

Anhang 4-G: Ergänzende Daten zur Studie LIBRETTO-431**Inhaltsverzeichnis**

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Anhang 4-G1: Ergänzende Angaben zur Studienpopulation

Tabelle 1: Vorangegangene Krebstherapie - RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
Patienten mit vorangegangener Krebstherapie	31 (27,0)	24 (32,9)	55 (29,3)
Vorangegangene Krebstherapie			
Chirurgischer Eingriff	17 (14,8)	18 (24,7)	35 (18,6)
Strahlentherapie	18 (15,7)	10 (13,7)	28 (14,9)
Systemische und lokoregionäre Therapie	5 (4,3)	7 (9,6)	12 (6,4)
Chirurgischer Eingriff: Behandlungsziel			
Kurativ	13 (11,3)	11 (15,1)	24 (12,8)
Palliativ	5 (4,3)	8 (11,0)	13 (6,9)
Strahlentherapie: Behandlungsgrund			
Kurativ	2 (1,7)	0	2 (1,1)
Palliativ	14 (12,2)	7 (9,6)	21 (11,2)
Neoadjuvant	0	1 (1,4)	1 (0,5)
Adjuvant	2 (1,7)	3 (4,1)	5 (2,7)
Systemische und lokoregionäre Therapie:			
Primäre Studienerkrankung	5 (4,3)	7 (9,6)	12 (6,4)
Systemische und lokoregionäre Therapie: Anzahl der Therapien			
1	5 (4,3)	7 (9,6)	12 (6,4)
Systemische und lokoregionäre Therapie: Behandlungsziel			
Kurativ	4 (3,5)	6 (8,2)	10 (5,3)
Nicht codiert	1 (0,9)	1 (1,4)	2 (1,1)
Systemische und lokoregionäre Therapie: Setting			
Adjuvant	3 (2,6)	6 (8,2)	9 (4,8)
Neoadjuvant	1 (0,9)	0	1 (0,5)
Nicht codiert	1 (0,9)	1 (1,4)	2 (1,1)
Systemische und lokoregionäre Therapie: Medikation			
Carboplatin	2 (1,7)	3 (4,1)	5 (2,7)
Cisplatin	4 (3,5)	4 (5,5)	8 (4,3)
Durvalumab	1 (0,9)	0	1 (0,5)
Paclitaxel	3 (2,6)	3 (4,1)	6 (3,2)
Pemetrexed	1 (0,9)	2 (2,7)	3 (1,6)
Vinorelbine	1 (0,9)	2 (2,7)	3 (1,6)
Systemische und lokoregionäre Therapie: Behandlungsschema			

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
Carboplatin, Cisplatin, Paclitaxel, Vinorelbine	1 (0,9)	0	1 (0,5)
Carboplatin, Paclitaxel	1 (0,9)	2 (2,7)	3 (1,6)
Carboplatin, Pemetrexed	0	1 (1,4)	1 (0,5)
Cisplatin, Paclitaxel	1 (0,9)	1 (1,4)	2 (1,1)
Cisplatin, Pemetrexed	1 (0,9)	1 (1,4)	2 (1,1)
Cisplatin, Vinorelbine	0	2 (2,7)	2 (1,1)
Cisplatin	1 (0,9)	1 (1,4)	2 (1,1)
Durvalumab	1 (0,9)	0	1 (0,5)
Immuntherapie (IO-Therapie)			
Ja	1 (0,9)	0	1 (0,5)
Nein	114 (99,1)	73 (100,0)	187 (99,5)
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; IO: Immunonkologie; kg: Kilogramm; mITT: Modifizierte ITT-Pembrolizumab Population; n: Anzahl der Patienten; N: Anzahl der Patienten in der Analyse; RCT: Randomisierte kontrollierte Studie.			

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Tabelle 2: Nachfolgende Antitumor-Therapien - RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
Chirurgischer Eingriff	0	0	0
Strahlentherapie	4 (3,5)	5 (6,8)	9 (4,8)
Systemische Therapie			
Gesamt	27 (23,5)	14 (19,2)	41 (21,8)
CARBOPLATIN	16 (13,9)	1 (1,4)	17 (9,0)
PEMETREXED	14 (12,2)	1 (1,4)	15 (8,0)
PRALSETINIB	6 (5,2)	5 (6,8)	11 (5,9)
BEVACIZUMAB	4 (3,5)	2 (2,7)	6 (3,2)
SELPERCATINIB	4 (3,5)	2 (2,7)	6 (3,2)
ATEZOLIZUMAB	3 (2,6)	2 (2,7)	5 (2,7)
DOCETAXEL	1 (0,9)	3 (4,1)	4 (2,1)
PACLITAXEL	4 (3,5)	0	4 (2,1)
PEMBROLIZUMAB	4 (3,5)	0	4 (2,1)
CISPLATIN	1 (0,9)	1 (1,4)	2 (1,1)
NIVOLUMAB	2 (1,7)	0	2 (1,1)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 (1,7)	0	2 (1,1)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0,9)	0	1 (0,5)
CAMRELIZUMAB	1 (0,9)	0	1 (0,5)
CATEQUENTINIB	1 (0,9)	0	1 (0,5)
DABRAFENIB	1 (0,9)	0	1 (0,5)
DENOSUMAB	1 (0,9)	0	1 (0,5)
DOCETAXEL;NINTEDANIB	0	1 (1,4)	1 (0,5)
GEMCITABINE	0	1 (1,4)	1 (0,5)
GIMERACIL;OTERACIL;TEGAFUR	0	1 (1,4)	1 (0,5)
INVESTIGATIONAL DRUG	0	1 (1,4)	1 (0,5)
IPILIMUMAB	1 (0,9)	0	1 (0,5)
RAMUCIRUMAB	1 (0,9)	0	1 (0,5)
RELATLIMAB	1 (0,9)	0	1 (0,5)
SACITUZUMAB GOVITECAN	1 (0,9)	0	1 (0,5)
TEGAFUR;URACIL	0	1 (1,4)	1 (0,5)
TEMOZOLOMIDE	0	1 (1,4)	1 (0,5)
TISLELIZUMAB	1 (0,9)	0	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
TRAMETINIB	1 (0,9)	0	1 (0,5)
ZOLEDRONIC ACID	0	1 (1,4)	1 (0,5)
Erste nachfolgende Therapielinie	27 (23,5)	14 (19,2)	41 (21,8)
CARBOPLATIN	15 (13,0)	1 (1,4)	16 (8,5)
PEMETREXED	12 (10,4)	0	12 (6,4)
PRALSETINIB	4 (3,5)	5 (6,8)	9 (4,8)
BEVACIZUMAB	4 (3,5)	2 (2,7)	6 (3,2)
SELPERCATINIB	3 (2,6)	2 (2,7)	5 (2,7)
ATEZOLIZUMAB	2 (1,7)	2 (2,7)	4 (2,1)
PACLITAXEL	4 (3,5)	0	4 (2,1)
PEMBROLIZUMAB	4 (3,5)	0	4 (2,1)
DOCETAXEL	0	3 (4,1)	3 (1,6)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 (1,7)	0	2 (1,1)
CAMRELIZUMAB	1 (0,9)	0	1 (0,5)
DOCETAXEL;NINTEDANIB	0	1 (1,4)	1 (0,5)
GEMCITABINE	0	1 (1,4)	1 (0,5)
INVESTIGATIONAL DRUG	0	1 (1,4)	1 (0,5)
IPILIMUMAB	1 (0,9)	0	1 (0,5)
NIVOLUMAB	1 (0,9)	0	1 (0,5)
RELATLIMAB	1 (0,9)	0	1 (0,5)
TEMOZOLOMIDE	0	1 (1,4)	1 (0,5)
TISLELIZUMAB	1 (0,9)	0	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
ZOLEDRONIC ACID	0	1 (1,4)	1 (0,5)
Zweite oder spätere nachfolgende Therapielinie	9 (7,8)	2 (2,7)	11 (5,9)
PEMETREXED	2 (1,7)	1 (1,4)	3 (1,6)
BEVACIZUMAB	1 (0,9)	1 (1,4)	2 (1,1)
CISPLATIN	1 (0,9)	1 (1,4)	2 (1,1)
PRALSETINIB	2 (1,7)	0	2 (1,1)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0,9)	0	1 (0,5)
ATEZOLIZUMAB	1 (0,9)	0	1 (0,5)
CARBOPLATIN	1 (0,9)	0	1 (0,5)
CATEQUENTINIB	1 (0,9)	0	1 (0,5)
DABRAFENIB	1 (0,9)	0	1 (0,5)
DENOSUMAB	1 (0,9)	0	1 (0,5)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
DOCETAXEL	1 (0,9)	0	1 (0,5)
GIMERACIL;OTERACIL;TEGAFUR	0	1 (1,4)	1 (0,5)
NIVOLUMAB	1 (0,9)	0	1 (0,5)
RAMUCIRUMAB	1 (0,9)	0	1 (0,5)
SACITUZUMAB GOVITECAN	1 (0,9)	0	1 (0,5)
SELPERCATINIB	1 (0,9)	0	1 (0,5)
TEGAFUR;URACIL	0	1 (1,4)	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
TRAMETINIB	1 (0,9)	0	1 (0,5)
Systemische Therapien: Behandlungsschema	27 (23,5)	14 (19,2)	41 (21,8)
PRALSETINIB	5 (4,3)	5 (6,8)	10 (5,3)
CARBOPLATIN, PEMETREXED	6 (5,2)	0	6 (3,2)
SELPERCATINIB	4 (3,5)	2 (2,7)	6 (3,2)
BEVACIZUMAB, CARBOPLATIN, PACLITAXEL, ATEZOLIZUMAB	2 (1,7)	0	2 (1,1)
CARBOPLATIN, PACLITAXEL	2 (1,7)	0	2 (1,1)
CARBOPLATIN, PEMBROLIZUMAB, PEMETREXED	2 (1,7)	0	2 (1,1)
DOCETAXEL	0	2 (2,7)	2 (1,1)
PEMETREXED	2 (1,7)	0	2 (1,1)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 (1,7)	0	2 (1,1)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0,9)	0	1 (0,5)
ATEZOLIZUMAB	1 (0,9)	0	1 (0,5)
ATEZOLIZUMAB, BEVACIZUMAB, DOCETAXEL	0	1 (1,4)	1 (0,5)
BEVACIZUMAB	0	1 (1,4)	1 (0,5)
BEVACIZUMAB, CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
BEVACIZUMAB, PEMETREXED	0	1 (1,4)	1 (0,5)
BEVACIZUMAB, PEMETREXED, CARBOPLATIN, CAMRELIZUMAB	1 (0,9)	0	1 (0,5)
BEVACIZUMAB, PEMETREXED, CISPLATIN	1 (0,9)	0	1 (0,5)
CARBOPLATIN	1 (0,9)	0	1 (0,5)
CATEQUENTINIB	1 (0,9)	0	1 (0,5)
CISPLATIN, PEMETREXED	0	1 (1,4)	1 (0,5)
DABRAFENIB, PRALSETINIB, TRAMETINIB	1 (0,9)	0	1 (0,5)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
DABRAFENIB, TRAMETINIB	1 (0,9)	0	1 (0,5)
DENOSUMAB	1 (0,9)	0	1 (0,5)
DOCETAXEL, RAMUCIRUMAB	1 (0,9)	0	1 (0,5)
DOCETAXEL;NINTEDANIB	0	1 (1,4)	1 (0,5)
GIMERACIL;OTERACIL;TEGAFUR	0	1 (1,4)	1 (0,5)
INVESTIGATIONAL DRUG	0	1 (1,4)	1 (0,5)
IPILIMUMAB, NIVOLUMAB, RELATLIMAB	1 (0,9)	0	1 (0,5)
NIVOLUMAB	1 (0,9)	0	1 (0,5)
PEMBROLIZUMAB	1 (0,9)	0	1 (0,5)
PEMBROLIZUMAB, CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
SACITUZUMAB GOVITECAN	1 (0,9)	0	1 (0,5)
TEGAFUR;URACIL	0	1 (1,4)	1 (0,5)
TEMOZOLOMIDE	0	1 (1,4)	1 (0,5)
TISLELIZUMAB	1 (0,9)	0	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
ZOLEDRONIC ACID, ATEZOLIZUMAB, CARBOPLATIN, GEMCITABINE	0	1 (1,4)	1 (0,5)
Systemische Therapien: Erstlinien- Behandlungsschema	27 (23,5)	14 (19,2)	41 (21,8)
PRALSETINIB	4 (3,5)	5 (6,8)	9 (4,8)
CARBOPLATIN, PEMETREXED	6 (5,2)	0	6 (3,2)
SELPERCATINIB	3 (2,6)	2 (2,7)	5 (2,7)
BEVACIZUMAB, CARBOPLATIN, PACLITAXEL, ATEZOLIZUMAB	2 (1,7)	0	2 (1,1)
CARBOPLATIN, PACLITAXEL	2 (1,7)	0	2 (1,1)
CARBOPLATIN, PEMBROLIZUMAB, PEMETREXED	2 (1,7)	0	2 (1,1)
DOCETAXEL	0	2 (2,7)	2 (1,1)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 (1,7)	0	2 (1,1)
ATEZOLIZUMAB, BEVACIZUMAB, DOCETAXEL	0	1 (1,4)	1 (0,5)
BEVACIZUMAB	0	1 (1,4)	1 (0,5)
BEVACIZUMAB, CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
BEVACIZUMAB, PEMETREXED, CARBOPLATIN, CAMRELIZUMAB	1 (0,9)	0	1 (0,5)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
DOCETAXEL;NINTEDANIB	0	1 (1,4)	1 (0,5)
INVESTIGATIONAL DRUG	0	1 (1,4)	1 (0,5)
IPILIMUMAB, NIVOLUMAB, RELATLIMAB	1 (0,9)	0	1 (0,5)
PEMBROLIZUMAB	1 (0,9)	0	1 (0,5)
PEMBROLIZUMAB, CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
PEMETREXED	1 (0,9)	0	1 (0,5)
TEMOZOLOMIDE	0	1 (1,4)	1 (0,5)
TISLELIZUMAB	1 (0,9)	0	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
ZOLEDRONIC ACID, ATEZOLIZUMAB, CARBOPLATIN, GEMCITABINE	0	1 (1,4)	1 (0,5)
Systemische Therapien: Zweit- oder Spätlinien- Behandlungsschema	9 (7,8)	2 (2,7)	11 (5,9)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0,9)	0	1 (0,5)
ATEZOLIZUMAB	1 (0,9)	0	1 (0,5)
BEVACIZUMAB	0	1 (1,4)	1 (0,5)
BEVACIZUMAB, PEMETREXED	0	1 (1,4)	1 (0,5)
BEVACIZUMAB, PEMETREXED, CISPLATIN	1 (0,9)	0	1 (0,5)
CARBOPLATIN	1 (0,9)	0	1 (0,5)
CATEQUENTINIB	1 (0,9)	0	1 (0,5)
CISPLATIN, PEMETREXED	0	1 (1,4)	1 (0,5)
DABRAFENIB, PRALSETINIB, TRAMETINIB	1 (0,9)	0	1 (0,5)
DABRAFENIB, TRAMETINIB	1 (0,9)	0	1 (0,5)
DENOSUMAB	1 (0,9)	0	1 (0,5)
DOCETAXEL, RAMUCIRUMAB	1 (0,9)	0	1 (0,5)
GIMERACIL;OTERACIL;TEGAFUR	0	1 (1,4)	1 (0,5)
NIVOLUMAB	1 (0,9)	0	1 (0,5)
PEMETREXED	1 (0,9)	0	1 (0,5)
PRALSETINIB	1 (0,9)	0	1 (0,5)
SACITUZUMAB GOVITECAN	1 (0,9)	0	1 (0,5)
SELPERCATINIB	1 (0,9)	0	1 (0,5)
TEGAFUR;URACIL	0	1 (1,4)	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; mITT: Modifizierte ITT-Pembrolizumab Population; n: Anzahl der Patienten; N: Anzahl der Patienten in der Analyse; RCT: Randomisierte kontrollierte Studie.			

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Anhang 4-G2: Zusammenfassende Statistiken für patientenberichtete Endpunkte

**Anhang 4-G2.1: Zusammenfassende Statistik für die Symptomskalen des EORTC
QLQ-C30**

Tabelle 3: Zusammenfassende Statistik der Symptomskala Fatigue des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Fatigue			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	26,1 (24,22)	32,7 (23,54)	28,7 (24,10)
Median (min; max)	22,2 (0,0; 100,0)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)
Q1-Q3	0,0-33,3	22,2-44,4	11,1-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

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Tabelle 4: Zusammenfassende Statistik der Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Übelkeit und Erbrechen			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	5,7 (12,83)	6,3 (13,00)	5,9 (12,86)
Median (min; max)	0,0 (0,0; 66,7)	0,0 (0,0; 66,7)	0,0 (0,0; 66,7)
Q1-Q3	0,0-0,0	0,0-16,7	0,0-0,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30nvsm_mitt.rtf

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 5: Zusammenfassende Statistik der Symptomskala Schmerz des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Schmerz			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	20,3 (21,31)	21,0 (22,32)	20,6 (21,64)
Median (min; max)	16,7 (0,0; 100,0)	16,7 (0,0; 83,3)	16,7 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30pasm_mitt.rtf

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Tabelle 6: Zusammenfassende Statistik der Symptomskala Dyspnoe des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Dyspnoe			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	23,8 (28,76)	30,3 (29,08)	26,3 (28,97)
Median (min; max)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30dysm_mitt.rtf

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Tabelle 7: Zusammenfassende Statistik der Symptomskala Schlaflosigkeit des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Schlaflosigkeit			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	23,5 (27,71)	29,3 (27,74)	25,7 (27,78)
Median (min; max)	0,0 (0,0; 100,0)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30insm_mitt.rtf

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 8: Zusammenfassende Statistik der Symptomskala Appetitlosigkeit des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Appetitlosigkeit			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	16,5 (24,95)	20,2 (26,07)	17,9 (25,37)
Median (min; max)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 9: Zusammenfassende Statistik der Symptomskala Verstopfung des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Verstopfung			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	11,7 (19,60)	15,2 (25,61)	13,1 (22,10)
Median (min; max)	0,0 (0,0; 66,7)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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Tabelle 10: Zusammenfassende Statistik der Symptomskala Diarrhö des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Diarrhö			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	3,5 (10,26)	4,5 (15,34)	3,9 (12,44)
Median (min; max)	0,0 (0,0; 33,3)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-0,0	0,0-0,0	0,0-0,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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Tabelle 11: Zusammenfassende Statistik der Symptomskala Finanzielle Schwierigkeiten des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Finanzielle Schwierigkeiten			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	21,9 (26,49)	23,7 (29,68)	22,6 (27,69)
Median (min; max)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30fism_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Anhang 4-G2.2: Zusammenfassende Statistik für NSCLC-SAQ

Tabelle 12: Zusammenfassende Statistik für NSCLC-SAQ Gesamtwertung des NSCLC-SAQ aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
NSCLC-SAQ Gesamtwertung			
Baseline			
Anzahl der Patienten, n (fehlend)	82 (33)	52 (21)	134 (54)
Mittelwert (SD)	6,1 (3,90)	5,7 (3,66)	6,0 (3,80)
Median (min; max)	5,5 (0,0; 18,0)	5,0 (0,0; 16,0)	5,5 (0,0; 18,0)
Q1-Q3	3,0-8,5	3,0-8,0	3,0-8,5
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 13: Zusammenfassende Statistik für NSCLC-SAQ Symptomskala Husten des NSCLC-SAQ aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Husten			
Baseline			
Anzahl der Patienten, n (fehlend)	82 (33)	52 (21)	134 (54)
Mittelwert (SD)	1,3 (1,04)	1,2 (0,91)	1,2 (0,99)
Median (min; max)	1,0 (0,0; 4,0)	1,0 (0,0; 3,0)	1,0 (0,0; 4,0)
Q1-Q3	0,0-2,0	1,0-2,0	1,0-2,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 14: Zusammenfassende Statistik für NSCLC-SAQ Symptomskala Schmerz des NSCLC-SAQ aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Schmerz			
Baseline			
Anzahl der Patienten, n (fehlend)	82 (33)	52 (21)	134 (54)
Mittelwert (SD)	1,0 (0,92)	0,9 (0,80)	1,0 (0,88)
Median (min; max)	1,0 (0,0; 3,0)	1,0 (0,0; 3,0)	1,0 (0,0; 3,0)
Q1-Q3	0,0-2,0	0,0-1,5	0,0-2,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 15: Zusammenfassende Statistik für NSCLC-SAQ Symptomskala Dyspnoe des NSCLC-SAQ aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Dyspnoe			
Baseline			
Anzahl der Patienten, n (fehlend)	82 (33)	52 (21)	134 (54)
Mittelwert (SD)	1,3 (1,10)	1,3 (1,08)	1,3 (1,09)
Median (min; max)	1,0 (0,0; 4,0)	1,0 (0,0; 4,0)	1,0 (0,0; 4,0)
Q1-Q3	0,0-2,0	0,0-2,0	0,0-2,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_nsdysm_mitt.rtf

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 16: Zusammenfassende Statistik für NSCLC-SAQ Symptomskala Müdigkeit des NSCLC-SAQ aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Müdigkeit			
Baseline			
Anzahl der Patienten, n (fehlend)	82 (33)	52 (21)	134 (54)
Mittelwert (SD)	1,5 (1,02)	1,4 (1,07)	1,4 (1,04)
Median (min; max)	1,5 (0,0; 4,0)	1,3 (0,0; 4,0)	1,5 (0,0; 4,0)
Q1-Q3	0,5-2,0	0,5-2,0	0,5-2,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_nsfatm_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 17: Zusammenfassende Statistik für NSCLC-SAQ Symptomskala Verminderter Appetit des NSCLC-SAQ aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Verminderter Appetit			
Baseline			
Anzahl der Patienten, n (fehlend)	82 (33)	52 (21)	134 (54)
Mittelwert (SD)	1,0 (1,21)	1,0 (1,08)	1,0 (1,16)
Median (min; max)	1,0 (0,0; 4,0)	1,0 (0,0; 4,0)	1,0 (0,0; 4,0)
Q1-Q3	0,0-2,0	0,0-2,0	0,0-2,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_nsappsm_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Anhang 4-G2.3: Zusammenfassende Statistik für EQ-5D VAS

Tabelle 18: Zusammenfassende Statistik für Gesundheitszustand - EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
EQ-5D VAS			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	65 (8)	170 (18)
Mittelwert (SD)	76,8 (17,83)	72,4 (18,58)	75,1 (18,19)
Median (min; max)	80,0 (20,0; 100,0)	75,0 (29,0; 100,0)	80,0 (20,0; 100,0)
Q1-Q3	70,0-90,0	60,0-88,0	64,0-90,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EQ-5D: Fragebogen der EuroQol-Gruppe zur Lebensqualität auf 5 Dimensionen; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung; VAS: Visuelle Analogskala.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_gol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_eq5dvassm_mitt.rtf

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Anhang 4-G2.4: Zusammenfassende Statistik für den globalen Gesundheitsstatus und die Funktionsskalen des EORTC QLQ-C30

Tabelle 19: Zusammenfassende Statistik des globalen Gesundheitsstatus des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Globaler Gesundheitsstatus			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	69,0 (21,70)	62,1 (22,46)	66,3 (22,18)
Median (min; max)	66,7 (16,7; 100,0)	66,7 (8,3; 100,0)	66,7 (8,3; 100,0)
Q1-Q3	50,0-83,3	50,0-83,3	50,0-83,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30ghsm_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 20: Zusammenfassende Statistik der Funktionsskala Körperliche Funktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Körperliche Funktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	84,8 (16,48)	80,9 (16,74)	83,3 (16,64)
Median (min; max)	86,7 (20,0; 100,0)	86,7 (26,7; 100,0)	86,7 (20,0; 100,0)
Q1-Q3	73,3-100,0	66,7-93,3	73,3-93,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30pfsm_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 21: Zusammenfassende Statistik der Funktionsskala Rollenfunktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Rollenfunktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	81,7 (27,88)	78,5 (25,95)	80,5 (27,12)
Median (min; max)	100,0 (0,0; 100,0)	83,3 (0,0; 100,0)	100,0 (0,0; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	66,7-100,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 22: Zusammenfassende Statistik der Funktionsskala Emotionale Funktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Emotionale Funktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	81,6 (19,22)	78,4 (19,28)	80,4 (19,25)
Median (min; max)	83,3 (0,0; 100,0)	83,3 (16,7; 100,0)	83,3 (0,0; 100,0)
Q1-Q3	66,7-100,0	66,7-91,7	66,7-100,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30efsm_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Tabelle 23: Zusammenfassende Statistik der Funktionsskala Kognitive Funktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Kognitive Funktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	93,0 (11,03)	85,6 (19,37)	90,2 (15,20)
Median (min; max)	100,0 (50,0; 100,0)	100,0 (16,7; 100,0)	100,0 (16,7; 100,0)
Q1-Q3	83,3-100,0	83,3-100,0	83,3-100,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

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Tabelle 24: Zusammenfassende Statistik der Funktionsskala Soziale Funktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
Soziale Funktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	66 (7)	171 (17)
Mittelwert (SD)	83,7 (21,92)	73,0 (26,44)	79,5 (24,26)
Median (min; max)	100,0 (16,7; 100,0)	83,3 (0,0; 100,0)	83,3 (0,0; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	66,7-100,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qol_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30sfsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

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Anhang 4-G2.5: Zusammenfassende Statistik für patientenberichtete Endpunkte nach Crossover

Tabelle 177: Zusammenfassende Statistik des globalen Gesundheitsstatus des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Globaler Gesundheitsstatus			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	69,0 (21,70)	52,2 (21,51)	69,0 (20,67)
Median (min; max)	66,7 (16,7; 100,0)	58,3 (8,3; 83,3)	66,7 (16,7; 100,0)
Q1-Q3	50,0-83,3	33,3-66,7	58,3-83,3
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	68,4 (19,67)	63,9 (20,80)	70,1 (17,60)
Median (min; max)	66,7 (16,7; 100,0)	66,7 (16,7; 100,0)	66,7 (33,3; 100,0)
Q1-Q3	50,0-83,3	50,0-83,3	58,3-83,3
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	60,9 (24,28)	63,1 (24,24)	71,0 (17,94)
Median (min; max)	66,7 (8,3; 100,0)	66,7 (0,0; 100,0)	75,0 (33,3; 100,0)
Q1-Q3	41,7-83,3	50,0-83,3	66,7-83,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP.Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30ghxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba_adsl_gba
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Tabelle 178: Zusammenfassende Statistik der Funktionsskala Körperliche Funktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Körperliche Funktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	84,8 (16,48)	75,3 (19,81)	84,8 (13,15)
Median (min; max)	86,7 (20,0; 100,0)	80,0 (26,7; 100,0)	86,7 (53,3; 100,0)
Q1-Q3	73,3-100,0	60,0-93,3	73,3-93,3
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	81,0 (17,98)	80,2 (17,55)	79,8 (17,13)
Median (min; max)	86,7 (20,0; 100,0)	83,3 (26,7; 100,0)	80,0 (33,3; 100,0)
Q1-Q3	73,3-96,7	73,3-93,3	73,3-93,3
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	73,2 (24,68)	72,4 (28,27)	77,0 (20,82)
Median (min; max)	80,0 (0,0; 100,0)	80,0 (13,3; 100,0)	80,0 (13,3; 100,0)
Q1-Q3	60,0-93,3	60,0-93,3	66,7-93,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_golxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30pfxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba, adsl_gba
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Tabelle 179: Zusammenfassende Statistik der Funktionsskala Rollenfunktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Rollenfunktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	81,7 (27,88)	73,5 (28,22)	82,1 (24,00)
Median (min; max)	100,0 (0,0; 100,0)	66,7 (0,0; 100,0)	100,0 (33,3; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	66,7-100,0
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	77,5 (23,75)	71,1 (27,66)	75,2 (23,53)
Median (min; max)	83,3 (0,0; 100,0)	66,7 (0,0; 100,0)	66,7 (33,3; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	66,7-100,0
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	70,5 (31,93)	67,8 (33,88)	74,7 (27,68)
Median (min; max)	66,7 (0,0; 100,0)	66,7 (0,0; 100,0)	83,3 (16,7; 100,0)
Q1-Q3	50,0-100,0	50,0-100,0	66,7-100,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP.Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30rfxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba, adsl_gba
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Tabelle 180: Zusammenfassende Statistik der Funktionsskala Emotionale Funktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Emotionale Funktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	81,6 (19,22)	73,1 (22,45)	82,1 (16,06)
Median (min; max)	83,3 (0,0; 100,0)	75,0 (16,7; 100,0)	83,3 (33,3; 100,0)
Q1-Q3	66,7-100,0	66,7-91,7	66,7-100,0
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	81,1 (20,56)	80,0 (16,89)	86,5 (17,90)
Median (min; max)	83,3 (0,0; 100,0)	75,0 (41,7; 100,0)	100,0 (33,3; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	66,7-100,0
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	76,8 (24,10)	77,5 (28,04)	85,1 (15,42)
Median (min; max)	83,3 (0,0; 100,0)	87,5 (0,0; 100,0)	91,7 (50,0; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	66,7-100,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP.Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30efxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba, adsl_gba
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Tabelle 181: Zusammenfassende Statistik der Funktionsskala Kognitive Funktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Kognitive Funktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	93,0 (11,03)	84,6 (20,11)	86,3 (19,07)
Median (min; max)	100,0 (50,0; 100,0)	100,0 (33,3; 100,0)	100,0 (16,7; 100,0)
Q1-Q3	83,3-100,0	66,7-100,0	83,3-100,0
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	84,1 (18,37)	83,9 (19,32)	84,2 (19,48)
Median (min; max)	83,3 (33,3; 100,0)	91,7 (33,3; 100,0)	100,0 (33,3; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	66,7-100,0
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	80,8 (20,71)	82,2 (23,95)	84,3 (17,65)
Median (min; max)	83,3 (16,7; 100,0)	91,7 (0,0; 100,0)	83,3 (33,3; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	83,3-100,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP.Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30cfxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba, adsl_gba
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Tabelle 182: Zusammenfassende Statistik der Funktionsskala Soziale Funktion des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Soziale Funktion			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	83,7 (21,92)	67,3 (29,77)	76,9 (23,45)
Median (min; max)	100,0 (16,7; 100,0)	66,7 (0,0; 100,0)	83,3 (16,7; 100,0)
Q1-Q3	66,7-100,0	50,0-100,0	66,7-100,0
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	78,6 (22,08)	73,3 (22,15)	78,6 (26,75)
Median (min; max)	83,3 (0,0; 100,0)	66,7 (33,3; 100,0)	83,3 (0,0; 100,0)
Q1-Q3	66,7-100,0	66,7-100,0	66,7-100,0
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	72,1 (25,08)	69,4 (29,39)	74,7 (26,72)
Median (min; max)	66,7 (0,0; 100,0)	66,7 (0,0; 100,0)	83,3 (16,7; 100,0)
Q1-Q3	58,3-100,0	66,7-100,0	66,7-100,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30sfxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba_adsl_gba
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Tabelle 183: Zusammenfassende Statistik der Symptomskala Fatigue des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Fatigue			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	26,1 (24,22)	39,5 (27,27)	27,9 (19,56)
Median (min; max)	22,2 (0,0; 100,0)	33,3 (0,0; 100,0)	33,3 (0,0; 66,7)
Q1-Q3	0,0-33,3	22,2-55,6	11,1-33,3
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	27,7 (22,77)	31,9 (23,66)	30,8 (26,30)
Median (min; max)	33,3 (0,0; 88,9)	33,3 (0,0; 100,0)	33,3 (0,0; 88,9)
Q1-Q3	11,1-33,3	22,2-33,3	0,0-44,4
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	36,8 (27,26)	36,3 (29,32)	31,0 (25,87)
Median (min; max)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)
Q1-Q3	16,7-55,6	22,2-44,4	11,1-44,4
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP.Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30faxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba, adsl_gba
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Tabelle 184: Zusammenfassende Statistik der Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Übelkeit und Erbrechen			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	5,7 (12,83)	10,5 (13,98)	3,4 (11,58)
Median (min; max)	0,0 (0,0; 66,7)	0,0 (0,0; 50,0)	0,0 (0,0; 66,7)
Q1-Q3	0,0-0,0	0,0-16,7	0,0-0,0
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	3,7 (10,42)	7,2 (10,43)	6,4 (11,22)
Median (min; max)	0,0 (0,0; 50,0)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Q1-Q3	0,0-0,0	0,0-16,7	0,0-16,7
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	8,0 (12,99)	6,7 (13,56)	5,1 (11,40)
Median (min; max)	0,0 (0,0; 50,0)	0,0 (0,0; 50,0)	0,0 (0,0; 50,0)
Q1-Q3	0,0-16,7	0,0-16,7	0,0-0,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_golxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30nvxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba_adsl_gba
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Tabelle 185: Zusammenfassende Statistik der Symptomskala Schmerz des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Schmerz			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	20,3 (21,31)	28,4 (23,49)	15,8 (20,21)
Median (min; max)	16,7 (0,0; 100,0)	16,7 (0,0; 83,3)	0,0 (0,0; 66,7)
Q1-Q3	0,0-33,3	16,7-50,0	0,0-33,3
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	18,3 (22,59)	25,0 (26,17)	17,1 (19,30)
Median (min; max)	16,7 (0,0; 100,0)	16,7 (0,0; 100,0)	16,7 (0,0; 66,7)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	26,9 (26,64)	32,2 (29,01)	19,2 (18,22)
Median (min; max)	16,7 (0,0; 100,0)	33,3 (0,0; 100,0)	16,7 (0,0; 50,0)
Q1-Q3	0,0-41,7	16,7-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30paxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba_adsl_gba
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Tabelle 186: Zusammenfassende Statistik der Symptomskala Dyspnoe des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Dyspnoe			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	23,8 (28,76)	30,9 (31,93)	29,9 (27,35)
Median (min; max)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	17,0 (22,37)	23,3 (29,23)	24,8 (29,34)
Median (min; max)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	23,7 (29,03)	28,9 (33,60)	22,2 (27,22)
Median (min; max)	16,7 (0,0; 100,0)	33,3 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30dyxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba_adsl_gba
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Tabelle 187: Zusammenfassende Statistik der Symptomskala Schlaflosigkeit des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Schlaflosigkeit			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	23,5 (27,71)	35,8 (27,62)	24,8 (27,27)
Median (min; max)	0,0 (0,0; 100,0)	33,3 (0,0; 100,0)	33,3 (0,0; 100,0)
Q1-Q3	0,0-33,3	33,3-33,3	0,0-33,3
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	18,5 (24,85)	25,6 (25,80)	15,4 (22,74)
Median (min; max)	0,0 (0,0; 100,0)	33,3 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	25,0 (31,57)	23,3 (32,93)	13,1 (18,52)
Median (min; max)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)	0,0 (0,0; 66,7)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30inxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba, adsl_gba
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Tabelle 188: Zusammenfassende Statistik der Symptomskala Appetitlosigkeit des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Appetitlosigkeit			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	16,5 (24,95)	29,6 (28,24)	13,7 (22,58)
Median (min; max)	0,0 (0,0; 100,0)	33,3 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	14,3 (24,80)	15,6 (20,96)	12,0 (20,92)
Median (min; max)	0,0 (0,0; 100,0)	0,0 (0,0; 66,7)	0,0 (0,0; 66,7)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	24,4 (29,61)	17,8 (29,99)	12,1 (20,10)
Median (min; max)	16,7 (0,0; 100,0)	0,0 (0,0; 100,0)	0,0 (0,0; 66,7)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30apxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba_adsl_gba
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Tabelle 189: Zusammenfassende Statistik der Symptomskala Verstopfung des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Verstopfung			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	11,7 (19,60)	28,4 (31,63)	6,0 (15,05)
Median (min; max)	0,0 (0,0; 66,7)	33,3 (0,0; 100,0)	0,0 (0,0; 66,7)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-0,0
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	8,6 (17,18)	17,8 (22,71)	7,7 (19,44)
Median (min; max)	0,0 (0,0; 66,7)	0,0 (0,0; 66,7)	0,0 (0,0; 100,0)
Q1-Q3	0,0-0,0	0,0-33,3	0,0-0,0
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	14,7 (23,26)	22,2 (28,14)	9,1 (22,47)
Median (min; max)	0,0 (0,0; 100,0)	16,7 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-0,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30coxsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba_adsl_gba
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Tabelle 190: Zusammenfassende Statistik der Symptomskala Diarrhö des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Diarrhö			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	3,5 (10,26)	3,7 (10,68)	5,1 (18,00)
Median (min; max)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)	0,0 (0,0; 100,0)
Q1-Q3	0,0-0,0	0,0-0,0	0,0-0,0
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	19,6 (24,73)	4,4 (11,52)	2,6 (9,00)
Median (min; max)	0,0 (0,0; 100,0)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Q1-Q3	0,0-33,3	0,0-0,0	0,0-0,0
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	10,9 (19,49)	12,2 (18,54)	4,0 (13,84)
Median (min; max)	0,0 (0,0; 66,7)	0,0 (0,0; 66,7)	0,0 (0,0; 66,7)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-0,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_golxover_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30dixsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba, adsl_gba
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Tabelle 191: Zusammenfassende Statistik der Symptomskala Finanzielle Schwierigkeiten des EORTC QLQ-C30 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
Finanzielle Schwierigkeiten			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	39 (1)
Mittelwert (SD)	21,9 (26,49)	25,9 (33,76)	22,2 (26,86)
Median (min; max)	0,0 (0,0; 100,0)	0,0 (0,0; 100,0)	33,3 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-66,7	0,0-33,3
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	19,9 (24,29)	25,6 (28,61)	21,4 (30,09)
Median (min; max)	0,0 (0,0; 100,0)	33,3 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	52 (63)	30 (2)	33 (7)
Mittelwert (SD)	26,9 (31,68)	23,3 (29,23)	22,2 (28,46)
Median (min; max)	33,3 (0,0; 100,0)	16,7 (0,0; 100,0)	0,0 (0,0; 100,0)
Q1-Q3	0,0-33,3	0,0-33,3	0,0-33,3
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP. Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_qolxover_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_c30fixsm_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqxs_gba_adsl_gba
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Tabelle 192: Zusammenfassende Statistik für Gesundheitszustand - EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT, zensierte Patienten

		Komparator	
Endpunkt Visite Merkmal	Selpercatinib (N=115)	Crossover (N=32)	Non-Crossover (N=40)
EQ-5D VAS			
Baseline			
Anzahl der Patienten, n (fehlend)	105 (10)	27 (5)	38 (2)
Mittelwert (SD)	76,8 (17,83)	65,8 (20,85)	77,1 (15,40)
Median (min; max)	80,0 (20,0; 100,0)	70,0 (29,0; 98,0)	79,5 (40,0; 100,0)
Q1-Q3	70,0-90,0	49,0-81,0	65,0-90,0
am Zeitpunkt der Zensierung			
Anzahl der Patienten, n (fehlend)	112 (3)	30 (2)	39 (1)
Mittelwert (SD)	78,4 (17,60)	72,8 (16,36)	78,3 (15,50)
Median (min; max)	81,0 (25,0; 100,0)	75,5 (30,0; 98,0)	81,0 (49,0; 100,0)
Q1-Q3	69,5-94,0	63,0-85,0	70,0-90,0
am Datenschnitt			
Anzahl der Patienten, n (fehlend)	51 (64)	30 (2)	33 (7)
Mittelwert (SD)	71,0 (22,15)	70,6 (23,43)	79,1 (14,72)
Median (min; max)	74,0 (10,0; 99,0)	77,0 (0,0; 99,0)	85,0 (41,0; 98,0)
Q1-Q3	59,0-91,0	56,0-85,0	70,0-90,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; EQ-5D: Fragebogen der EuroQol-Gruppe zur Lebensqualität auf 5 Dimensionen; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung; VAS: Visuelle Analogskala. Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab. Das Datum der Zensur wird definiert als das Datum der letzten auswertbaren Messung bis zur Zensierung (Todesdatum, letzter Behandlungstag, Datum der Progression) , gemäß dem PRO SAP.Falls kein Wert für den Patienten nach der Zensur verfügbar ist, gibt es keinen Wert, der für den Zeitpunkt des Datenschnittes berücksichtigt werden kann.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_golxover_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_eq5dvaxsm_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adqsx_gba, adsl_gba
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Anhang 4-G3: Ergänzende Angaben zur Sicherheit

Anhang 4-G3.1: Unerwünschte Ereignisse nach SOC und PT

Table 25: Results for TEAEs occurred in ≥10% or in ≥10 patients and ≥1% in any treatment arm within analysis population - study LIBRETTO-431, mSAF

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
TEAEs occurred in ≥10% or in ≥10 patients and ≥1% in any treatment arm within analysis population					
Investigations	93/115 (80.9)	0.7 [0.49; 1.18]	53/72 (73.6)	2.1 [1.18; 4.96]	1.35 [0.96; 1.90] 0.082
Aspartate aminotransferase increased	71/115 (61.7)	2.1 [1.48; 7.66]	30/72 (41.7)	NE [4.96; NE]	1.85 [1.20; 2.84] 0.004
Alanine aminotransferase increased	68/115 (59.1)	2.8 [1.48; 13.14]	29/72 (40.3)	NE [7.16; NE]	1.70 [1.10; 2.64] 0.016
Blood bilirubin increased*	47/115 (40.9)	NE [11.96; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] <0.001
Blood creatinine increased	28/115 (24.3)	NE [NE; NE]	13/72 (18.1)	NE [NE; NE]	1.28 [0.66; 2.47] 0.474
Platelet count decreased	23/115 (20.0)	NE [NE; NE]	14/72 (19.4)	NE [NE; NE]	0.97 [0.50; 1.88] 0.911
White blood cell count decreased	23/115 (20.0)	NE [NE; NE]	20/72 (27.8)	NE [NE; NE]	0.69 [0.38; 1.25] 0.215
Neutrophil count decreased	22/115 (19.1)	NE [NE; NE]	20/72 (27.8)	NE [NE; NE]	0.66 [0.36; 1.22] 0.183
Electrocardiogram QT prolonged	21/115 (18.3)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	14.18 [1.91; 105.43] <0.001
Weight increased	19/115 (16.5)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	1.62 [0.68; 3.86] 0.270
Bilirubin conjugated increased	17/115 (14.8)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	10.98 [1.46; 82.55] 0.003
Blood alkaline phosphatase increased	12/115 (10.4)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	1.58 [0.56; 4.49] 0.384
Gamma- glutamyltransferase increased	11/115 (9.6)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	1.35 [0.47; 3.90] 0.576
Gastrointestinal disorders	89/115 (77.4)	1.4 [0.72; 3.45]	54/72 (75.0)	0.3 [0.13; 0.79]	0.78 [0.56; 1.10] 0.178

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Diarrhoea	57/115 (49.6)	10.4 [6.44; NE]	19/72 (26.4)	NE [16.03; NE]	1.99 [1.18; 3.34] 0.008
Dry mouth	46/115 (40.0)	NE [14.36; NE]	4/72 (5.6)	NE [NE; NE]	8.54 [3.07; 23.74] <0.001
Constipation	24/115 (20.9)	NE [NE; NE]	29/72 (40.3)	NE [2.89; NE]	0.42 [0.24; 0.72] 0.001
Abdominal pain	16/115 (13.9)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	2.21 [0.74; 6.62] 0.147
Nausea	16/115 (13.9)	NE [NE; NE]	30/72 (41.7)	NE [1.64; NE]	0.24 [0.13; 0.44] <0.001
Vomiting	15/115 (13.0)	NE [NE; NE]	18/72 (25.0)	NE [NE; NE]	0.43 [0.22; 0.86] 0.014
Abdominal pain upper	14/115 (12.2)	NE [NE; NE]	10/72 (13.9)	NE [NE; NE]	0.80 [0.35; 1.80] 0.585
Stomatitis	10/115 (8.7)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	2.05 [0.56; 7.45] 0.267
General disorders and administration site conditions	71/115 (61.7)	5.1 [1.91; 9.00]	50/72 (69.4)	1.5 [0.39; 4.83]	0.67 [0.46; 0.96] 0.030
Oedema peripheral	28/115 (24.3)	NE [NE; NE]	8/72 (11.1)	NE [NE; NE]	2.08 [0.95; 4.57] 0.062
Fatigue	18/115 (15.7)	NE [NE; NE]	17/72 (23.6)	NE [NE; NE]	0.56 [0.29; 1.08] 0.082
Asthenia	16/115 (13.9)	NE [NE; NE]	21/72 (29.2)	NE [NE; NE]	0.40 [0.21; 0.76] 0.004
Pyrexia	15/115 (13.0)	NE [NE; NE]	18/72 (25.0)	NE [23.89; NE]	0.44 [0.22; 0.88] 0.017
Metabolism and nutrition disorders	60/115 (52.2)	12.6 [7.00; 21.49]	34/72 (47.2)	15.9 [2.56; NE]	0.92 [0.60; 1.40] 0.709
Decreased appetite	20/115 (17.4)	NE [NE; NE]	20/72 (27.8)	NE [NE; NE]	0.52 [0.28; 0.96] 0.035
Hypoalbuminaemia	17/115 (14.8)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	1.83 [0.67; 4.98] 0.228

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Hypokalaemia	15/115 (13.0)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	1.19 [0.48; 2.92] 0.706
Hypocalcaemia*	10/115 (8.7)	NE [NE; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] 0.013
Hyperglycaemia	4/115 (3.5)	NE [27.07; NE]	9/72 (12.5)	NE [NE; NE]	0.24 [0.07; 0.78] 0.010
Infections and infestations	59/115 (51.3)	12.7 [8.25; 19.98]	38/72 (52.8)	12.3 [8.05; 17.08]	0.86 [0.57; 1.29] 0.465
COVID-19	25/115 (21.7)	NE [22.21; NE]	14/72 (19.4)	NE [20.44; NE]	0.83 [0.43; 1.59] 0.568
Skin and subcutaneous tissue disorders	59/115 (51.3)	10.4 [5.49; NE]	38/72 (52.8)	7.1 [2.30; NE]	0.83 [0.55; 1.25] 0.376
Rash	26/115 (22.6)	NE [NE; NE]	17/72 (23.6)	NE [NE; NE]	0.86 [0.47; 1.59] 0.637
Pruritus	13/115 (11.3)	31.0 [NE; NE]	16/72 (22.2)	NE [NE; NE]	0.40 [0.19; 0.84] 0.013
Vascular disorders	59/115 (51.3)	9.0 [3.25; NE]	10/72 (13.9)	NE [NE; NE]	4.70 [2.40; 9.20] <0.001
Hypertension	54/115 (47.0)	NE [3.38; NE]	5/72 (6.9)	NE [NE; NE]	8.95 [3.58; 22.40] <0.001
Respiratory, thoracic and mediastinal disorders	41/115 (35.7)	NE [22.14; NE]	32/72 (44.4)	17.5 [6.70; NE]	0.66 [0.42; 1.06] 0.082
Cough	12/115 (10.4)	NE [NE; NE]	12/72 (16.7)	NE [NE; NE]	0.54 [0.24; 1.21] 0.129
Dyspnoea	4/115 (3.5)	NE [NE; NE]	8/72 (11.1)	NE [NE; NE]	0.25 [0.08; 0.85] 0.016
Musculoskeletal and connective tissue disorders	40/115 (34.8)	NE [21.13; NE]	23/72 (31.9)	NE [13.83; NE]	1.10 [0.66; 1.83] 0.721
Arthralgia	14/115 (12.2)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	1.20 [0.48; 2.97] 0.700
Back pain	12/115 (10.4)	30.2 [30.19; NE]	8/72 (11.1)	NE [NE; NE]	0.79 [0.32; 1.97] 0.610

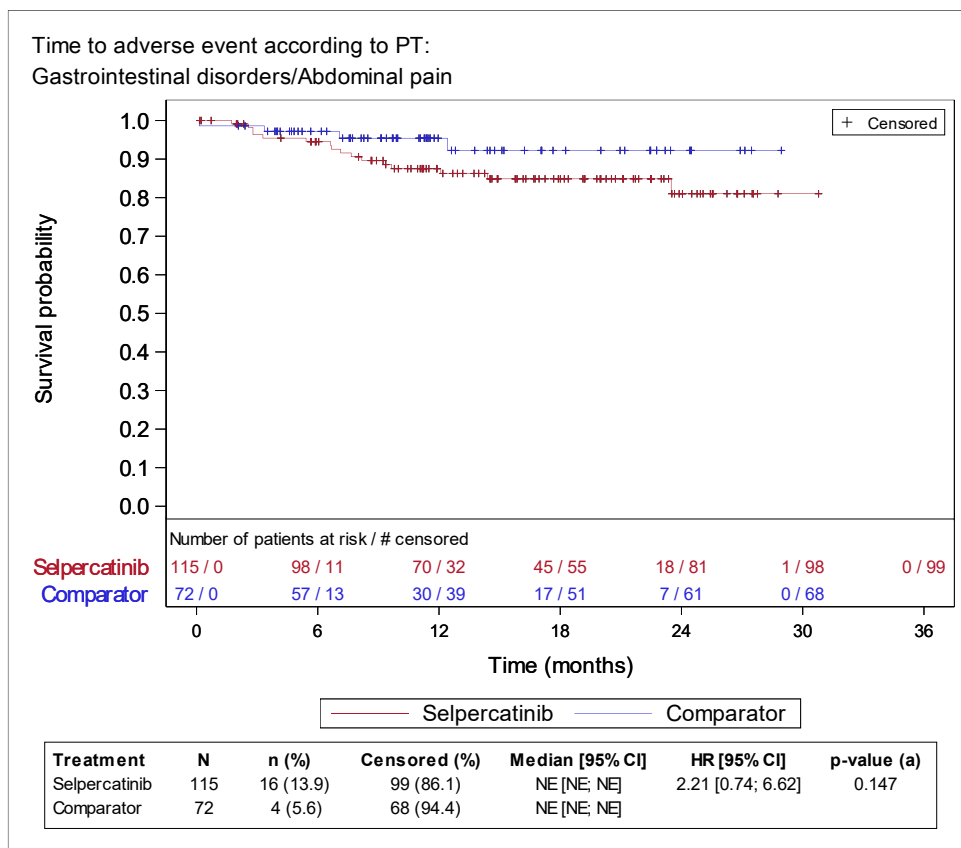
SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Nervous system disorders	34/115 (29.6)	NE [NE; NE]	24/72 (33.3)	NE [21.68; NE]	0.80 [0.48; 1.35] 0.409
Headache	17/115 (14.8)	NE [NE; NE]	8/72 (11.1)	NE [NE; NE]	1.20 [0.51; 2.78] 0.676
Blood and lymphatic system disorders	32/115 (27.8)	NE [NE; NE]	47/72 (65.3)	2.2 [1.38; 5.78]	0.30 [0.19; 0.48] <0.001
Anaemia	14/115 (12.2)	NE [NE; NE]	40/72 (55.6)	4.2 [2.14; NE]	0.14 [0.08; 0.26] <0.001
Leukopenia	11/115 (9.6)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	0.94 [0.36; 2.43] 0.897
Neutropenia	4/115 (3.5)	NE [NE; NE]	14/72 (19.4)	NE [NE; NE]	0.17 [0.05; 0.51] <0.001
Eye disorders	19/115 (16.5)	34.6 [NE; NE]	16/72 (22.2)	NE [NE; NE]	0.63 [0.32; 1.23] 0.173
Lacrimation increased	2/115 (1.7)	NE [NE; NE]	9/72 (12.5)	NE [NE; NE]	0.12 [0.03; 0.57] 0.001
Cardiac disorders	16/115 (13.9)	NE [NE; NE]	16/72 (22.2)	NE [NE; NE]	0.59 [0.29; 1.18] 0.130
Psychiatric disorders	14/115 (12.2)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	2.11 [0.69; 6.43] 0.177
Renal and urinary disorders	14/115 (12.2)	NE [NE; NE]	10/72 (13.9)	NE [NE; NE]	0.81 [0.36; 1.83] 0.610
Reproductive system and breast disorders	13/115 (11.3)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	7.19 [0.94; 54.98] 0.026
Endocrine disorders	12/115 (10.4)	NE [NE; NE]	11/72 (15.3)	NE [NE; NE]	0.65 [0.29; 1.48] 0.298
Hepatobiliary disorders	12/115 (10.4)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	2.40 [0.68; 8.51] 0.162
Injury, poisoning and procedural complications	12/115 (10.4)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	0.91 [0.36; 2.31] 0.837

SOC	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
		Median time to event ^a [95% CI]		Median time to event ^a [95% CI]	
	Preferred term	n/N (%)	n/N (%)		
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class. a: In months; b: from unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

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Figure 1: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Abdominal pain - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

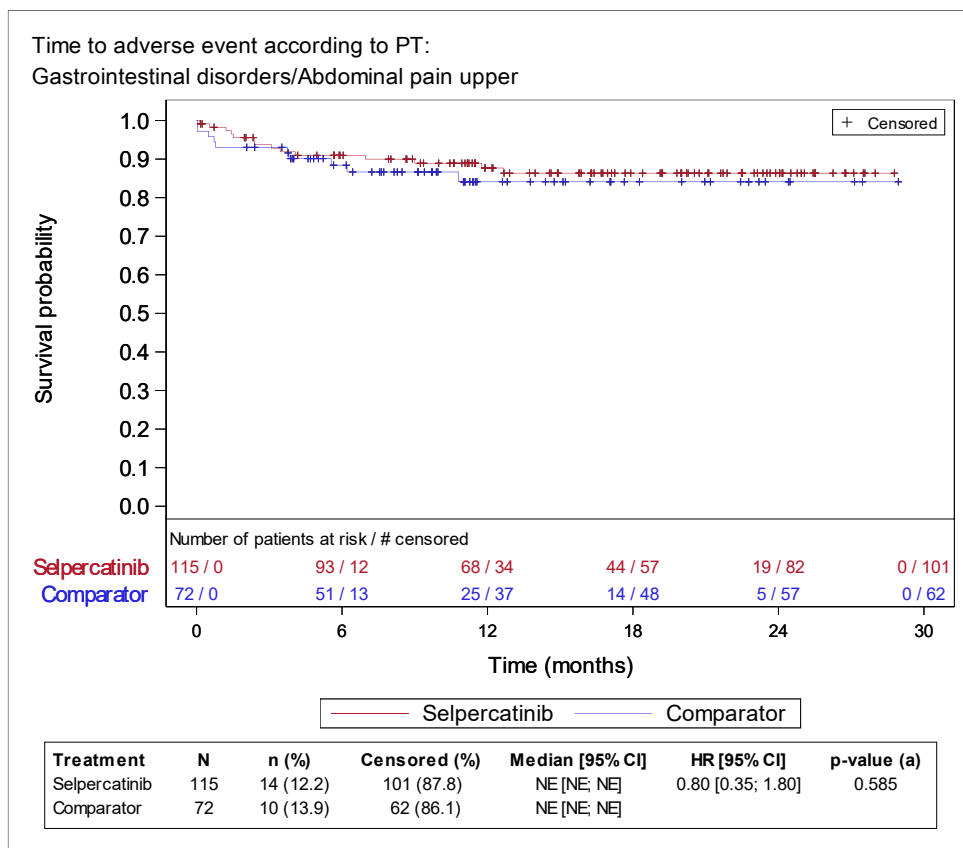
HR is based on the unstratified Cox proportional hazards model.

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Figure 2: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Abdominal pain upper - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

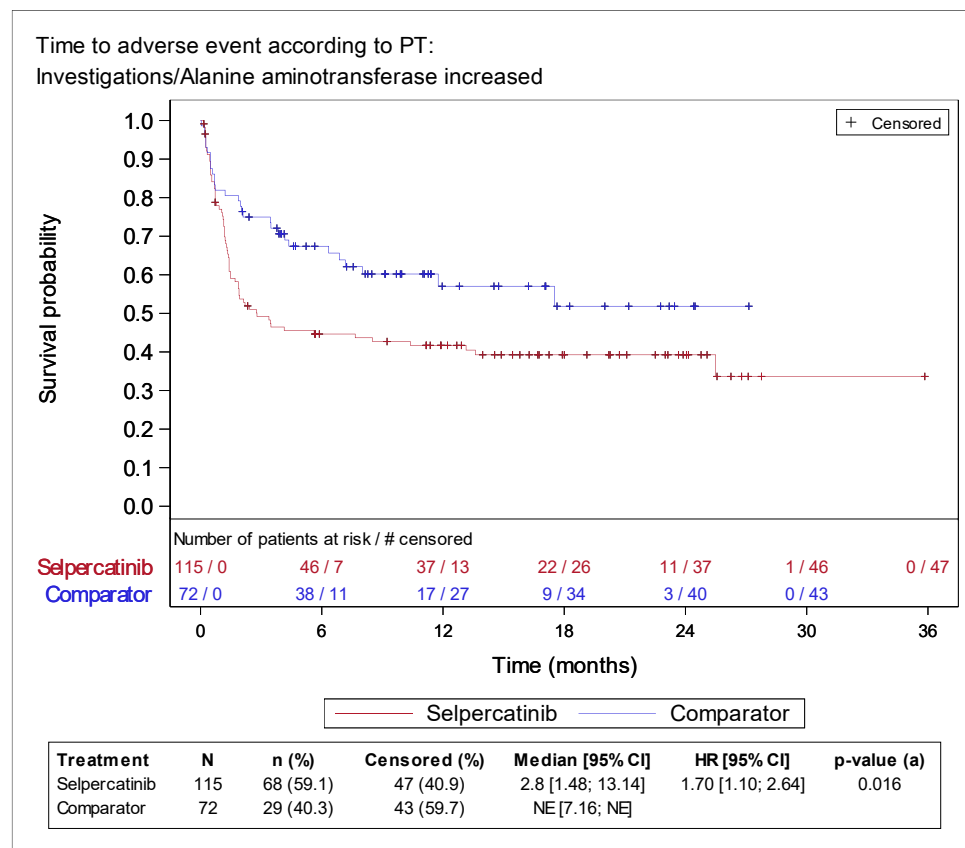
HR is based on the unstratified Cox proportional hazards model.

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Figure 3: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Alanine aminotransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

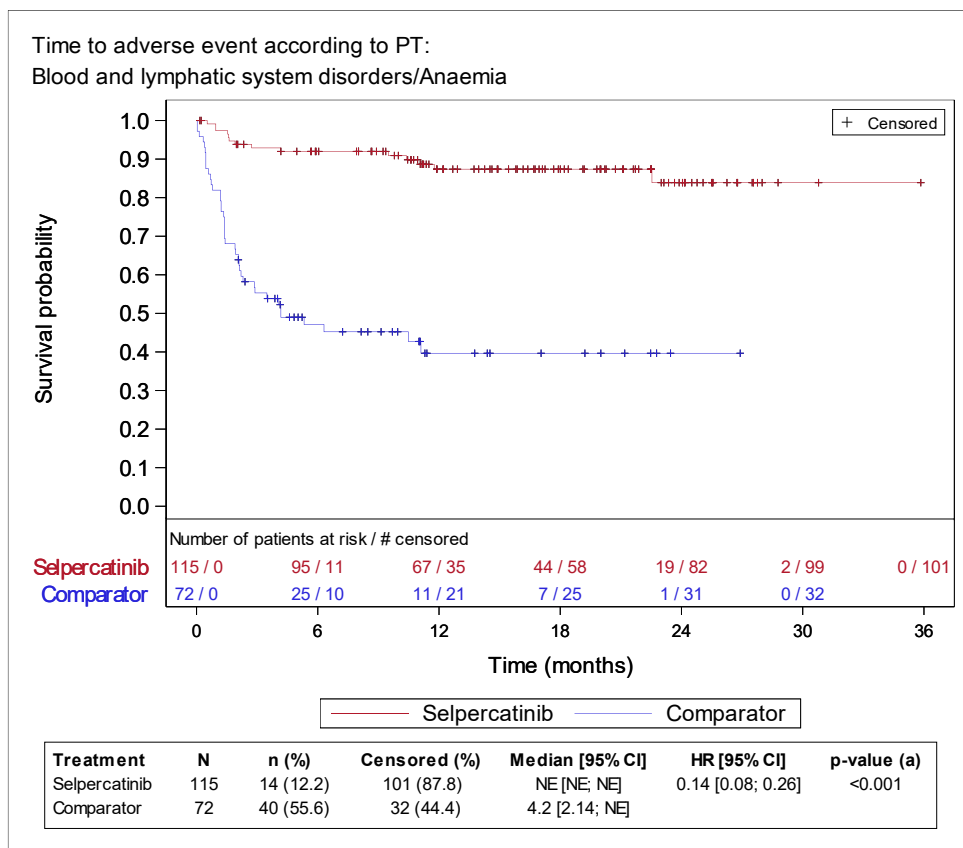
HR is based on the unstratified Cox proportional hazards model.

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Figure 4: Kaplan-Meier Plot - Time to adverse event according to PT: Blood and lymphatic system disorders/Anaemia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

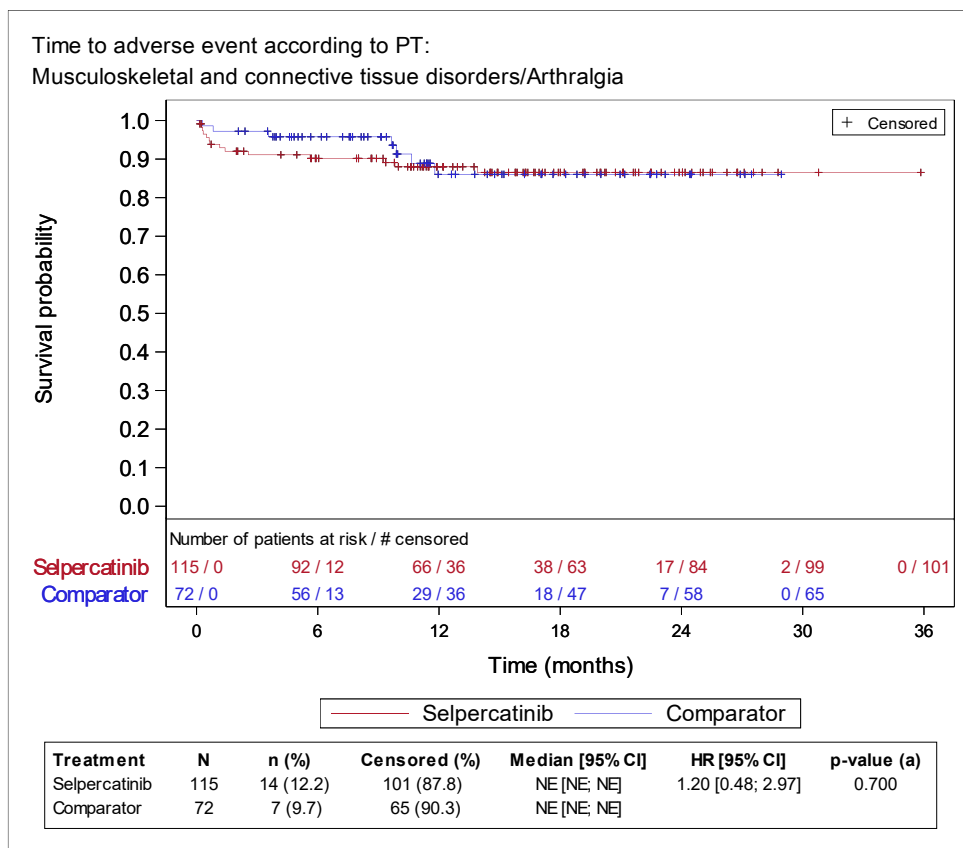
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Figure 5: Kaplan-Meier Plot - Time to adverse event according to PT: Musculoskeletal and connective tissue disorders/Arthralgia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

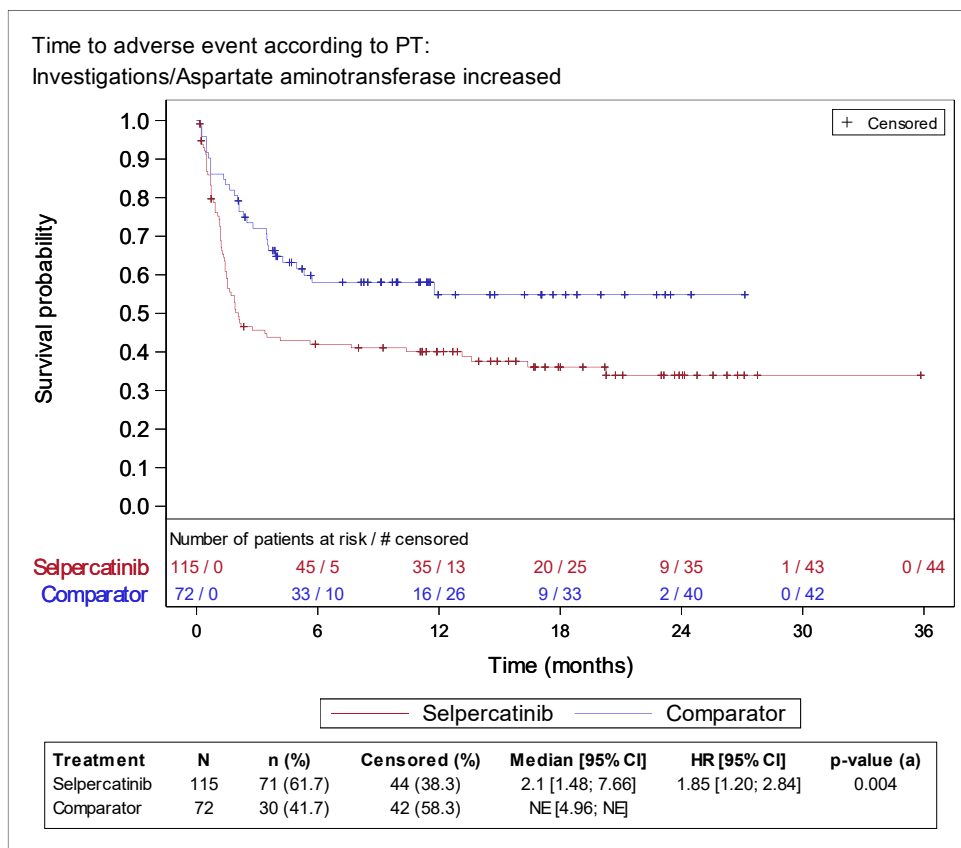
HR is based on the unstratified Cox proportional hazards model.

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Figure 6: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Aspartate aminotransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

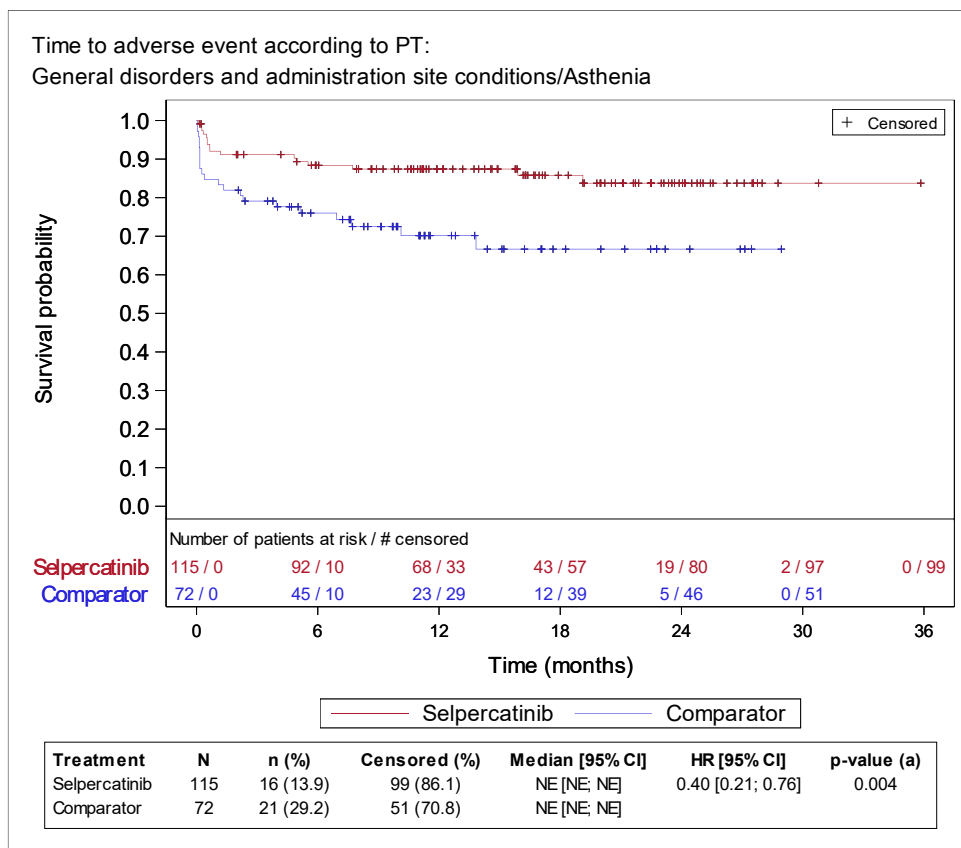
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Figure 7: Kaplan-Meier Plot - Time to adverse event according to PT: General disorders and administration site conditions/Asthenia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

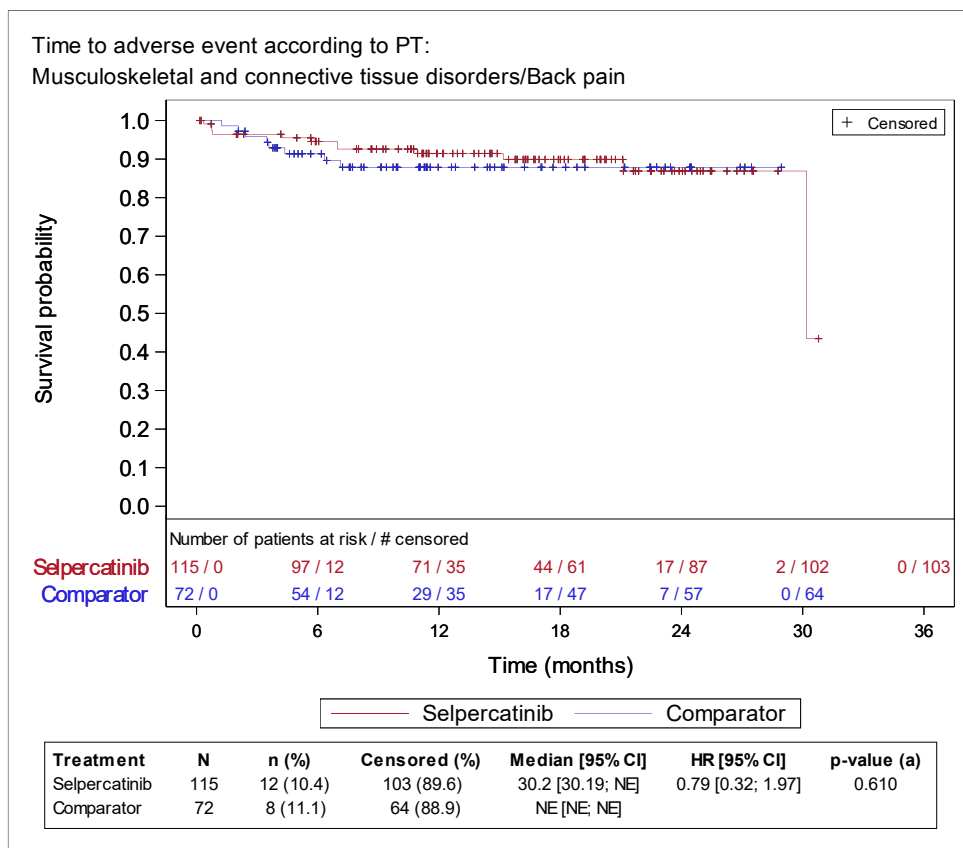
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Figure 8: Kaplan-Meier Plot - Time to adverse event according to PT: Musculoskeletal and connective tissue disorders/Back pain - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

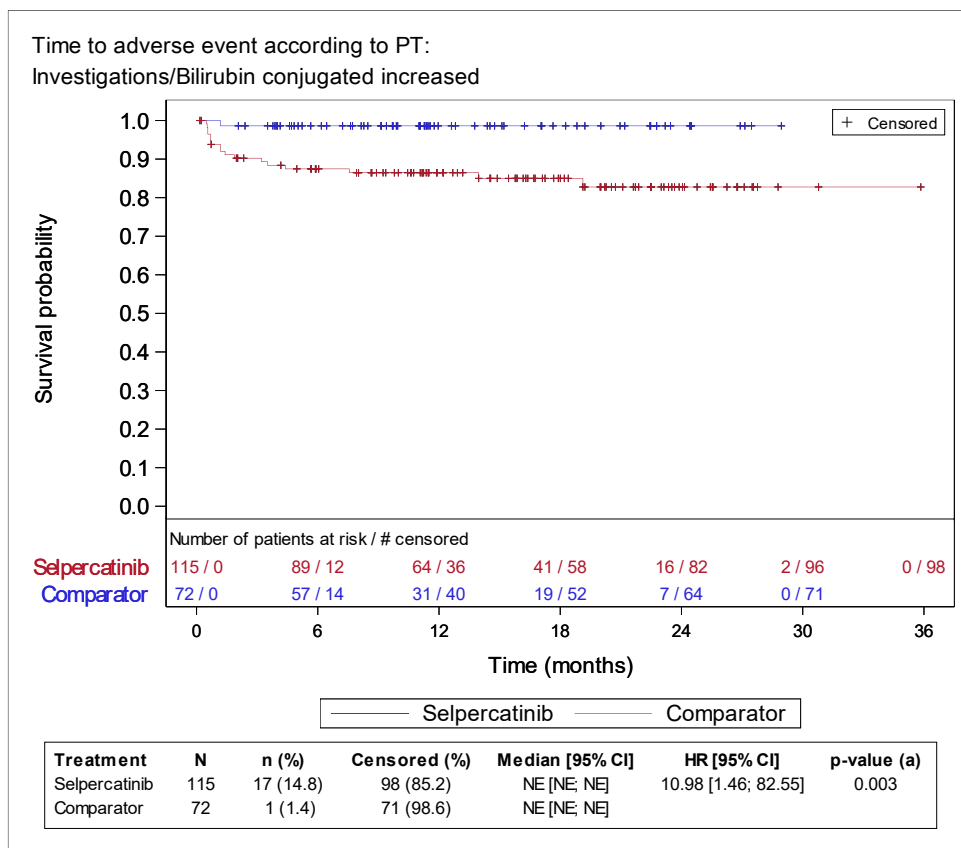
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Figure 9: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Bilirubin conjugated increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

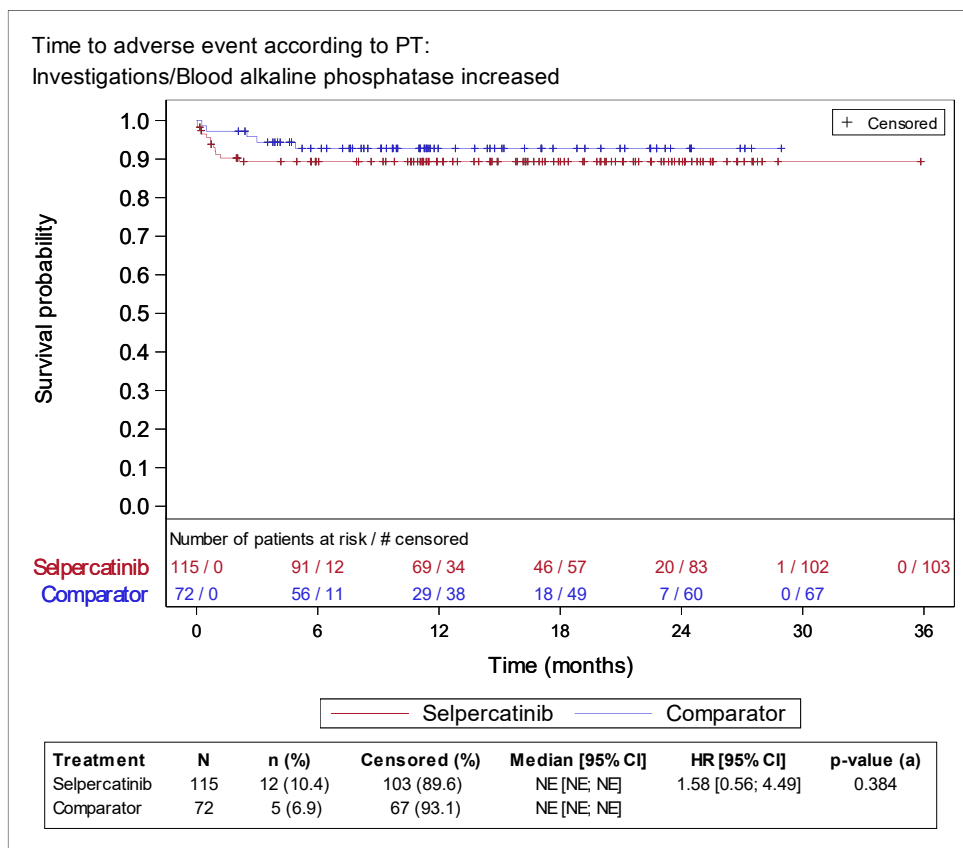
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Figure 10: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Blood alkaline phosphatase increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

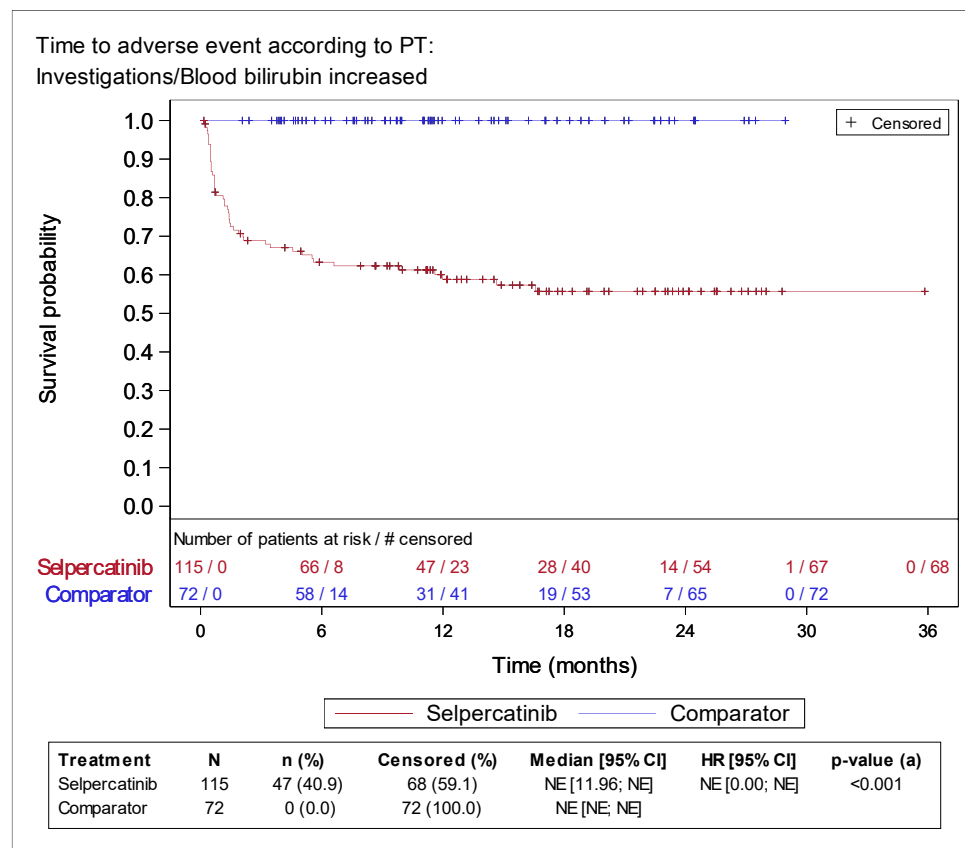
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Figure 11: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Blood bilirubin increased - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

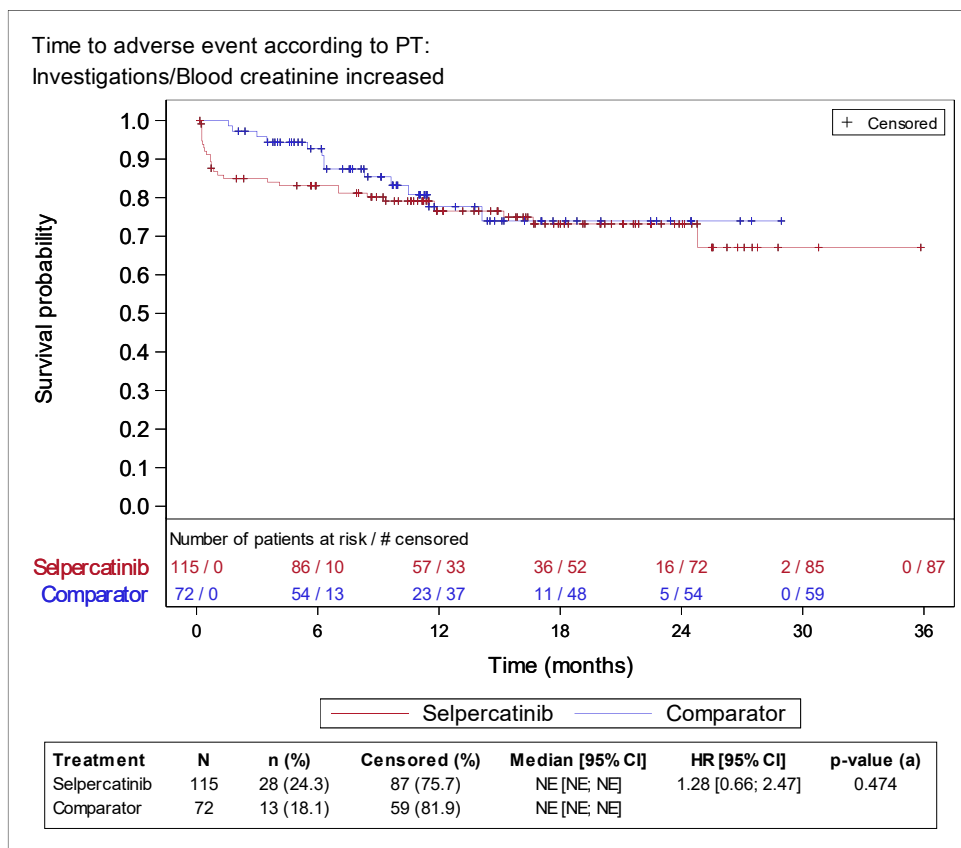
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx011_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 12: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Blood creatinine increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

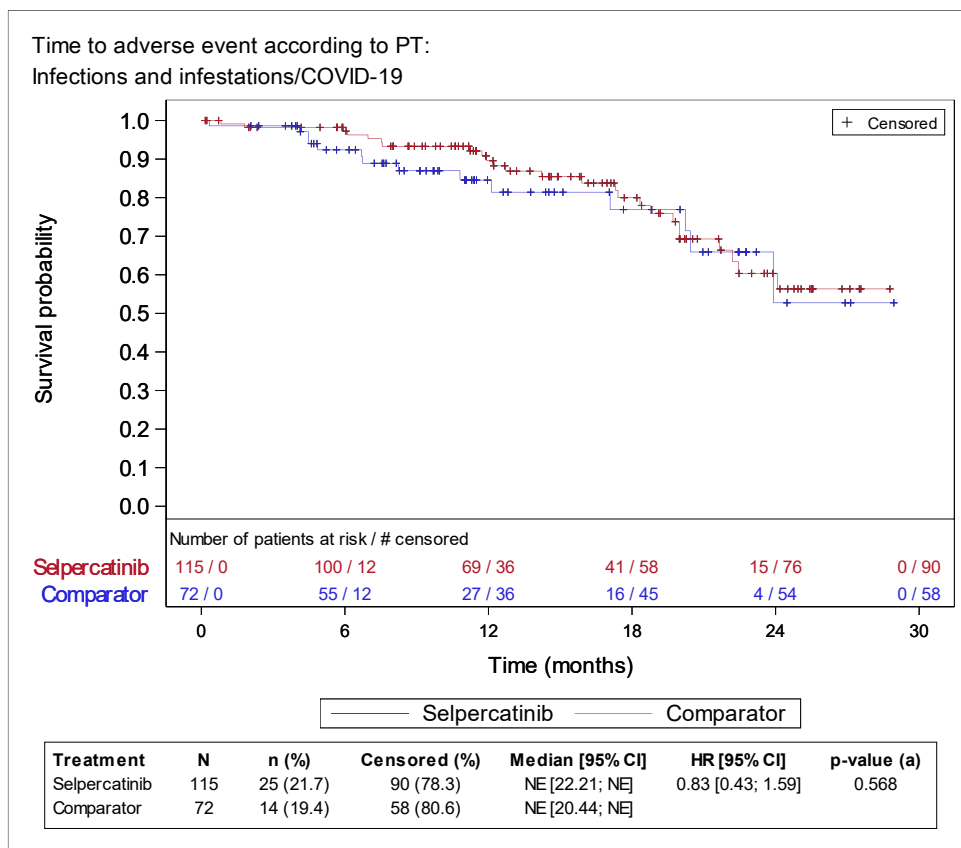
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx012_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 13: Kaplan-Meier Plot - Time to adverse event according to PT: Infections and infestations/COVID-19 - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

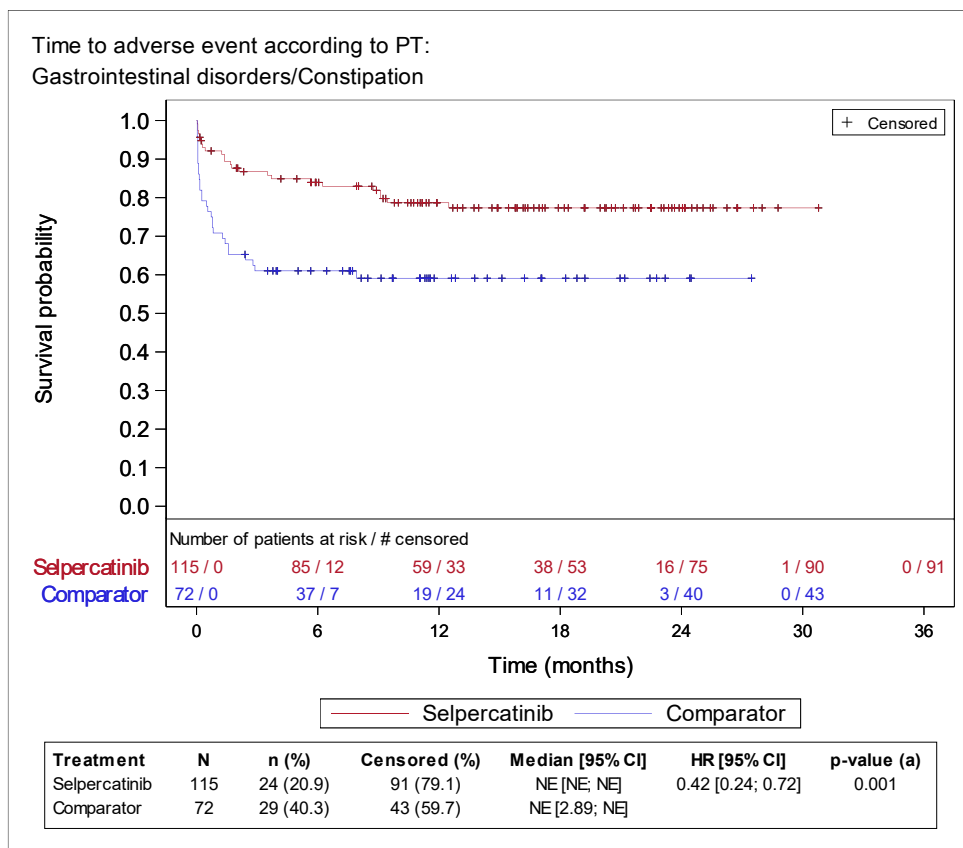
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx013_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 14: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Constipation - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

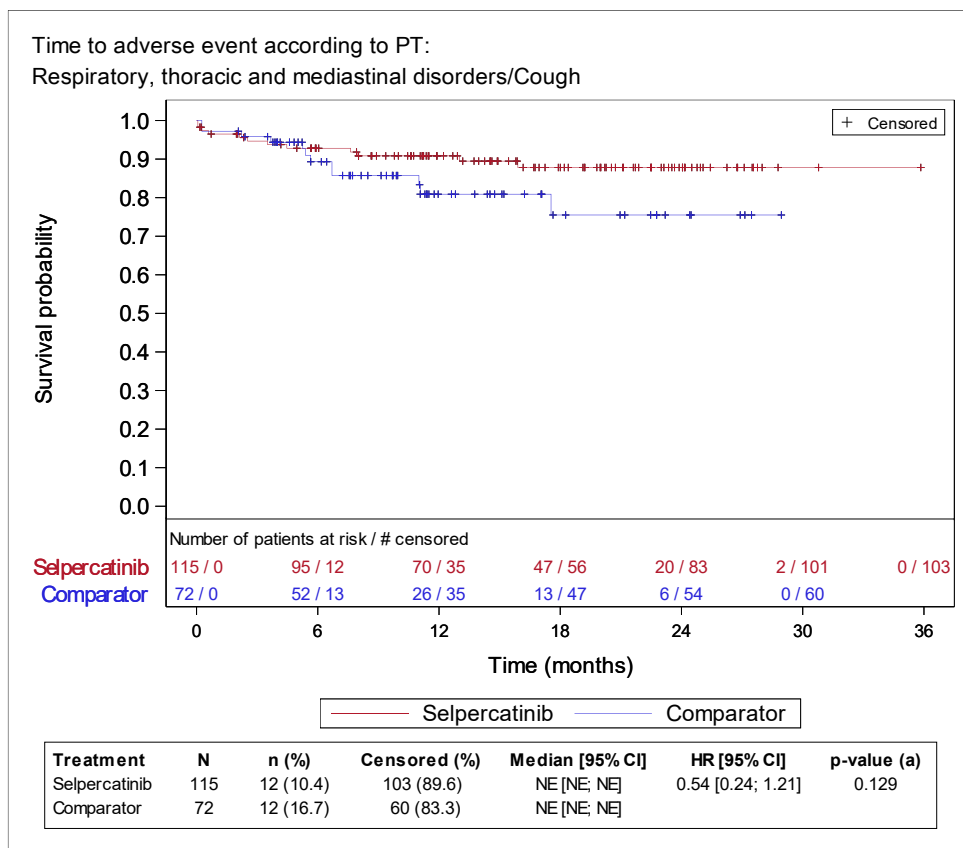
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx014_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 15: Kaplan-Meier Plot - Time to adverse event according to PT: Respiratory, thoracic and mediastinal disorders/Cough - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

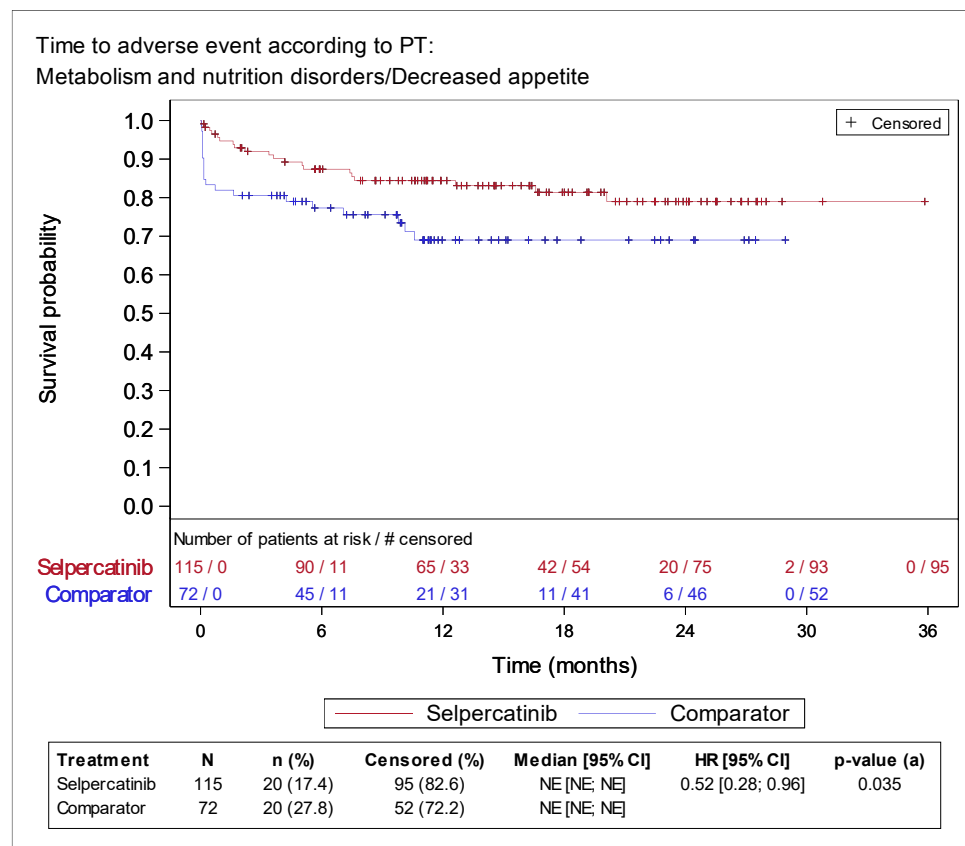
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx015_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 16: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Decreased appetite - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

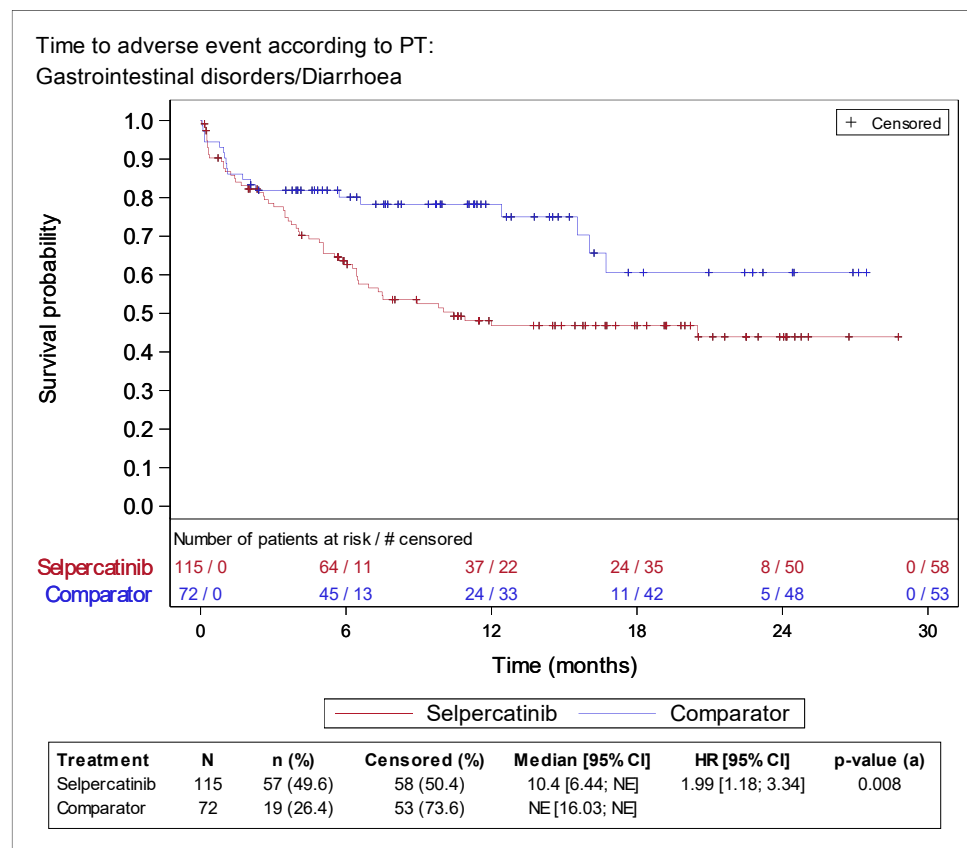
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx016_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 17: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Diarrhoea - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

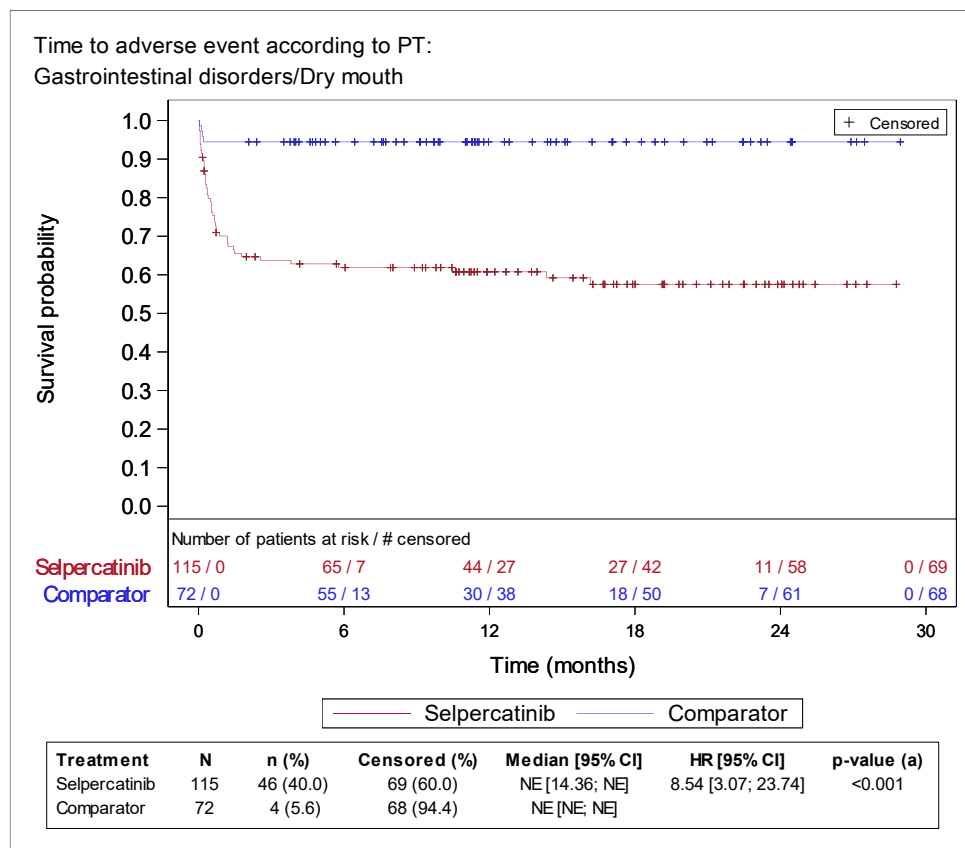
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 18: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Dry mouth - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

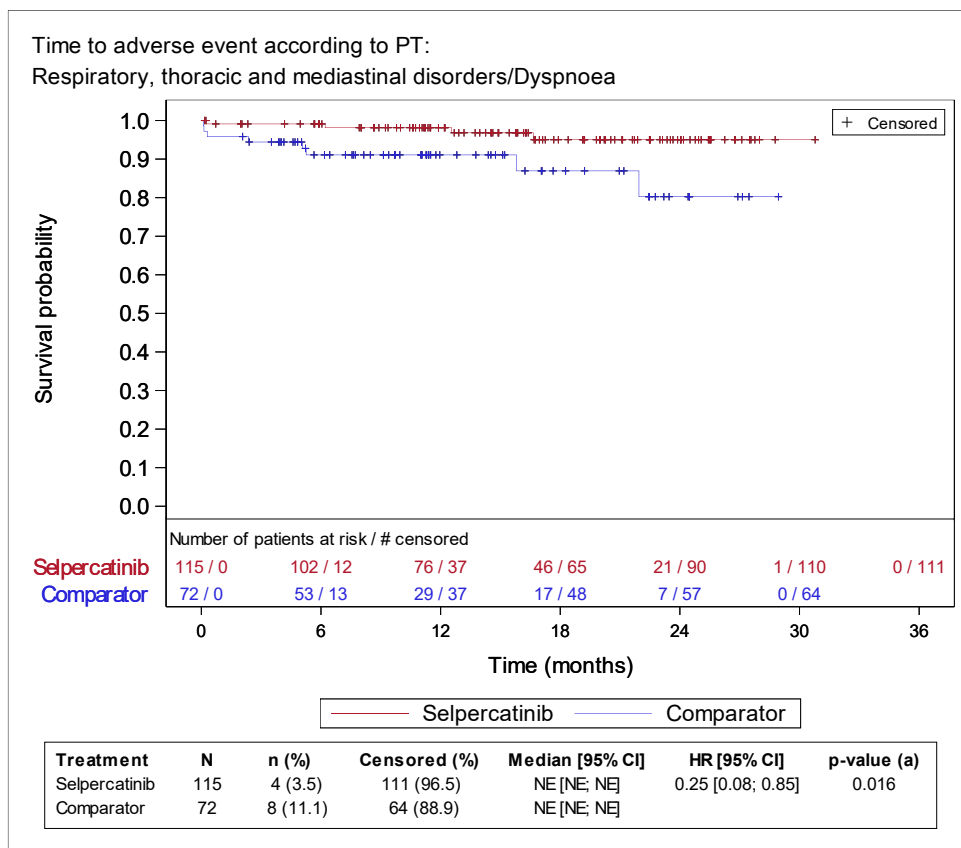
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Figure 19: Kaplan-Meier Plot - Time to adverse event according to PT: Respiratory, thoracic and mediastinal disorders/Dyspnoea - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

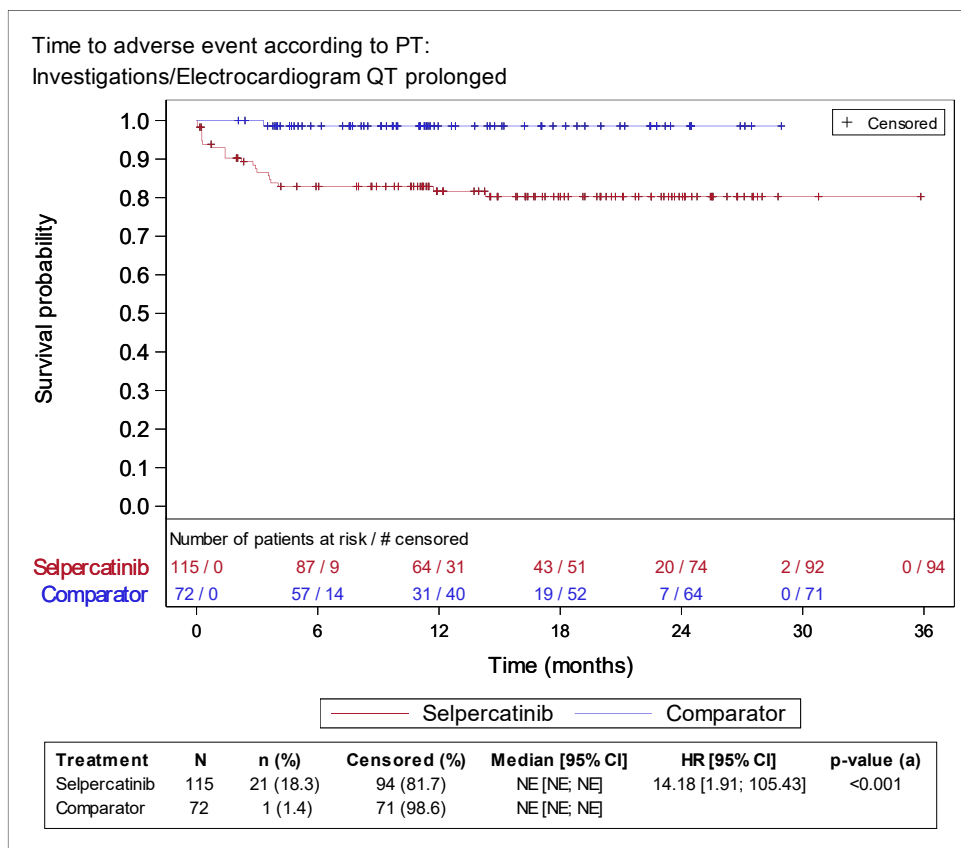
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx019_msaf.rtf

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Figure 20: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Electrocardiogram QT prolonged - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

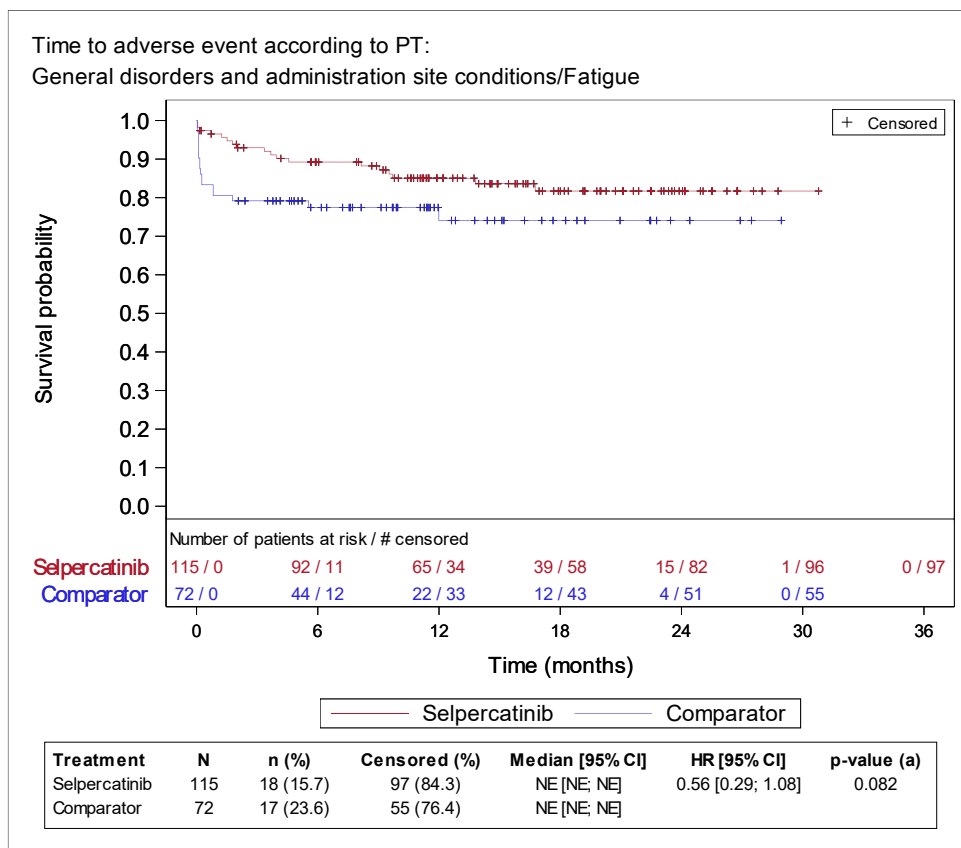
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx020_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 21: Kaplan-Meier Plot - Time to adverse event according to PT: General disorders and administration site conditions/Fatigue - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

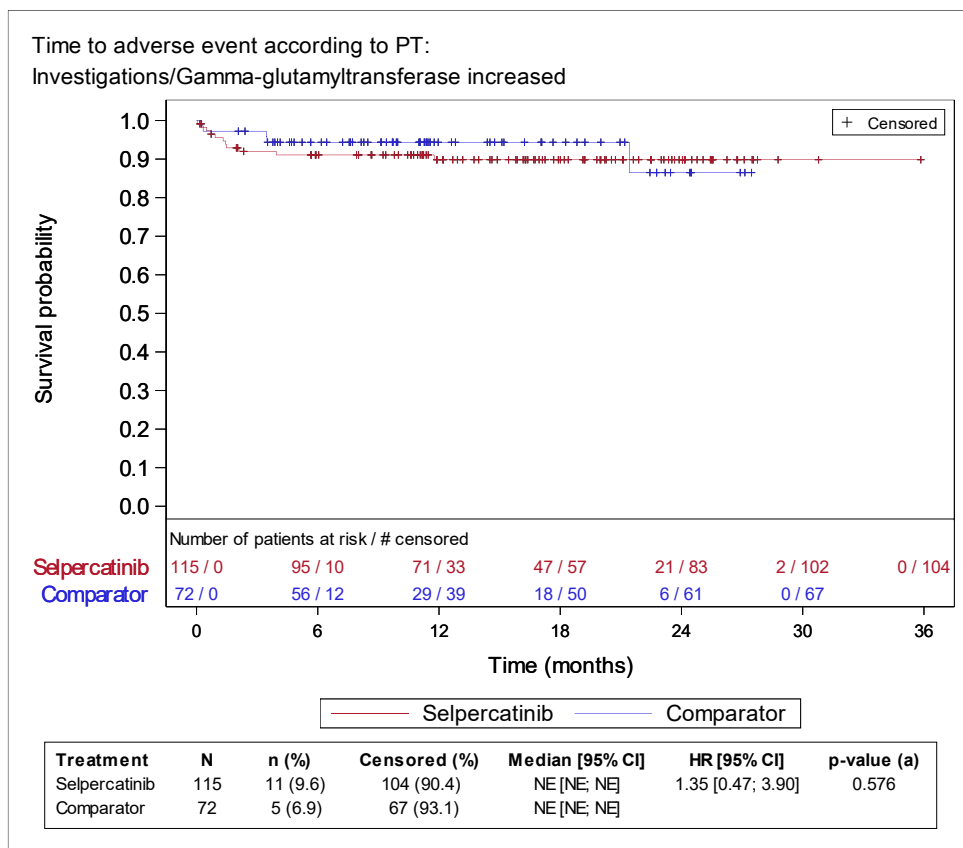
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx021_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 22: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Gamma-glutamyltransferase increased - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

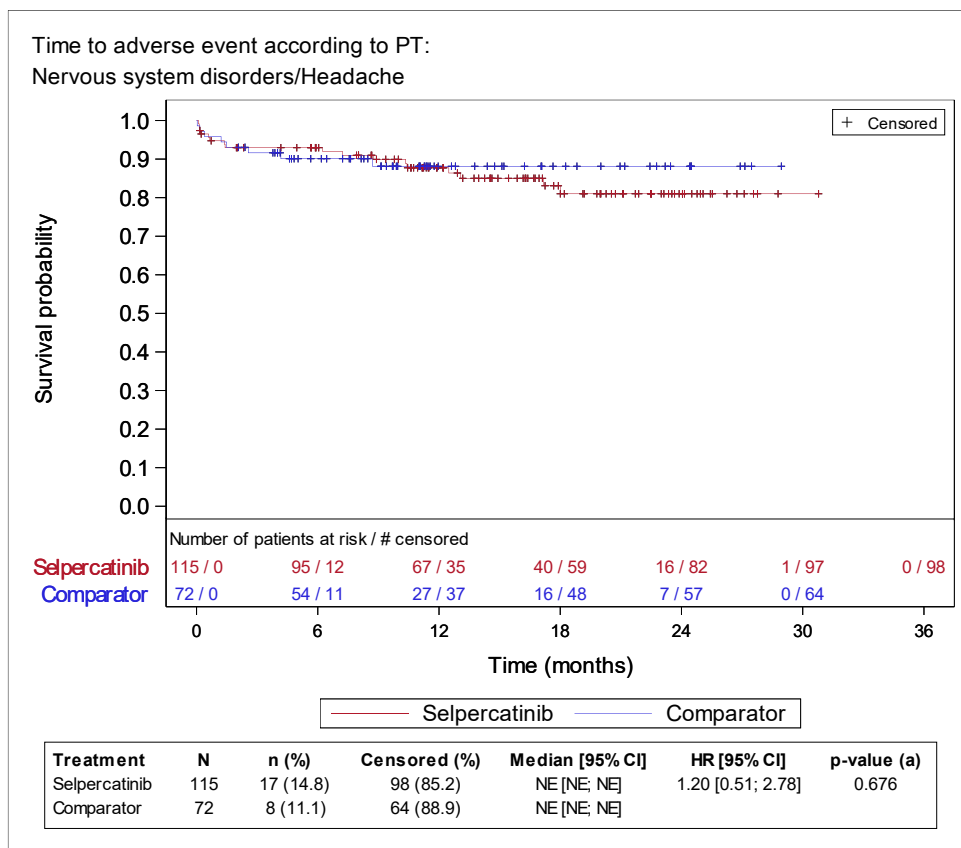
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx022_msaf.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 23: Kaplan-Meier Plot - Time to adverse event according to PT: Nervous system disorders/Headache - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

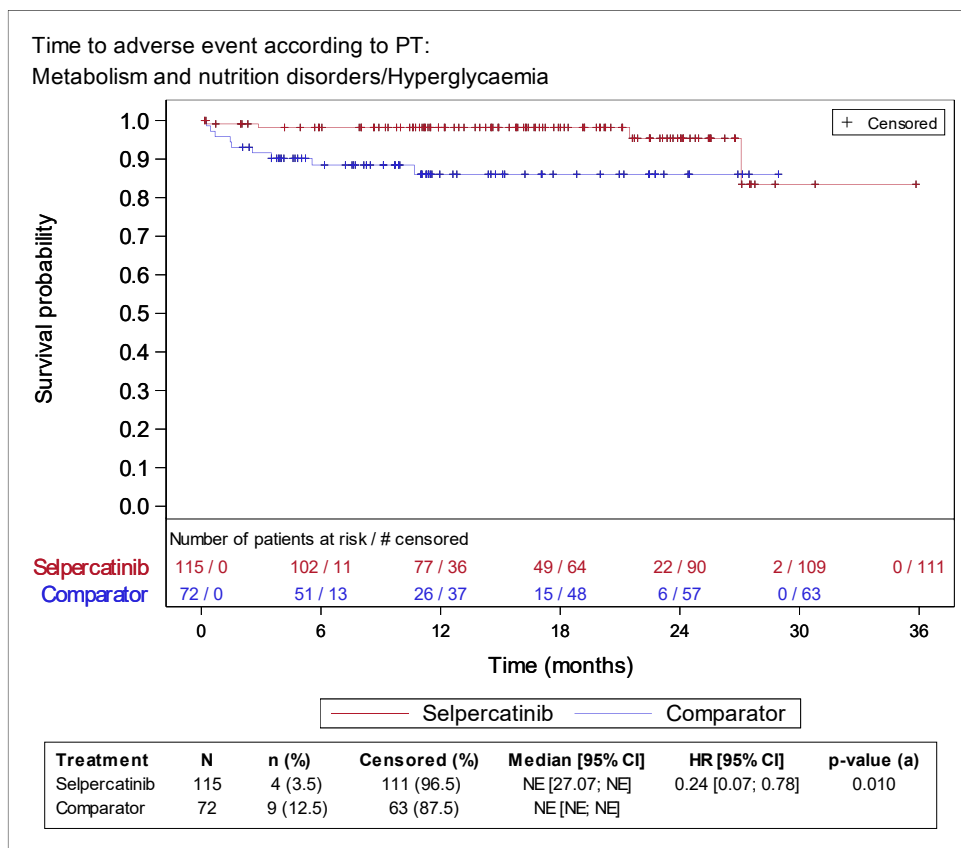
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx023_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 24: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Hyperglycaemia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

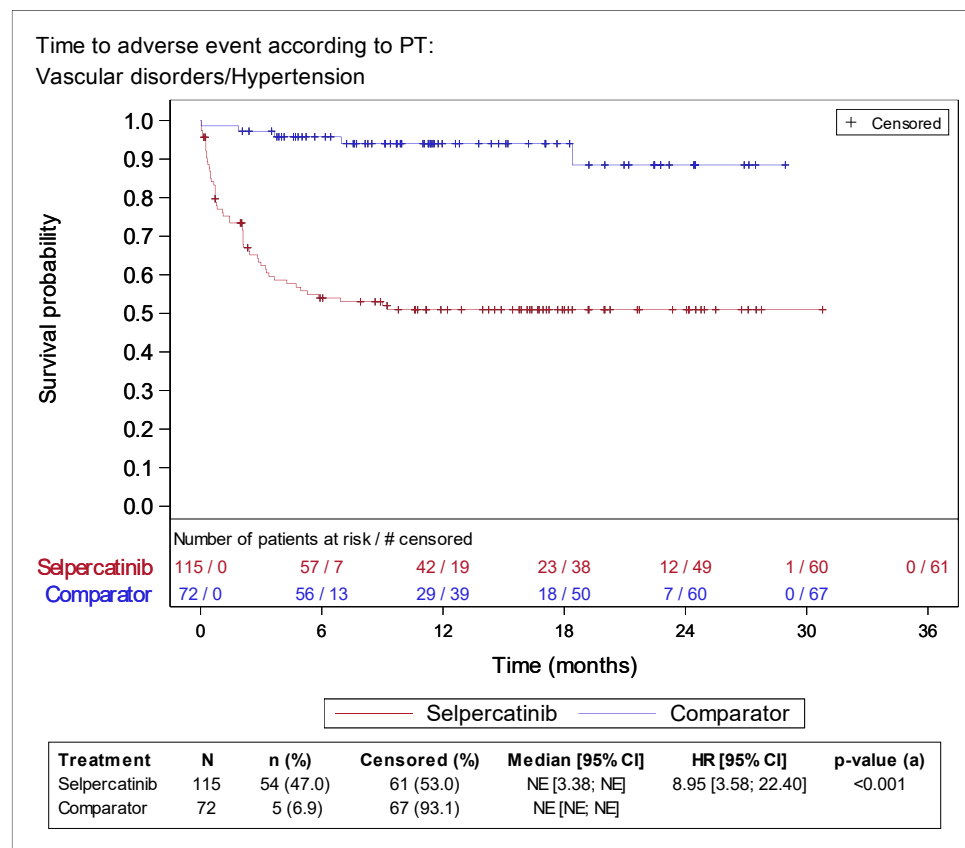
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx024_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 25: Kaplan-Meier Plot - Time to adverse event according to PT: Vascular disorders/Hypertension - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

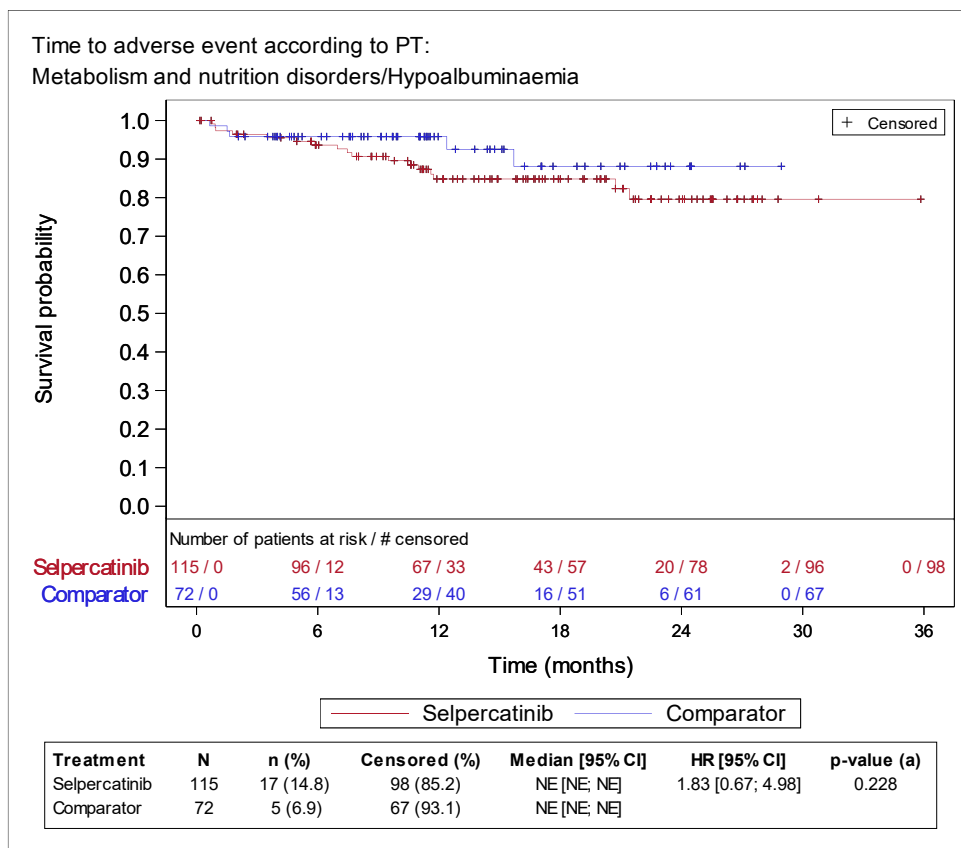
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx025_msaf.rtf

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02OCT2025 / 04:32

Figure 26: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Hypoalbuminaemia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

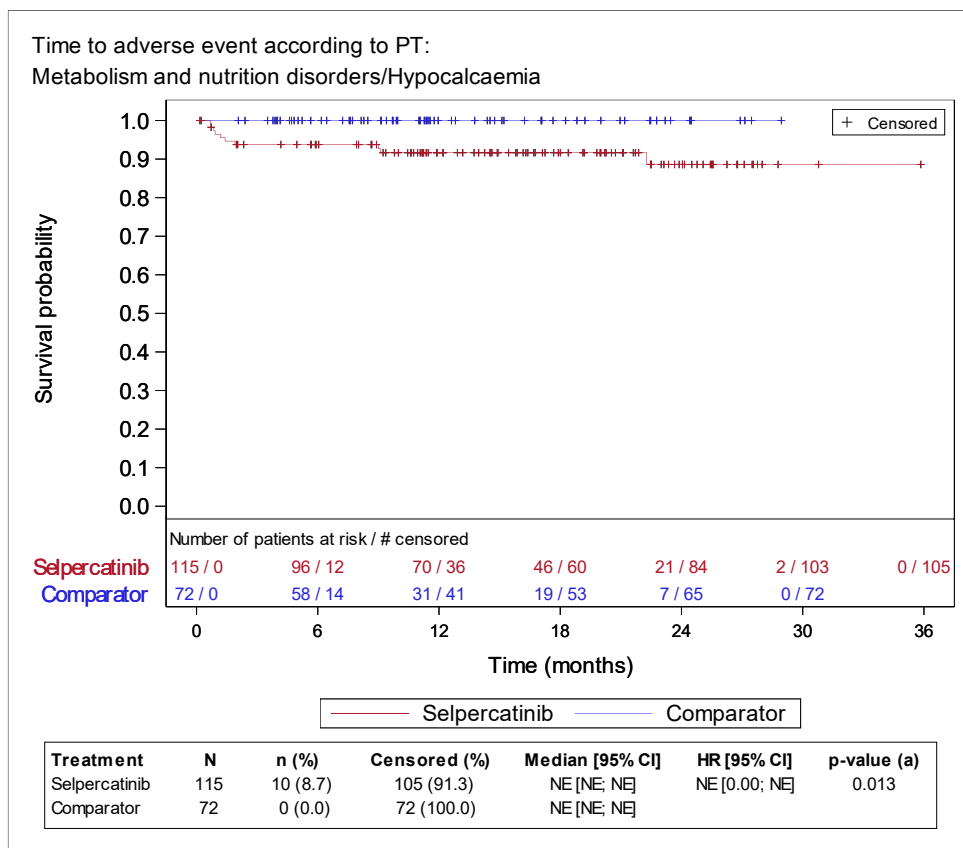
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 27: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Hypocalcaemia - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

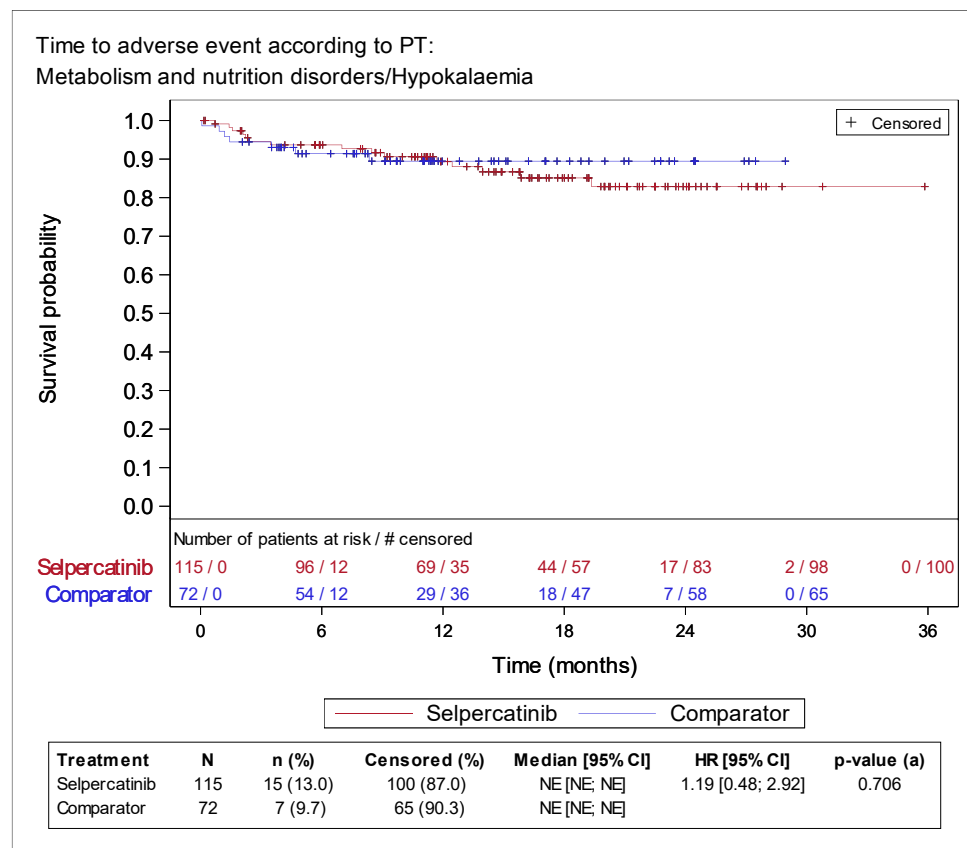
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx027_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 28: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Hypokalaemia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

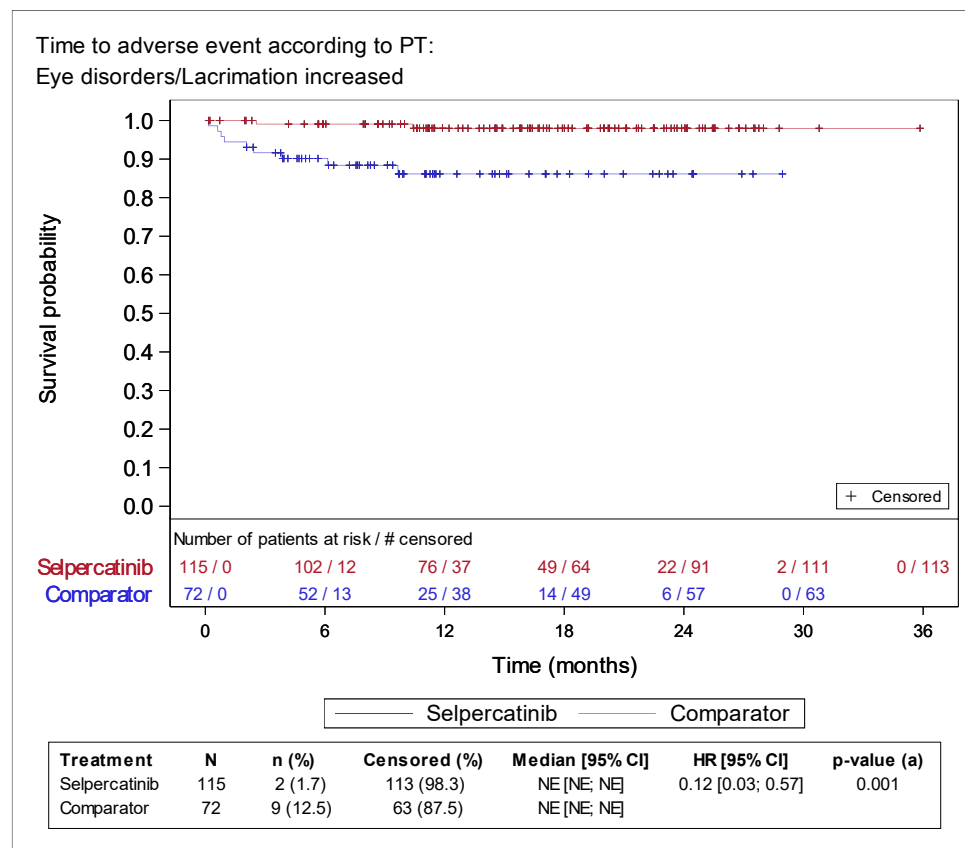
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx028_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 29: Kaplan-Meier Plot - Time to adverse event according to PT: Eye disorders/Lacrimation increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

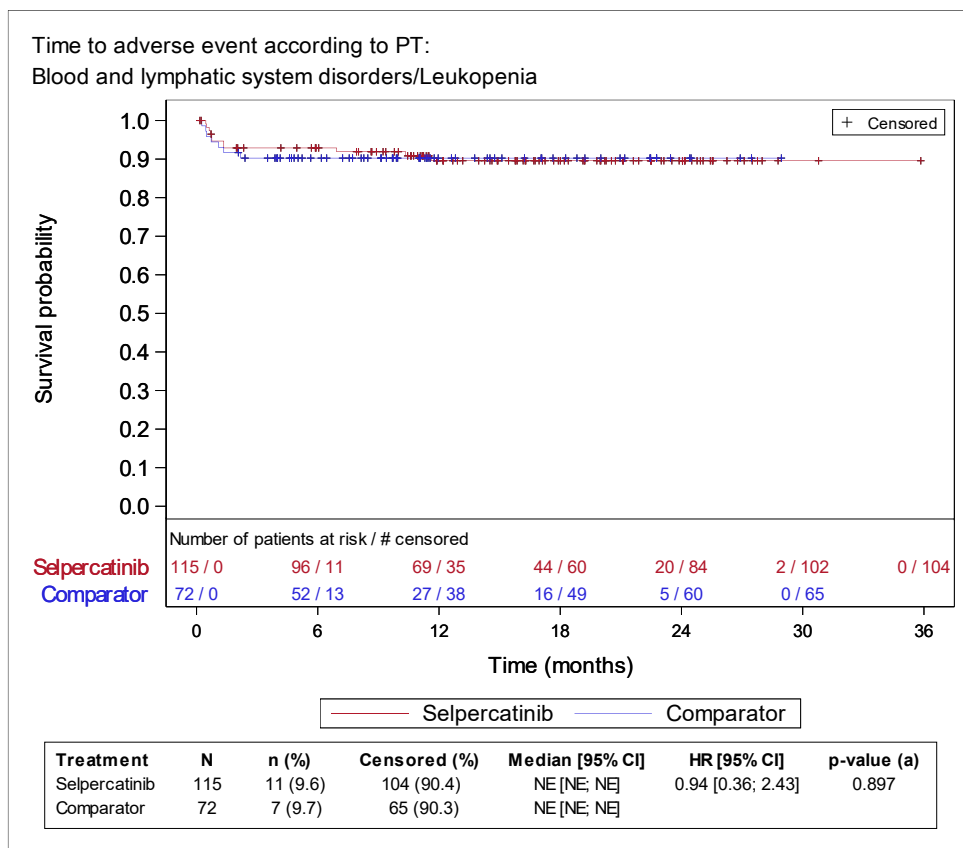
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aeppx029_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 30: Kaplan-Meier Plot - Time to adverse event according to PT: Blood and lymphatic system disorders/Leukopenia - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

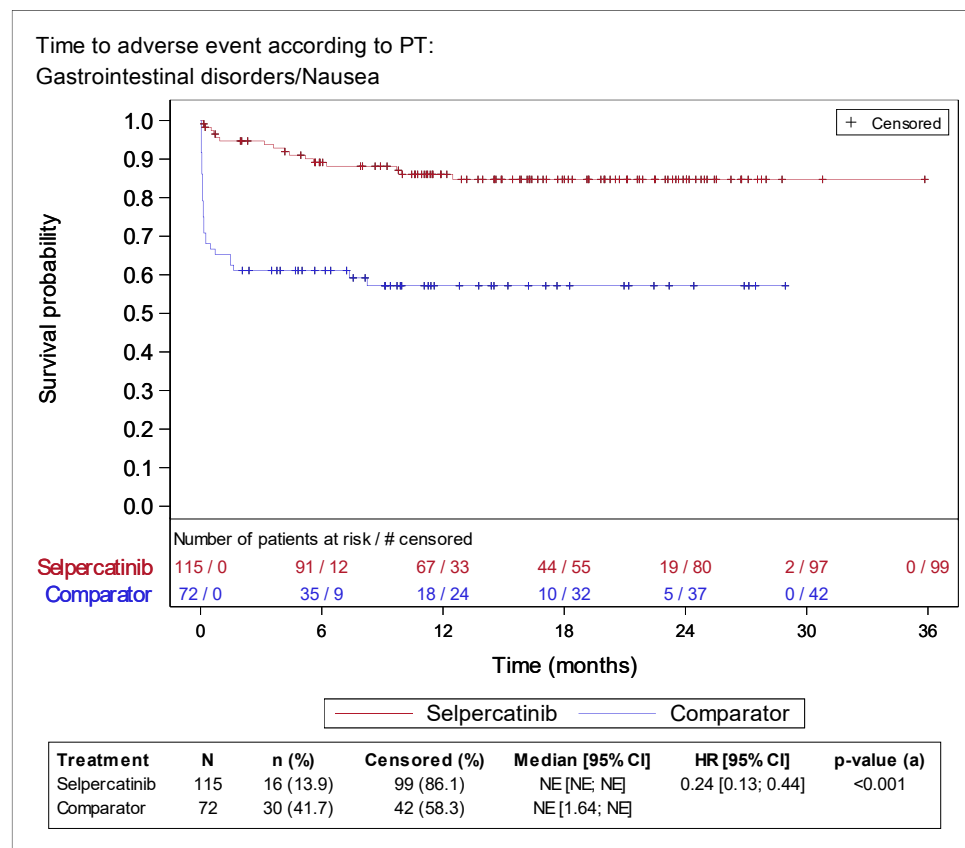
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 31: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Nausea - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

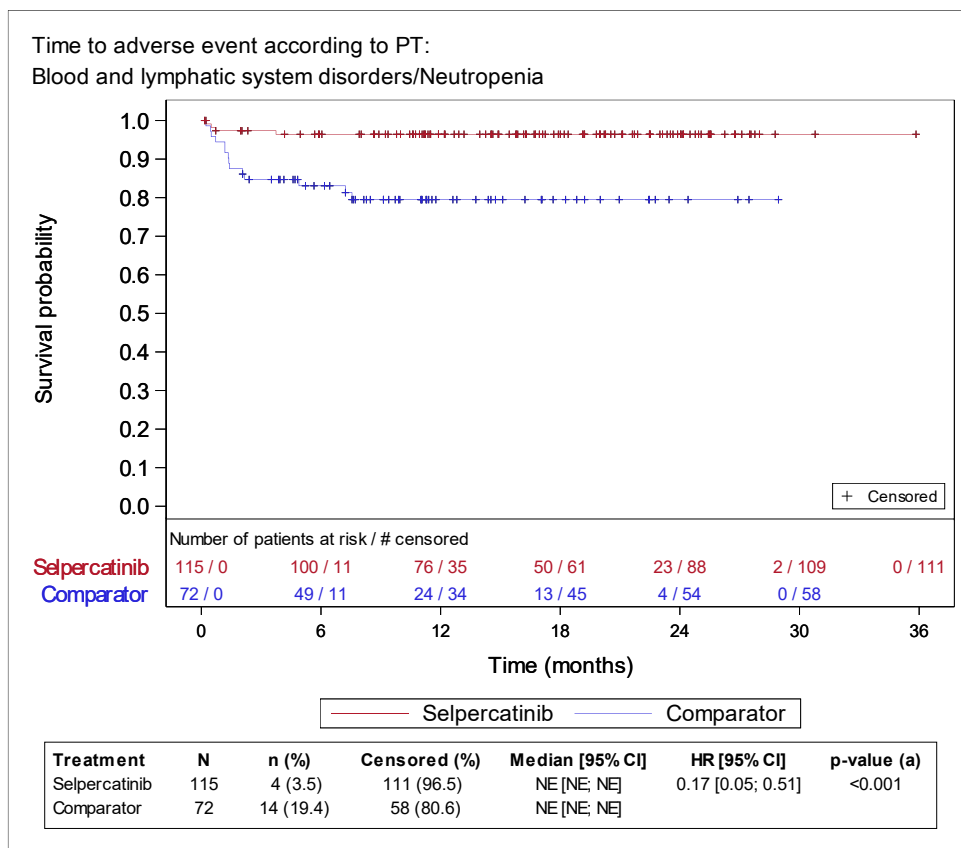
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 32: Kaplan-Meier Plot - Time to adverse event according to PT: Blood and lymphatic system disorders/Neutropenia - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

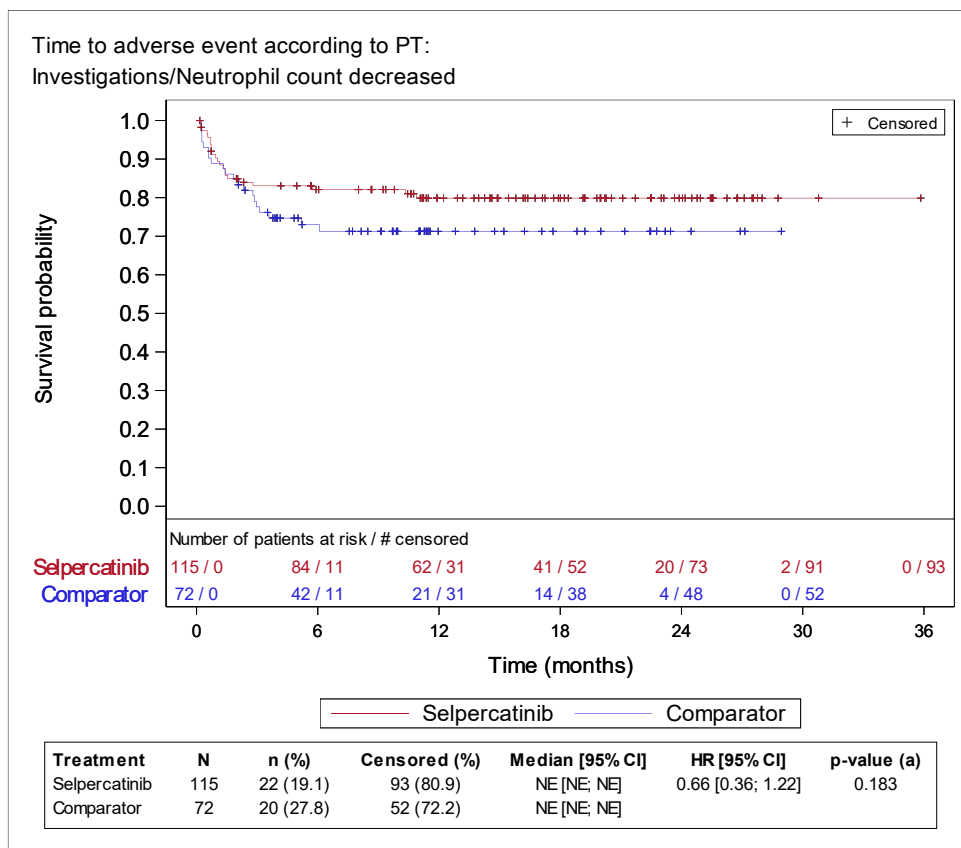
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 33: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Neutrophil count decreased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

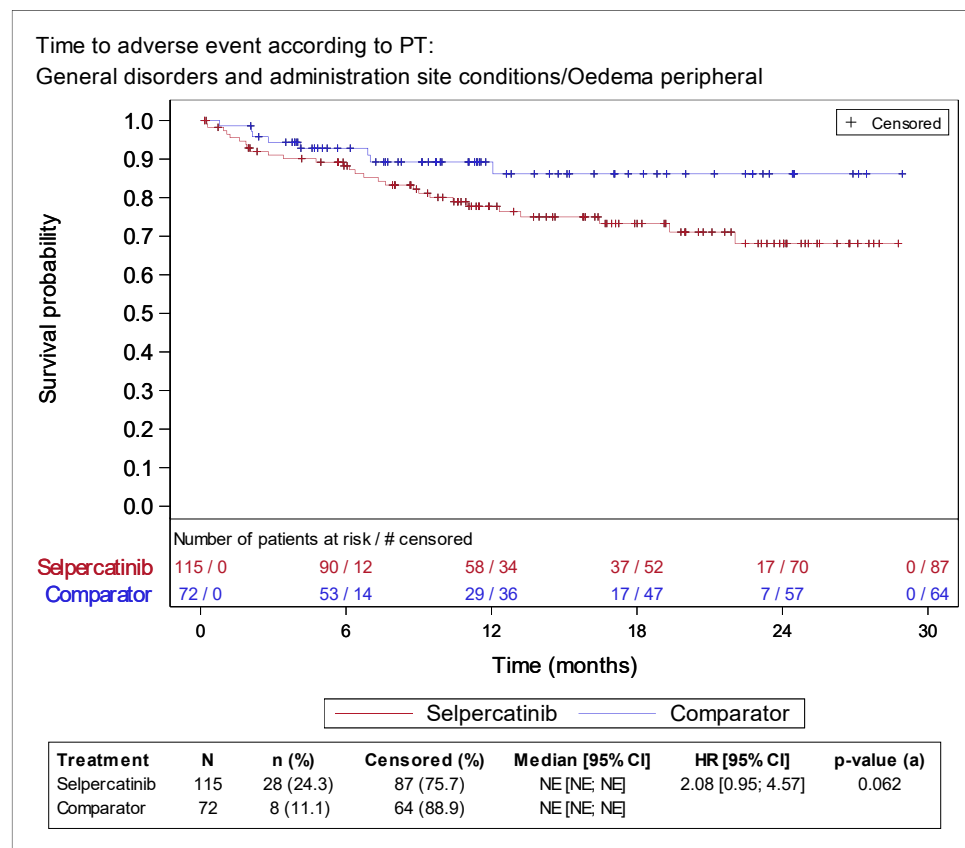
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 34: Kaplan-Meier Plot - Time to adverse event according to PT: General disorders and administration site conditions/Oedema peripheral - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

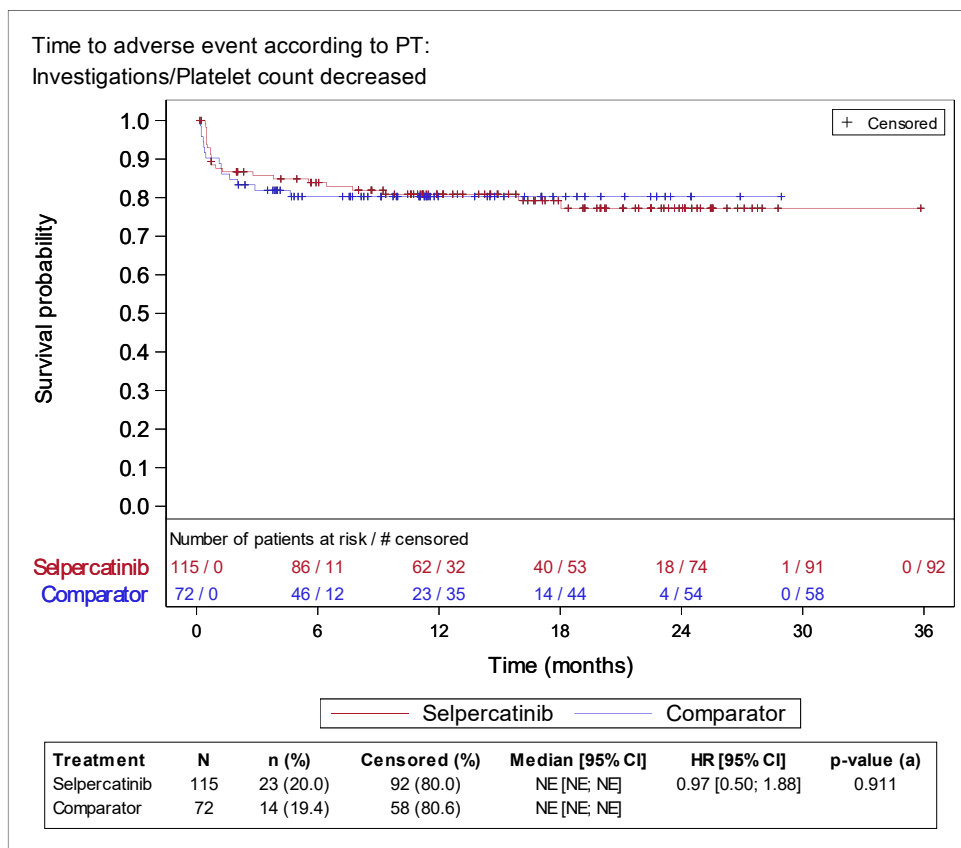
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 35: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Platelet count decreased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

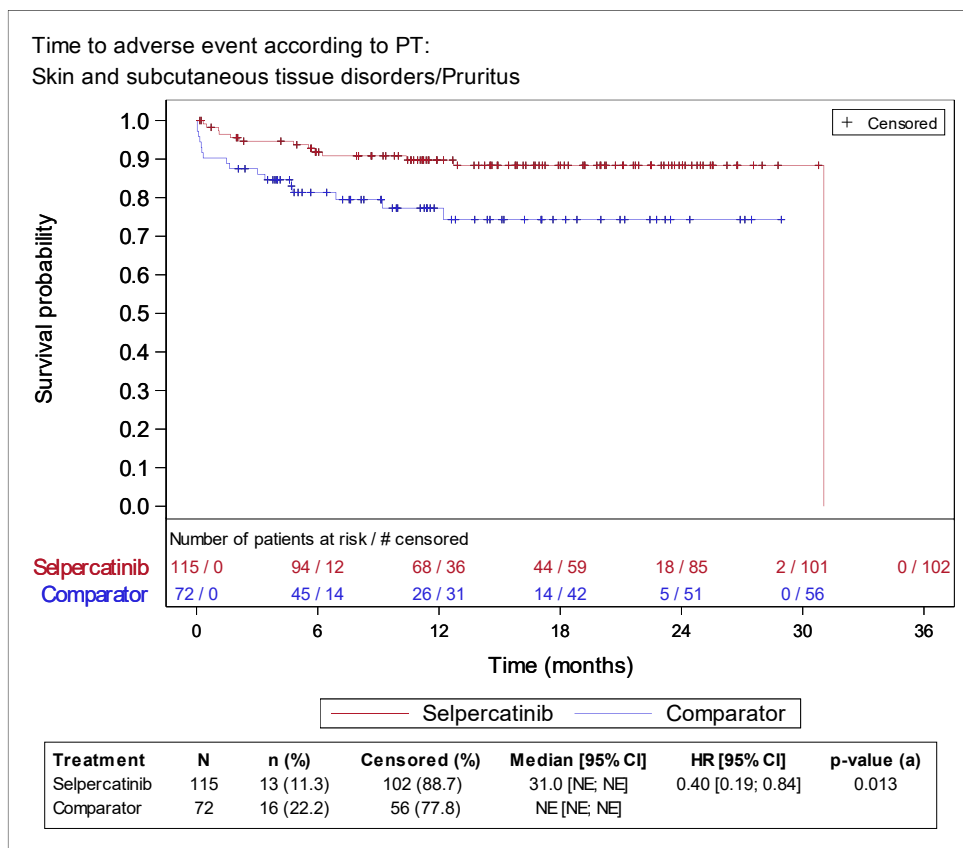
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Figure 36: Kaplan-Meier Plot - Time to adverse event according to PT: Skin and subcutaneous tissue disorders/Pruritus - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

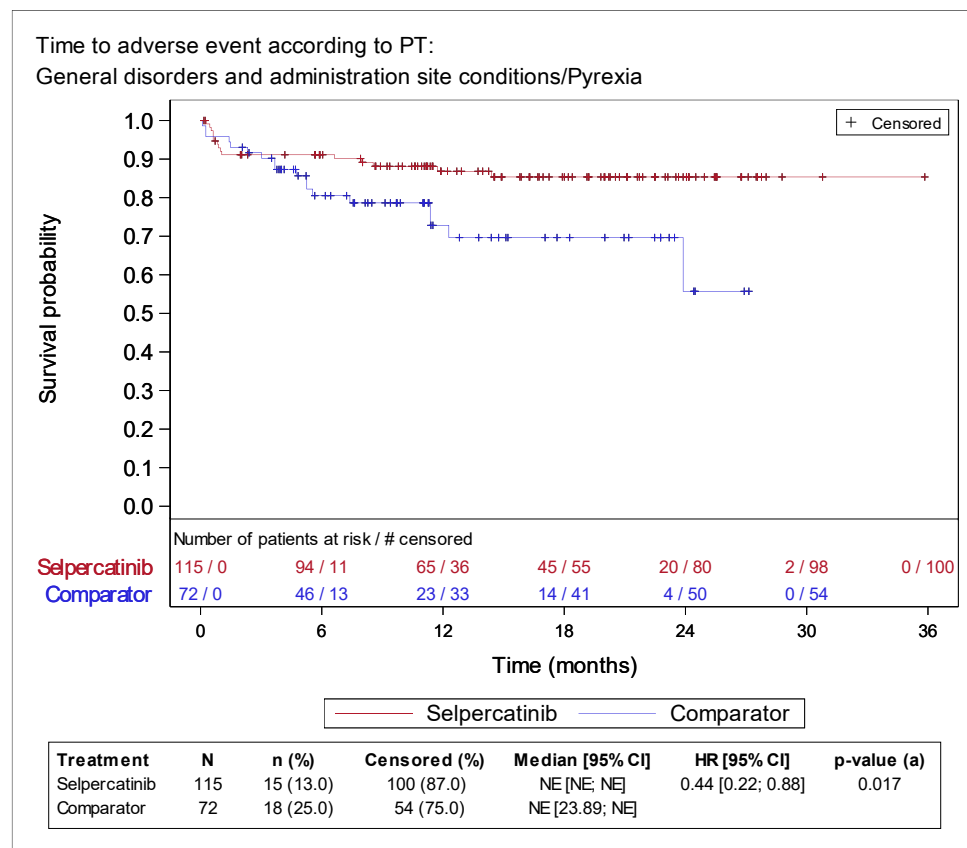
HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 37: Kaplan-Meier Plot - Time to adverse event according to PT: General disorders and administration site conditions/Pyrexia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

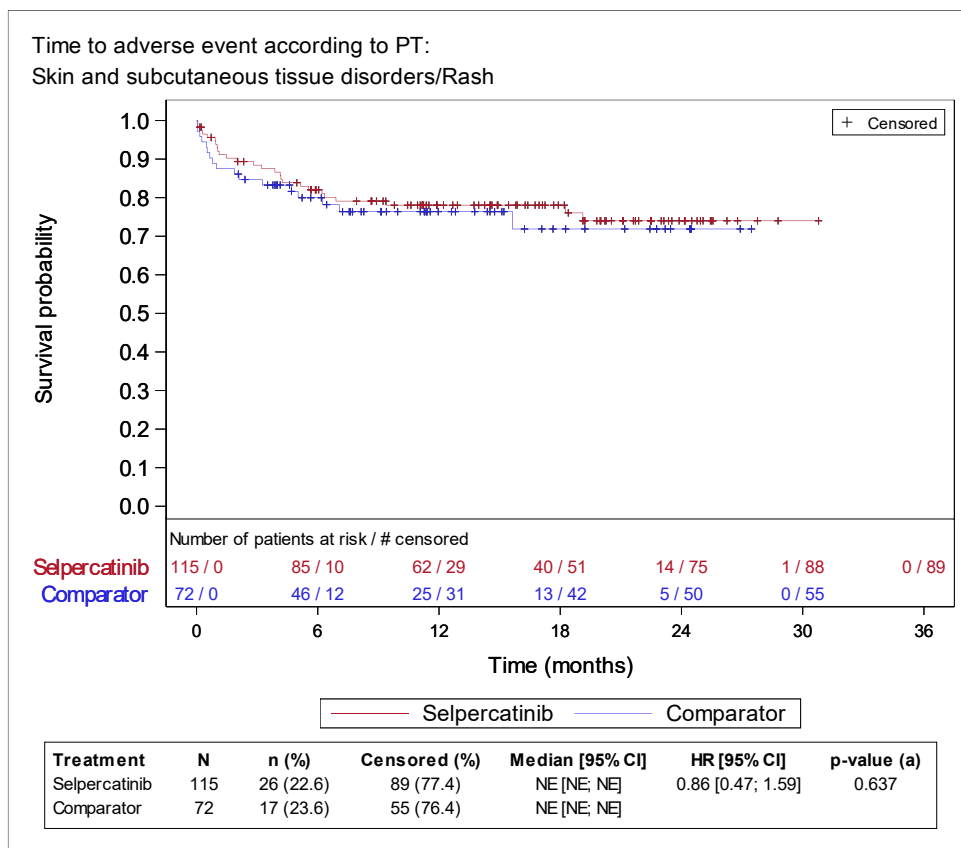
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 38: Kaplan-Meier Plot - Time to adverse event according to PT: Skin and subcutaneous tissue disorders/Rash - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

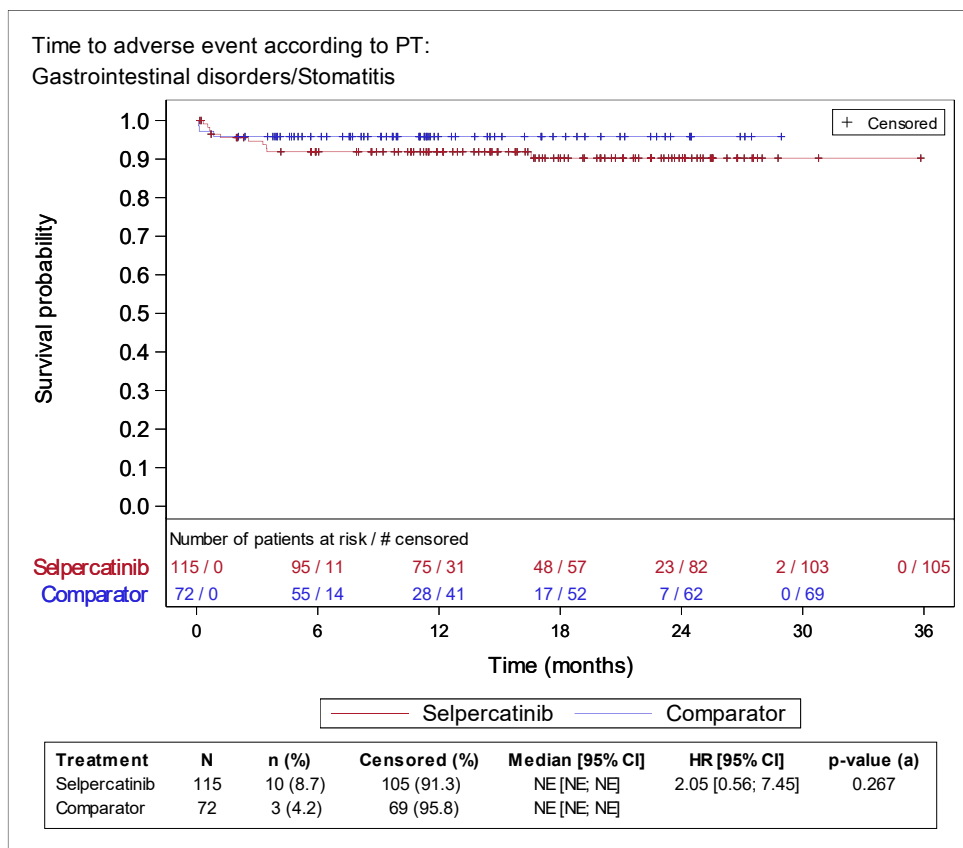
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 39: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Stomatitis - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

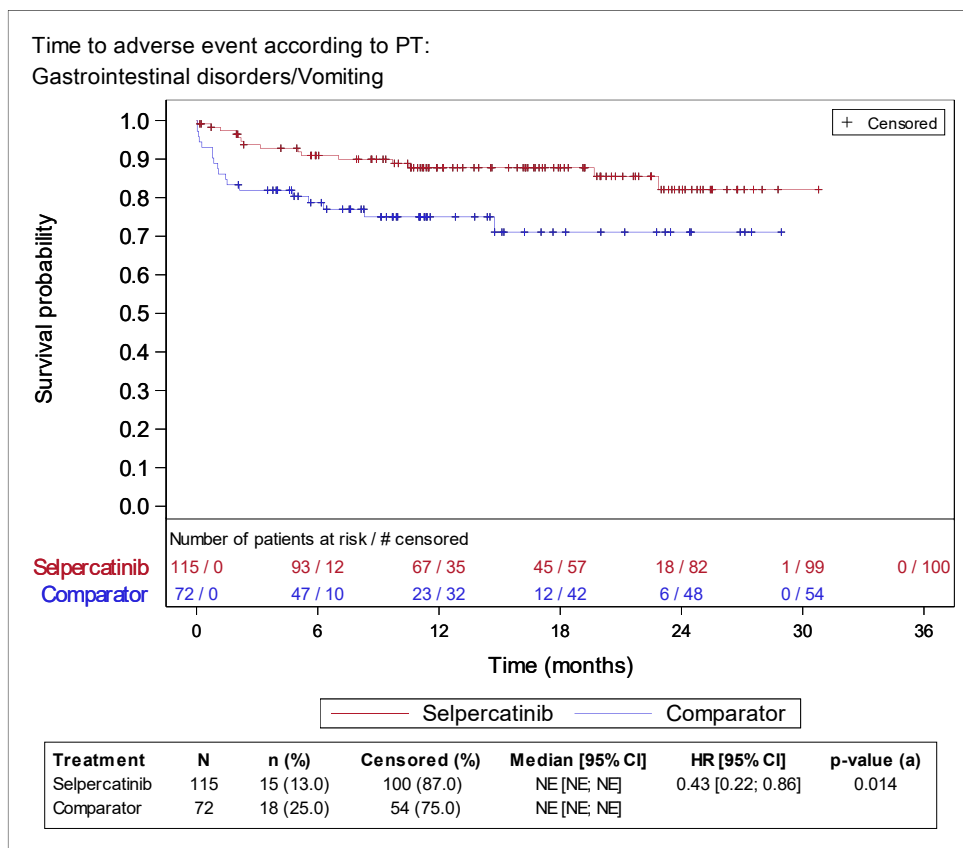
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 40: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Vomiting - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

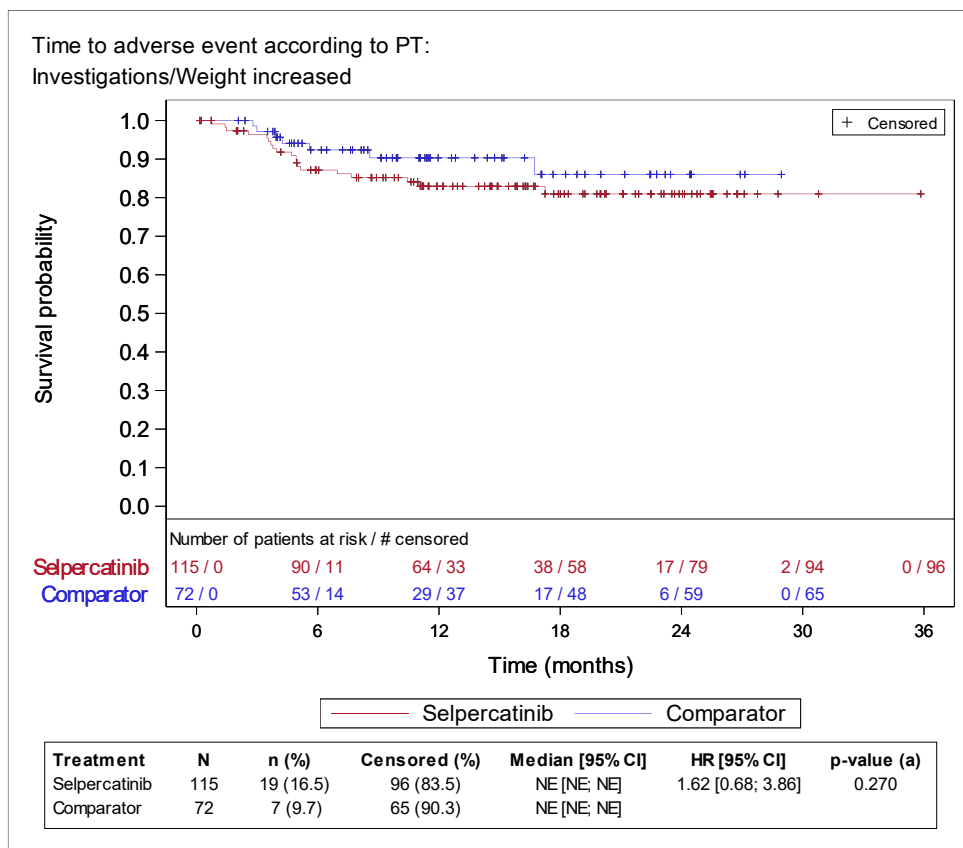
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 41: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Weight increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

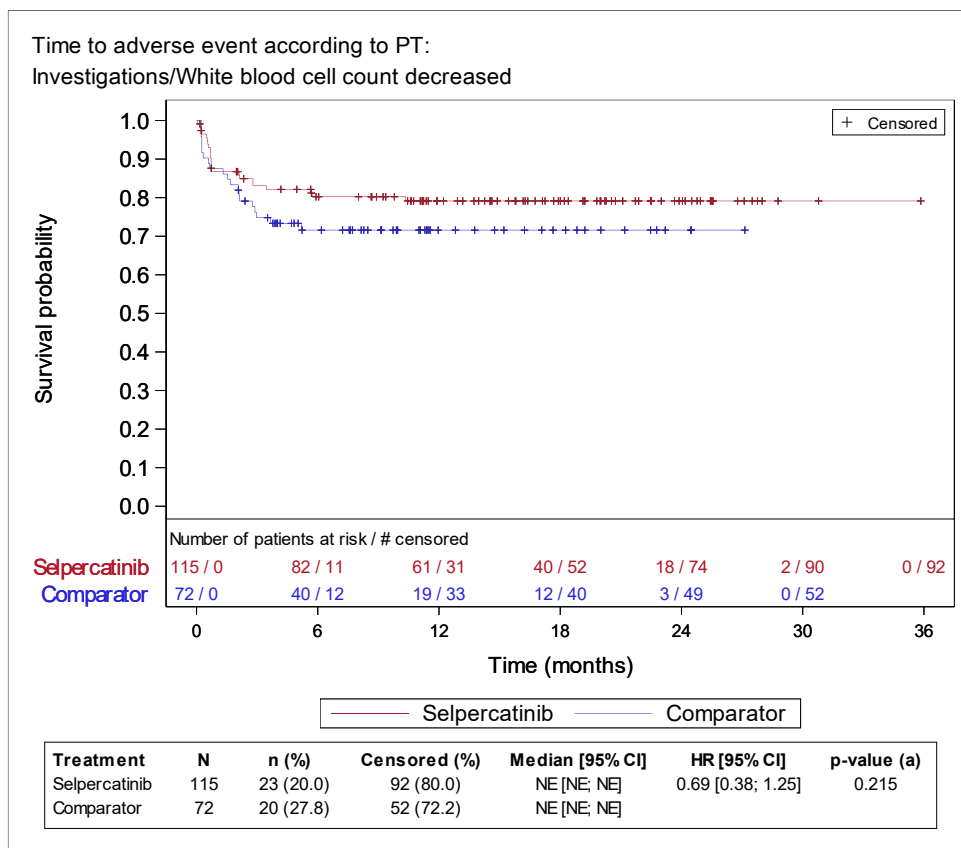
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
02OCT2025 / 04:32

Figure 42: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/White blood cell count decreased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

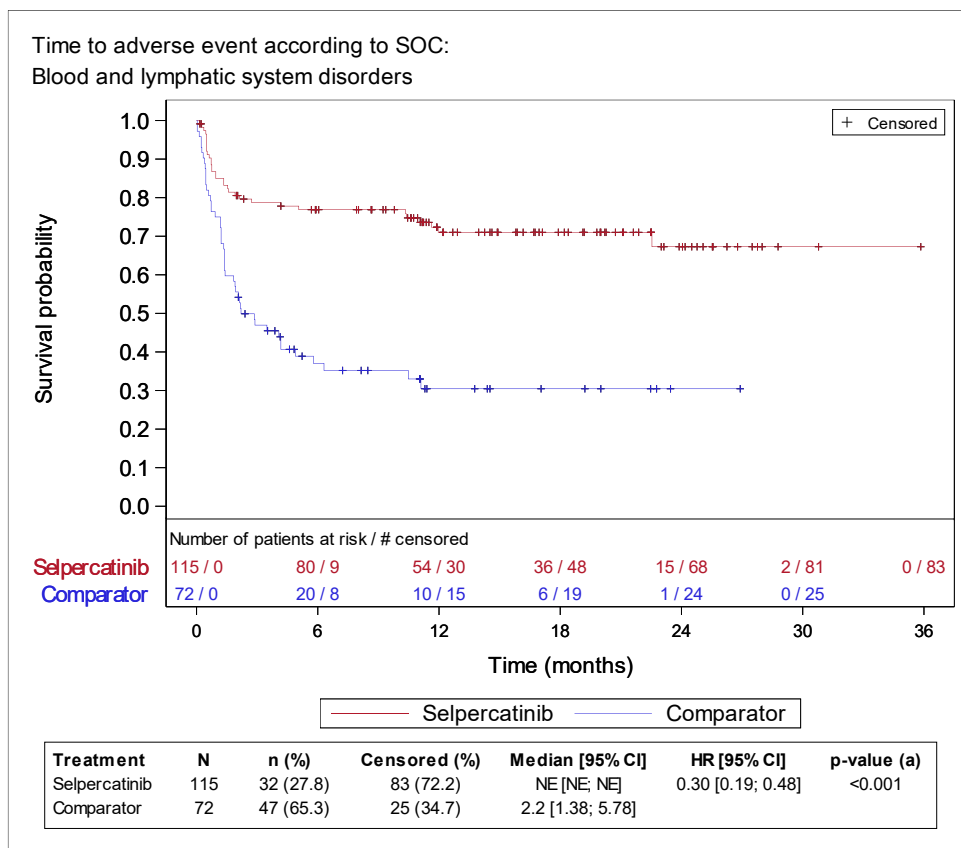
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 43: Kaplan-Meier Plot - Time to adverse event according to SOC: Blood and lymphatic system disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

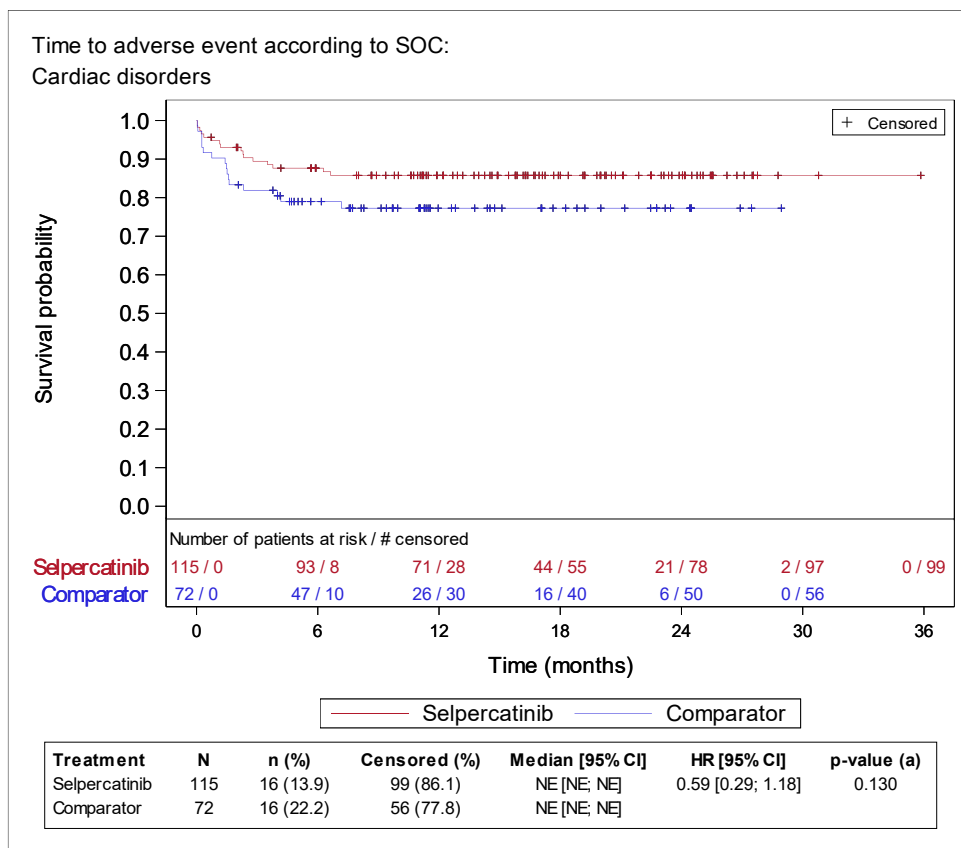
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 44: Kaplan-Meier Plot - Time to adverse event according to SOC: Cardiac disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

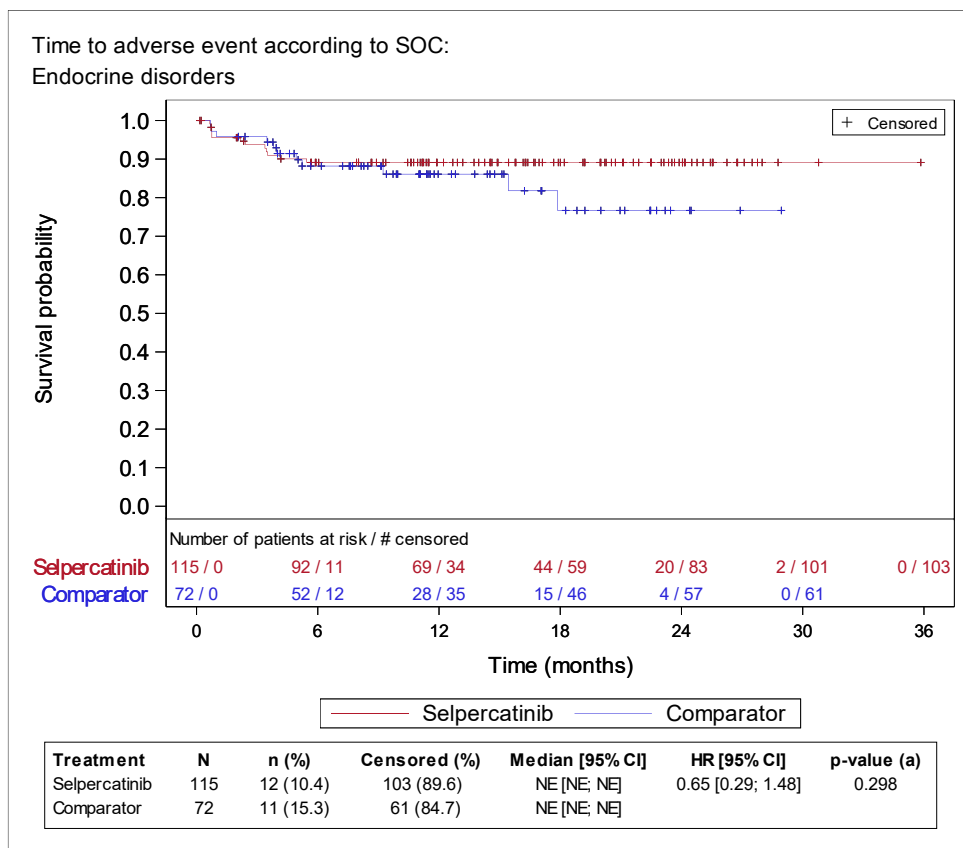
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Figure 45: Kaplan-Meier Plot - Time to adverse event according to SOC: Endocrine disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

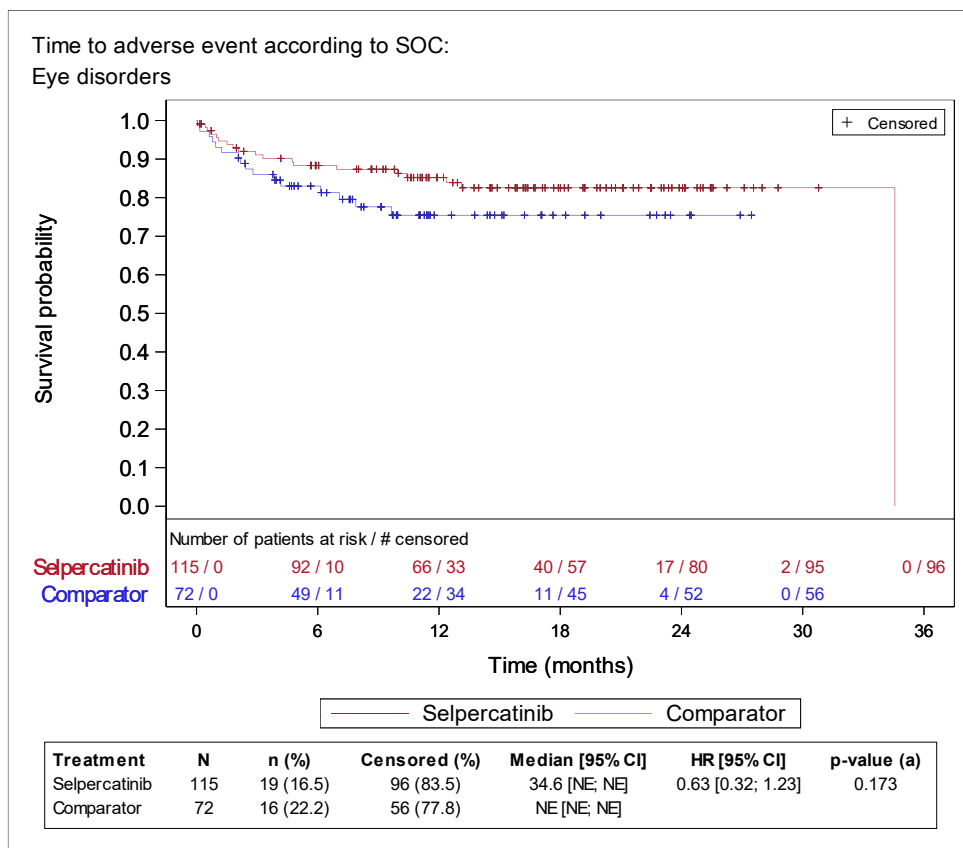
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 46: Kaplan-Meier Plot - Time to adverse event according to SOC: Eye disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

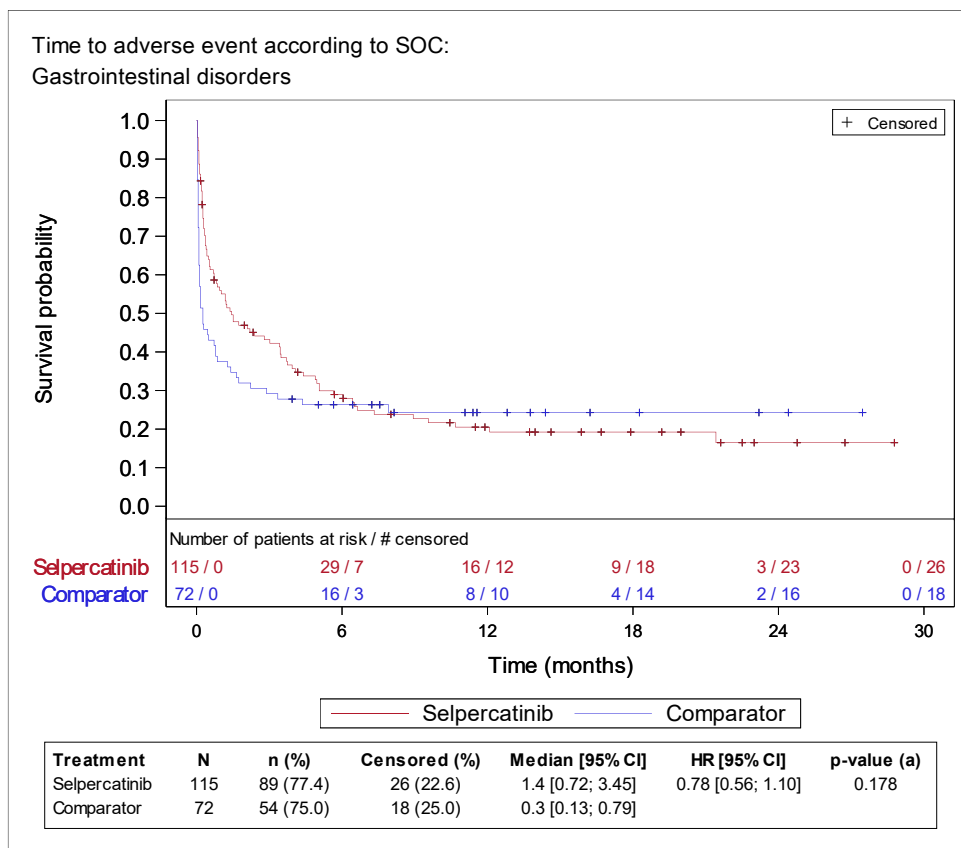
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 47: Kaplan-Meier Plot - Time to adverse event according to SOC: Gastrointestinal disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

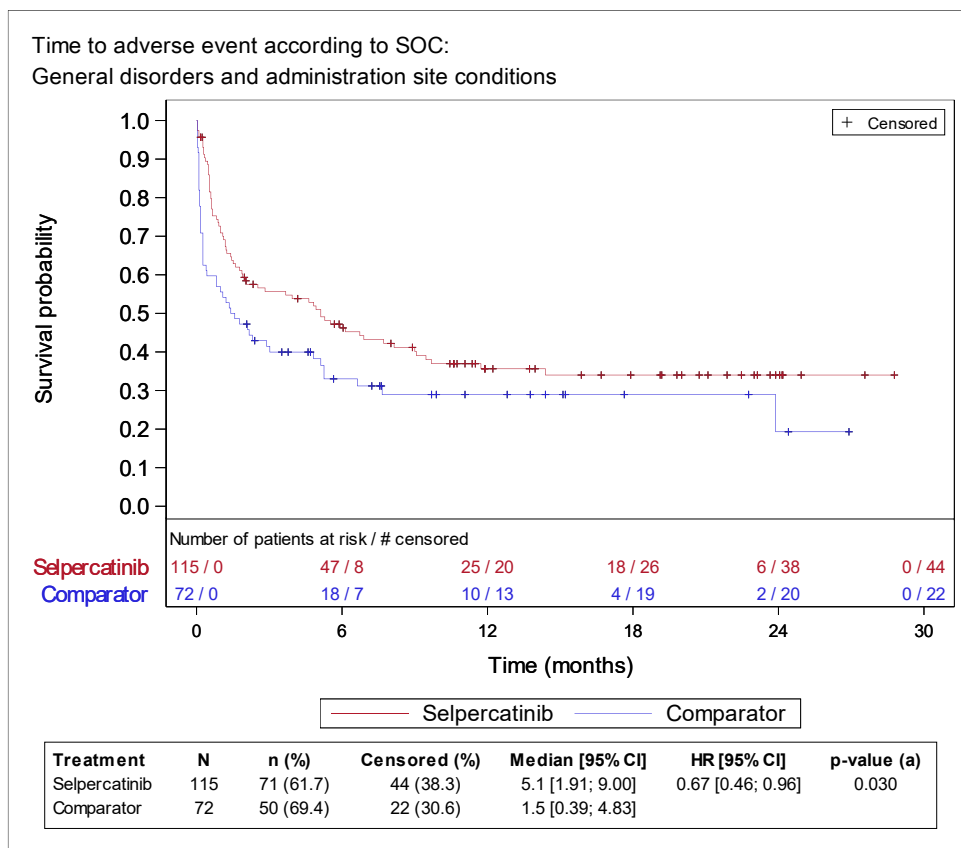
HR is based on the unstratified Cox proportional hazards model.

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Figure 48: Kaplan-Meier Plot - Time to adverse event according to SOC: General disorders and administration site conditions - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

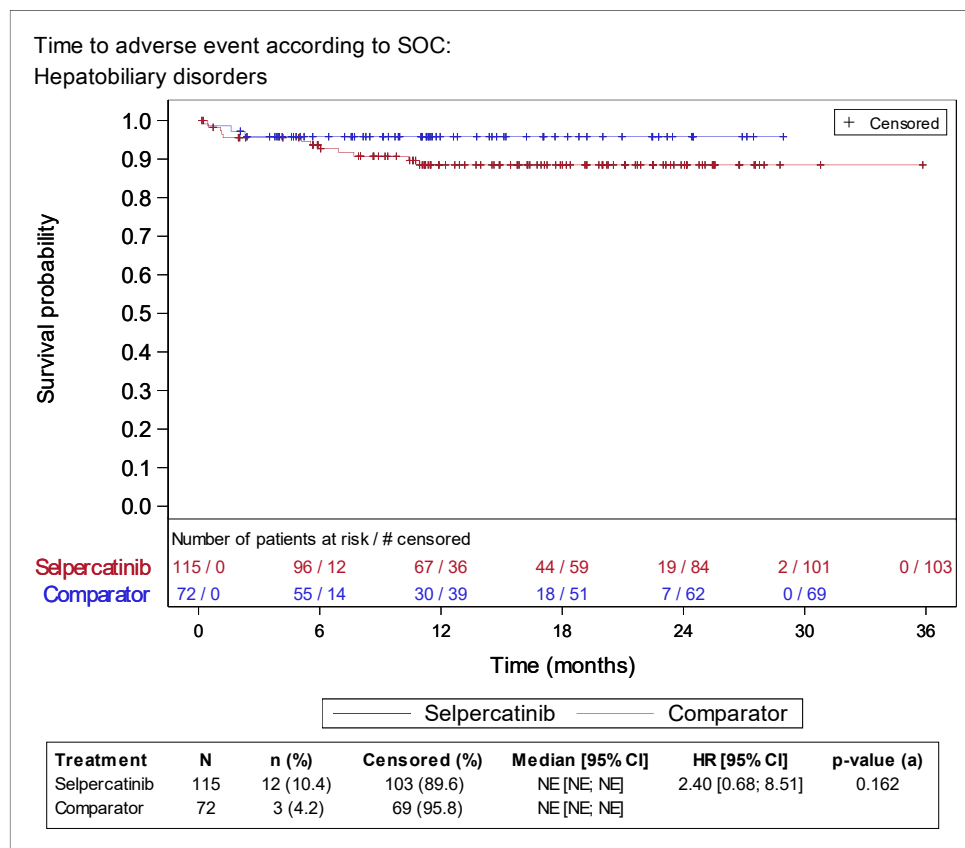
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Figure 49: Kaplan-Meier Plot - Time to adverse event according to SOC: Hepatobiliary disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

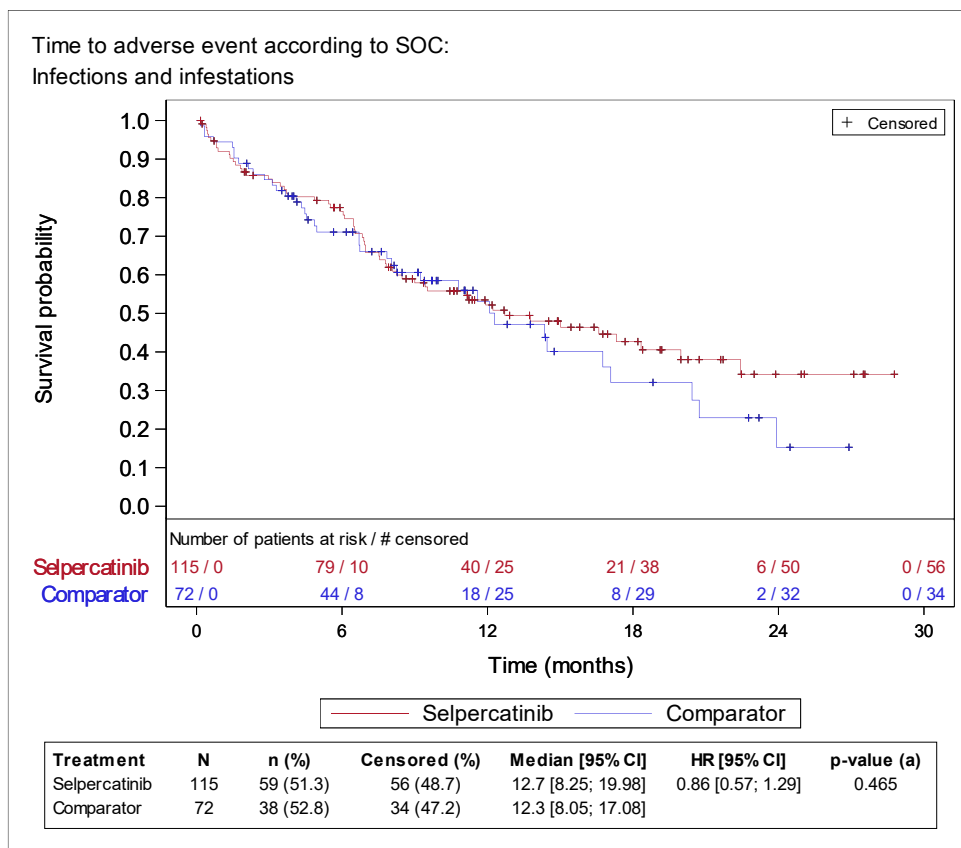
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 50: Kaplan-Meier Plot - Time to adverse event according to SOC: Infections and infestations - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

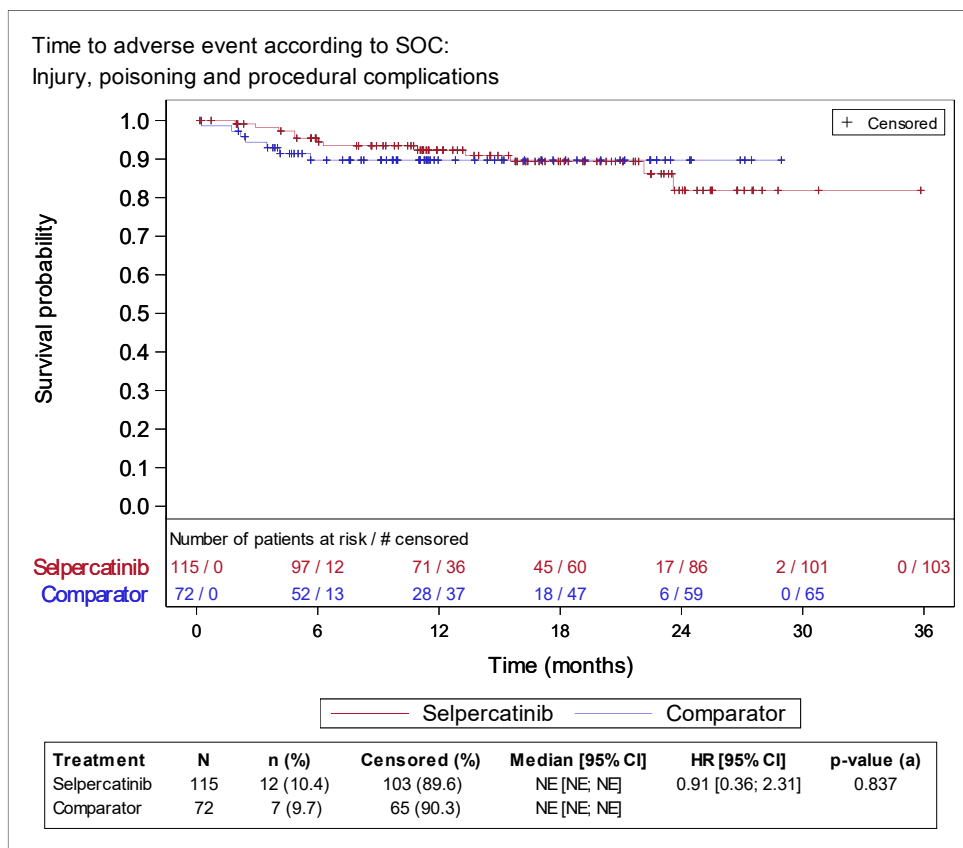
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Figure 51: Kaplan-Meier Plot - Time to adverse event according to SOC: Injury, poisoning and procedural complications - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

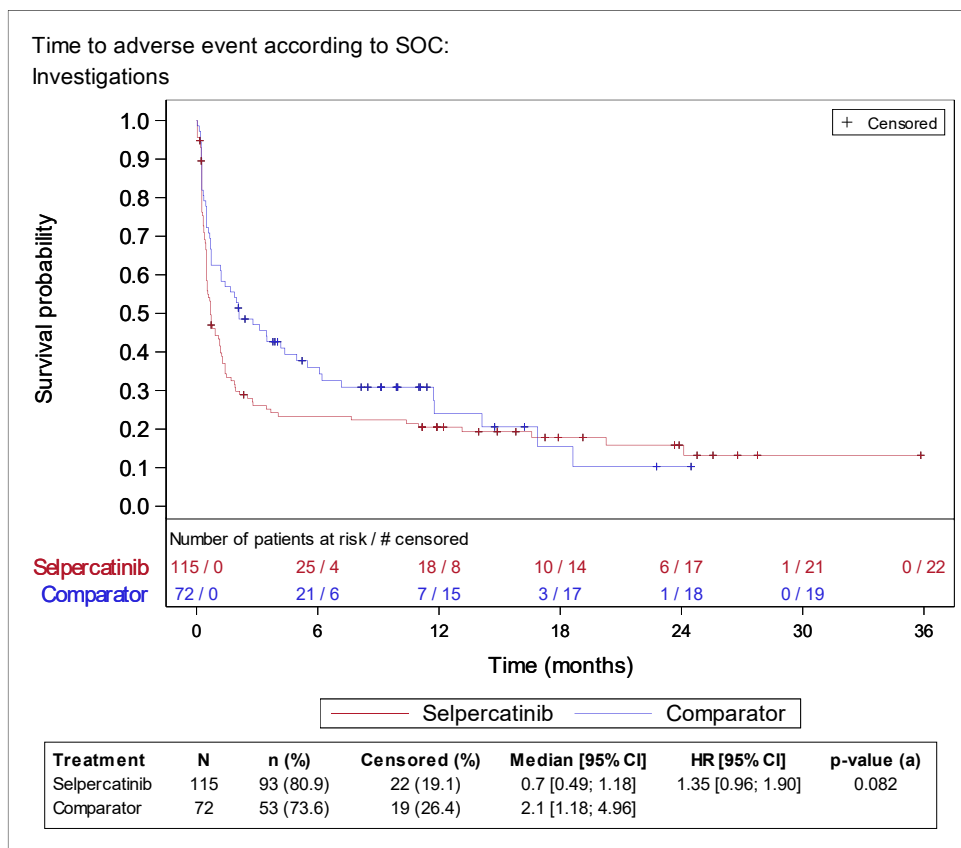
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 52: Kaplan-Meier Plot - Time to adverse event according to SOC: Investigations - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

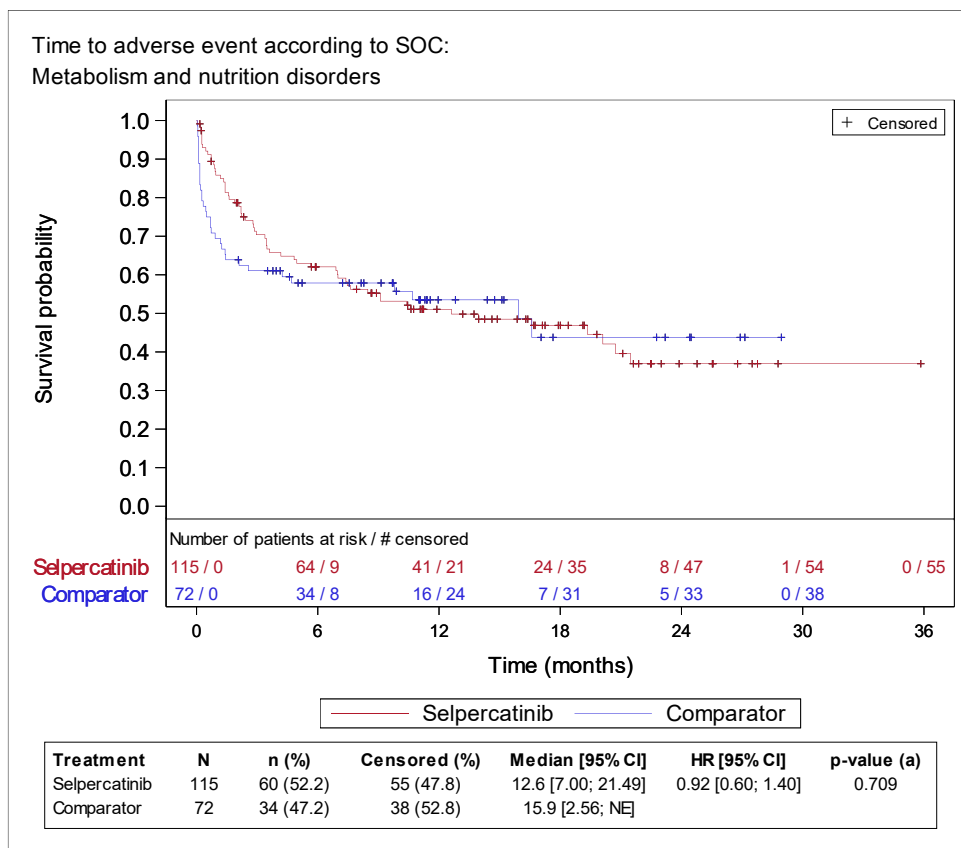
HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 53: Kaplan-Meier Plot - Time to adverse event according to SOC: Metabolism and nutrition disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

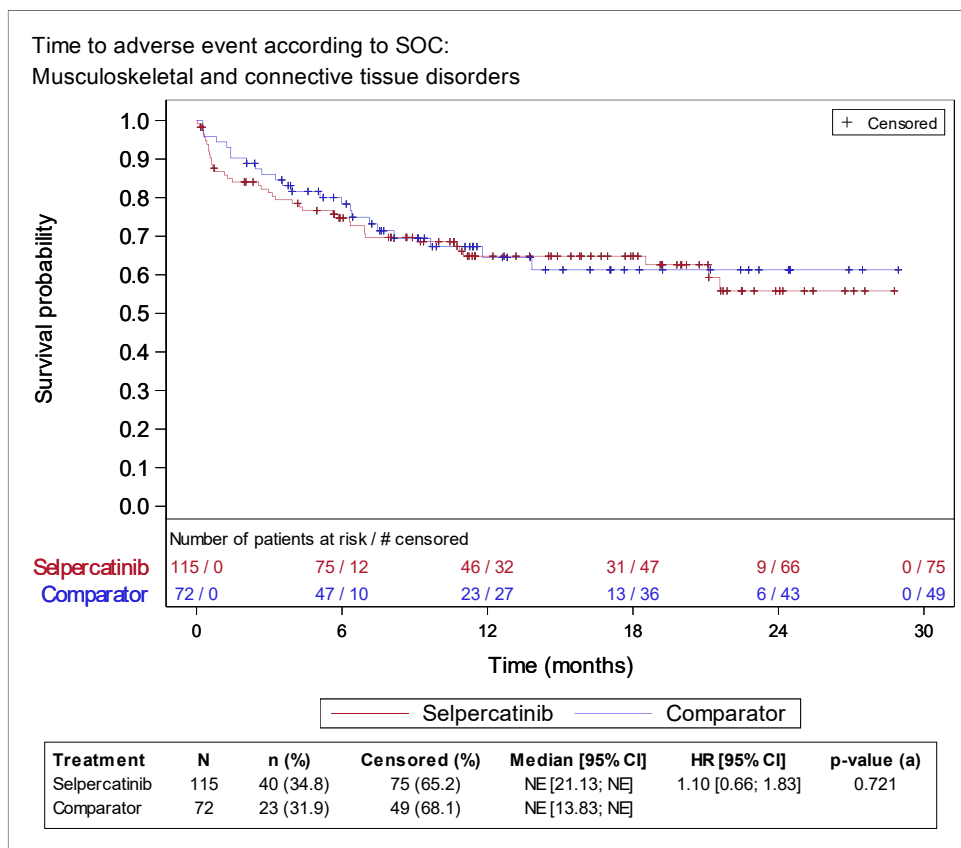
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 54: Kaplan-Meier Plot - Time to adverse event according to SOC: Musculoskeletal and connective tissue disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

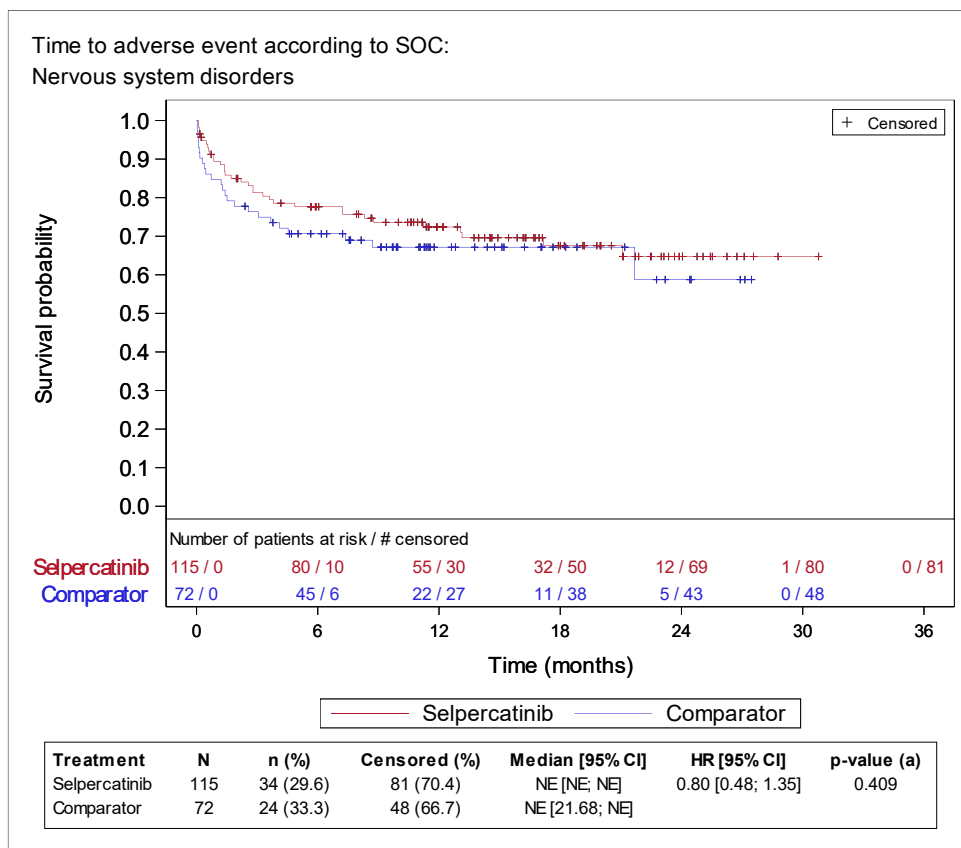
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 55: Kaplan-Meier Plot - Time to adverse event according to SOC: Nervous system disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

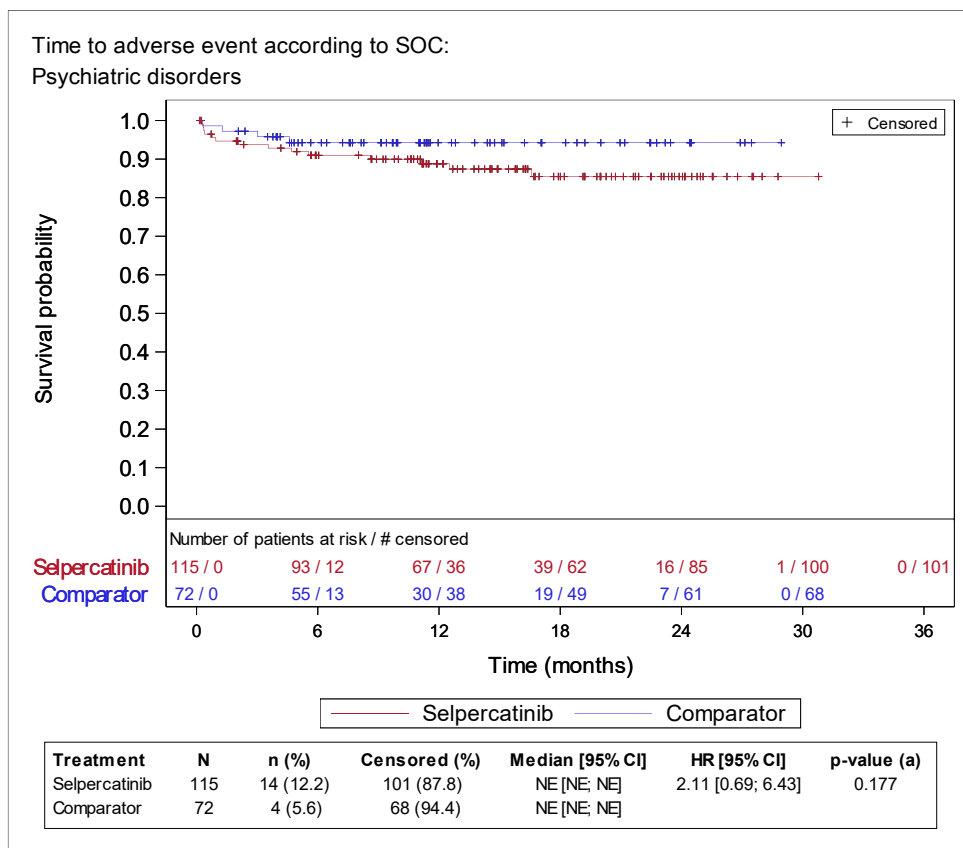
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 56: Kaplan-Meier Plot - Time to adverse event according to SOC: Psychiatric disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

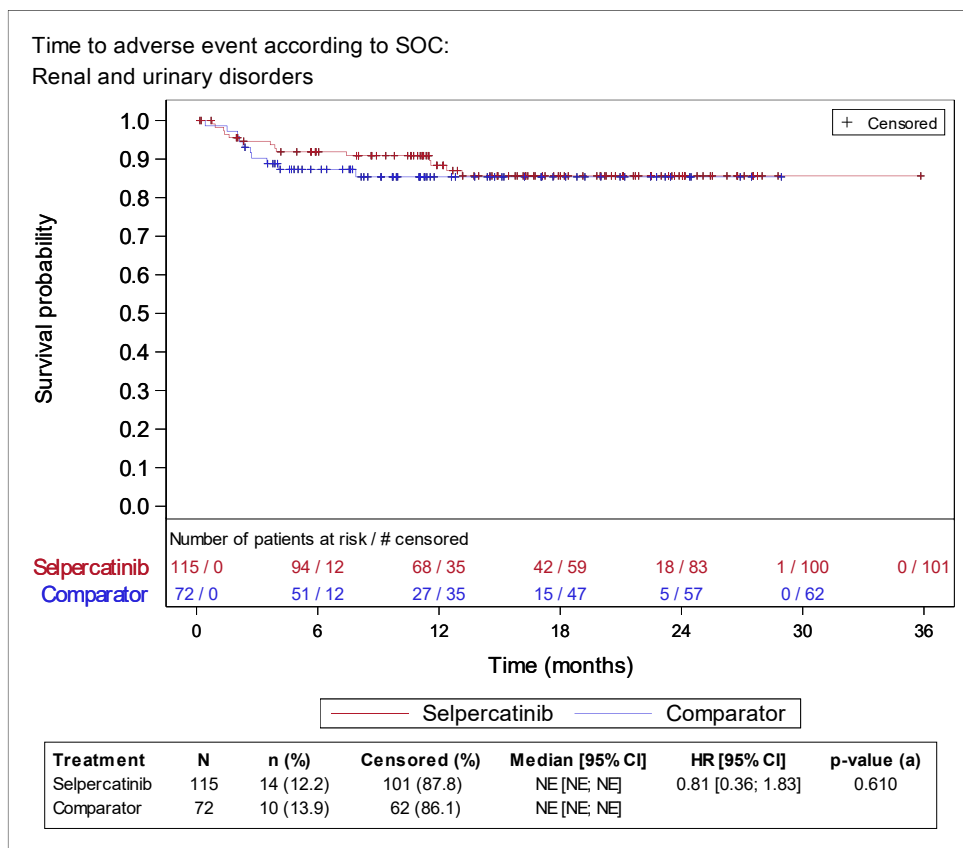
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 57: Kaplan-Meier Plot - Time to adverse event according to SOC: Renal and urinary disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

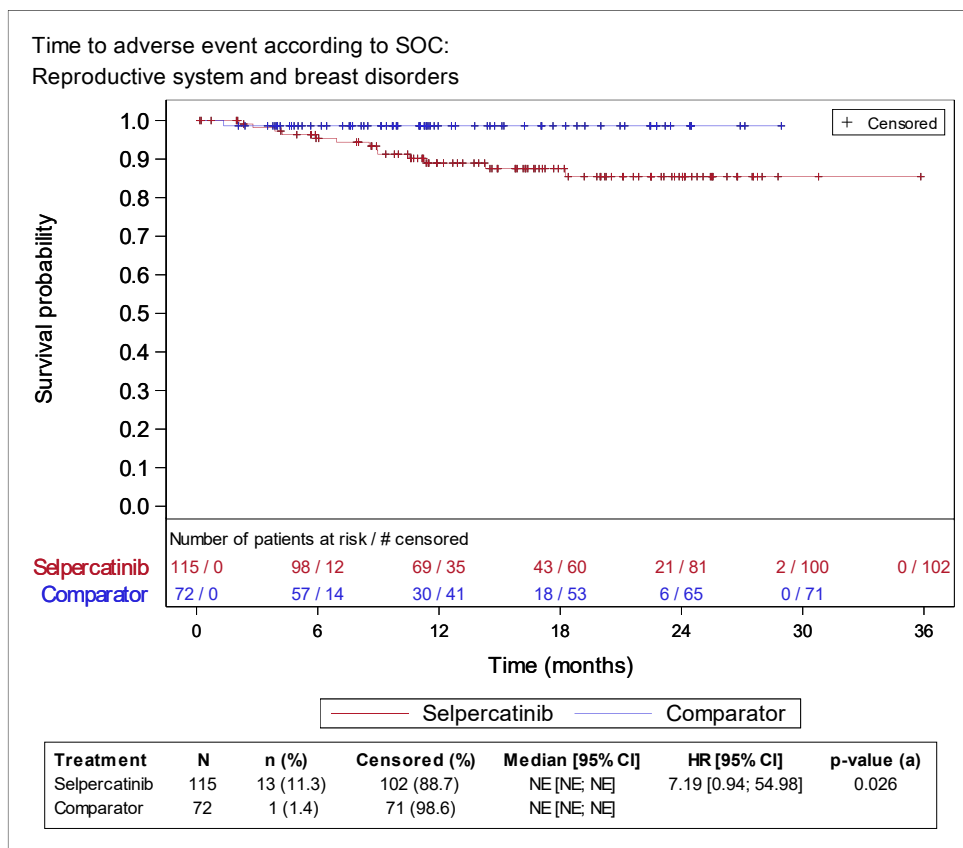
HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 58: Kaplan-Meier Plot - Time to adverse event according to SOC: Reproductive system and breast disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

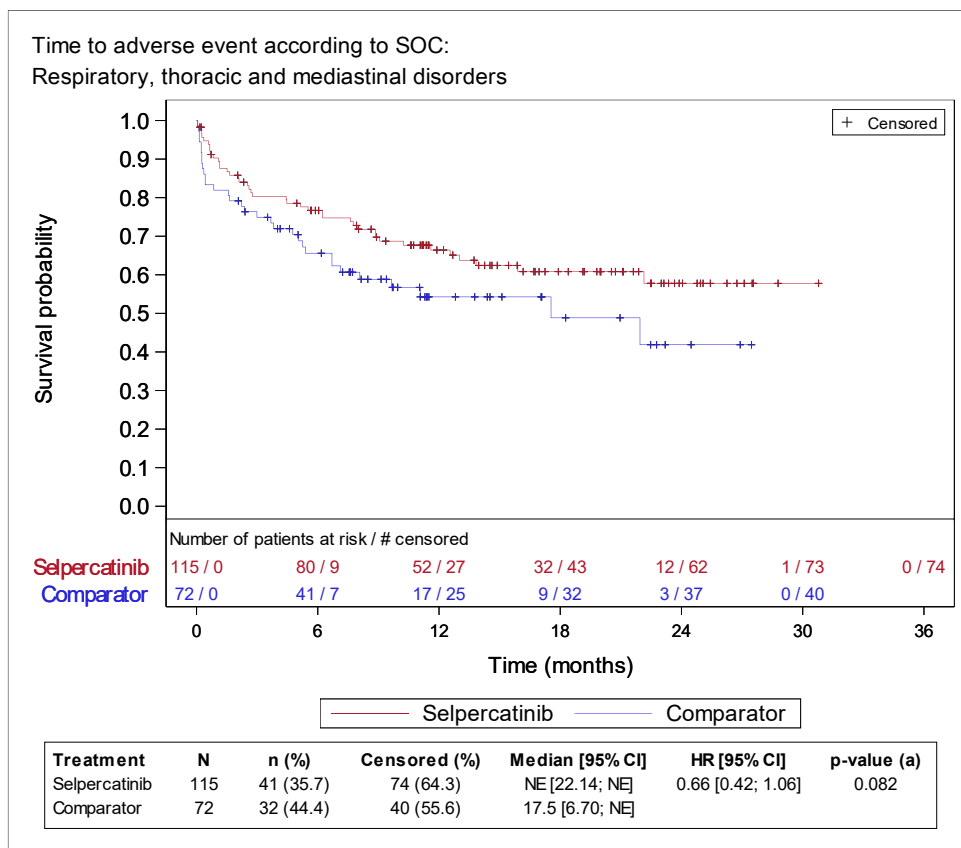
HR is based on the unstratified Cox proportional hazards model.

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02OCT2025 / 04:32

Figure 59: Kaplan-Meier Plot - Time to adverse event according to SOC: Respiratory, thoracic and mediastinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

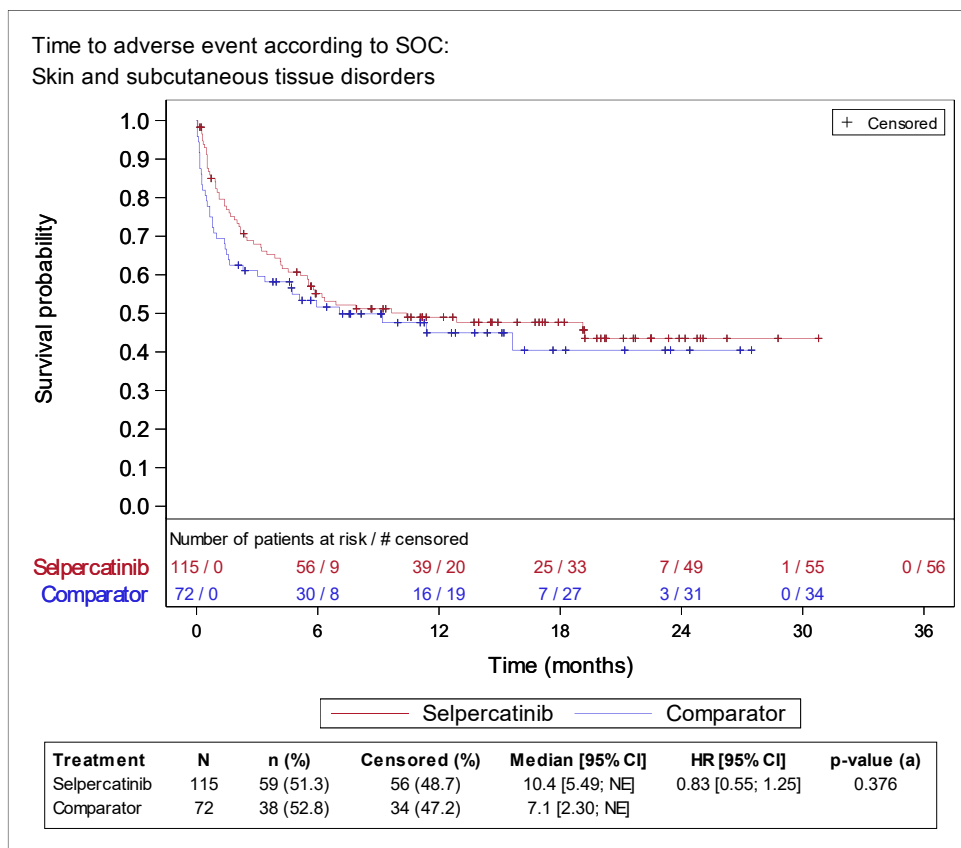
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 60: Kaplan-Meier Plot - Time to adverse event according to SOC: Skin and subcutaneous tissue disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

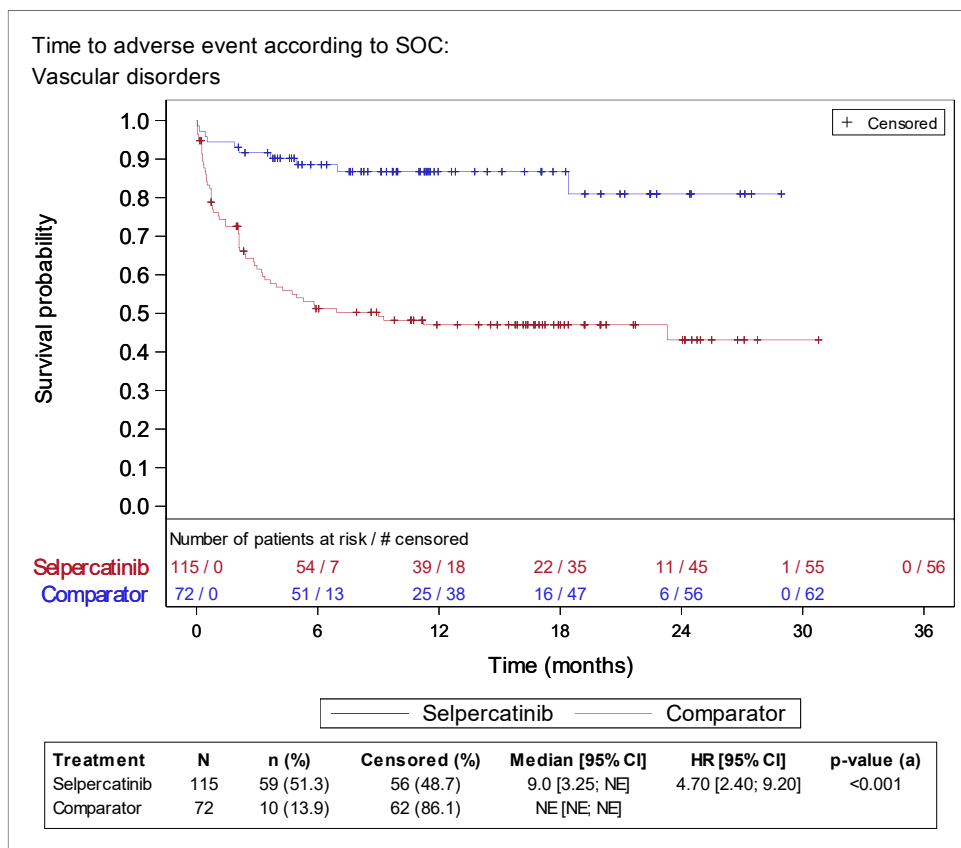
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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02OCT2025 / 04:32

Figure 61: Kaplan-Meier Plot - Time to adverse event according to SOC: Vascular disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Anhang 4-G3.2: Schwerwiegende unerwünschte Ereignisse nach SOC und PT

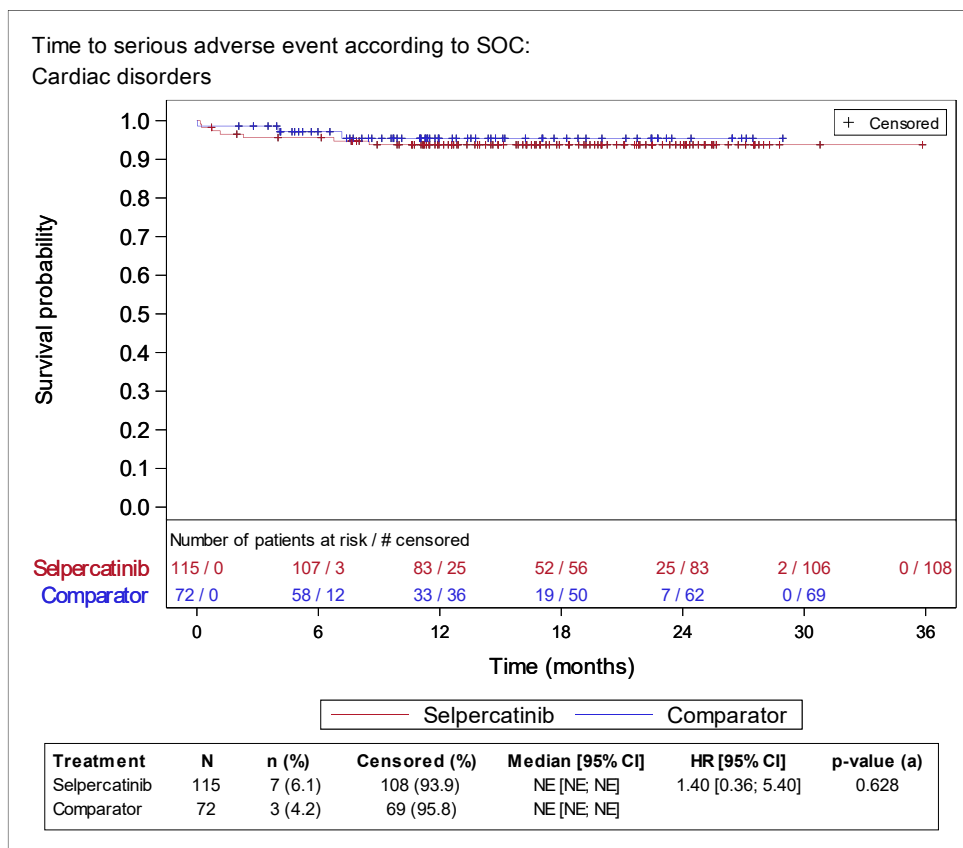
Table 26: Results for Serious TEAEs occurred in $\geq 5\%$ or in ≥ 10 patients and $\geq 1\%$ in any treatment arm within analysis population - study LIBRETTO-431, mSAF

SOC	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		
	Preferred term	n/N (%)	Median time to event ^a [95% CI]	Median time to event ^a [95% CI]	HR [95% CI] p-value ^b
Serious TEAEs occurred in ≥5% or in ≥10 patients and ≥1% in any treatment arm within analysis population					
Infections and infestations	10/115 (8.7)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	1.61 [0.44; 5.87] 0.467
Respiratory, thoracic and mediastinal disorders	9/115 (7.8)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	4.69 [0.59; 37.22] 0.107
Gastrointestinal disorders	8/115 (7.0)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	1.36 [0.36; 5.16] 0.647
Cardiac disorders	7/115 (6.1)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	1.40 [0.36; 5.40] 0.628
Investigations	1/115 (0.9)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	0.14 [0.02; 1.30] 0.045
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class. a: In months; b: from unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					

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02OCT2025 / 04:32

Figure 62: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Cardiac disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

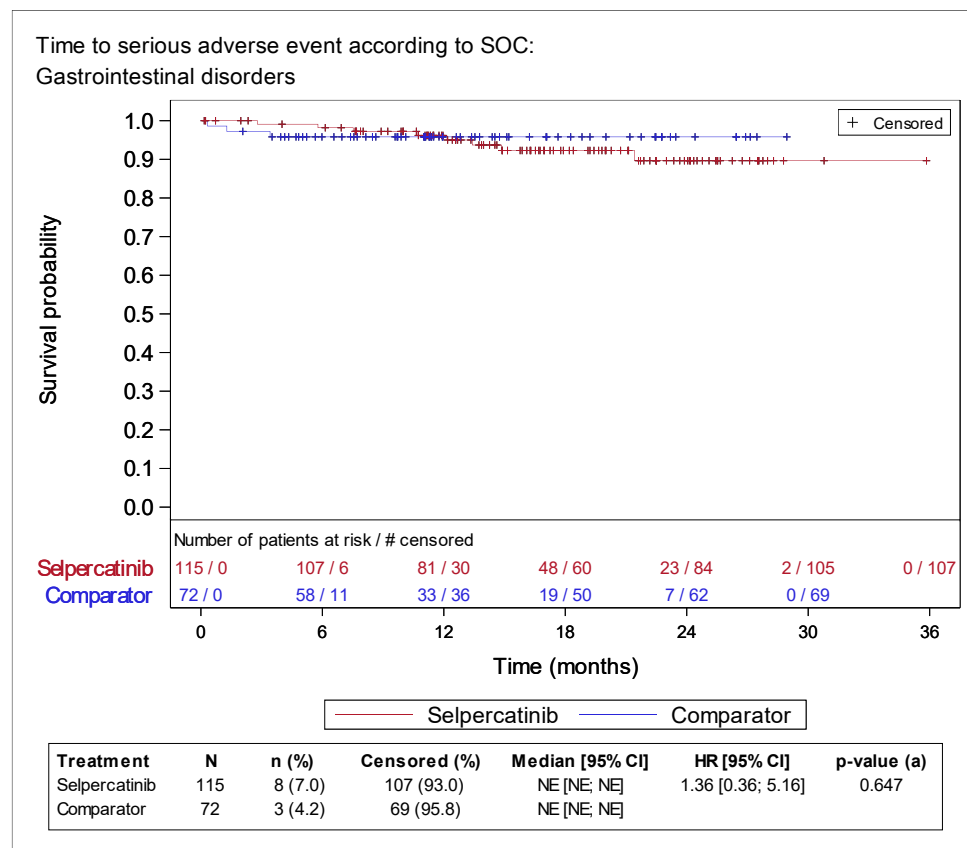
HR is based on the unstratified Cox proportional hazards model.

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Figure 63: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Gastrointestinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

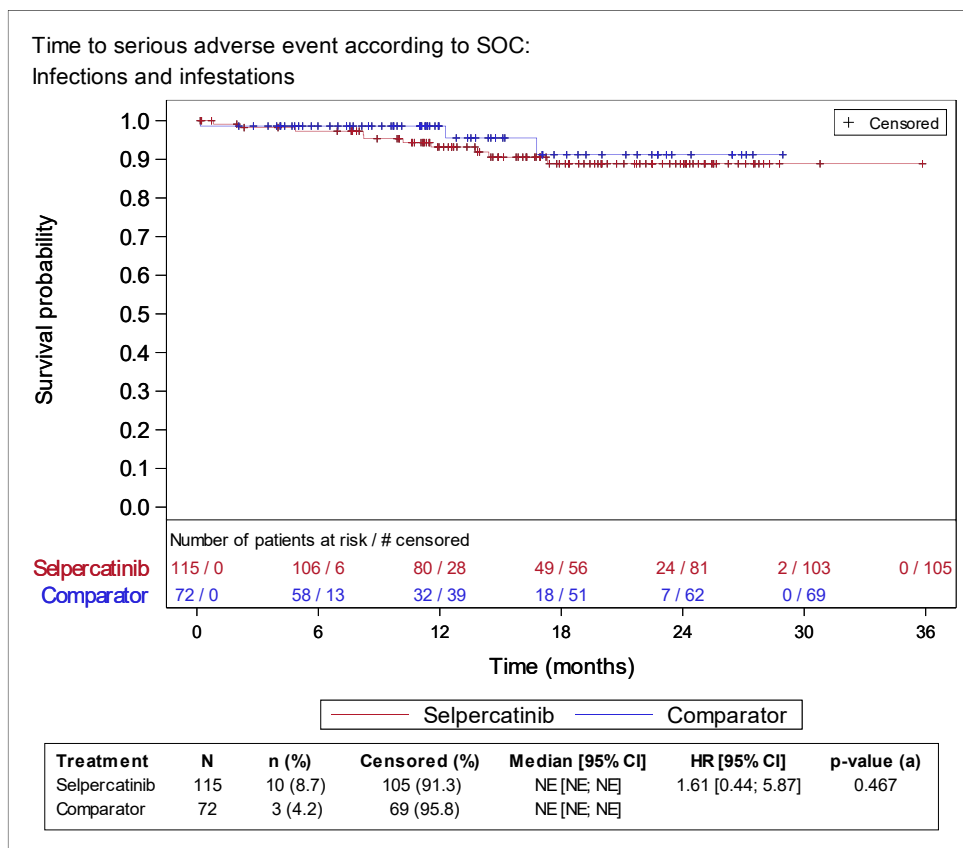
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Figure 64: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Infections and infestations - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

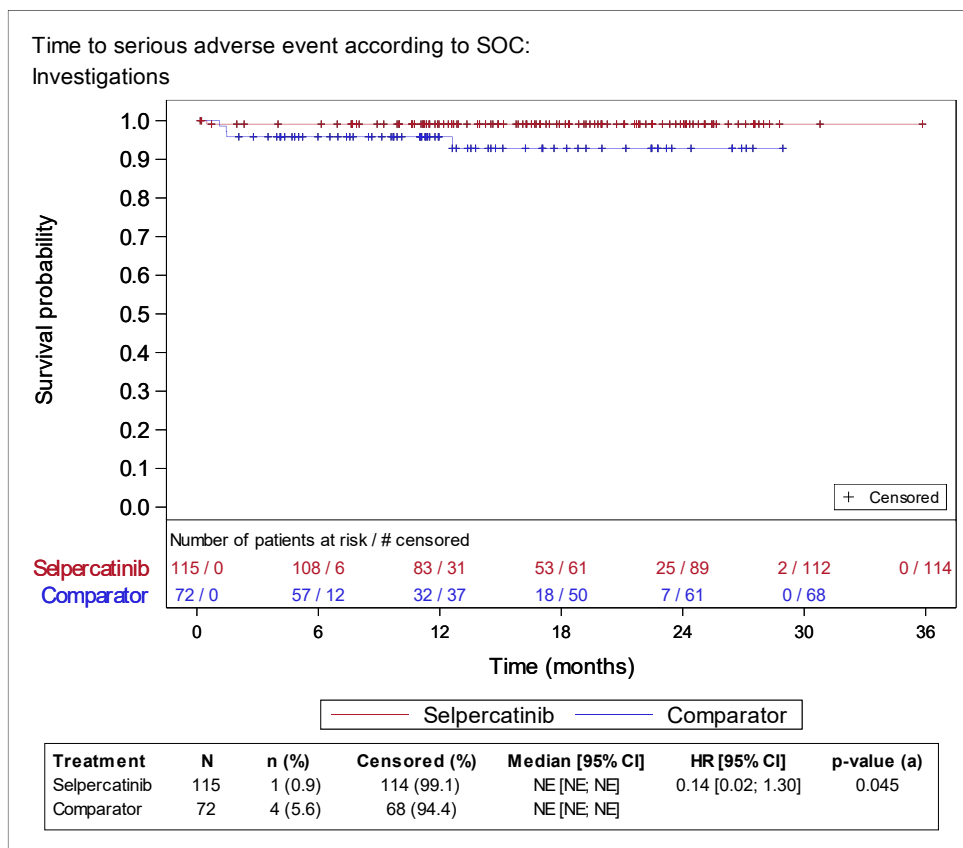
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_saespx003_msaf.rtf

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Figure 65: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Investigations - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

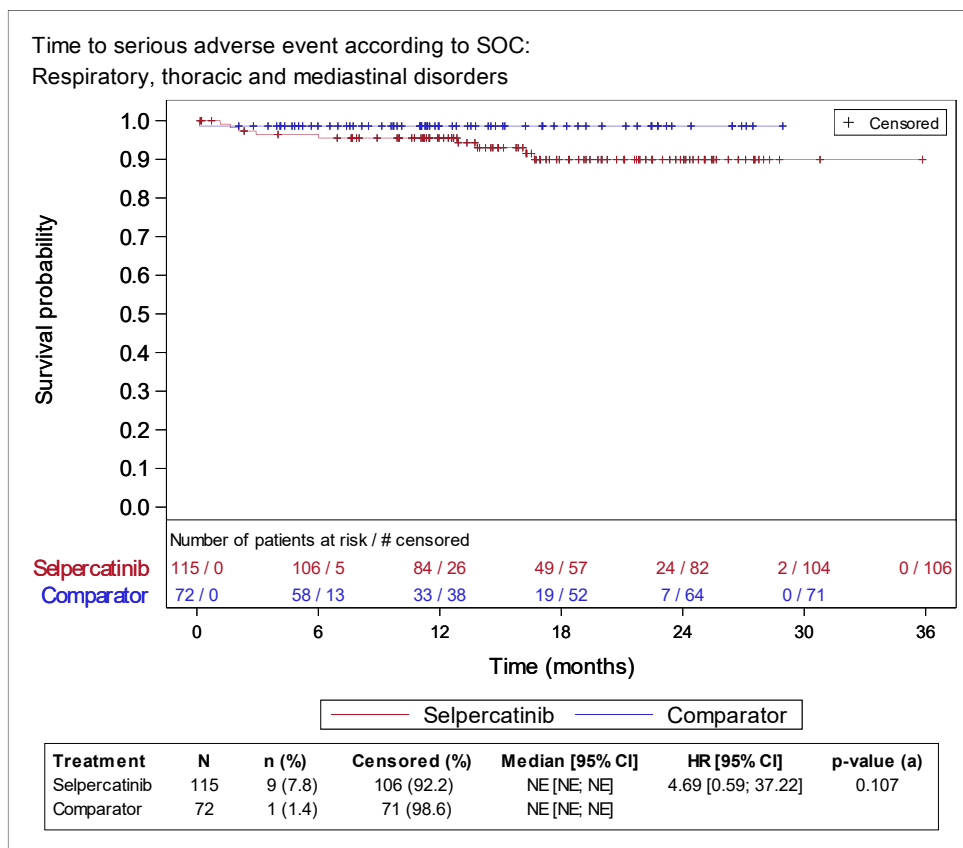
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Figure 66: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Respiratory, thoracic and mediastinal disorders - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_saespx005_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteae_gba
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Anhang 4-G3.3: Schwere unerwünschte Ereignisse nach SOC und PT

Table 27: Results for TEAEs with CTCAE grade ≥ 3 occurred in $\geq 5\%$ or in ≥ 10 patients and $\geq 1\%$ in any treatment arm within analysis population - study LIBRETTO-431, mSAF

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
TEAEs with CTCAE grade ≥3 occurred in ≥5% or in ≥10 patients and ≥1% in any treatment arm within analysis population					
Investigations	40/115 (34.8)	NE [24.90; NE]	14/72 (19.4)	NE [NE; NE]	1.85 [1.01; 3.41] 0.044
Alanine aminotransferase increased*	25/115 (21.7)	NE [NE; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] <0.001
Aspartate aminotransferase increased*	14/115 (12.2)	NE [NE; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] 0.002
Electrocardiogram QT prolonged*	9/115 (7.8)	NE [NE; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] 0.015
Platelet count decreased	3/115 (2.6)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	0.32 [0.07; 1.38] 0.107
Neutrophil count decreased	2/115 (1.7)	NE [NE; NE]	10/72 (13.9)	NE [NE; NE]	0.11 [0.02; 0.50] <0.001
White blood cell count decreased	2/115 (1.7)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	0.28 [0.05; 1.52] 0.114
Vascular disorders	26/115 (22.6)	NE [NE; NE]	2/72 (2.8)	NE [NE; NE]	8.72 [2.07; 36.75] <0.001
Hypertension	24/115 (20.9)	NE [NE; NE]	2/72 (2.8)	NE [NE; NE]	8.05 [1.90; 34.09] <0.001
Gastrointestinal disorders	9/115 (7.8)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	1.17 [0.36; 3.81] 0.798
Infections and infestations	9/115 (7.8)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	4.45 [0.56; 35.30] 0.122
Respiratory, thoracic and mediastinal disorders	7/115 (6.1)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	0.75 [0.24; 2.38] 0.624
Cardiac disorders	6/115 (5.2)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	1.23 [0.31; 4.93] 0.767
General disorders and administration site conditions	6/115 (5.2)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	0.53 [0.16; 1.74] 0.285

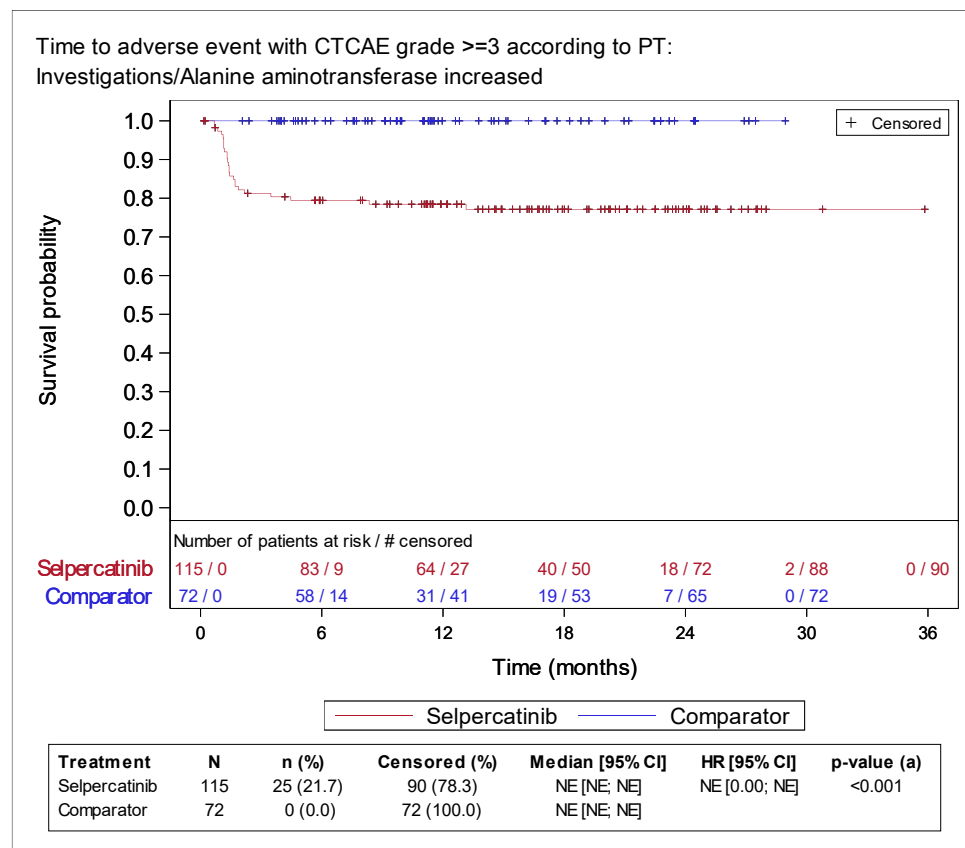
SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Metabolism and nutrition disorders	6/115 (5.2)	29.2 [29.21; NE]	6/72 (8.3)	NE [NE; NE]	0.50 [0.15; 1.64] 0.243
Blood and lymphatic system disorders	1/115 (0.9)	NE [NE; NE]	17/72 (23.6)	NE [NE; NE]	0.03 [0.00; 0.23] <0.001
Anaemia	1/115 (0.9)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	0.08 [0.01; 0.62] 0.002
Neutropenia*	0/115 (0.0)	NE [NE; NE]	10/72 (13.9)	NE [NE; NE]	0.00 [0.00; NE] <0.001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class. a: In months; b: from unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

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Figure 67: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Alanine aminotransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

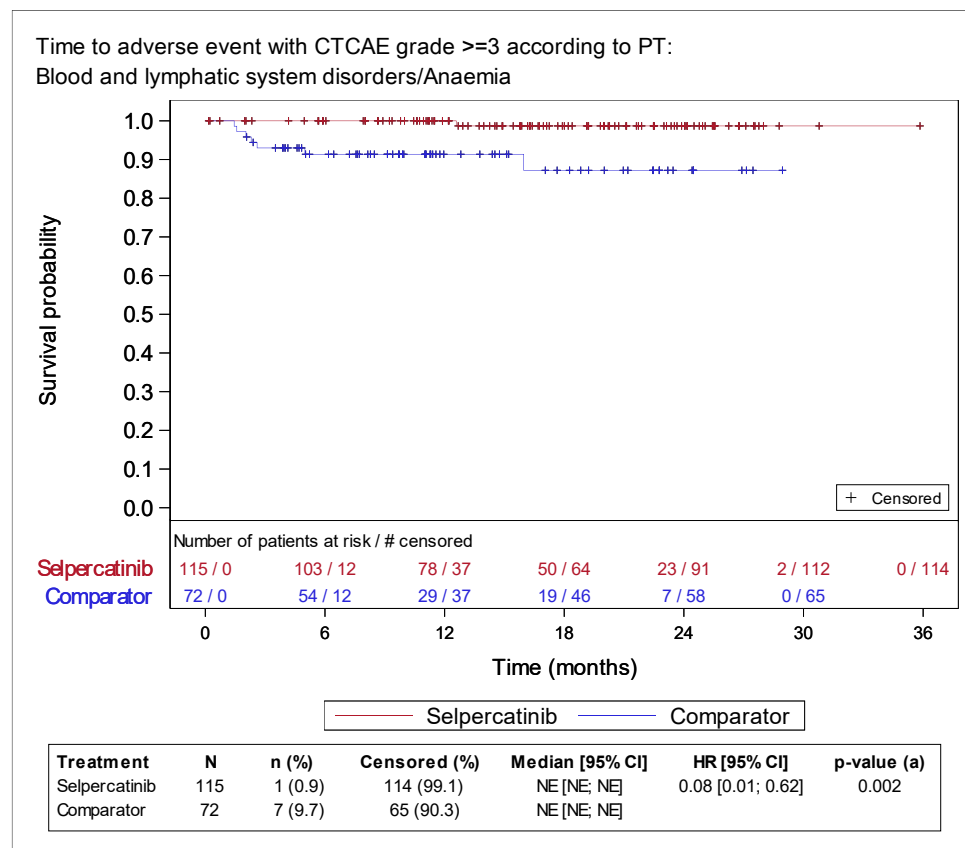
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

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Figure 68: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Blood and lymphatic system disorders/Anaemia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

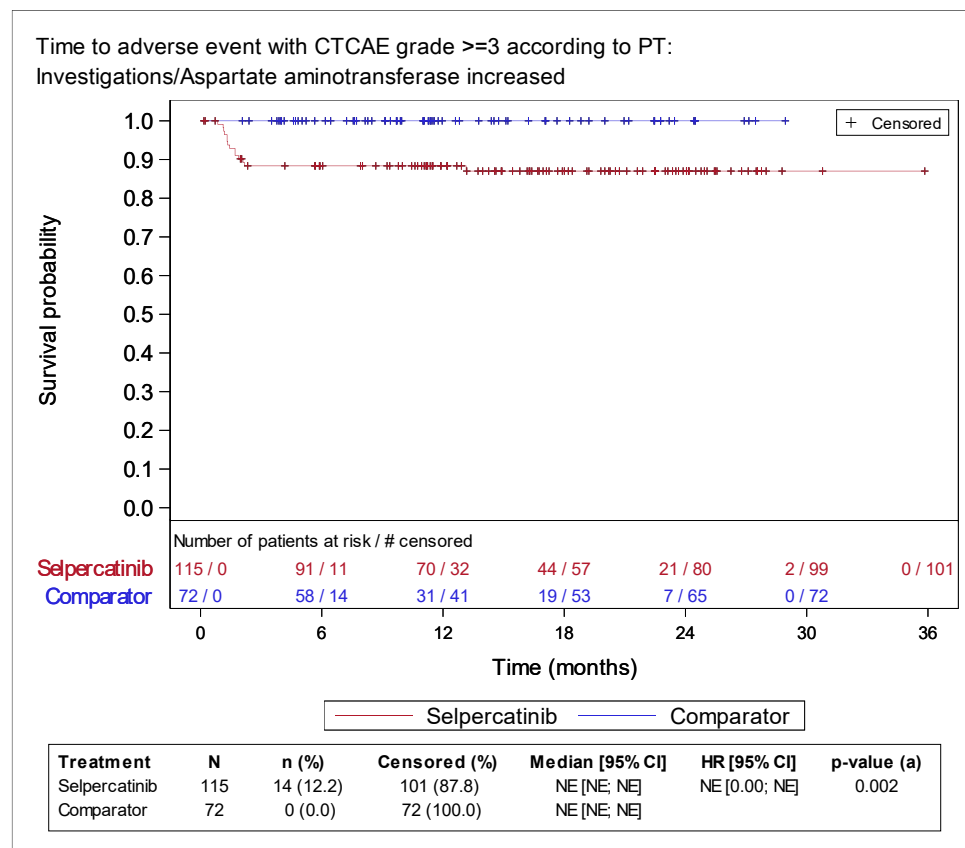
HR is based on the unstratified Cox proportional hazards model.

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Figure 69: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Aspartate aminotransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

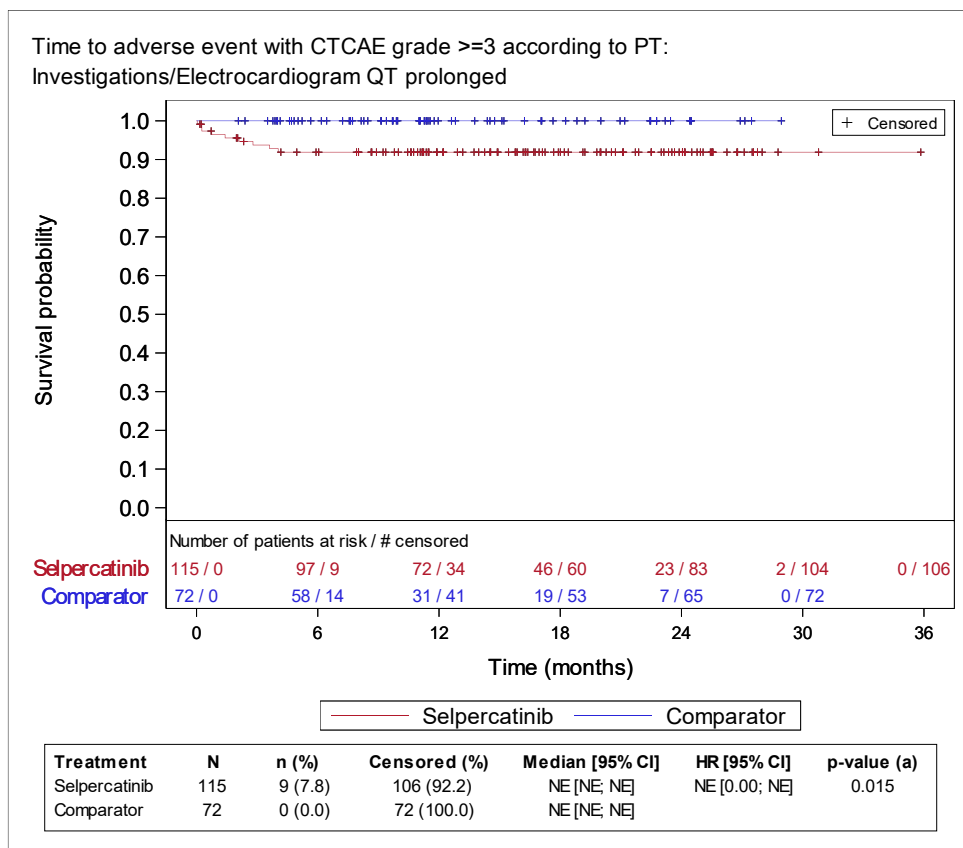
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

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Figure 70: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Electrocardiogram QT prolonged - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

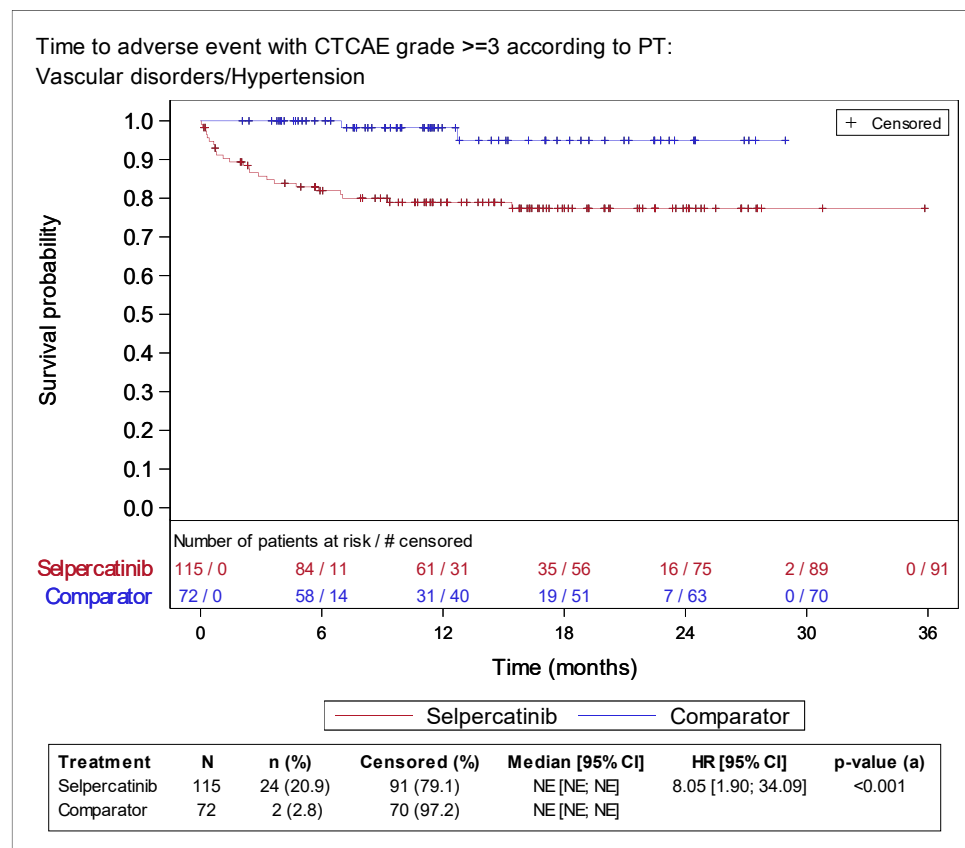
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

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Figure 71: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Vascular disorders/Hypertension - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

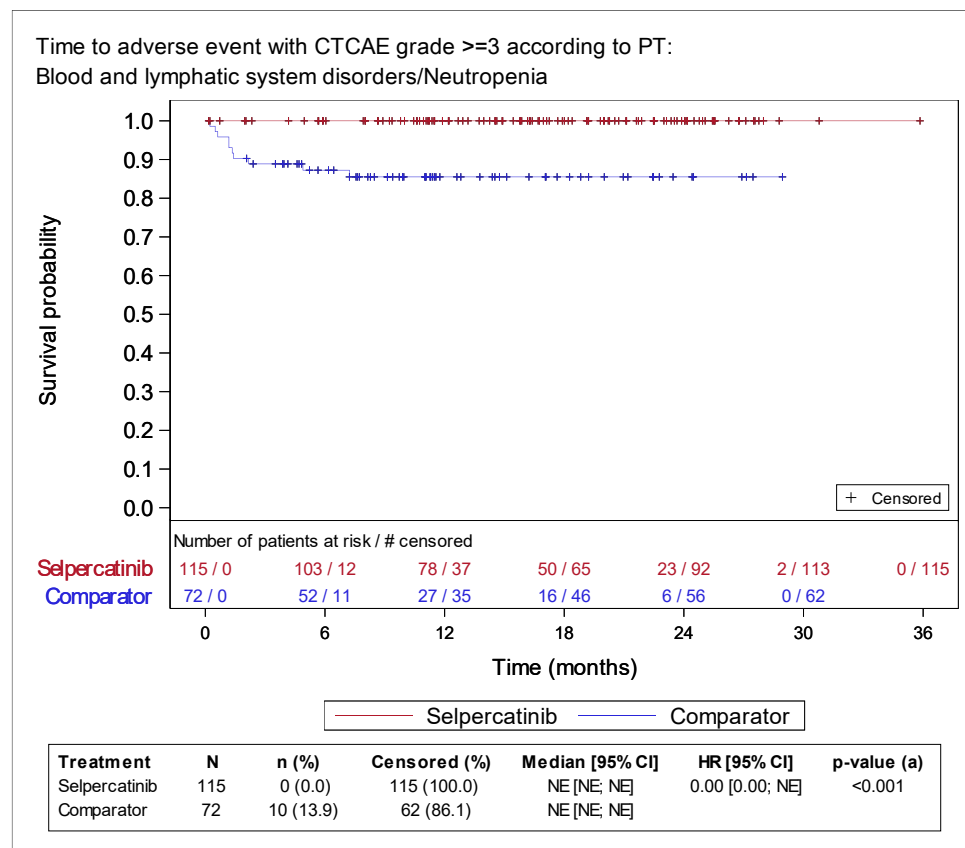
HR is based on the unstratified Cox proportional hazards model.

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Figure 72: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Blood and lymphatic system disorders/Neutropenia - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

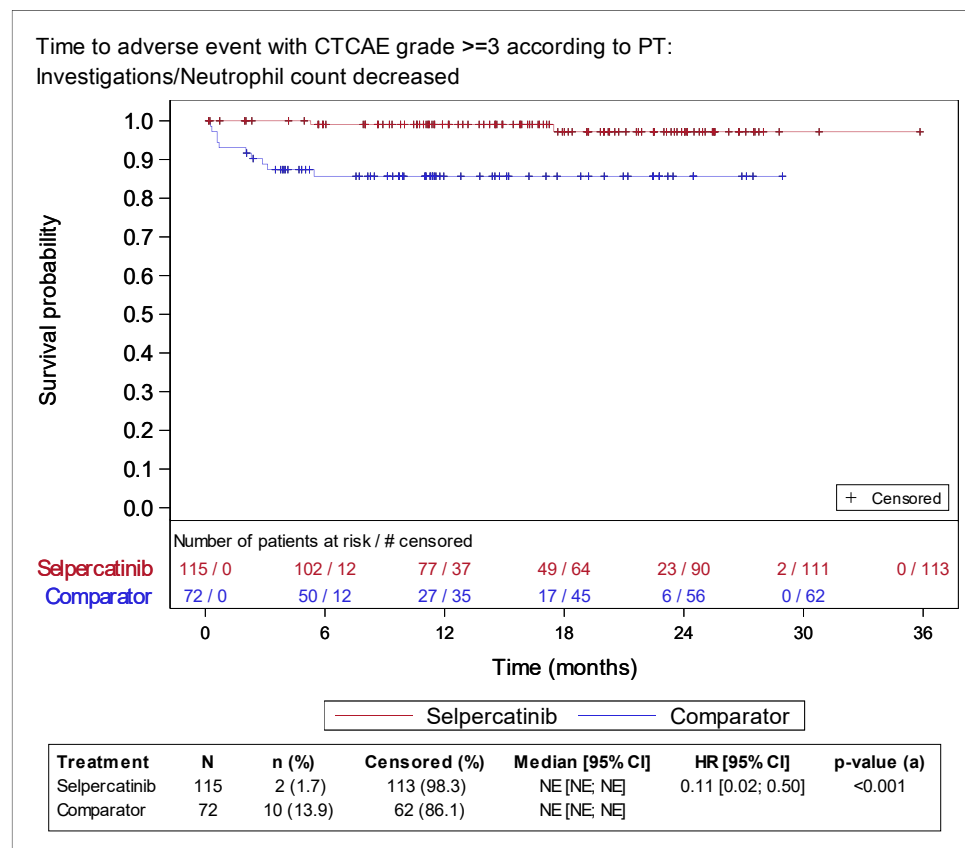
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Figure 73: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Neutrophil count decreased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

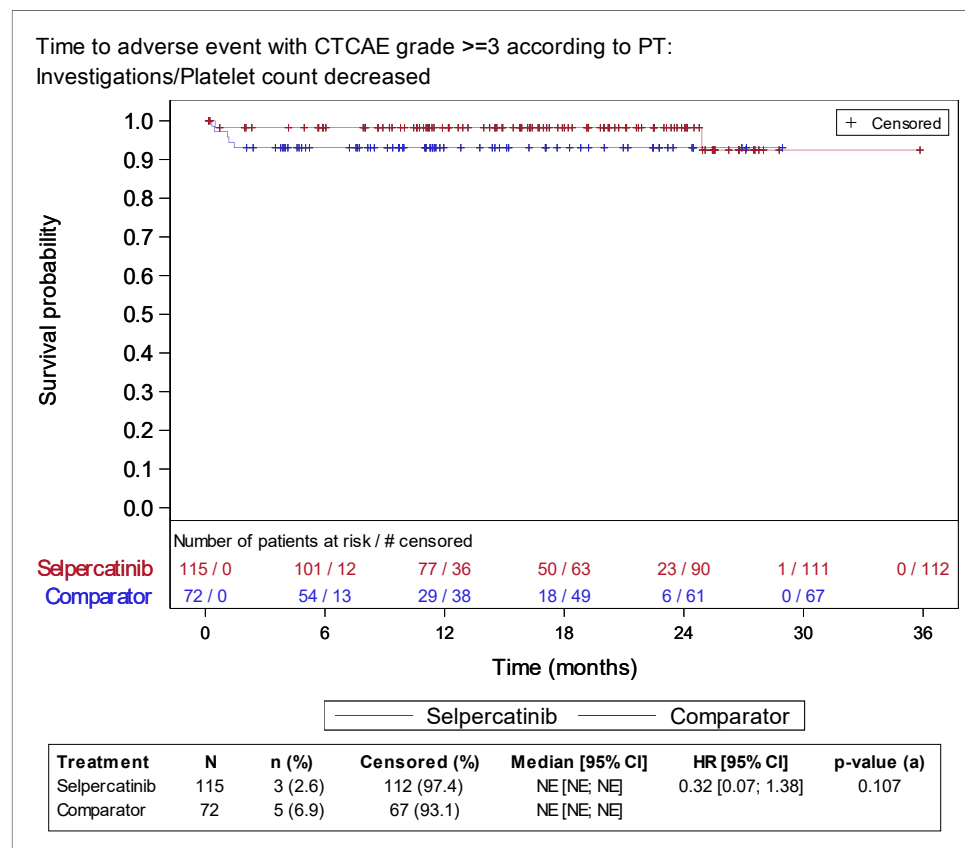
HR is based on the unstratified Cox proportional hazards model.

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Figure 74: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Platelet count decreased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

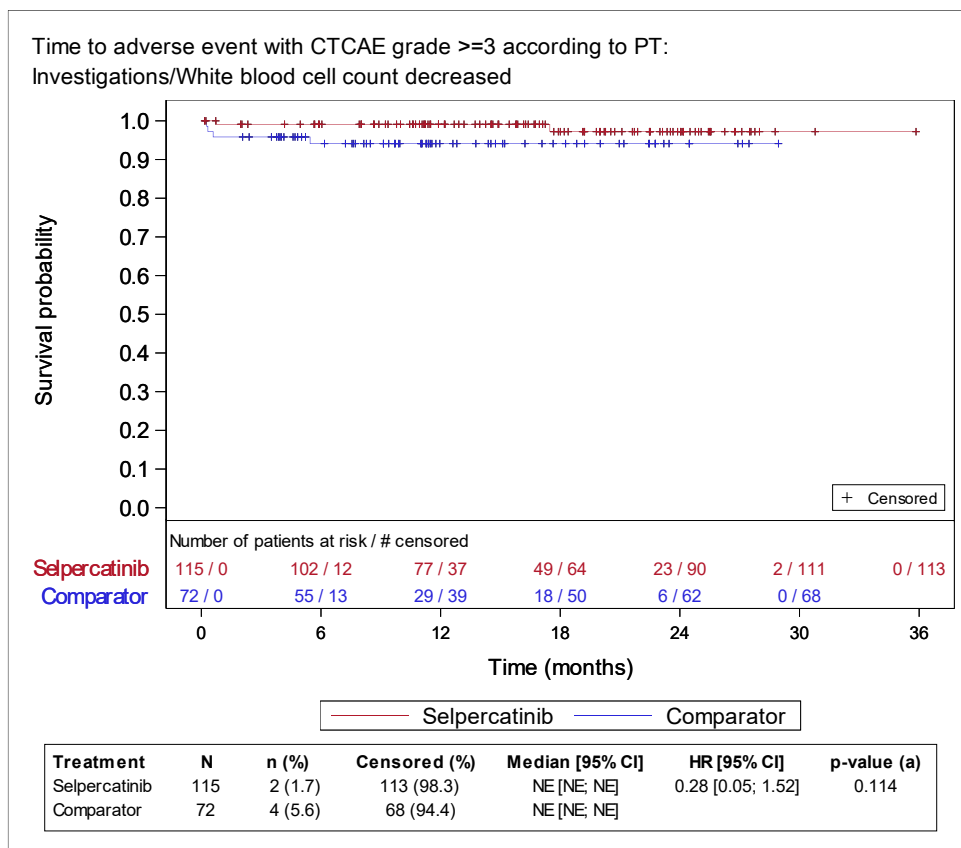
HR is based on the unstratified Cox proportional hazards model.

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Figure 75: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/White blood cell count decreased - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

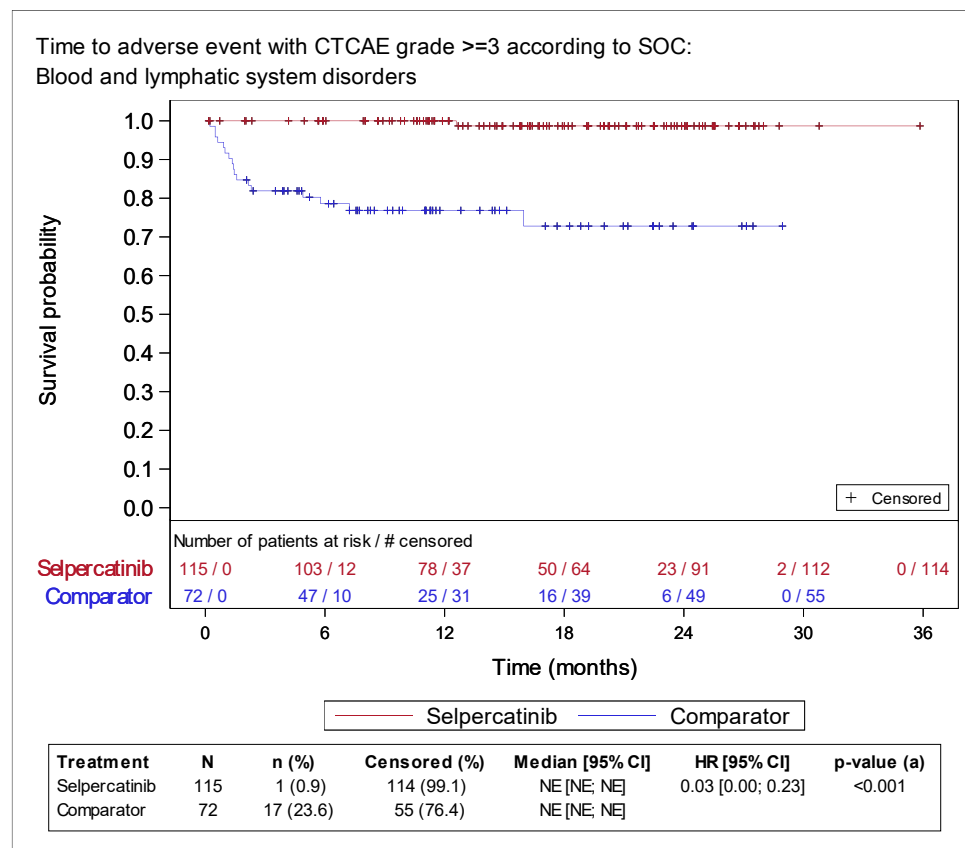
HR is based on the unstratified Cox proportional hazards model.

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Figure 76: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Blood and lymphatic system disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

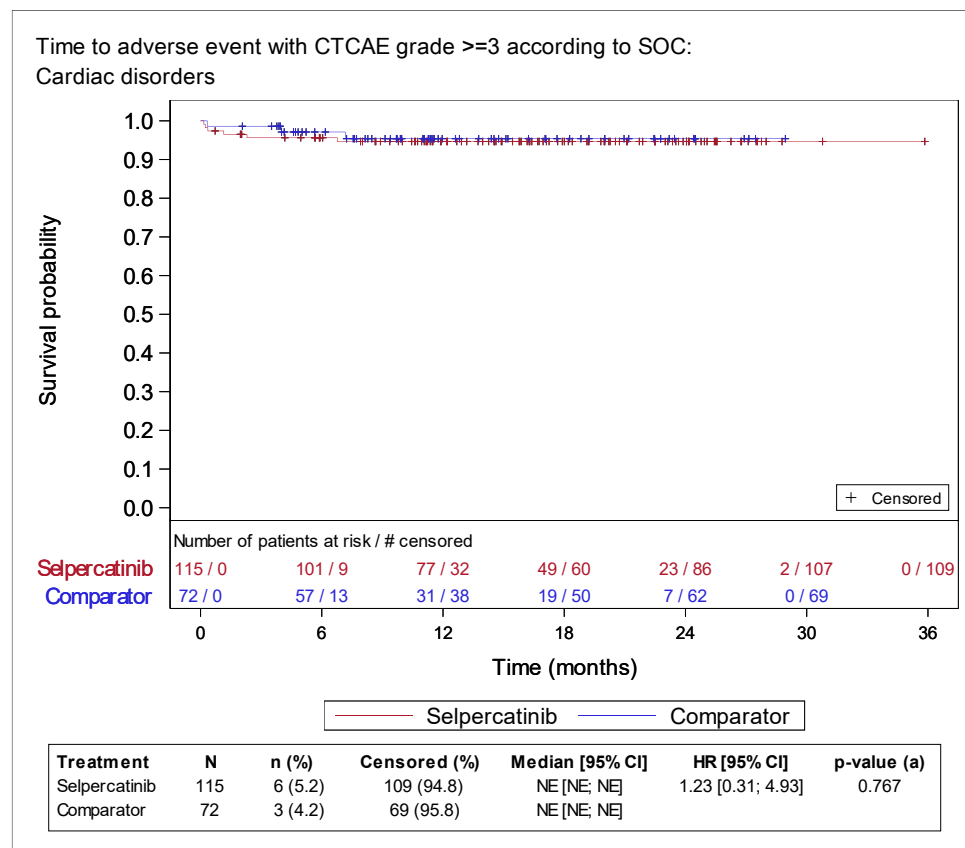
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_gr3spx001_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Figure 77: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Cardiac disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

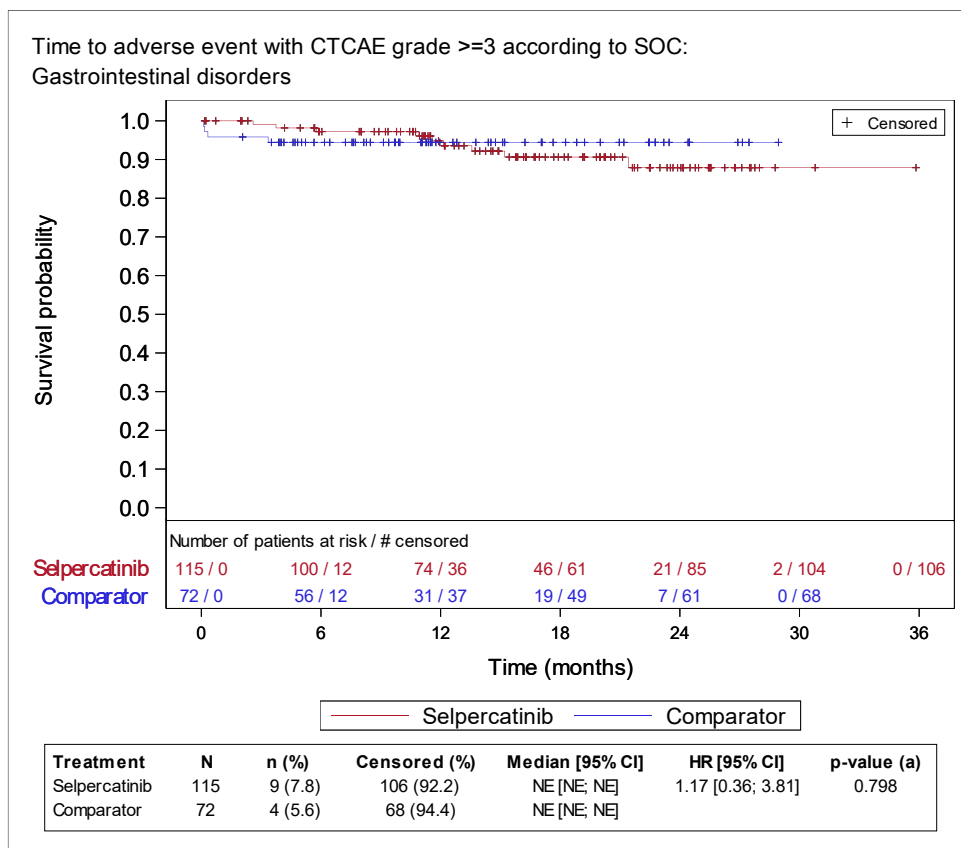
HR is based on the unstratified Cox proportional hazards model.

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Figure 78: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Gastrointestinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

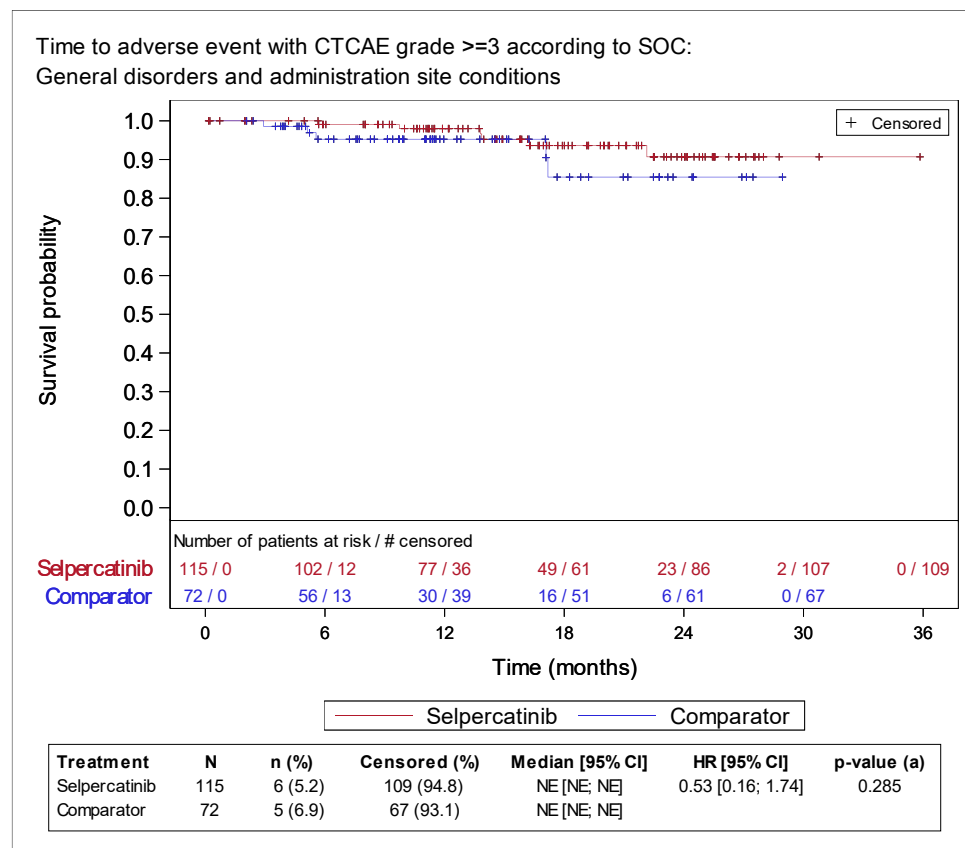
HR is based on the unstratified Cox proportional hazards model.

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Figure 79: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: General disorders and administration site conditions - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

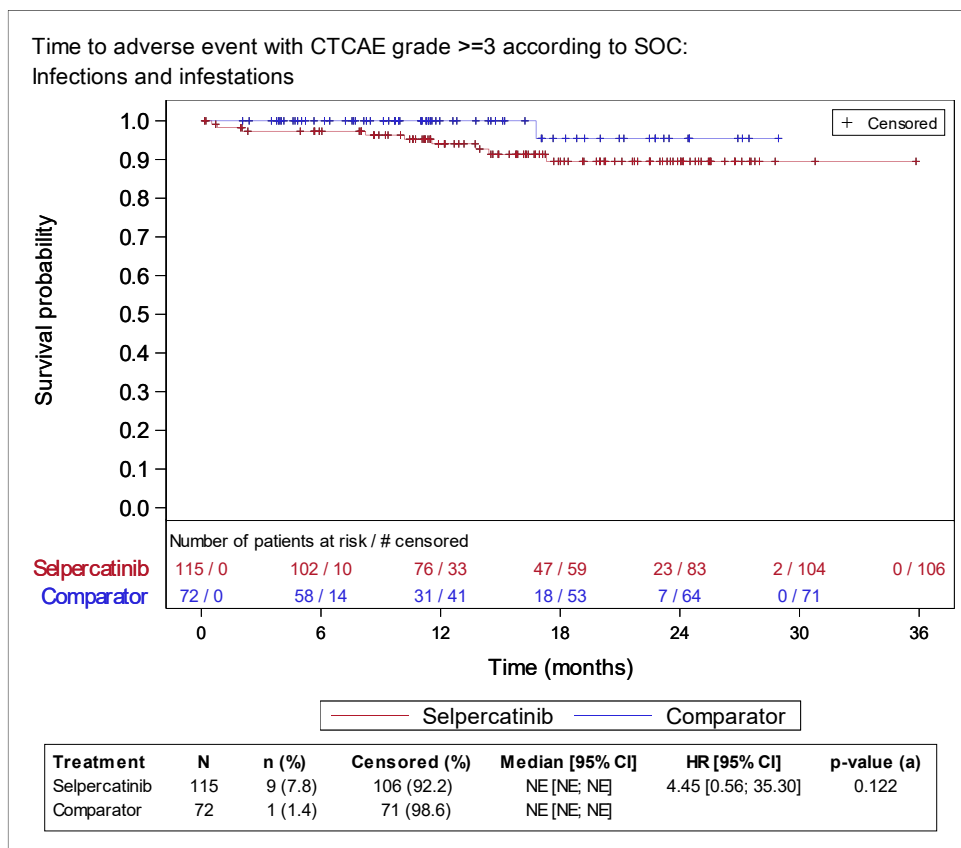
HR is based on the unstratified Cox proportional hazards model.

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Figure 80: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Infections and infestations - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

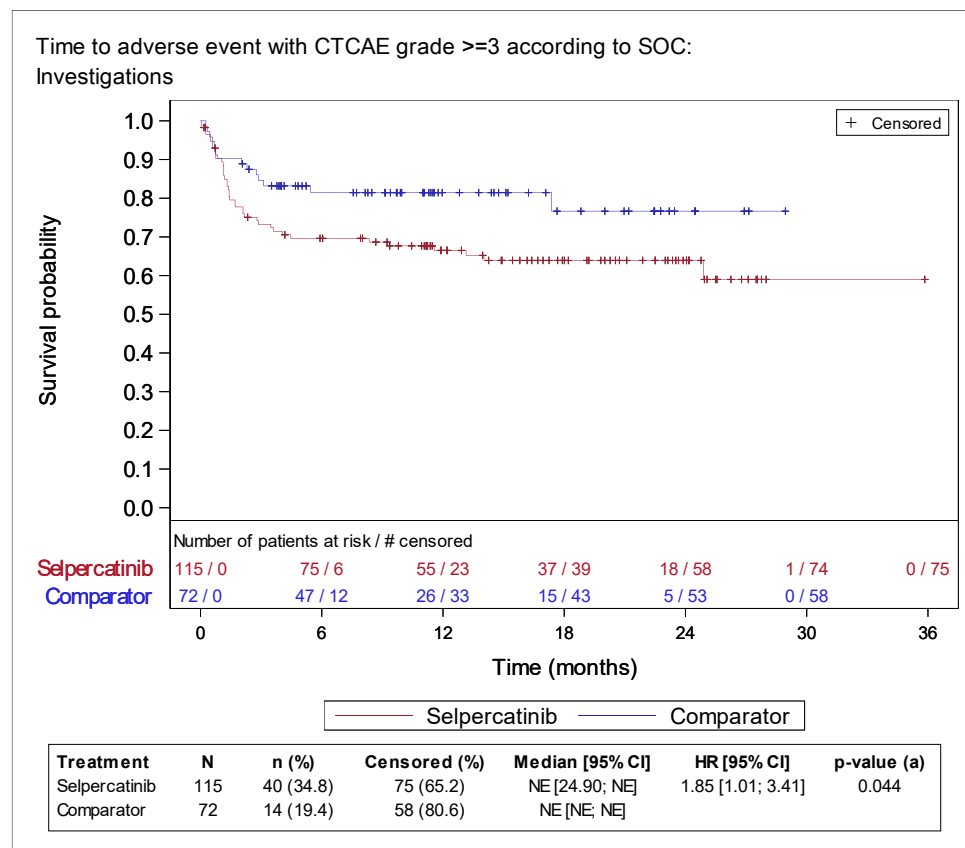
HR is based on the unstratified Cox proportional hazards model.

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Figure 81: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Investigations - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

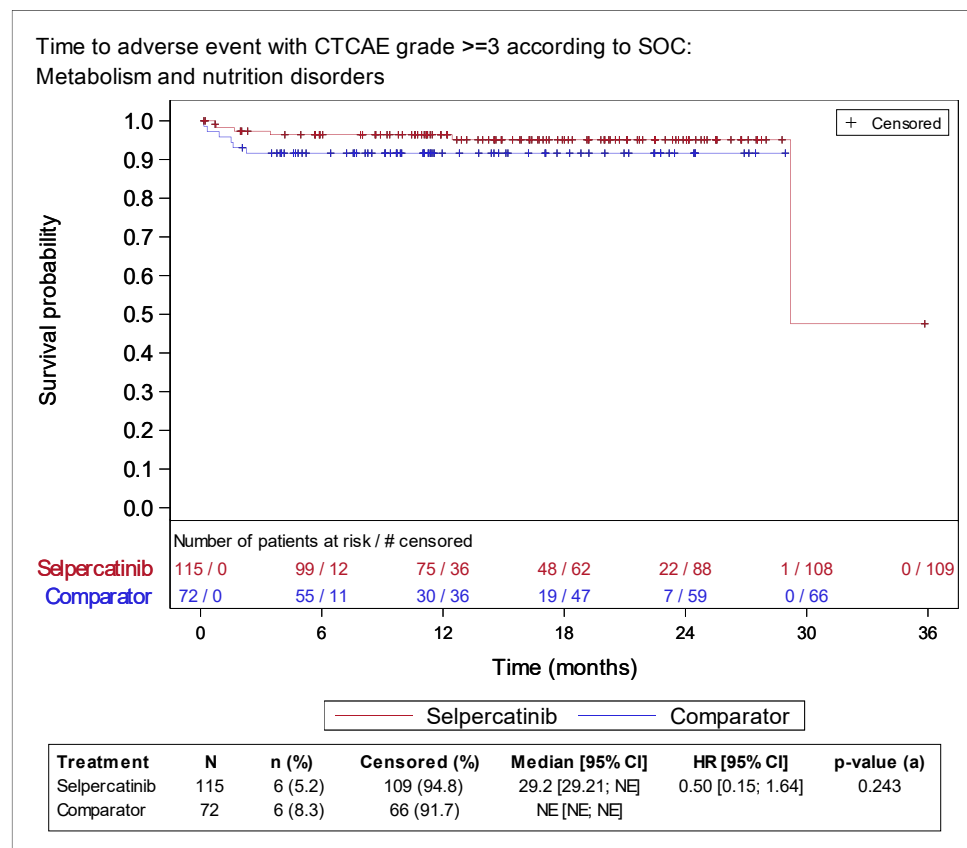
HR is based on the unstratified Cox proportional hazards model.

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteae_gba_02OCT2025 / 04:32

Figure 82: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Metabolism and nutrition disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

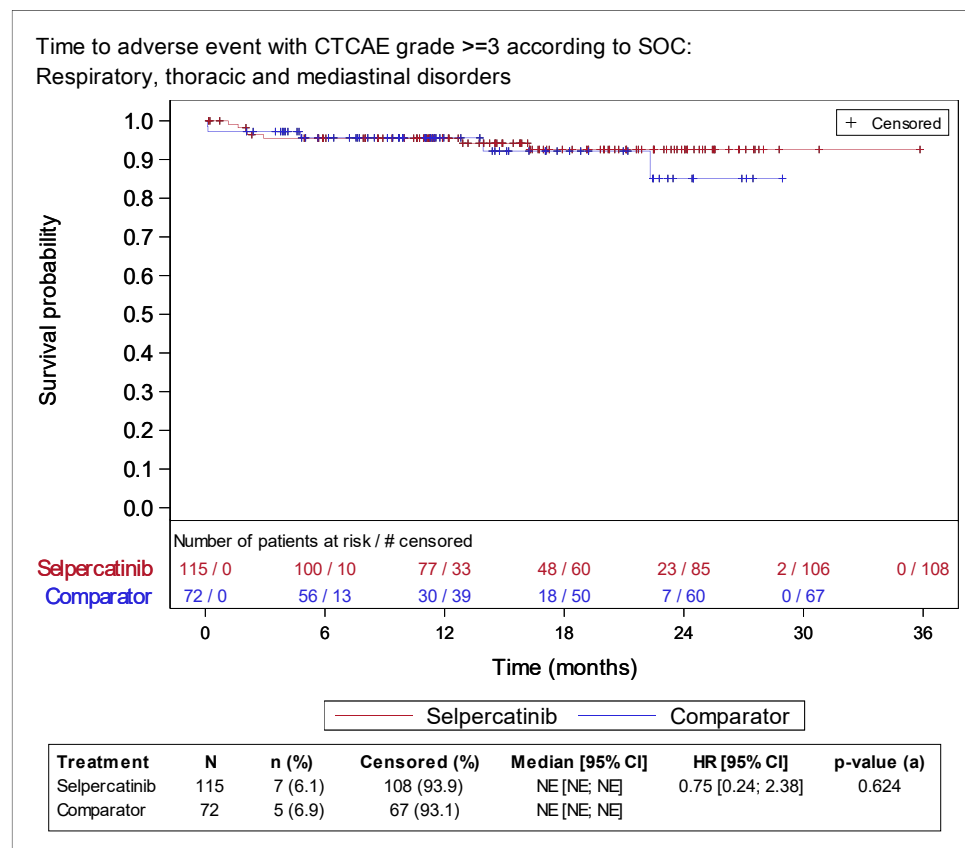
HR is based on the unstratified Cox proportional hazards model.

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteae_gba
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Figure 83: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Respiratory, thoracic and mediastinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

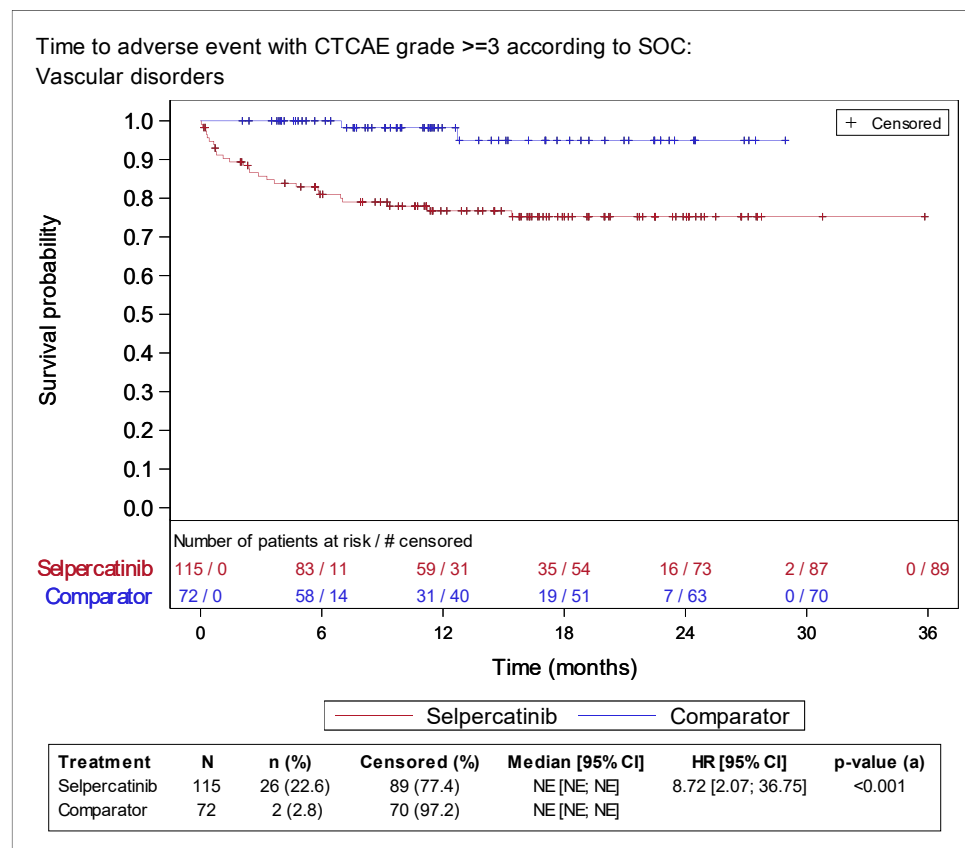
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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Figure 84: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Vascular disorders - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc230501.sas

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**Anhang 4-G3.4: Behandlungsbedingte unerwünschte Ereignisse, die zum
Behandlungsabbruch führen nach SOC und PT**

Tabelle 28: Behandlungsbedingte unerwünschte Ereignisse, die zum Behandlungsabbruch führen - Studie LIBRETTO-431, mSAF

SOC Preferred term	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72) n (%)	Gesamt (N=187) n (%)
Behandlungsbedingte unerwünschte Ereignisse, die zum Behandlungsabbruch führen	10 (8,7)	2 (2,8)	12 (6,4)
Cardiac disorders	3 (2,6)	0 (0,0)	3 (1,6)
Myocardial infarction	2 (1,7)	0 (0,0)	2 (1,1)
Cardiac arrest	1 (0,9)	0 (0,0)	1 (0,5)
Respiratory, thoracic and mediastinal disorders	2 (1,7)	0 (0,0)	2 (1,1)
Acute respiratory failure	1 (0,9)	0 (0,0)	1 (0,5)
Interstitial lung disease	1 (0,9)	0 (0,0)	1 (0,5)
General disorders and administration site conditions	1 (0,9)	0 (0,0)	1 (0,5)
Asthenia	1 (0,9)	0 (0,0)	1 (0,5)
Infections and infestations	1 (0,9)	0 (0,0)	1 (0,5)
Soft tissue infection	1 (0,9)	0 (0,0)	1 (0,5)
Injury, poisoning and procedural complications	1 (0,9)	0 (0,0)	1 (0,5)
Femur fracture	1 (0,9)	0 (0,0)	1 (0,5)
Investigations	1 (0,9)	1 (1,4)	2 (1,1)
Alanine aminotransferase increased	1 (0,9)	0 (0,0)	1 (0,5)
Neutrophil count decreased	0 (0,0)	1 (1,4)	1 (0,5)
Skin and subcutaneous tissue disorders	1 (0,9)	0 (0,0)	1 (0,5)
Drug eruption	1 (0,9)	0 (0,0)	1 (0,5)
Gastrointestinal disorders	0 (0,0)	1 (1,4)	1 (0,5)
Intestinal obstruction	0 (0,0)	1 (1,4)	1 (0,5)
Datenschnitt: 01. Mai 2023; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; SOC: System Organ Class.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aeldst_sm_dc230501.sas

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/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adae

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**Anhang 4-G3.5: Zusatztablette zum Resolved-Status unerwünschter Ereignisse nach
SOC und PT**

Table 25.1: Duration of TEAEs occurred in $\geq 10\%$ or in ≥ 10 patients and $\geq 1\%$ in any treatment arm within analysis population for significant SOC and PTs - study LIBRETTO-431, mSAF

		Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab
Duration of Adverse Events (resolved and unresolved) (in months)			
PT: Aspartate aminotransferase increased	Number of events Mean (SD) Median Min, Max	246 1.16 (1.722) 0.62 0.0, 12.8	70 1.76 (2.334) 0.76 0.1, 14.5
PT: Alanine aminotransferase increased	Number of events Mean (SD) Median Min, Max	234 0.89 (1.196) 0.53 0.1, 12.8	75 1.40 (1.810) 0.72 0.1, 9.9
PT: Blood bilirubin increased	Number of events Mean (SD) Median Min, Max	185 1.16 (2.065) 0.72 0.1, 20.0	0
PT: Electrocardiogram QT prolonged	Number of events Mean (SD) Median Min, Max	39 1.51 (2.219) 0.72 0.0, 10.1	1 20.86 (NE) 20.86 20.9, 20.9
PT: Bilirubin conjugated increased	Number of events Mean (SD) Median Min, Max	44 1.57 (3.657) 0.72 0.1, 24.3	1 0.23 (NE) 0.23 0.2, 0.2
PT: Diarrhoea	Number of events Mean (SD) Median Min, Max	176 2.31 (4.849) 0.16 0.0, 24.0	26 1.95 (4.696) 0.13 0.0, 19.5
PT: Dry mouth	Number of events Mean (SD) Median Min, Max	57 10.53 (9.758) 7.03 0.3, 29.8	4 12.33 (14.449) 6.90 1.9, 33.6
PT: Constipation	Number of events Mean (SD) Median Min, Max	35 2.70 (4.438) 0.53 0.0, 17.1	55 3.72 (7.796) 0.26 0.0, 33.6
PT: Nausea	Number of events Mean (SD) Median Min, Max	22 3.05 (5.572) 0.85 0.0, 24.4	69 1.29 (2.972) 0.26 0.0, 18.4
PT: Vomiting	Number of events Mean (SD) Median Min, Max	31 1.35 (4.604) 0.03 0.0, 24.9	26 1.55 (4.653) 0.21 0.0, 21.0
SOC: General disorders and administration site conditions	Number of events Mean (SD) Median Min, Max	214 4.50 (6.614) 0.94 0.0, 26.6	170 3.30 (6.591) 0.48 0.0, 33.6

		Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab
PT: Asthenia	Number of events Mean (SD) Median Min, Max	39 3.08 (4.844) 0.72 0.0, 17.9	55 3.50 (7.282) 0.49 0.1, 31.5
PT: Pyrexia	Number of events Mean (SD) Median Min, Max	29 0.17 (0.211) 0.10 0.0, 1.1	36 0.22 (0.568) 0.10 0.0, 3.5
PT: Decreased appetite	Number of events Mean (SD) Median Min, Max	24 6.95 (7.954) 2.38 0.1, 23.2	29 4.07 (6.807) 0.56 0.1, 21.6
PT: Hypocalcaemia	Number of events Mean (SD) Median Min, Max	24 1.20 (1.352) 0.74 0.1, 6.4	0
PT: Hyperglycaemia	Number of events Mean (SD) Median Min, Max	7 2.08 (2.802) 1.41 0.3, 8.3	18 5.23 (7.545) 1.81 0.5, 22.1
PT: Pruritus	Number of events Mean (SD) Median Min, Max	24 4.35 (7.013) 1.59 0.0, 27.3	20 5.35 (7.666) 1.49 0.0, 26.1
SOC: Vascular disorders	Number of events Mean (SD) Median Min, Max	125 5.87 (8.057) 1.35 0.0, 29.2	21 2.62 (5.409) 0.79 0.0, 24.1
PT: Hypertension	Number of events Mean (SD) Median Min, Max	116 6.00 (8.231) 1.33 0.0, 29.2	16 2.64 (5.824) 0.77 0.0, 24.1
PT: Dyspnoea	Number of events Mean (SD) Median Min, Max	9 3.73 (5.947) 0.92 0.1, 18.0	10 4.09 (6.675) 0.31 0.1, 17.8
SOC: Blood and lymphatic system disorders	Number of events Mean (SD) Median Min, Max	72 1.80 (3.394) 0.72 0.0, 17.9	291 1.45 (3.141) 0.49 0.0, 23.1
PT: Anaemia	Number of events Mean (SD) Median Min, Max	21 3.62 (5.426) 0.82 0.4, 17.9	164 2.05 (3.859) 0.72 0.0, 23.1
PT: Neutropenia	Number of events Mean (SD) Median Min, Max	11 0.50 (0.466) 0.46 0.0, 1.4	43 0.53 (0.494) 0.26 0.1, 2.2
PT: Lacrimation increased	Number of events Mean (SD) Median Min, Max	4 5.40 (1.652) 5.72 3.1, 7.0	11 10.53 (10.081) 5.72 1.6, 33.6

		Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab
SOC: Reproductive system and breast disorders	Number of events Mean (SD) Median Min, Max	14 8.31 (6.511) 8.53 0.2, 17.1	1 26.15 (NE) 26.15 26.2, 26.2
SOC: Reproductive system and breast disorders	Number of events Mean (SD) Median Min, Max	5 1.47 (1.130) 2.07 0.2, 2.6	0
Number of resolved Adverse Events			
PT: Aspartate aminotransferase increased	n/N (%)	241/246 98.0	66/70 94.3
PT: Alanine aminotransferase increased	n/N (%)	232/234 99.1	73/75 97.3
PT: Blood bilirubin increased	n/N (%)	179/185 96.8	0/0
PT: Electrocardiogram QT prolonged	n/N (%)	38/39 97.4	0/1
PT: Bilirubin conjugated increased	n/N (%)	43/44 97.7	1/1 100.0
PT: Diarrhoea	n/N (%)	161/176 91.5	24/26 92.3
PT: Dry mouth	n/N (%)	31/57 54.4	3/4 75.0
PT: Constipation	n/N (%)	31/35 88.6	47/55 85.5
PT: Nausea	n/N (%)	17/22 77.3	67/69 97.1
PT: Vomiting	n/N (%)	28/31 90.3	24/26 92.3
SOC: General disorders and administration site conditions	n/N (%)	163/214 76.2	147/170 86.5
PT: Asthenia	n/N (%)	31/39 79.5	47/55 85.5
PT: Pyrexia	n/N (%)	29/29 100.0	36/36 100.0
PT: Decreased appetite	n/N (%)	16/24 66.7	22/29 75.9
PT: Hypocalcaemia	n/N (%)	21/24 87.5	0/0
PT: Hyperglycaemia	n/N (%)	7/7 100.0	14/18 77.8
PT: Pruritus	n/N (%)	18/24 75.0	17/20 85.0
SOC: Vascular disorders	n/N (%)	87/125 69.6	19/21 90.5
PT: Hypertension	n/N (%)	81/116 69.8	15/16 93.8

		Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab
PT: Dyspnoea	n/N (%)	7/9 77.8	8/10 80.0
SOC: Blood and lymphatic system disorders	n/N (%)	68/72 94.4	280/291 96.2
PT: Anaemia	n/N (%)	17/21 81.0	153/164 93.3
PT: Neutropenia	n/N (%)	11/11 100.0	43/43 100.0
PT: Lacrimation increased	n/N (%)	2/4 50.0	6/11 54.5
SOC: Reproductive system and breast disorders	n/N (%)	5/14 35.7	0/1
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: ECOG: Eastern Cooperative Oncology Group; kg: kilogram; Max: Maximum; Min: Minimum; mSAF: Modified Safety-Pembrolizumab Population; NE: Not evaluable/not calculated; PT: Preferred Term; SD: Standard Deviation. n/N refers to number of events rather than number of patients.			

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Table 26.1: Duration of serious TEAEs occurred in $\geq 10\%$ or in ≥ 10 patients and $\geq 1\%$ in any treatment arm within analysis population for significant SOC and PTs - study LIBRETTO-431, mSAF

		Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab
Duration of Adverse Events (resolved and unresolved) (in months)			
SOC: Investigations	Number of events	1	15
	Mean (SD)	0.10 (NE)	0.27 (0.527)
	Median	0.10	0.10
	Min, Max	0.1, 0.1	0.0, 2.1
Number of resolved Adverse Events			
SOC: Investigations	n/N (%)	1/1 100.0	15/15 100.0
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg). Abbreviations: ECOG: Eastern Cooperative Oncology Group; kg: kilogram; Max: Maximum; Min: Minimum; mSAF: Modified Safety-Pembrolizumab Population; NE: Not evaluable/not calculated; PT: Preferred Term; SD: Standard Deviation. n/N refers to number of events rather than number of patients.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aesig_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_saesig_msaf.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adae_gba

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Table 27.1: Duration of TEAEs with CTCAE grade ≥ 3 occurred in $\geq 10\%$ or in ≥ 10 patients and $\geq 1\%$ in any treatment arm within analysis population for significant SOC and PTs - study LIBRETTO-431, mSAF

		Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab
Duration of Adverse Events (resolved and unresolved) (in months)			
SOC: Investigations	Number of events Mean (SD) Median Min, Max	84 0.94 (2.135) 0.31 0.0, 12.9	46 0.25 (0.311) 0.13 0.0, 1.9
PT: Alanine aminotransferase increased	Number of events Mean (SD) Median Min, Max	30 0.39 (0.337) 0.28 0.1, 1.9	0
PT: Aspartate aminotransferase increased	Number of events Mean (SD) Median Min, Max	18 0.45 (0.436) 0.34 0.0, 1.9	0
PT: Electrocardiogram QT prolonged	Number of events Mean (SD) Median Min, Max	14 1.84 (2.773) 0.74 0.2, 10.1	0
PT: Neutrophil count decreased	Number of events Mean (SD) Median Min, Max	2 0.31 (0.023) 0.31 0.3, 0.3	20 0.27 (0.191) 0.20 0.1, 0.8
SOC: Vascular disorders	Number of events Mean (SD) Median Min, Max	37 2.57 (6.263) 0.16 0.0, 29.2	3 0.50 (0.411) 0.69 0.0, 0.8
PT: Hypertension	Number of events Mean (SD) Median Min, Max	35 2.55 (6.434) 0.16 0.0, 29.2	3 0.50 (0.411) 0.69 0.0, 0.8
SOC: Blood and lymphatic system disorders	Number of events Mean (SD) Median Min, Max	1 11.96 (NE) 11.96 12.0, 12.0	42 0.43 (0.638) 0.23 0.1, 3.6
PT: Anaemia	Number of events Mean (SD) Median Min, Max	1 11.96 (NE) 11.96 12.0, 12.0	9 0.47 (0.353) 0.46 0.1, 1.1
PT: Neutropenia	Number of events Mean (SD) Median Min, Max	0	15 0.25 (0.104) 0.26 0.1, 0.4
Number of resolved Adverse Events			
SOC: Investigations	n/N (%)	81/84 96.4	45/46 97.8
PT: Alanine aminotransferase increased	n/N (%)	30/30 100.0	0/0

		Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab
PT: Aspartate aminotransferase increased	n/N (%)	18/18 100.0	0/0
PT: Electrocardiogram QT prolonged	n/N (%)	13/14 92.9	0/0
PT: Neutrophil count decreased	n/N (%)	2/2 100.0	20/20 100.0
SOC: Vascular disorders	n/N (%)	33/37 89.2	3/3 100.0
PT: Hypertension	n/N (%)	31/35 88.6	3/3 100.0
SOC: Blood and lymphatic system disorders	n/N (%)	0/1	41/42 97.6
PT: Anaemia	n/N (%)	0/1	8/9 88.9
PT: Neutropenia	n/N (%)	0/0	15/15 100.0
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg). Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; kg: kilogram; Max: Maximum; Min: Minimum; mSAF: Modified Safety-Pembrolizumab Population; NE: Not evaluable/not calculated; PT: Preferred Term; SD: Standard Deviation. n/N refers to number of events rather than number of patients.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aesig_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aegr3sig_msaf.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adae_gba
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Anhang 4-G3.6: Zusammenfassende Statistik für FACT-GP5

Tabelle 29: Zusammenfassende Statistik für FACT-GP5 Nebenwirkungen des FACT-GP5 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Visite Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)	Gesamt (N=188)
FACT-GP5 Nebenwirkungen			
Baseline			
Anzahl der Patienten, n (fehlend)	78 (37)	50 (23)	128 (60)
Mittelwert (SD)	0,3 (0,60)	0,4 (0,86)	0,3 (0,71)
Median (min; max)	0,0 (0,0; 3,0)	0,0 (0,0; 4,0)	0,0 (0,0; 4,0)
Q1-Q3	0,0-0,0	0,0-0,0	0,0-0,0
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; FACT-GP5: Functional Assessment of Cancer Therapy - Side Effects; kg: Kilogramm; Max: Maximum; Min: Minimum; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_gol_sm_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_gp5sm_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqs

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Anhang 4-G3.7: Zusammenfassende Statistik für PRO-CTCAE

Table 30: PRO-CTCAE Arm or Leg Swelling - Frequency - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Arm or Leg Swelling - Frequency - Worst score		
Never	19 (16,5)	17 (23,3)
Rarely	18 (15,7)	9 (12,3)
Occasionally	19 (16,5)	21 (28,8)
Frequently	27 (23,5)	8 (11,0)
Almost constantly	28 (24,3)	11 (15,1)
Missing	4 (3,5)	7 (9,6)
Arm or Leg Swelling - Frequency - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	13 (11,3)	13 (17,8)
Rarely	12 (10,4)	6 (8,2)
Occasionally	14 (12,2)	13 (17,8)
Frequently	19 (16,5)	7 (9,6)
Almost constantly	20 (17,4)	10 (13,7)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcalsfsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 31: PRO-CTCAE Chills - Frequency - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Chills - Frequency - Worst score		
Never	31 (27,0)	22 (30,1)
Rarely	21 (18,3)	12 (16,4)
Occasionally	32 (27,8)	18 (24,7)
Frequently	24 (20,9)	13 (17,8)
Almost constantly	3 (2,6)	1 (1,4)
Missing	4 (3,5)	7 (9,6)
Chills - Frequency - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	21 (18,3)	17 (23,3)
Rarely	12 (10,4)	7 (9,6)
Occasionally	25 (21,7)	14 (19,2)
Frequently	18 (15,7)	10 (13,7)
Almost constantly	2 (1,7)	1 (1,4)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctchifsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 32: PRO-CTCAE Diarrhea - Frequency - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Diarrhea - Frequency - Worst score		
Never	9 (7,8)	15 (20,5)
Rarely	17 (14,8)	25 (34,2)
Occasionally	29 (25,2)	13 (17,8)
Frequently	41 (35,7)	11 (15,1)
Almost constantly	15 (13,0)	2 (2,7)
Missing	4 (3,5)	7 (9,6)
Diarrhea - Frequency - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	10 (8,7)	13 (17,8)
Rarely	9 (7,8)	14 (19,2)
Occasionally	16 (13,9)	11 (15,1)
Frequently	33 (28,7)	10 (13,7)
Almost constantly	10 (8,7)	1 (1,4)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcdiafsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqscctc

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Table 33: PRO-CTCAE Headache - Frequency - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Headache - Frequency - Worst score		
Never	18 (15,7)	11 (15,1)
Rarely	30 (26,1)	15 (20,5)
Occasionally	34 (29,6)	21 (28,8)
Frequently	25 (21,7)	15 (20,5)
Almost constantly	4 (3,5)	4 (5,5)
Missing	4 (3,5)	7 (9,6)
Headache - Frequency - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	17 (14,8)	9 (12,3)
Rarely	12 (10,4)	12 (16,4)
Occasionally	26 (22,6)	15 (20,5)
Frequently	19 (16,5)	10 (13,7)
Almost constantly	4 (3,5)	3 (4,1)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcheafsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 34: PRO-CTCAE Nausea - Frequency - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Nausea - Frequency - Worst score		
Never	32 (27,8)	3 (4,1)
Rarely	32 (27,8)	8 (11,0)
Occasionally	32 (27,8)	17 (23,3)
Frequently	10 (8,7)	32 (43,8)
Almost constantly	5 (4,3)	6 (8,2)
Missing	4 (3,5)	7 (9,6)
Nausea - Frequency - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	31 (27,0)	2 (2,7)
Rarely	19 (16,5)	5 (6,8)
Occasionally	18 (15,7)	12 (16,4)
Frequently	8 (7,0)	26 (35,6)
Almost constantly	2 (1,7)	4 (5,5)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcnaufsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 35: PRO-CTCAE Vomiting - Frequency - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Vomiting - Frequency - Worst score		
Never	61 (53,0)	20 (27,4)
Rarely	28 (24,3)	12 (16,4)
Occasionally	15 (13,0)	25 (34,2)
Frequently	7 (6,1)	8 (11,0)
Almost constantly	0	1 (1,4)
Missing	4 (3,5)	7 (9,6)
Vomiting - Frequency - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	47 (40,9)	14 (19,2)
Rarely	17 (14,8)	10 (13,7)
Occasionally	10 (8,7)	21 (28,8)
Frequently	4 (3,5)	3 (4,1)
Almost constantly	0	1 (1,4)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcvomfsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 36: PRO-CTCAE Arm or Leg Swelling - Interfere - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Arm or Leg Swelling - Interfere - Worst score		
Not at all	15 (13,0)	8 (11,0)
A little bit	24 (20,9)	13 (17,8)
Somewhat	26 (22,6)	19 (26,0)
Quite a bit	15 (13,0)	5 (6,8)
Very much	7 (6,1)	3 (4,1)
Missing	28 (24,3)	25 (34,2)
Arm or Leg Swelling - Interfere - Baseline-adjusted Worst score		
Baseline Missing	78 (67,8)	41 (56,2)
Same as Baseline	1 (0,9)	1 (1,4)
A little bit	1 (0,9)	0
Somewhat	4 (3,5)	3 (4,1)
Quite a bit	2 (1,7)	3 (4,1)
Very much	1 (0,9)	0
Missing	28 (24,3)	25 (34,2)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcalsism_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 37: PRO-CTCAE Decreased Appetite - Interfere - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Decreased Appetite - Interfere - Worst score		
Not at all	17 (14,8)	1 (1,4)
A little bit	28 (24,3)	15 (20,5)
Somewhat	23 (20,0)	15 (20,5)
Quite a bit	18 (15,7)	16 (21,9)
Very much	7 (6,1)	13 (17,8)
Missing	22 (19,1)	13 (17,8)
Decreased Appetite - Interfere - Baseline-adjusted Worst score		
Baseline Missing	65 (56,5)	38 (52,1)
Same as Baseline	12 (10,4)	1 (1,4)
A little bit	5 (4,3)	2 (2,7)
Somewhat	3 (2,6)	5 (6,8)
Quite a bit	4 (3,5)	9 (12,3)
Very much	4 (3,5)	5 (6,8)
Missing	22 (19,1)	13 (17,8)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcdecism_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqscctc

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Table 38: PRO-CTCAE Fatigue - Interfere - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Fatigue - Interfere - Worst score		
Not at all	8 (7,0)	0
A little bit	34 (29,6)	9 (12,3)
Somewhat	25 (21,7)	18 (24,7)
Quite a bit	20 (17,4)	17 (23,3)
Very much	20 (17,4)	20 (27,4)
Missing	8 (7,0)	9 (12,3)
Fatigue - Interfere - Baseline-adjusted Worst score		
Baseline Missing	63 (54,8)	33 (45,2)
Same as Baseline	16 (13,9)	4 (5,5)
A little bit	3 (2,6)	3 (4,1)
Somewhat	9 (7,8)	7 (9,6)
Quite a bit	9 (7,8)	9 (12,3)
Very much	7 (6,1)	8 (11,0)
Missing	8 (7,0)	9 (12,3)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcfatism_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 39: PRO-CTCAE Headache - Interfere - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Headache - Interfere - Worst score		
Not at all	19 (16,5)	6 (8,2)
A little bit	35 (30,4)	18 (24,7)
Somewhat	21 (18,3)	21 (28,8)
Quite a bit	13 (11,3)	7 (9,6)
Very much	3 (2,6)	2 (2,7)
Missing	24 (20,9)	19 (26,0)
Headache - Interfere - Baseline-adjusted Worst score		
Baseline Missing	69 (60,0)	40 (54,8)
Same as Baseline	7 (6,1)	1 (1,4)
A little bit	4 (3,5)	2 (2,7)
Somewhat	8 (7,0)	7 (9,6)
Quite a bit	3 (2,6)	2 (2,7)
Very much	0	2 (2,7)
Missing	24 (20,9)	19 (26,0)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcheaism_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 40: PRO-CTCAE Watery Eyes - Interfere - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Watery Eyes - Interfere - Worst score		
Not at all	15 (13,0)	5 (6,8)
A little bit	30 (26,1)	20 (27,4)
Somewhat	14 (12,2)	25 (34,2)
Quite a bit	13 (11,3)	8 (11,0)
Very much	3 (2,6)	2 (2,7)
Missing	40 (34,8)	13 (17,8)
Watery Eyes - Interfere - Baseline-adjusted Worst score		
Baseline Missing	65 (56,5)	54 (74,0)
Same as Baseline	4 (3,5)	1 (1,4)
A little bit	1 (0,9)	2 (2,7)
Somewhat	2 (1,7)	2 (2,7)
Quite a bit	3 (2,6)	1 (1,4)
Very much	0	0
Missing	40 (34,8)	13 (17,8)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctewatism_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 41: PRO-CTCAE Arm or Leg Swelling - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Arm or Leg Swelling - Severity - Worst score		
None	5 (4,3)	1 (1,4)
Mild	26 (22,6)	21 (28,8)
Moderate	34 (29,6)	15 (20,5)
Severe	16 (13,9)	7 (9,6)
Very severe	11 (9,6)	5 (6,8)
Missing	23 (20,0)	24 (32,9)
Arm or Leg Swelling - Severity - Baseline-adjusted Worst score		
Baseline Missing	83 (72,2)	42 (57,5)
Same as Baseline	1 (0,9)	0
Mild	0	0
Moderate	2 (1,7)	2 (2,7)
Severe	5 (4,3)	4 (5,5)
Very severe	1 (0,9)	1 (1,4)
Missing	23 (20,0)	24 (32,9)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcalessm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqscctc

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Table 42: PRO-CTCAE Chills - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Chills - Severity - Worst score		
None	6 (5,2)	1 (1,4)
Mild	35 (30,4)	14 (19,2)
Moderate	24 (20,9)	17 (23,3)
Severe	11 (9,6)	10 (13,7)
Very severe	4 (3,5)	2 (2,7)
Missing	35 (30,4)	29 (39,7)
Chills - Severity - Baseline-adjusted Worst score		
Baseline Missing	67 (58,3)	35 (47,9)
Same as Baseline	5 (4,3)	1 (1,4)
Mild	1 (0,9)	0
Moderate	2 (1,7)	4 (5,5)
Severe	3 (2,6)	2 (2,7)
Very severe	2 (1,7)	2 (2,7)
Missing	35 (30,4)	29 (39,7)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcchissm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 43: PRO-CTCAE Constipation - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Constipation - Severity - Worst score		
None	12 (10,4)	3 (4,1)
Mild	45 (39,1)	14 (19,2)
Moderate	28 (24,3)	22 (30,1)
Severe	17 (14,8)	18 (24,7)
Very severe	9 (7,8)	9 (12,3)
Missing	4 (3,5)	7 (9,6)
Constipation - Severity - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	15 (13,0)	5 (6,8)
Mild	24 (20,9)	8 (11,0)
Moderate	19 (16,5)	18 (24,7)
Severe	14 (12,2)	14 (19,2)
Very severe	6 (5,2)	4 (5,5)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_cteconssm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 44: PRO-CTCAE Decreased Appetite - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Decreased Appetite - Severity - Worst score		
None	18 (15,7)	6 (8,2)
Mild	38 (33,0)	9 (12,3)
Moderate	28 (24,3)	20 (27,4)
Severe	18 (15,7)	14 (19,2)
Very severe	9 (7,8)	17 (23,3)
Missing	4 (3,5)	7 (9,6)
Decreased Appetite - Severity - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	24 (20,9)	5 (6,8)
Mild	14 (12,2)	7 (9,6)
Moderate	18 (15,7)	15 (20,5)
Severe	14 (12,2)	9 (12,3)
Very severe	8 (7,0)	13 (17,8)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcdecsm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 45: PRO-CTCAE Dry Mouth - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Dry Mouth - Severity - Worst score		
None	4 (3,5)	6 (8,2)
Mild	19 (16,5)	13 (17,8)
Moderate	31 (27,0)	25 (34,2)
Severe	28 (24,3)	15 (20,5)
Very severe	29 (25,2)	7 (9,6)
Missing	4 (3,5)	7 (9,6)
Dry Mouth - Severity - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	8 (7,0)	9 (12,3)
Mild	9 (7,8)	7 (9,6)
Moderate	19 (16,5)	20 (27,4)
Severe	21 (18,3)	8 (11,0)
Very severe	21 (18,3)	5 (6,8)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcdryssm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 46: PRO-CTCAE Fatigue - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Fatigue - Severity - Worst score		
None	4 (3,5)	2 (2,7)
Mild	33 (28,7)	6 (8,2)
Moderate	38 (33,0)	21 (28,8)
Severe	19 (16,5)	17 (23,3)
Very severe	17 (14,8)	20 (27,4)
Missing	4 (3,5)	7 (9,6)
Fatigue - Severity - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	19 (16,5)	8 (11,0)
Mild	11 (9,6)	2 (2,7)
Moderate	24 (20,9)	14 (19,2)
Severe	12 (10,4)	13 (17,8)
Very severe	12 (10,4)	12 (16,4)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcfatssm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 47: PRO-CTCAE Headache - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Headache - Severity - Worst score		
None	2 (1,7)	1 (1,4)
Mild	47 (40,9)	21 (28,8)
Moderate	29 (25,2)	17 (23,3)
Severe	11 (9,6)	12 (16,4)
Very severe	4 (3,5)	4 (5,5)
Missing	22 (19,1)	18 (24,7)
Headache - Severity - Baseline-adjusted Worst score		
Baseline Missing	71 (61,7)	40 (54,8)
Same as Baseline	7 (6,1)	2 (2,7)
Mild	0	0
Moderate	10 (8,7)	6 (8,2)
Severe	5 (4,3)	5 (6,8)
Very severe	0	2 (2,7)
Missing	22 (19,1)	18 (24,7)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcheassm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 48: PRO-CTCAE Itching - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Itching - Severity - Worst score		
None	15 (13,0)	14 (19,2)
Mild	51 (44,3)	15 (20,5)
Moderate	28 (24,3)	24 (32,9)
Severe	14 (12,2)	8 (11,0)
Very severe	3 (2,6)	5 (6,8)
Missing	4 (3,5)	7 (9,6)
Itching - Severity - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	14 (12,2)	11 (15,1)
Mild	34 (29,6)	9 (12,3)
Moderate	17 (14,8)	18 (24,7)
Severe	11 (9,6)	7 (9,6)
Very severe	2 (1,7)	4 (5,5)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcitcssm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 49: PRO-CTCAE Nausea - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Nausea - Severity - Worst score		
None	8 (7,0)	1 (1,4)
Mild	35 (30,4)	12 (16,4)
Moderate	22 (19,1)	24 (32,9)
Severe	10 (8,7)	16 (21,9)
Very severe	4 (3,5)	10 (13,7)
Missing	36 (31,3)	10 (13,7)
Nausea - Severity - Baseline-adjusted Worst score		
Baseline Missing	62 (53,9)	51 (69,9)
Same as Baseline	8 (7,0)	1 (1,4)
Mild	1 (0,9)	0
Moderate	5 (4,3)	4 (5,5)
Severe	3 (2,6)	5 (6,8)
Very severe	0	2 (2,7)
Missing	36 (31,3)	10 (13,7)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctcnaussm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 50: PRO-CTCAE Vomiting - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Vomiting - Severity - Worst score		
None	4 (3,5)	0
Mild	23 (20,0)	14 (19,2)
Moderate	11 (9,6)	19 (26,0)
Severe	9 (7,8)	9 (12,3)
Very severe	3 (2,6)	4 (5,5)
Missing	65 (56,5)	27 (37,0)
Vomiting - Severity - Baseline-adjusted Worst score		
Baseline Missing	43 (37,4)	41 (56,2)
Same as Baseline	6 (5,2)	3 (4,1)
Mild	0	0
Moderate	0	1 (1,4)
Severe	0	1 (1,4)
Very severe	1 (0,9)	0
Missing	65 (56,5)	27 (37,0)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctevomssm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Table 51: PRO-CTCAE Watery Eyes - Severity - study LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Watery Eyes - Severity - Worst score		
None	36 (31,3)	6 (8,2)
Mild	41 (35,7)	20 (27,4)
Moderate	16 (13,9)	25 (34,2)
Severe	14 (12,2)	10 (13,7)
Very severe	4 (3,5)	5 (6,8)
Missing	4 (3,5)	7 (9,6)
Watery Eyes - Severity - Baseline-adjusted Worst score		
Baseline Missing	33 (28,7)	17 (23,3)
Same as Baseline	29 (25,2)	7 (9,6)
Mild	24 (20,9)	13 (17,8)
Moderate	12 (10,4)	19 (26,0)
Severe	9 (7,8)	6 (8,2)
Very severe	4 (3,5)	4 (5,5)
Missing	4 (3,5)	7 (9,6)
Data cutoff: 01MAY2023; Modified ITT-Pembrolizumab Population. Abbreviations: CTCAE: Common Terminology Criteria for Adverse Events; ITT: Intention-to-treat Population; mITT: Modified ITT-Pembrolizumab Population; n: Number of patients; N: Total number of patients in the analysis; PRO: Patient Reported Outcome.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_proctcae_sm_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_ctewatssm_mitt.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adqsctc

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Anhang 4-G4: Ergänzende Angaben zu Subgruppenanalysen

Anhang 4-G4.1: Subgruppen - Nicht signifikant

Tabelle 57: Subgruppen für das Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,996)					
<65 Jahre	14/76 (18,4)	NE [NE; NE]	7/45 (15,6)	NE [NE; NE]	1,22 [0,49; 3,01] 0,673
≥65 Jahre	8/39 (20,5)	NE [21,85; NE]	4/28 (14,3)	NE [NE; NE]	1,34 [0,40; 4,45] 0,632
Baseline ECOG (p-Wert des Interaktionsterms: 0,313)					
0	5/41 (12,2)	NE [NE; NE]	1/25 (4,0)	NE [NE; NE]	3,09 [0,36; 26,46] 0,278
1	17/74 (23,0)	NE [NE; NE]	10/48 (20,8)	NE [NE; NE]	1,00 [0,46; 2,20] 0,991
Geschlecht (p-Wert des Interaktionsterms: 0,629)					
Männlich	10/61 (16,4)	NE [NE; NE]	3/34 (8,8)	NE [NE; NE]	1,68 [0,46; 6,13] 0,422
Weiblich	12/54 (22,2)	NE [NE; NE]	8/39 (20,5)	NE [NE; NE]	1,10 [0,45; 2,68] 0,840
Geografische Region (p-Wert des Interaktionsterms: 0,620)					
Ostasiatisch	12/65 (18,5)	NE [NE; NE]	6/35 (17,1)	NE [NE; NE]	1,04 [0,39; 2,76] 0,945
Nicht-Ostasiatisch	10/50 (20,0)	NE [NE; NE]	5/38 (13,2)	NE [NE; NE]	1,51 [0,51; 4,41] 0,451
Raucherstatus (p-Wert des Interaktionsterms: 0,486)					
Nie	14/72 (19,4)	NE [NE; NE]	9/50 (18,0)	NE [NE; NE]	1,06 [0,46; 2,46] 0,887
Ehemals/Aktuell	8/43 (18,6)	NE [NE; NE]	2/23 (8,7)	NE [NE; NE]	2,08 [0,44; 9,78] 0,343
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,933)					
Ja	8/23 (34,8)	NE [15,47; NE]	3/14 (21,4)	NE [9,72; NE]	1,37 [0,36; 5,20] 0,639
Nein	5/44 (11,4)	NE [21,19; NE]	2/23 (8,7)	NE [NE; NE]	1,31 [0,25; 6,81] 0,747

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	9/48 (18,8)	NE [NE; NE]	6/36 (16,7)	NE [NE; NE]	1,06 [0,38; 2,99] 0,908
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,356)					
Ja	4/16 (25,0)	NE [15,47; NE]	4/13 (30,8)	NE [9,26; NE]	0,72 [0,18; 2,87] 0,637
Nein	18/98 (18,4)	NE [NE; NE]	7/60 (11,7)	NE [NE; NE]	1,57 [0,65; 3,75] 0,309
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,318)					
TPS <50%	8/48 (16,7)	NE [NE; NE]	4/27 (14,8)	NE [NE; NE]	0,89 [0,27; 2,98] 0,855
TPS ≥50%	4/19 (21,1)	NE [12,88; NE]	1/13 (7,7)	NE [NE; NE]	2,92 [0,33; 26,16] 0,315
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,605)					
TPS <50%	8/48 (16,7)	NE [NE; NE]	4/27 (14,8)	NE [NE; NE]	0,89 [0,27; 2,98] 0,855
TPS ≥50%	4/19 (21,1)	NE [12,88; NE]	1/13 (7,7)	NE [NE; NE]	2,92 [0,33; 26,16] 0,315
Unbekannt	10/48 (20,8)	NE [NE; NE]	6/33 (18,2)	NE [NE; NE]	1,14 [0,42; 3,15] 0,795
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,711)					
Negativ	2/26 (7,7)	NE [NE; NE]	1/12 (8,3)	NE [NE; NE]	0,42 [0,03; 5,30] 0,492
Positiv	11/49 (22,4)	NE [21,85; NE]	6/34 (17,6)	NE [NE; NE]	1,36 [0,50; 3,68] 0,548
Unbekannt	9/40 (22,5)	NE [NE; NE]	4/27 (14,8)	NE [NE; NE]	1,60 [0,49; 5,21] 0,428
Krankheitsstatus (p-Wert des Interaktionsterms: 0,707)					
III*	2/6 (33,3)	NE [12,48; NE]	0/6 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,208
IVA	9/44 (20,5)	NE [NE; NE]	4/33 (12,1)	NE [NE; NE]	1,60 [0,49; 5,20] 0,431

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	11/65 (16,9)	NE [NE; NE]	7/34 (20,6)	NE [NE; NE]	0,85 [0,33; 2,20] 0,738
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,516)					
Asiatisch	12/66 (18,2)	NE [NE; NE]	6/35 (17,1)	NE [NE; NE]	1,03 [0,39; 2,75] 0,952
Nicht asiatisch	10/49 (20,4)	NE [NE; NE]	4/34 (11,8)	NE [NE; NE]	1,72 [0,54; 5,49] 0,352
RET-Probenart (p-Wert des Interaktionsterms: 0,589)					
Blut	2/9 (22,2)	NE [7,72; NE]	1/10 (10,0)	NE [9,26; NE]	2,35 [0,21; 25,97] 0,473
Gewebe	20/106 (18,9)	NE [NE; NE]	10/63 (15,9)	NE [NE; NE]	1,15 [0,54; 2,46] 0,715
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 1,000)					
CCDC6*	0/9 (0,0)	NE [NE; NE]	0/6 (0,0)	NE [NE; NE]	NE
KIF5B	9/50 (18,0)	NE [NE; NE]	7/36 (19,4)	NE [NE; NE]	0,75 [0,28; 2,01] 0,560
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. * SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_os_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adtte

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Tabelle 58: Subgruppen für die Progressionsfreies Überleben (BICR Beurteilung) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit* [95% KI]	n/N (%)	Mediane Ereigniszeit* [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,560)					
<65 Jahre	30/76 (39,5)	24,8 [14,06; NE]	28/45 (62,2)	10,9 [7,10; 16,82]	0,51 [0,30; 0,85] 0,009
≥65 Jahre	15/39 (38,5)	NE [14,03; NE]	13/28 (46,4)	15,6 [11,10; NE]	0,67 [0,32; 1,42] 0,295
Baseline ECOG (p-Wert des Interaktionsterms: 0,945)					
0	14/41 (34,1)	NE [16,82; NE]	14/25 (56,0)	19,3 [10,91; 27,63]	0,56 [0,27; 1,18] 0,121
1	31/74 (41,9)	19,1 [14,03; NE]	27/48 (56,3)	11,2 [7,03; 16,82]	0,56 [0,33; 0,94] 0,026
Geschlecht (p-Wert des Interaktionsterms: 0,075)					
Männlich	20/61 (32,8)	NE [19,29; NE]	21/34 (61,8)	11,4 [7,10; 16,82]	0,36 [0,19; 0,67] <0,001
Weiblich	25/54 (46,3)	16,8 [9,23; NE]	20/39 (51,3)	14,2 [7,36; NE]	0,85 [0,47; 1,53] 0,599
Geografische Region (p-Wert des Interaktionsterms: 0,616)					
Ostasiatisch	23/65 (35,4)	NE [14,06; NE]	19/35 (54,3)	11,2 [7,10; NE]	0,50 [0,27; 0,93] 0,025
Nicht-Ostasiatisch	22/50 (44,0)	24,8 [13,93; NE]	22/38 (57,9)	15,6 [9,26; 24,87]	0,61 [0,34; 1,11] 0,103
Raucherstatus (p-Wert des Interaktionsterms: 0,772)					
Nie	31/72 (43,1)	19,3 [14,06; NE]	29/50 (58,0)	11,2 [8,77; 19,29]	0,59 [0,36; 0,99] 0,043
Ehemals/Aktuell	14/43 (32,6)	NE [14,03; NE]	12/23 (52,2)	16,8 [7,36; NE]	0,53 [0,24; 1,15] 0,104
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,416)					
Ja	13/23 (56,5)	11,2 [8,80; NE]	9/14 (64,3)	10,9 [3,78; NE]	0,67 [0,28; 1,60] 0,376
Nein	14/44 (31,8)	NE [16,56; NE]	8/23 (34,8)	NE [11,10; NE]	0,82 [0,34; 1,97] 0,656

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	18/48 (37,5)	NE [16,36; NE]	24/36 (66,7)	11,4 [7,03; 19,29]	0,41 [0,22; 0,77] 0,004
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,633)					
Ja	9/16 (56,3)	14,1 [8,94; NE]	10/13 (76,9)	6,9 [3,29; 15,64]	0,47 [0,19; 1,18] 0,102
Nein	36/98 (36,7)	NE [16,89; NE]	31/60 (51,7)	16,8 [11,10; 27,63]	0,58 [0,36; 0,95] 0,028
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,400)					
TPS <50%	19/48 (39,6)	NE [14,03; NE]	14/27 (51,9)	11,4 [4,86; NE]	0,56 [0,28; 1,13] 0,102
TPS ≥50%	10/19 (52,6)	16,8 [7,06; 24,84]	8/13 (61,5)	10,9 [6,74; NE]	0,91 [0,36; 2,31] 0,846
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,497)					
TPS <50%	19/48 (39,6)	NE [14,03; NE]	14/27 (51,9)	11,4 [4,86; NE]	0,56 [0,28; 1,13] 0,102
TPS ≥50%	10/19 (52,6)	16,8 [7,06; 24,84]	8/13 (61,5)	10,9 [6,74; NE]	0,91 [0,36; 2,31] 0,846
Unbekannt	16/48 (33,3)	NE [14,06; NE]	19/33 (57,6)	14,2 [9,26; NE]	0,47 [0,24; 0,92] 0,024
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,651)					
Negativ	11/26 (42,3)	19,3 [11,20; NE]	4/12 (33,3)	NE [4,73; NE]	0,92 [0,29; 2,98] 0,894
Positiv	21/49 (42,9)	24,8 [13,70; NE]	23/34 (67,6)	10,9 [6,74; 16,76]	0,51 [0,28; 0,92] 0,024
Unbekannt	13/40 (32,5)	NE [16,36; NE]	14/27 (51,9)	16,8 [9,26; NE]	0,55 [0,26; 1,18] 0,122
Krankheitsstatus (p-Wert des Interaktionsterms: 0,966)					
III	2/6 (33,3)	NE [6,80; NE]	3/6 (50,0)	11,4 [4,86; NE]	0,65 [0,11; 3,91] 0,634
IVA	13/44 (29,5)	NE [17,31; NE]	14/33 (42,4)	19,3 [10,91; NE]	0,58 [0,27; 1,24] 0,157

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	30/65 (46,2)	16,9 [12,45; NE]	24/34 (70,6)	9,9 [4,86; 15,64]	0,51 [0,30; 0,87] 0,012
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,524)					
Asiatisch	23/66 (34,8)	NE [14,06; NE]	19/35 (54,3)	11,2 [7,10; NE]	0,50 [0,27; 0,92] 0,023
Nicht asiatisch	22/49 (44,9)	19,1 [13,70; NE]	19/34 (55,9)	15,6 [7,36; NE]	0,64 [0,35; 1,20] 0,162
RET-Probenart (p-Wert des Interaktionsterms: 0,722)					
Blut	8/9 (88,9)	11,1 [4,67; 19,09]	8/10 (80,0)	6,7 [1,38; 14,19]	0,56 [0,20; 1,56] 0,261
Gewebe	37/106 (34,9)	NE [17,31; NE]	33/63 (52,4)	15,6 [10,94; 27,63]	0,56 [0,35; 0,90] 0,015
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,573)					
CCDC6	1/9 (11,1)	NE [13,70; NE]	2/6 (33,3)	16,8 [4,86; NE]	0,23 [0,02; 2,60] 0,199
KIF5B	26/50 (52,0)	16,8 [11,24; NE]	23/36 (63,9)	10,9 [6,74; 14,19]	0,48 [0,27; 0,85] 0,010
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

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 Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba
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Tabelle 59: Subgruppen für die Zeit bis zur ZNS-Progression bzw. zum ersten Auftreten einer ZNS-Metastase (BICR Beurteilung) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mZNS

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,668)					
<65 Jahre	5/71 (7,0)	NE [22,57; NE]	7/39 (17,9)	NE [11,40; NE]	0,31 [0,10; 0,98] 0,035
≥65 Jahre	3/36 (8,3)	NE [NE; NE]	3/23 (13,0)	NE [NE; NE]	0,52 [0,10; 2,58] 0,412
Baseline ECOG (p-Wert des Interaktionsterms: 0,856)					
0	4/34 (11,8)	NE [22,57; NE]	2/19 (10,5)	NE [NE; NE]	1,03 [0,19; 5,66] 0,974
1	4/73 (5,5)	NE [NE; NE]	8/43 (18,6)	NE [11,40; NE]	0,22 [0,07; 0,74] 0,007
Geografische Region (p-Wert des Interaktionsterms: 0,186)					
Ostasiatisch	2/64 (3,1)	NE [NE; NE]	8/33 (24,2)	NE [11,17; NE]	0,09 [0,02; 0,44] <0,001
Nicht-Ostasiatisch	6/43 (14,0)	NE [22,57; NE]	2/29 (6,9)	NE [NE; NE]	1,67 [0,33; 8,46] 0,529
Raucherstatus (p-Wert des Interaktionsterms: 0,332)					
Nie	7/66 (10,6)	NE [22,57; NE]	8/43 (18,6)	NE [11,40; NE]	0,45 [0,16; 1,25] 0,118
Ehemals/Aktuell	1/41 (2,4)	NE [NE; NE]	2/19 (10,5)	NE [NE; NE]	0,23 [0,02; 2,48] 0,182
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,455)					
Ja	6/23 (26,1)	NE [8,97; NE]	5/14 (35,7)	NE [4,76; NE]	0,61 [0,19; 2,01] 0,414
Nein	1/44 (2,3)	NE [NE; NE]	2/20 (10,0)	NE [11,17; NE]	0,15 [0,01; 1,72] 0,081
Unbekannt	1/40 (2,5)	NE [22,57; NE]	3/28 (10,7)	NE [NE; NE]	0,16 [0,02; 1,54] 0,070
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,146)					
Ja	2/15 (13,3)	NE [NE; NE]	4/11 (36,4)	6,9 [3,78; NE]	0,22 [0,04; 1,23] 0,065

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	6/91 (6,6)	NE [NE; NE]	6/51 (11,8)	NE [NE; NE]	0,47 [0,15; 1,46] 0,182
Krankheitsstatus (p-Wert des Interaktionsterms: 0,964)					
III*	0/5 (0,0)	NE [NE; NE]	2/5 (40,0)	NE [11,17; NE]	0,00 [0,00; NE] 0,187
IVA	1/38 (2,6)	NE [NE; NE]	3/27 (11,1)	NE [NE; NE]	0,20 [0,02; 1,94] 0,123
IVB	7/64 (10,9)	NE [NE; NE]	5/30 (16,7)	NE [NE; NE]	0,50 [0,16; 1,58] 0,231
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,148)					
Asiatisch	2/65 (3,1)	NE [NE; NE]	8/33 (24,2)	NE [11,17; NE]	0,09 [0,02; 0,44] <0,001
Nicht asiatisch	6/42 (14,3)	NE [22,57; NE]	2/25 (8,0)	NE [NE; NE]	1,40 [0,27; 7,23] 0,690
RET-Probenart (p-Wert des Interaktionsterms: 0,484)					
Blut	2/9 (22,2)	NE [4,80; NE]	2/9 (22,2)	NE [4,76; NE]	0,63 [0,09; 4,49] 0,641
Gewebe	6/98 (6,1)	NE [NE; NE]	8/53 (15,1)	NE [NE; NE]	0,34 [0,12; 0,97] 0,035
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,986)					
CCDC6*	0/7 (0,0)	NE [NE; NE]	0/4 (0,0)	NE [NE; NE]	NE
KIF5B	7/49 (14,3)	NE [22,57; NE]	4/34 (11,8)	NE [NE; NE]	0,81 [0,23; 2,80] 0,735

Subgruppe	Selpercatinib	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	Mediane Ereigniszeit ^a [95% KI]	
Datenschnitt: 01. Mai 2023; Modifizierte ZNS-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; bzw.: beziehungsweise; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mZNS: Modifizierte ZNS-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection; ZNS: Zentrales Nervensystem. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt.				
* SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.				

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_cnsp1_sub_mcns_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adttcns

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Tabelle 60: Subgruppen für die Dauer des Ansprechens (bestätigt, BICR Beurteilung) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit* [95% KI]	n/N (%)	Mediane Ereigniszeit* [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,714)					
<65 Jahre	23/66 (34,8)	24,2 [15,41; NE]	19/33 (57,6)	9,8 [6,01; NE]	0,45 [0,24; 0,83] 0,008
≥65 Jahre	10/33 (30,3)	NE [15,21; NE]	7/18 (38,9)	23,3 [9,89; NE]	0,51 [0,19; 1,37] 0,176
Baseline ECOG (p-Wert des Interaktionsterms: 0,816)					
0	11/36 (30,6)	24,2 [17,94; NE]	11/20 (55,0)	11,5 [6,01; NE]	0,43 [0,18; 0,99] 0,041
1	22/63 (34,9)	NE [14,95; NE]	15/31 (48,4)	12,7 [6,14; NE]	0,48 [0,25; 0,94] 0,029
Geschlecht (p-Wert des Interaktionsterms: 0,204)					
Männlich	17/57 (29,8)	24,2 [17,94; NE]	13/24 (54,2)	11,5 [6,14; NE]	0,32 [0,15; 0,67] 0,002
Weiblich	16/42 (38,1)	17,7 [12,32; NE]	13/27 (48,1)	12,7 [7,43; NE]	0,68 [0,32; 1,41] 0,298
Geografische Region (p-Wert des Interaktionsterms: 0,346)					
Ostasiatisch	19/59 (32,2)	NE [14,95; NE]	10/23 (43,5)	12,7 [7,92; NE]	0,61 [0,28; 1,31] 0,196
Nicht-Ostasiatisch	14/40 (35,0)	24,2 [15,41; NE]	16/28 (57,1)	10,8 [6,01; NE]	0,33 [0,16; 0,71] 0,003
Raucherstatus (p-Wert des Interaktionsterms: 0,655)					
Nie	24/63 (38,1)	24,2 [15,21; NE]	17/32 (53,1)	9,9 [6,14; NE]	0,51 [0,27; 0,96] 0,035
Ehemals/Aktuell	9/36 (25,0)	NE [15,41; NE]	9/19 (47,4)	12,7 [9,79; NE]	0,37 [0,15; 0,95] 0,033
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,788)					
Ja	8/18 (44,4)	24,2 [7,66; NE]	4/9 (44,4)	9,8 [3,45; NE]	0,66 [0,19; 2,27] 0,506
Nein	9/36 (25,0)	NE [15,21; NE]	5/15 (33,3)	NE [5,78; NE]	0,58 [0,19; 1,75] 0,328

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	16/45 (35,6)	NE [15,93; NE]	17/27 (63,0)	11,5 [6,01; 23,26]	0,39 [0,20; 0,78] 0,006
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,795)					
Ja	6/13 (46,2)	15,9 [7,75; NE]	6/8 (75,0)	7,6 [1,91; NE]	0,43 [0,14; 1,35] 0,138
Nein	27/86 (31,4)	24,2 [17,74; NE]	20/43 (46,5)	12,7 [9,79; NE]	0,48 [0,27; 0,87] 0,013
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,506)					
TPS <50%	15/42 (35,7)	NE [12,62; NE]	10/19 (52,6)	9,9 [4,21; NE]	0,41 [0,18; 0,95] 0,032
TPS ≥50%	7/15 (46,7)	17,7 [7,66; NE]	7/12 (58,3)	9,8 [3,98; NE]	0,53 [0,17; 1,61] 0,256
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,729)					
TPS <50%	15/42 (35,7)	NE [12,62; NE]	10/19 (52,6)	9,9 [4,21; NE]	0,41 [0,18; 0,95] 0,032
TPS ≥50%	7/15 (46,7)	17,7 [7,66; NE]	7/12 (58,3)	9,8 [3,98; NE]	0,53 [0,17; 1,61] 0,256
Unbekannt	11/42 (26,2)	NE [15,93; NE]	9/20 (45,0)	18,0 [9,59; NE]	0,49 [0,20; 1,17] 0,103
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,874)					
Negativ	10/24 (41,7)	17,9 [9,79; NE]	3/8 (37,5)	NE [1,91; NE]	0,49 [0,12; 2,05] 0,317
Positiv	14/40 (35,0)	24,2 [12,62; NE]	16/26 (61,5)	9,9 [5,55; 23,26]	0,41 [0,20; 0,86] 0,015
Unbekannt	9/35 (25,7)	NE [15,93; NE]	7/17 (41,2)	18,0 [9,59; NE]	0,57 [0,21; 1,53] 0,260
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,408)					
Asiatisch	19/60 (31,7)	NE [14,95; NE]	10/23 (43,5)	12,7 [7,92; NE]	0,60 [0,28; 1,29] 0,185
Nicht asiatisch	14/39 (35,9)	24,2 [15,41; NE]	14/26 (53,8)	10,8 [5,78; NE]	0,35 [0,16; 0,76] 0,006
RET-Probenart (p-Wert des Interaktionsterms: 0,867)					

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Blut	7/8 (87,5)	9,8 [5,36; 17,74]	7/9 (77,8)	5,4 [1,91; NE]	0,52 [0,17; 1,57] 0,250
Gewebe	26/91 (28,6)	NE [24,18; NE]	19/42 (45,2)	18,0 [9,66; NE]	0,48 [0,27; 0,88] 0,015
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,354)					
CCDC6	1/9 (11,1)	NE [12,32; NE]	2/5 (40,0)	12,7 [3,45; NE]	0,13 [0,01; 1,53] 0,062
KIF5B	22/45 (48,9)	17,7 [9,86; NE]	16/27 (59,3)	9,8 [5,55; NE]	0,43 [0,22; 0,85] 0,013
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw. <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw. <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_dorc_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adtteir

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Tabelle 61: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Fatigue (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,196)					
<65 Jahre	41/76 (53,9)	5,1 [2,23; 18,73]	24/45 (53,3)	3,6 [1,54; 6,28]	0,77 [0,47; 1,28] 0,301
≥65 Jahre	25/39 (64,1)	1,4 [0,82; 4,21]	16/28 (57,1)	2,6 [0,95; 5,52]	1,39 [0,74; 2,63] 0,304
Baseline ECOG (p-Wert des Interaktionsterms: 0,942)					
0	26/41 (63,4)	2,7 [1,45; 8,64]	14/25 (56,0)	2,4 [0,95; NE]	0,88 [0,45; 1,69] 0,691
1	40/74 (54,1)	4,2 [1,45; 19,35]	26/48 (54,2)	3,6 [1,54; 5,78]	0,94 [0,57; 1,55] 0,779
Geografische Region (p-Wert des Interaktionsterms: 0,731)					
Ostasiatisch	38/65 (58,5)	1,5 [0,85; 14,32]	21/35 (60,0)	2,5 [0,99; NE]	1,03 [0,60; 1,76] 0,969
Nicht-Ostasiatisch	28/50 (56,0)	4,2 [2,23; 18,73]	19/38 (50,0)	3,6 [1,48; 6,28]	0,82 [0,45; 1,48] 0,505
Raucherstatus (p-Wert des Interaktionsterms: 0,071)					
Nie	37/72 (51,4)	4,3 [1,48; NE]	28/50 (56,0)	2,5 [1,28; 5,36]	0,72 [0,44; 1,18] 0,185
Ehemals/Aktuell	29/43 (67,4)	2,7 [0,79; 6,28]	12/23 (52,2)	5,4 [0,92; NE]	1,46 [0,74; 2,87] 0,291
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,647)					
Ja	12/23 (52,2)	10,9 [0,76; NE]	7/14 (50,0)	1,5 [0,72; NE]	0,74 [0,28; 1,94] 0,548
Nein	25/44 (56,8)	3,4 [0,85; 5,06]	14/23 (60,9)	5,0 [0,95; NE]	1,15 [0,60; 2,21] 0,703
Unbekannt	29/48 (60,4)	3,6 [1,41; 14,72]	19/36 (52,8)	2,5 [1,48; NE]	0,96 [0,54; 1,72] 0,864
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,661)					
Ja	5/16 (31,3)	NE [1,45; NE]	2/13 (15,4)	NE [3,98; NE]	1,35 [0,26; 6,97] 0,721

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	60/98 (61,2)	2,9 [1,45; 5,09]	38/60 (63,3)	2,4 [1,48; 5,36]	0,91 [0,60; 1,38] 0,624
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,971)					
Negativ	14/26 (53,8)	3,6 [1,38; NE]	7/12 (58,3)	2,5 [0,79; NE]	0,94 [0,37; 2,35] 0,907
Positiv	28/49 (57,1)	2,7 [1,41; 18,73]	18/34 (52,9)	2,6 [1,48; 5,65]	0,95 [0,52; 1,74] 0,865
Unbekannt	24/40 (60,0)	4,2 [0,85; 19,35]	15/27 (55,6)	5,4 [1,54; 6,28]	1,00 [0,52; 1,93] 0,947
Krankheitsstatus (p-Wert des Interaktionsterms: 0,794)					
III	4/6 (66,7)	3,4 [0,76; NE]	4/6 (66,7)	4,6 [2,33; NE]	1,11 [0,25; 5,01] 0,919
IVA	27/44 (61,4)	2,2 [0,85; 5,42]	21/33 (63,6)	1,5 [0,89; 5,36]	0,89 [0,50; 1,57] 0,672
IVB	35/65 (53,8)	4,1 [1,48; 19,35]	15/34 (44,1)	5,4 [1,48; NE]	0,99 [0,54; 1,82] 0,943
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,649)					
Asiatisch	39/66 (59,1)	3,2 [0,85; 14,32]	21/35 (60,0)	2,5 [0,99; NE]	1,03 [0,61; 1,76] 0,957
Nicht asiatisch	27/49 (55,1)	4,2 [2,17; 18,73]	17/34 (50,0)	3,6 [1,54; 6,28]	0,79 [0,42; 1,46] 0,443
RET-Probenart (p-Wert des Interaktionsterms: 0,819)					
Blut	5/9 (55,6)	5,4 [0,76; NE]	4/10 (40,0)	5,0 [0,72; NE]	0,78 [0,21; 2,92] 0,707
Gewebe	61/106 (57,5)	3,2 [1,48; 8,64]	36/63 (57,1)	2,5 [1,48; 5,52]	0,93 [0,62; 1,41] 0,711
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,717)					
CCDC6	5/9 (55,6)	2,7 [0,76; NE]	5/6 (83,3)	3,1 [0,92; NE]	0,76 [0,22; 2,64] 0,615
KIF5B	27/50 (54,0)	5,4 [1,45; 22,21]	16/36 (44,4)	4,0 [1,48; NE]	0,80 [0,42; 1,51] 0,485

Subgruppe	Selpercatinib	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	Mediane Ereigniszeit ^a [95% KI]	
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht erreehenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt.				
Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.				

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10fa_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteqol_gba

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Tabelle 62: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Übelkeit und Erbrechen (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,824)					
<65 Jahre	26/76 (34,2)	NE [10,41; NE]	23/45 (51,1)	2,9 [1,48; 12,02]	0,32 [0,18; 0,57] <0,001
≥65 Jahre	14/39 (35,9)	NE [5,42; NE]	19/28 (67,9)	3,3 [0,89; 8,05]	0,30 [0,15; 0,61] <0,001
Baseline ECOG (p-Wert des Interaktionsterms: 0,709)					
0	15/41 (36,6)	NE [4,93; NE]	15/25 (60,0)	3,3 [0,95; 9,10]	0,33 [0,16; 0,70] 0,002
1	25/74 (33,8)	NE [10,41; NE]	27/48 (56,3)	2,8 [1,64; 8,48]	0,29 [0,16; 0,51] <0,001
Geschlecht (p-Wert des Interaktionsterms: 0,491)					
Männlich	18/61 (29,5)	NE [16,82; NE]	20/34 (58,8)	3,5 [1,64; 9,17]	0,24 [0,12; 0,48] <0,001
Weiblich	22/54 (40,7)	10,4 [4,93; NE]	22/39 (56,4)	2,3 [0,82; 8,05]	0,38 [0,21; 0,69] 0,001
Geografische Region (p-Wert des Interaktionsterms: 0,864)					
Ostasiatisch	22/65 (33,8)	NE [11,17; NE]	21/35 (60,0)	3,3 [1,94; 9,17]	0,32 [0,17; 0,60] <0,001
Nicht-Ostasiatisch	18/50 (36,0)	16,8 [7,89; NE]	21/38 (55,3)	3,1 [0,82; 7,75]	0,28 [0,15; 0,55] <0,001
Raucherstatus (p-Wert des Interaktionsterms: 0,568)					
Nie	27/72 (37,5)	17,2 [9,00; NE]	28/50 (56,0)	3,3 [1,94; 8,05]	0,33 [0,19; 0,57] <0,001
Ehemals/Aktuell	13/43 (30,2)	NE [8,64; NE]	14/23 (60,9)	2,7 [0,89; 13,34]	0,27 [0,12; 0,58] <0,001
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,103)					
Ja	10/23 (43,5)	7,9 [3,22; NE]	7/14 (50,0)	3,5 [0,72; NE]	0,40 [0,15; 1,09] 0,066
Nein	17/44 (38,6)	14,6 [5,03; NE]	13/23 (56,5)	7,8 [0,99; 13,34]	0,45 [0,22; 0,96] 0,034

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	13/48 (27,1)	NE [16,82; NE]	22/36 (61,1)	2,3 [0,89; 8,48]	0,19 [0,09; 0,39] <0,001
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,510)					
Ja	4/16 (25,0)	NE [7,66; NE]	2/13 (15,4)	NE [0,95; NE]	0,45 [0,07; 2,89] 0,387
Nein	36/98 (36,7)	NE [10,41; NE]	40/60 (66,7)	2,9 [1,64; 6,97]	0,30 [0,19; 0,48] <0,001
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,484)					
TPS <50%	17/48 (35,4)	NE [8,64; NE]	19/27 (70,4)	2,9 [0,99; 9,10]	0,27 [0,13; 0,53] <0,001
TPS ≥50%	7/19 (36,8)	10,4 [4,93; NE]	5/13 (38,5)	1,5 [0,72; NE]	0,43 [0,13; 1,36] 0,139
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,820)					
TPS <50%	17/48 (35,4)	NE [8,64; NE]	19/27 (70,4)	2,9 [0,99; 9,10]	0,27 [0,13; 0,53] <0,001
TPS ≥50%	7/19 (36,8)	10,4 [4,93; NE]	5/13 (38,5)	1,5 [0,72; NE]	0,43 [0,13; 1,36] 0,139
Unbekannt	16/48 (33,3)	NE [9,00; NE]	18/33 (54,5)	3,9 [0,95; 8,48]	0,30 [0,15; 0,62] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,081)					
Negativ	4/26 (15,4)	NE [NE; NE]	9/12 (75,0)	2,7 [0,89; NE]	0,14 [0,04; 0,46] <0,001
Positiv	24/49 (49,0)	9,0 [5,42; 16,82]	18/34 (52,9)	3,1 [0,82; 9,10]	0,44 [0,24; 0,83] 0,009
Unbekannt	12/40 (30,0)	NE [11,17; NE]	15/27 (55,6)	3,9 [0,95; 9,17]	0,28 [0,13; 0,63] 0,001
Krankheitsstatus (p-Wert des Interaktionsterms: 0,500)					
III	3/6 (50,0)	6,7 [1,38; NE]	4/6 (66,7)	5,9 [0,72; NE]	0,54 [0,10; 2,97] 0,469
IVA	16/44 (36,4)	NE [4,93; NE]	20/33 (60,6)	2,9 [0,89; 9,17]	0,36 [0,18; 0,71] 0,002

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	21/65 (32,3)	NE [11,17; NE]	18/34 (52,9)	3,1 [0,99; 8,05]	0,24 [0,12; 0,46] <0,001
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,826)					
Asiatisch	23/66 (34,8)	NE [11,17; NE]	21/35 (60,0)	3,3 [1,94; 9,17]	0,33 [0,18; 0,61] <0,001
Nicht asiatisch	17/49 (34,7)	16,8 [8,64; NE]	18/34 (52,9)	3,4 [0,82; 9,10]	0,28 [0,14; 0,57] <0,001
RET-Probenart (p-Wert des Interaktionsterms: 0,602)					
Blut	4/9 (44,4)	NE [2,83; NE]	3/10 (30,0)	NE [0,76; NE]	0,50 [0,11; 2,35] 0,384
Gewebe	36/106 (34,0)	NE [11,93; NE]	39/63 (61,9)	3,1 [1,94; 7,75]	0,29 [0,18; 0,47] <0,001
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,599)					
CCDC6	4/9 (44,4)	NE [0,76; NE]	5/6 (83,3)	2,0 [0,72; NE]	0,37 [0,10; 1,39] 0,132
KIF5B	22/50 (44,0)	11,2 [6,74; NE]	16/36 (44,4)	3,5 [0,89; 9,10]	0,45 [0,23; 0,88] 0,017
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. ***** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10nv_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 63: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Schmerz (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,776)					
0	18/41 (43,9)	10,4 [1,91; NE]	12/25 (48,0)	4,4 [0,95; NE]	0,76 [0,37; 1,58] 0,456
1	36/74 (48,6)	7,7 [3,48; 22,97]	26/48 (54,2)	4,7 [1,61; 9,46]	0,64 [0,38; 1,07] 0,081
Geschlecht (p-Wert des Interaktionsterms: 0,412)					
Männlich	30/61 (49,2)	10,4 [2,96; NE]	18/34 (52,9)	6,3 [2,27; NE]	0,79 [0,43; 1,43] 0,417
Weiblich	24/54 (44,4)	7,7 [4,63; NE]	20/39 (51,3)	2,6 [0,82; 9,46]	0,59 [0,33; 1,07] 0,083
Geografische Region (p-Wert des Interaktionsterms: 0,461)					
Ostasiatisch	32/65 (49,2)	10,4 [4,99; NE]	21/35 (60,0)	2,6 [1,51; 9,46]	0,58 [0,33; 1,01] 0,054
Nicht-Ostasiatisch	22/50 (44,0)	7,0 [3,09; NE]	17/38 (44,7)	4,7 [2,27; NE]	0,83 [0,44; 1,58] 0,560
Raucherstatus (p-Wert des Interaktionsterms: 0,644)					
Nie	35/72 (48,6)	9,8 [3,48; NE]	27/50 (54,0)	4,2 [1,58; 7,16]	0,63 [0,38; 1,05] 0,073
Ehemals/Aktuell	19/43 (44,2)	10,4 [3,48; NE]	11/23 (47,8)	4,9 [0,95; NE]	0,81 [0,38; 1,70] 0,572
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,371)					
Ja	13/23 (56,5)	7,7 [1,41; 22,97]	6/14 (42,9)	4,2 [0,76; NE]	0,79 [0,28; 2,19] 0,643
Nein	23/44 (52,3)	6,1 [2,83; NE]	14/23 (60,9)	4,7 [1,68; 7,16]	0,81 [0,42; 1,59] 0,527
Unbekannt	18/48 (37,5)	NE [4,21; NE]	18/36 (50,0)	4,4 [0,89; 9,92]	0,51 [0,26; 0,99] 0,042
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,764)					
Ja	7/16 (43,8)	7,7 [1,41; NE]	4/13 (30,8)	4,9 [0,79; NE]	0,88 [0,25; 3,03] 0,827

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	46/98 (46,9)	10,4 [4,99; 22,97]	34/60 (56,7)	4,2 [1,61; 7,16]	0,65 [0,42; 1,02] 0,060
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,210)					
TPS <50%	26/48 (54,2)	9,8 [2,14; 22,97]	15/27 (55,6)	4,7 [1,68; NE]	0,94 [0,50; 1,79] 0,841
TPS ≥50%	9/19 (47,4)	7,0 [2,23; NE]	7/13 (53,8)	2,9 [0,72; 6,31]	0,40 [0,14; 1,12] 0,071
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,333)					
TPS <50%	26/48 (54,2)	9,8 [2,14; 22,97]	15/27 (55,6)	4,7 [1,68; NE]	0,94 [0,50; 1,79] 0,841
TPS ≥50%	9/19 (47,4)	7,0 [2,23; NE]	7/13 (53,8)	2,9 [0,72; 6,31]	0,40 [0,14; 1,12] 0,071
Unbekannt	19/48 (39,6)	NE [3,58; NE]	16/33 (48,5)	6,2 [0,89; 9,92]	0,60 [0,31; 1,16] 0,123
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,262)					
Negativ	14/26 (53,8)	9,8 [0,82; NE]	7/12 (58,3)	4,7 [1,64; NE]	0,96 [0,38; 2,42] 0,918
Positiv	26/49 (53,1)	7,0 [2,23; 22,97]	16/34 (47,1)	4,2 [0,82; NE]	0,80 [0,43; 1,50] 0,479
Unbekannt	14/40 (35,0)	NE [4,63; NE]	15/27 (55,6)	6,2 [0,89; 9,92]	0,45 [0,22; 0,94] 0,030
Krankheitsstatus (p-Wert des Interaktionsterms: 0,968)					
III	4/6 (66,7)	2,8 [0,76; NE]	6/6 (100,0)	3,4 [1,51; NE]	1,08 [0,27; 4,36] 0,909
IVA	23/44 (52,3)	5,4 [1,54; 20,93]	18/33 (54,5)	2,9 [0,89; NE]	0,80 [0,43; 1,50] 0,488
IVB	27/65 (41,5)	21,5 [5,75; NE]	14/34 (41,2)	6,3 [1,61; NE]	0,70 [0,37; 1,34] 0,282
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,460)					
Asiatisch	32/66 (48,5)	10,4 [4,99; NE]	21/35 (60,0)	2,6 [1,51; 9,46]	0,57 [0,33; 0,99] 0,046

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	22/49 (44,9)	7,0 [2,96; NE]	15/34 (44,1)	4,7 [2,27; NE]	0,83 [0,43; 1,61] 0,575
RET-Probenart (p-Wert des Interaktionsterms: 0,437)					
Blut	4/9 (44,4)	7,7 [0,76; NE]	4/10 (40,0)	4,2 [0,76; NE]	0,13 [0,01; 1,23] 0,036
Gewebe	50/106 (47,2)	10,4 [3,48; 22,97]	34/63 (54,0)	4,7 [1,68; 9,46]	0,72 [0,46; 1,12] 0,138
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,687)					
CCDC6	5/9 (55,6)	4,2 [0,76; NE]	3/6 (50,0)	4,4 [0,76; NE]	1,21 [0,29; 5,07] 0,800
KIF5B	29/50 (58,0)	7,0 [2,83; 20,93]	18/36 (50,0)	4,2 [1,58; 9,92]	0,73 [0,40; 1,33] 0,288
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. **** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. ***** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10pa_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 64: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Dyspnoe (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,313)					
<65 Jahre	24/76 (31,6)	NE [14,49; NE]	15/45 (33,3)	NE [4,17; NE]	0,78 [0,41; 1,49] 0,433
≥65 Jahre	20/39 (51,3)	6,3 [2,07; NE]	11/28 (39,3)	9,9 [1,61; NE]	1,28 [0,61; 2,67] 0,513
Baseline ECOG (p-Wert des Interaktionsterms: 0,247)					
0	16/41 (39,0)	15,4 [6,44; NE]	11/25 (44,0)	4,2 [0,95; NE]	0,60 [0,27; 1,30] 0,188
1	28/74 (37,8)	NE [6,24; NE]	15/48 (31,3)	NE [5,78; NE]	1,16 [0,62; 2,18] 0,646
Geschlecht (p-Wert des Interaktionsterms: 0,455)					
Männlich	25/61 (41,0)	15,4 [5,65; NE]	12/34 (35,3)	NE [5,39; NE]	1,11 [0,56; 2,22] 0,773
Weiblich	19/54 (35,2)	14,5 [8,35; NE]	14/39 (35,9)	NE [1,45; NE]	0,78 [0,39; 1,56] 0,478
Geografische Region (p-Wert des Interaktionsterms: 0,528)					
Ostasiatisch	26/65 (40,0)	NE [3,45; NE]	13/35 (37,1)	NE [2,83; NE]	1,10 [0,57; 2,14] 0,786
Nicht-Ostasiatisch	18/50 (36,0)	15,4 [8,35; NE]	13/38 (34,2)	NE [3,35; NE]	0,71 [0,34; 1,45] 0,340
Raucherstatus (p-Wert des Interaktionsterms: 0,324)					
Nie	26/72 (36,1)	NE [11,07; NE]	18/50 (36,0)	NE [2,46; NE]	0,77 [0,42; 1,40] 0,385
Ehemals/Aktuell	18/43 (41,9)	13,1 [2,63; NE]	8/23 (34,8)	NE [3,91; NE]	1,30 [0,56; 2,99] 0,545
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,528)					
Ja	7/23 (30,4)	NE [2,63; NE]	6/14 (42,9)	4,2 [0,76; NE]	0,51 [0,16; 1,60] 0,240
Nein	19/44 (43,2)	11,1 [2,07; NE]	10/23 (43,5)	7,4 [1,45; NE]	1,04 [0,48; 2,25] 0,918

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	18/48 (37,5)	NE [6,44; NE]	10/36 (27,8)	NE [4,90; NE]	1,04 [0,48; 2,25] 0,932
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,347)					
Ja	5/16 (31,3)	NE [4,34; NE]	1/13 (7,7)	NE [5,39; NE]	2,23 [0,26; 19,30] 0,455
Nein	39/98 (39,8)	15,4 [6,44; NE]	25/60 (41,7)	NE [3,35; NE]	0,88 [0,53; 1,46] 0,618
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,095)					
TPS <50%	22/48 (45,8)	11,1 [3,29; NE]	9/27 (33,3)	NE [3,91; NE]	1,39 [0,64; 3,02] 0,410
TPS ≥50%	4/19 (21,1)	NE [8,35; NE]	5/13 (38,5)	3,8 [0,72; NE]	0,26 [0,07; 0,98] 0,033
Unbekannt	18/48 (37,5)	NE [5,09; NE]	12/33 (36,4)	NE [2,83; NE]	0,94 [0,45; 1,95] 0,844
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,735)					
Negativ	9/26 (34,6)	NE [3,45; NE]	5/12 (41,7)	NE [0,92; NE]	0,76 [0,25; 2,28] 0,622
Positiv	21/49 (42,9)	13,9 [5,03; NE]	10/34 (29,4)	NE [3,35; NE]	1,12 [0,52; 2,38] 0,784
Unbekannt	14/40 (35,0)	NE [5,09; NE]	11/27 (40,7)	9,9 [1,68; NE]	0,80 [0,36; 1,76] 0,563
Krankheitsstatus (p-Wert des Interaktionsterms: 0,222)					
III	1/6 (16,7)	NE [2,07; NE]	3/6 (50,0)	9,9 [1,45; NE]	0,35 [0,04; 3,38] 0,341
IVA	18/44 (40,9)	15,4 [3,29; NE]	16/33 (48,5)	4,9 [1,61; NE]	0,76 [0,38; 1,49] 0,420
IVB	25/65 (38,5)	14,5 [6,28; NE]	7/34 (20,6)	NE [5,39; NE]	1,56 [0,67; 3,60] 0,298
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,469)					
Asiatisch	26/66 (39,4)	NE [3,45; NE]	13/35 (37,1)	NE [2,83; NE]	1,08 [0,55; 2,10] 0,831

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	18/49 (36,7)	15,4 [8,35; NE]	12/34 (35,3)	5,8 [2,46; NE]	0,65 [0,31; 1,37] 0,252
RET-Probenart (p-Wert des Interaktionsterms: 0,577)					
Blut	2/9 (22,2)	NE [0,79; NE]	2/10 (20,0)	NE [0,72; NE]	0,47 [0,06; 3,51] 0,453
Gewebe	42/106 (39,6)	15,4 [6,44; NE]	24/63 (38,1)	NE [4,17; NE]	0,96 [0,58; 1,59] 0,868
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,781)					
CCDC6	3/9 (33,3)	NE [0,76; NE]	2/6 (33,3)	NE [0,92; NE]	1,11 [0,18; 6,71] 0,975
KIF5B	18/50 (36,0)	15,4 [11,07; NE]	12/36 (33,3)	NE [3,35; NE]	0,62 [0,30; 1,31] 0,211
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10dy_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba
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Tabelle 65: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Schlaflosigkeit (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,174)					
<65 Jahre	31/76 (40,8)	15,3 [4,86; NE]	16/45 (35,6)	12,0 [4,21; NE]	0,94 [0,51; 1,72] 0,839
≥65 Jahre	21/39 (53,8)	7,1 [3,38; NE]	8/28 (28,6)	22,4 [3,02; NE]	1,84 [0,81; 4,15] 0,139
Baseline ECOG (p-Wert des Interaktionsterms: 0,954)					
0	17/41 (41,5)	11,0 [3,98; NE]	8/25 (32,0)	NE [2,92; NE]	1,21 [0,52; 2,80] 0,665
1	35/74 (47,3)	10,4 [4,80; NE]	16/48 (33,3)	19,0 [4,63; NE]	1,18 [0,65; 2,14] 0,577
Geschlecht (p-Wert des Interaktionsterms: 0,931)					
Männlich	27/61 (44,3)	13,8 [4,99; NE]	10/34 (29,4)	22,4 [4,24; NE]	1,24 [0,60; 2,56] 0,571
Weiblich	25/54 (46,3)	8,3 [3,88; NE]	14/39 (35,9)	12,0 [2,83; NE]	1,22 [0,64; 2,36] 0,543
Geografische Region (p-Wert des Interaktionsterms: 0,587)					
Ostasiatisch	32/65 (49,2)	7,1 [3,98; NE]	15/35 (42,9)	12,0 [2,83; NE]	1,05 [0,57; 1,94] 0,875
Nicht-Ostasiatisch	20/50 (40,0)	11,1 [4,99; NE]	9/38 (23,7)	NE [4,24; NE]	1,43 [0,65; 3,15] 0,368
Raucherstatus (p-Wert des Interaktionsterms: 0,843)					
Nie	33/72 (45,8)	8,3 [4,37; NE]	17/50 (34,0)	19,0 [3,22; NE]	1,18 [0,66; 2,12] 0,577
Ehemals/Aktuell	19/43 (44,2)	13,8 [4,21; NE]	7/23 (30,4)	NE [4,21; NE]	1,30 [0,55; 3,10] 0,545
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,604)					
Ja	9/23 (39,1)	13,8 [1,45; NE]	3/14 (21,4)	NE [4,24; NE]	1,58 [0,42; 5,90] 0,494
Nein	23/44 (52,3)	4,4 [3,98; 11,07]	9/23 (39,1)	NE [2,83; NE]	1,50 [0,69; 3,24] 0,306

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	20/48 (41,7)	NE [5,13; NE]	12/36 (33,3)	19,0 [3,22; NE]	0,94 [0,46; 1,92] 0,863
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,626)					
Ja	5/16 (31,3)	NE [4,34; NE]	2/13 (15,4)	NE [0,95; NE]	0,97 [0,18; 5,16] 0,957
Nein	47/98 (48,0)	8,9 [4,21; NE]	22/60 (36,7)	19,0 [4,63; NE]	1,29 [0,78; 2,15] 0,321
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,693)					
TPS <50%	24/48 (50,0)	8,9 [4,37; NE]	8/27 (29,6)	NE [5,09; NE]	1,75 [0,79; 3,91] 0,164
TPS ≥50%	7/19 (36,8)	15,3 [4,21; NE]	3/13 (23,1)	NE [2,37; NE]	1,33 [0,34; 5,15] 0,682
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,508)					
TPS <50%	24/48 (50,0)	8,9 [4,37; NE]	8/27 (29,6)	NE [5,09; NE]	1,75 [0,79; 3,91] 0,164
TPS ≥50%	7/19 (36,8)	15,3 [4,21; NE]	3/13 (23,1)	NE [2,37; NE]	1,33 [0,34; 5,15] 0,682
Unbekannt	21/48 (43,8)	13,8 [2,83; NE]	13/33 (39,4)	19,0 [2,83; NE]	0,95 [0,48; 1,91] 0,887
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,324)					
Negativ	10/26 (38,5)	NE [4,21; NE]	2/12 (16,7)	NE [2,92; NE]	2,79 [0,61; 12,75] 0,168
Positiv	25/49 (51,0)	7,1 [4,34; 15,28]	10/34 (29,4)	12,0 [4,24; NE]	1,40 [0,67; 2,91] 0,373
Unbekannt	17/40 (42,5)	13,8 [2,83; NE]	12/27 (44,4)	19,0 [2,37; NE]	0,85 [0,40; 1,78] 0,663
Krankheitsstatus (p-Wert des Interaktionsterms: 0,754)					
III	3/6 (50,0)	15,3 [2,83; NE]	4/6 (66,7)	12,5 [1,45; NE]	0,82 [0,16; 4,08] 0,806
IVA	21/44 (47,7)	5,0 [3,52; NE]	11/33 (33,3)	NE [4,21; NE]	1,48 [0,71; 3,07] 0,289

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	28/65 (43,1)	11,0 [4,99; NE]	9/34 (26,5)	19,0 [4,24; NE]	1,26 [0,59; 2,67] 0,556
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,784)					
Asiatisch	32/66 (48,5)	8,9 [4,17; NE]	15/35 (42,9)	12,0 [2,83; NE]	1,03 [0,56; 1,91] 0,926
Nicht asiatisch	20/49 (40,8)	11,0 [4,86; NE]	9/34 (26,5)	NE [4,21; NE]	1,24 [0,56; 2,72] 0,596
RET-Probenart (p-Wert des Interaktionsterms: 0,453)					
Blut	5/9 (55,6)	6,1 [0,76; NE]	4/10 (40,0)	4,2 [0,85; NE]	0,82 [0,21; 3,13] 0,754
Gewebe	47/106 (44,3)	11,0 [4,99; NE]	20/63 (31,7)	19,0 [12,02; NE]	1,29 [0,76; 2,18] 0,341
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,775)					
CCDC6	6/9 (66,7)	5,0 [0,76; NE]	3/6 (50,0)	NE [2,37; NE]	1,41 [0,35; 5,69] 0,629
KIF5B	27/50 (54,0)	8,3 [4,21; 15,28]	9/36 (25,0)	22,4 [4,63; NE]	1,74 [0,82; 3,71] 0,148
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10sl_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 66: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Appetitlosigkeit (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,692)					
<65 Jahre	24/76 (31,6)	26,3 [12,62; NE]	16/45 (35,6)	NE [1,54; NE]	0,58 [0,30; 1,09] 0,087
≥65 Jahre	17/39 (43,6)	6,3 [2,14; NE]	14/28 (50,0)	5,0 [1,61; NE]	0,80 [0,39; 1,62] 0,531
Baseline ECOG (p-Wert des Interaktionsterms: 0,194)					
0	16/41 (39,0)	26,3 [6,44; NE]	14/25 (56,0)	4,2 [0,99; 7,72]	0,41 [0,20; 0,85] 0,014
1	25/74 (33,8)	NE [7,82; NE]	16/48 (33,3)	NE [6,31; NE]	0,81 [0,43; 1,52] 0,502
Geschlecht (p-Wert des Interaktionsterms: 0,887)					
Männlich	21/61 (34,4)	NE [8,35; NE]	15/34 (44,1)	6,6 [2,83; NE]	0,62 [0,32; 1,21] 0,160
Weiblich	20/54 (37,0)	19,9 [6,44; NE]	15/39 (38,5)	7,7 [1,48; NE]	0,64 [0,32; 1,26] 0,192
Geografische Region (p-Wert des Interaktionsterms: 0,368)					
Ostasiatisch	24/65 (36,9)	19,9 [7,82; NE]	18/35 (51,4)	5,0 [0,99; NE]	0,52 [0,28; 0,96] 0,033
Nicht-Ostasiatisch	17/50 (34,0)	26,3 [6,87; NE]	12/38 (31,6)	NE [4,93; NE]	0,79 [0,37; 1,66] 0,528
Raucherstatus (p-Wert des Interaktionsterms: 0,752)					
Nie	26/72 (36,1)	26,3 [12,62; NE]	19/50 (38,0)	6,6 [2,14; NE]	0,65 [0,36; 1,19] 0,156
Ehemals/Aktuell	15/43 (34,9)	NE [6,44; NE]	11/23 (47,8)	7,7 [0,99; NE]	0,60 [0,28; 1,32] 0,198
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,103)					
Ja	6/23 (26,1)	NE [6,28; NE]	7/14 (50,0)	4,2 [0,76; NE]	0,23 [0,07; 0,73] 0,007
Nein	18/44 (40,9)	12,6 [4,17; NE]	9/23 (39,1)	NE [2,14; NE]	1,10 [0,49; 2,45] 0,818

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	17/48 (35,4)	26,3 [6,97; NE]	14/36 (38,9)	7,7 [1,54; NE]	0,54 [0,26; 1,12] 0,093
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,520)					
Ja	3/16 (18,8)	NE [6,28; NE]	1/13 (7,7)	NE [6,08; NE]	1,10 [0,11; 10,67] 0,932
Nein	38/98 (38,8)	19,9 [6,97; NE]	29/60 (48,3)	6,3 [1,61; NE]	0,62 [0,38; 1,01] 0,051
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,243)					
TPS <50%	21/48 (43,8)	12,6 [4,01; NE]	12/27 (44,4)	9,9 [1,41; NE]	0,83 [0,40; 1,71] 0,622
TPS ≥50%	5/19 (26,3)	NE [5,42; NE]	5/13 (38,5)	4,6 [0,72; NE]	0,39 [0,11; 1,34] 0,121
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,465)					
TPS <50%	21/48 (43,8)	12,6 [4,01; NE]	12/27 (44,4)	9,9 [1,41; NE]	0,83 [0,40; 1,71] 0,622
TPS ≥50%	5/19 (26,3)	NE [5,42; NE]	5/13 (38,5)	4,6 [0,72; NE]	0,39 [0,11; 1,34] 0,121
Unbekannt	15/48 (31,3)	26,3 [19,91; NE]	13/33 (39,4)	6,6 [2,14; NE]	0,53 [0,25; 1,13] 0,092
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,723)					
Negativ	9/26 (34,6)	NE [4,01; NE]	6/12 (50,0)	9,9 [0,79; NE]	0,60 [0,21; 1,72] 0,345
Positiv	22/49 (44,9)	7,0 [4,93; NE]	14/34 (41,2)	4,9 [1,48; NE]	0,73 [0,37; 1,44] 0,360
Unbekannt	10/40 (25,0)	NE [19,91; NE]	10/27 (37,0)	NE [2,14; NE]	0,46 [0,19; 1,13] 0,082
Krankheitsstatus (p-Wert des Interaktionsterms: 0,343)					
III	3/6 (50,0)	NE [0,76; NE]	2/6 (33,3)	NE [0,76; NE]	1,44 [0,24; 8,64] 0,685
IVA	17/44 (38,6)	18,6 [5,68; NE]	16/33 (48,5)	6,6 [0,99; NE]	0,57 [0,29; 1,14] 0,107

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	21/65 (32,3)	26,3 [19,91; NE]	12/34 (35,3)	7,7 [4,21; NE]	0,61 [0,30; 1,26] 0,178
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,284)					
Asiatisch	24/66 (36,4)	NE [7,82; NE]	18/35 (51,4)	5,0 [0,99; NE]	0,51 [0,27; 0,94] 0,028
Nicht asiatisch	17/49 (34,7)	26,3 [6,87; NE]	10/34 (29,4)	NE [4,93; NE]	0,86 [0,39; 1,90] 0,713
RET-Probenart (p-Wert des Interaktionsterms: 0,480)					
Blut	4/9 (44,4)	26,3 [4,93; NE]	2/10 (20,0)	NE [1,61; NE]	0,57 [0,09; 3,51] 0,552
Gewebe	37/106 (34,9)	NE [8,35; NE]	28/63 (44,4)	6,6 [2,83; NE]	0,61 [0,37; 0,99] 0,045
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,134)					
CCDC6	6/9 (66,7)	8,3 [0,76; NE]	2/6 (33,3)	NE [0,76; NE]	1,82 [0,35; 9,41] 0,463
KIF5B	22/50 (44,0)	18,6 [5,68; NE]	15/36 (41,7)	4,2 [0,89; NE]	0,52 [0,26; 1,02] 0,053
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. ***** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10ap_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 67: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Verstopfung (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,266)					
<65 Jahre	34/76 (44,7)	14,5 [4,17; NE]	22/45 (48,9)	5,0 [1,54; NE]	0,59 [0,34; 1,02] 0,055
≥65 Jahre	20/39 (51,3)	4,1 [1,45; NE]	13/28 (46,4)	3,1 [1,84; NE]	1,09 [0,54; 2,20] 0,817
Baseline ECOG (p-Wert des Interaktionsterms: 0,506)					
0	20/41 (48,8)	7,5 [2,17; NE]	11/25 (44,0)	3,5 [0,99; NE]	0,88 [0,42; 1,87] 0,750
1	34/74 (45,9)	7,8 [3,65; NE]	24/48 (50,0)	5,0 [2,14; 9,92]	0,66 [0,39; 1,12] 0,117
Geschlecht (p-Wert des Interaktionsterms: 0,915)					
Männlich	27/61 (44,3)	20,3 [4,14; NE]	15/34 (44,1)	6,4 [2,14; NE]	0,75 [0,39; 1,42] 0,364
Weiblich	27/54 (50,0)	6,3 [2,23; NE]	20/39 (51,3)	2,9 [1,48; 7,72]	0,76 [0,43; 1,37] 0,351
Geografische Region (p-Wert des Interaktionsterms: 0,256)					
Ostasiatisch	29/65 (44,6)	14,5 [4,34; NE]	19/35 (54,3)	6,4 [1,48; 9,92]	0,57 [0,32; 1,03] 0,061
Nicht-Ostasiatisch	25/50 (50,0)	4,2 [2,20; NE]	16/38 (42,1)	3,5 [2,76; NE]	0,99 [0,53; 1,88] 0,980
Raucherstatus (p-Wert des Interaktionsterms: 0,696)					
Nie	35/72 (48,6)	7,5 [3,55; NE]	25/50 (50,0)	3,2 [1,61; 9,92]	0,68 [0,41; 1,15] 0,148
Ehemals/Aktuell	19/43 (44,2)	9,0 [2,89; NE]	10/23 (43,5)	3,5 [1,64; NE]	0,86 [0,40; 1,86] 0,698
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,092)					
Ja	12/23 (52,2)	3,5 [1,45; NE]	4/14 (28,6)	NE [0,82; NE]	1,90 [0,61; 5,91] 0,263
Nein	21/44 (47,7)	4,4 [2,83; NE]	12/23 (52,2)	5,0 [1,22; NE]	0,91 [0,45; 1,85] 0,780

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	21/48 (43,8)	20,3 [5,59; NE]	19/36 (52,8)	3,2 [2,14; 7,72]	0,39 [0,20; 0,75] 0,004
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,365)					
Ja	9/16 (56,3)	5,0 [1,45; NE]	3/13 (23,1)	NE [1,22; NE]	1,21 [0,32; 4,63] 0,789
Nein	45/98 (45,9)	7,8 [3,61; NE]	32/60 (53,3)	3,5 [2,37; 7,72]	0,69 [0,44; 1,09] 0,110
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,321)					
TPS <50%	22/48 (45,8)	14,5 [2,89; NE]	14/27 (51,9)	2,9 [1,61; NE]	0,75 [0,38; 1,48] 0,392
TPS ≥50%	8/19 (42,1)	6,7 [1,45; NE]	3/13 (23,1)	NE [0,82; NE]	1,60 [0,42; 6,06] 0,479
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,439)					
TPS <50%	22/48 (45,8)	14,5 [2,89; NE]	14/27 (51,9)	2,9 [1,61; NE]	0,75 [0,38; 1,48] 0,392
TPS ≥50%	8/19 (42,1)	6,7 [1,45; NE]	3/13 (23,1)	NE [0,82; NE]	1,60 [0,42; 6,06] 0,479
Unbekannt	24/48 (50,0)	7,8 [3,61; NE]	18/33 (54,5)	3,2 [1,48; 6,54]	0,60 [0,32; 1,12] 0,102
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,059)					
Negativ	9/26 (34,6)	NE [2,89; NE]	7/12 (58,3)	1,4 [0,79; NE]	0,46 [0,17; 1,27] 0,115
Positiv	27/49 (55,1)	5,6 [2,69; 20,27]	12/34 (35,3)	7,7 [2,89; NE]	1,33 [0,67; 2,63] 0,422
Unbekannt	18/40 (45,0)	10,0 [3,61; NE]	16/27 (59,3)	3,2 [1,54; 6,54]	0,51 [0,25; 1,01] 0,047
Krankheitsstatus (p-Wert des Interaktionsterms: 0,733)					
III	3/6 (50,0)	6,7 [1,91; NE]	4/6 (66,7)	5,8 [0,85; NE]	1,01 [0,20; 5,14] 0,986
IVA	21/44 (47,7)	9,0 [2,89; NE]	19/33 (57,6)	2,9 [1,22; 6,54]	0,63 [0,33; 1,19] 0,146

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	30/65 (46,2)	7,8 [3,55; NE]	12/34 (35,3)	7,7 [2,14; NE]	0,95 [0,48; 1,86] 0,865
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,239)					
Asiatisch	29/66 (43,9)	14,5 [4,34; NE]	19/35 (54,3)	6,4 [1,48; 9,92]	0,56 [0,31; 1,01] 0,052
Nicht asiatisch	25/49 (51,0)	3,6 [2,10; 20,27]	14/34 (41,2)	3,2 [2,14; NE]	1,01 [0,52; 1,95] 0,991
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,154)					
CCDC6	4/9 (44,4)	22,0 [3,61; NE]	3/6 (50,0)	NE [0,72; NE]	0,42 [0,08; 2,14] 0,285
KIF5B	32/50 (64,0)	3,5 [1,45; 9,95]	12/36 (33,3)	9,9 [2,37; NE]	1,55 [0,79; 3,02] 0,202
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10co_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 68: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Diarrhö (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,371)					
<65 Jahre	50/76 (65,8)	4,9 [2,89; 6,44]	16/45 (35,6)	12,0 [2,96; NE]	1,84 [1,05; 3,24] 0,032
≥65 Jahre	26/39 (66,7)	4,1 [2,17; 5,75]	8/28 (28,6)	NE [4,86; NE]	2,79 [1,26; 6,17] 0,008
Baseline ECOG (p-Wert des Interaktionsterms: 0,219)					
0	24/41 (58,5)	3,3 [2,14; 9,72]	10/25 (40,0)	12,0 [1,68; NE]	1,42 [0,67; 2,97] 0,354
1	52/74 (70,3)	4,2 [2,96; 5,85]	14/48 (29,2)	19,6 [7,20; NE]	2,73 [1,51; 4,94] <0,001
Geschlecht (p-Wert des Interaktionsterms: 0,817)					
Männlich	42/61 (68,9)	5,0 [2,89; 6,47]	10/34 (29,4)	NE [4,99; NE]	2,34 [1,17; 4,67] 0,013
Weiblich	34/54 (63,0)	3,5 [2,14; 6,31]	14/39 (35,9)	10,6 [4,86; NE]	2,10 [1,12; 3,93] 0,017
Geografische Region (p-Wert des Interaktionsterms: 0,470)					
Ostasiatisch	47/65 (72,3)	3,5 [2,83; 5,62]	12/35 (34,3)	12,0 [7,20; NE]	2,54 [1,34; 4,82] 0,003
Nicht-Ostasiatisch	29/50 (58,0)	5,0 [2,83; 9,00]	12/38 (31,6)	10,6 [4,86; NE]	1,82 [0,93; 3,56] 0,078
Raucherstatus (p-Wert des Interaktionsterms: 0,692)					
Nie	46/72 (63,9)	4,7 [2,89; 6,47]	15/50 (30,0)	19,6 [4,99; NE]	2,28 [1,27; 4,09] 0,004
Ehemals/Aktuell	30/43 (69,8)	4,1 [2,20; 5,85]	9/23 (39,1)	10,6 [1,48; NE]	1,88 [0,89; 3,98] 0,095
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,204)					
Ja	18/23 (78,3)	3,4 [2,17; 6,31]	3/14 (21,4)	NE [7,20; NE]	4,72 [1,37; 16,28] 0,007
Nein	27/44 (61,4)	4,1 [2,14; 5,59]	8/23 (34,8)	NE [2,96; NE]	2,41 [1,09; 5,32] 0,024

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	31/48 (64,6)	5,7 [2,86; 7,43]	13/36 (36,1)	12,0 [2,46; NE]	1,48 [0,77; 2,83] 0,236
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,354)					
Ja	13/16 (81,3)	3,1 [1,41; 5,62]	2/13 (15,4)	7,2 [1,48; NE]	3,78 [0,83; 17,15] 0,064
Nein	63/98 (64,3)	4,9 [2,89; 6,31]	22/60 (36,7)	12,0 [4,99; NE]	1,98 [1,22; 3,23] 0,005
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,503)					
TPS <50%	30/48 (62,5)	4,7 [2,83; 6,44]	9/27 (33,3)	12,0 [4,86; NE]	2,20 [1,04; 4,65] 0,034
TPS ≥50%	12/19 (63,2)	5,6 [1,41; 9,72]	5/13 (38,5)	7,0 [0,72; NE]	1,47 [0,52; 4,20] 0,465
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,666)					
TPS <50%	30/48 (62,5)	4,7 [2,83; 6,44]	9/27 (33,3)	12,0 [4,86; NE]	2,20 [1,04; 4,65] 0,034
TPS ≥50%	12/19 (63,2)	5,6 [1,41; 9,72]	5/13 (38,5)	7,0 [0,72; NE]	1,47 [0,52; 4,20] 0,465
Unbekannt	34/48 (70,8)	3,0 [2,20; 6,24]	10/33 (30,3)	19,6 [4,99; NE]	2,52 [1,24; 5,13] 0,008
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,977)					
Negativ	13/26 (50,0)	5,5 [3,48; NE]	3/12 (25,0)	NE [0,89; NE]	2,38 [0,67; 8,42] 0,166
Positiv	33/49 (67,3)	4,9 [2,14; 6,31]	11/34 (32,4)	10,6 [2,96; NE]	2,03 [1,02; 4,04] 0,038
Unbekannt	30/40 (75,0)	3,2 [2,20; 6,24]	10/27 (37,0)	19,6 [2,66; NE]	2,28 [1,11; 4,69] 0,022
Krankheitsstatus (p-Wert des Interaktionsterms: 0,765)					
III	3/6 (50,0)	7,4 [3,32; NE]	1/6 (16,7)	NE [4,86; NE]	5,64 [0,55; 57,53] 0,106
IVA	28/44 (63,6)	3,5 [2,14; 6,47]	12/33 (36,4)	NE [2,46; NE]	1,88 [0,95; 3,69] 0,064

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	45/65 (69,2)	4,1 [2,83; 6,24]	11/34 (32,4)	12,0 [7,00; NE]	1,99 [1,03; 3,86] 0,038
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,861)					
Asiatisch	47/66 (71,2)	3,5 [2,83; 5,75]	12/35 (34,3)	12,0 [7,20; NE]	2,48 [1,31; 4,71] 0,004
Nicht asiatisch	29/49 (59,2)	5,0 [2,20; 7,85]	9/34 (26,5)	NE [4,86; NE]	2,25 [1,06; 4,76] 0,029
RET-Probenart (p-Wert des Interaktionsterms: 0,478)					
Blut	9/9 (100,0)	1,4 [0,69; 3,22]	3/10 (30,0)	3,0 [0,89; NE]	3,20 [0,86; 11,88] 0,067
Gewebe	67/106 (63,2)	5,0 [3,48; 6,44]	21/63 (33,3)	19,6 [7,20; NE]	2,13 [1,30; 3,48] 0,002
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,864)					
CCDC6	9/9 (100,0)	6,2 [0,76; 9,72]	2/6 (33,3)	NE [1,45; NE]	3,24 [0,68; 15,44] 0,117
KIF5B	38/50 (76,0)	3,5 [2,14; 5,42]	10/36 (27,8)	10,6 [4,86; NE]	2,76 [1,37; 5,57] 0,003
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10di_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 69: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Symptomskala Finanzielle Schwierigkeiten (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,126)					
<65 Jahre	22/76 (28,9)	NE [15,28; NE]	19/45 (42,2)	7,1 [1,41; NE]	0,45 [0,24; 0,85] 0,011
≥65 Jahre	14/39 (35,9)	19,0 [6,24; NE]	9/28 (32,1)	NE [2,60; NE]	0,94 [0,41; 2,18] 0,885
Baseline ECOG (p-Wert des Interaktionsterms: 0,212)					
0	10/41 (24,4)	NE [NE; NE]	11/25 (44,0)	4,4 [1,05; NE]	0,42 [0,18; 0,98] 0,041
1	26/74 (35,1)	19,0 [7,26; NE]	17/48 (35,4)	NE [3,52; NE]	0,73 [0,39; 1,35] 0,314
Geschlecht (p-Wert des Interaktionsterms: 0,093)					
Männlich	23/61 (37,7)	NE [7,26; NE]	11/34 (32,4)	NE [1,68; NE]	0,91 [0,44; 1,87] 0,792
Weiblich	13/54 (24,1)	NE [18,99; NE]	17/39 (43,6)	4,4 [1,41; NE]	0,39 [0,19; 0,80] 0,008
Geografische Region (p-Wert des Interaktionsterms: 0,388)					
Ostasiatisch	21/65 (32,3)	19,0 [13,90; NE]	16/35 (45,7)	6,7 [1,28; NE]	0,45 [0,23; 0,87] 0,015
Nicht-Ostasiatisch	15/50 (30,0)	NE [6,24; NE]	12/38 (31,6)	NE [3,52; NE]	0,78 [0,37; 1,68] 0,527
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,900)					
Ja	4/23 (17,4)	NE [NE; NE]	4/14 (28,6)	NE [0,79; NE]	0,54 [0,13; 2,15] 0,371
Nein	14/44 (31,8)	NE [6,28; NE]	10/23 (43,5)	7,1 [1,68; NE]	0,67 [0,30; 1,52] 0,342
Unbekannt	18/48 (37,5)	19,0 [7,89; NE]	14/36 (38,9)	6,7 [1,05; NE]	0,58 [0,28; 1,18] 0,123
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,286)					
Ja	4/16 (25,0)	NE [4,34; NE]	1/13 (7,7)	NE [0,79; NE]	1,98 [0,22; 17,80] 0,536

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	32/98 (32,7)	NE [13,90; NE]	27/60 (45,0)	7,1 [1,68; NE]	0,55 [0,33; 0,93] 0,022
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,616)					
TPS <50%	12/48 (25,0)	NE [NE; NE]	9/27 (33,3)	NE [3,52; NE]	0,67 [0,28; 1,59] 0,353
TPS ≥50%	4/19 (21,1)	NE [15,28; NE]	4/13 (30,8)	NE [0,72; NE]	0,49 [0,12; 1,98] 0,309
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,906)					
TPS <50%	12/48 (25,0)	NE [NE; NE]	9/27 (33,3)	NE [3,52; NE]	0,67 [0,28; 1,59] 0,353
TPS ≥50%	4/19 (21,1)	NE [15,28; NE]	4/13 (30,8)	NE [0,72; NE]	0,49 [0,12; 1,98] 0,309
Unbekannt	20/48 (41,7)	19,0 [6,28; NE]	15/33 (45,5)	4,4 [0,89; NE]	0,55 [0,28; 1,10] 0,082
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,602)					
Negativ	7/26 (26,9)	NE [6,24; NE]	3/12 (25,0)	NE [0,99; NE]	1,11 [0,29; 4,31] 0,878
Positiv	12/49 (24,5)	NE [15,28; NE]	11/34 (32,4)	NE [1,68; NE]	0,53 [0,23; 1,20] 0,124
Unbekannt	17/40 (42,5)	19,0 [6,74; NE]	14/27 (51,9)	4,4 [0,85; NE]	0,49 [0,24; 1,02] 0,049
Krankheitsstatus (p-Wert des Interaktionsterms: 0,759)					
III	3/6 (50,0)	6,7 [2,07; NE]	4/6 (66,7)	2,0 [0,72; NE]	0,38 [0,07; 2,11] 0,251
IVA	11/44 (25,0)	NE [NE; NE]	13/33 (39,4)	NE [1,68; NE]	0,52 [0,23; 1,17] 0,110
IVB	22/65 (33,8)	NE [7,89; NE]	11/34 (32,4)	9,6 [1,68; NE]	0,71 [0,34; 1,47] 0,353
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,336)					
Asiatisch	21/66 (31,8)	NE [13,90; NE]	16/35 (45,7)	6,7 [1,28; NE]	0,44 [0,23; 0,85] 0,013

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	15/49 (30,6)	NE [5,65; NE]	10/34 (29,4)	NE [1,68; NE]	0,84 [0,38; 1,87] 0,669
RET-Probenart (p-Wert des Interaktionsterms: 0,820)					
Blut	3/9 (33,3)	NE [1,45; NE]	2/10 (20,0)	NE [0,72; NE]	0,78 [0,13; 4,77] 0,788
Gewebe	33/106 (31,1)	NE [15,28; NE]	26/63 (41,3)	9,6 [2,60; NE]	0,58 [0,35; 0,98] 0,038
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,176)					
CCDC6	2/9 (22,2)	NE [2,04; NE]	3/6 (50,0)	NE [0,76; NE]	0,30 [0,05; 1,86] 0,174
KIF5B	20/50 (40,0)	15,3 [6,24; NE]	9/36 (25,0)	NE [3,84; NE]	1,21 [0,55; 2,66] 0,642
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10fd_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 70: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des EORTC QLQ-C30 globalen Gesundheitsstatus (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,407)					
<65 Jahre	37/76 (48,7)	7,0 [3,58; NE]	17/45 (37,8)	8,4 [2,27; NE]	1,14 [0,64; 2,02] 0,658
≥65 Jahre	26/39 (66,7)	2,4 [0,85; 4,99]	15/28 (53,6)	5,4 [2,83; NE]	1,60 [0,84; 3,02] 0,151
Baseline ECOG (p-Wert des Interaktionsterms: 0,958)					
0	22/41 (53,7)	6,3 [2,83; 19,38]	10/25 (40,0)	8,0 [0,82; NE]	1,21 [0,57; 2,56] 0,615
1	41/74 (55,4)	4,5 [2,37; 6,97]	22/48 (45,8)	6,3 [2,83; NE]	1,26 [0,75; 2,12] 0,396
Geschlecht (p-Wert des Interaktionsterms: 0,839)					
Männlich	35/61 (57,4)	4,1 [2,14; 8,57]	16/34 (47,1)	7,0 [2,27; NE]	1,29 [0,72; 2,34] 0,414
Weiblich	28/54 (51,9)	5,0 [2,83; 19,38]	16/39 (41,0)	8,1 [3,48; NE]	1,22 [0,66; 2,26] 0,522
Geografische Region (p-Wert des Interaktionsterms: 0,770)					
Ostasiatisch	37/65 (56,9)	3,5 [1,54; 4,99]	17/35 (48,6)	8,0 [1,81; NE]	1,31 [0,74; 2,32] 0,370
Nicht-Ostasiatisch	26/50 (52,0)	7,0 [3,58; 19,38]	15/38 (39,5)	7,0 [3,48; NE]	1,09 [0,58; 2,07] 0,783
Raucherstatus (p-Wert des Interaktionsterms: 0,570)					
Nie	37/72 (51,4)	6,1 [2,99; NE]	20/50 (40,0)	8,1 [2,27; NE]	1,11 [0,64; 1,92] 0,700
Ehemals/Aktuell	26/43 (60,5)	4,1 [1,48; 7,82]	12/23 (52,2)	6,3 [2,37; NE]	1,47 [0,74; 2,91] 0,286
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,895)					
Ja	11/23 (47,8)	4,5 [0,76; NE]	5/14 (35,7)	NE [0,82; NE]	1,45 [0,50; 4,17] 0,501
Nein	27/44 (61,4)	3,5 [1,18; 6,97]	13/23 (56,5)	5,4 [1,54; NE]	1,31 [0,68; 2,55] 0,415

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	25/48 (52,1)	8,3 [2,99; NE]	14/36 (38,9)	8,1 [2,37; NE]	1,09 [0,57; 2,10] 0,798
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,541)					
Ja	5/16 (31,3)	NE [1,54; NE]	3/13 (23,1)	NE [3,58; NE]	0,76 [0,18; 3,24] 0,711
Nein	58/98 (59,2)	3,7 [2,40; 6,11]	29/60 (48,3)	8,0 [2,37; NE]	1,33 [0,85; 2,07] 0,216
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,073)					
TPS <50%	28/48 (58,3)	3,5 [1,54; 5,55]	10/27 (37,0)	14,0 [3,48; NE]	2,07 [1,01; 4,28] 0,042
TPS ≥50%	10/19 (52,6)	7,0 [2,40; NE]	6/13 (46,2)	4,7 [0,72; NE]	0,72 [0,26; 1,99] 0,526
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,118)					
TPS <50%	28/48 (58,3)	3,5 [1,54; 5,55]	10/27 (37,0)	14,0 [3,48; NE]	2,07 [1,01; 4,28] 0,042
TPS ≥50%	10/19 (52,6)	7,0 [2,40; NE]	6/13 (46,2)	4,7 [0,72; NE]	0,72 [0,26; 1,99] 0,526
Unbekannt	25/48 (52,1)	4,5 [2,37; NE]	16/33 (48,5)	3,7 [1,54; NE]	0,92 [0,49; 1,73] 0,785
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,646)					
Negativ	13/26 (50,0)	3,5 [0,82; NE]	6/12 (50,0)	14,0 [1,81; NE]	1,39 [0,53; 3,67] 0,504
Positiv	28/49 (57,1)	6,1 [3,52; 8,57]	12/34 (35,3)	8,4 [3,48; NE]	1,42 [0,72; 2,81] 0,313
Unbekannt	22/40 (55,0)	3,5 [1,54; NE]	14/27 (51,9)	6,3 [1,51; NE]	0,97 [0,50; 1,90] 0,923
Krankheitsstatus (p-Wert des Interaktionsterms: 0,219)					
III	3/6 (50,0)	NE [0,76; NE]	5/6 (83,3)	1,2 [0,72; NE]	0,55 [0,13; 2,31] 0,373
IVA	24/44 (54,5)	6,1 [2,33; 19,38]	17/33 (51,5)	5,4 [1,94; NE]	1,00 [0,53; 1,87] 1,000

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	36/65 (55,4)	4,2 [2,37; 8,57]	10/34 (29,4)	8,4 [7,00; NE]	1,95 [0,97; 3,94] 0,057
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,788)					
Asiatisch	37/66 (56,1)	3,5 [1,54; NE]	17/35 (48,6)	8,0 [1,81; NE]	1,28 [0,72; 2,27] 0,416
Nicht asiatisch	26/49 (53,1)	6,9 [3,58; 14,06]	13/34 (38,2)	6,3 [2,37; NE]	1,07 [0,55; 2,08] 0,844
RET-Probenart (p-Wert des Interaktionsterms: 0,568)					
Blut	5/9 (55,6)	8,6 [0,76; NE]	2/10 (20,0)	NE [0,85; NE]	1,95 [0,38; 10,10] 0,425
Gewebe	58/106 (54,7)	4,3 [2,76; 7,82]	30/63 (47,6)	7,0 [2,83; NE]	1,18 [0,76; 1,83] 0,469
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,173)					
CCDC6	5/9 (55,6)	14,1 [0,76; NE]	5/6 (83,3)	4,9 [0,76; NE]	0,41 [0,11; 1,55] 0,172
KIF5B	28/50 (56,0)	6,3 [2,83; 19,38]	13/36 (36,1)	7,0 [1,68; NE]	1,29 [0,66; 2,50] 0,458
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10gh_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 71: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Funktionsskala Körperliche Funktion (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,340)					
<65 Jahre	31/76 (40,8)	19,4 [6,80; NE]	18/45 (40,0)	8,8 [1,64; NE]	0,70 [0,39; 1,25] 0,227
≥65 Jahre	20/39 (51,3)	5,6 [2,17; NE]	13/28 (46,4)	7,0 [1,84; NE]	1,14 [0,57; 2,30] 0,709
Baseline ECOG (p-Wert des Interaktionsterms: 0,468)					
0	17/41 (41,5)	14,1 [4,67; NE]	12/25 (48,0)	7,0 [0,95; NE]	0,67 [0,32; 1,41] 0,292
1	34/74 (45,9)	11,2 [4,04; NE]	19/48 (39,6)	8,8 [1,91; NE]	0,92 [0,52; 1,63] 0,778
Geschlecht (p-Wert des Interaktionsterms: 0,101)					
Männlich	31/61 (50,8)	11,2 [4,17; 21,45]	13/34 (38,2)	NE [6,08; NE]	1,11 [0,58; 2,16] 0,747
Weiblich	20/54 (37,0)	NE [4,93; NE]	18/39 (46,2)	6,7 [1,28; NE]	0,58 [0,31; 1,10] 0,091
Geografische Region (p-Wert des Interaktionsterms: 0,367)					
Ostasiatisch	29/65 (44,6)	19,4 [4,37; NE]	18/35 (51,4)	6,7 [1,28; NE]	0,68 [0,38; 1,24] 0,203
Nicht-Ostasiatisch	22/50 (44,0)	8,6 [4,21; NE]	13/38 (34,2)	NE [6,08; NE]	1,07 [0,54; 2,14] 0,838
Raucherstatus (p-Wert des Interaktionsterms: 0,134)					
Nie	27/72 (37,5)	21,5 [6,80; NE]	20/50 (40,0)	8,8 [1,45; NE]	0,65 [0,36; 1,17] 0,152
Ehemals/Aktuell	24/43 (55,8)	4,9 [2,46; 19,35]	11/23 (47,8)	7,2 [1,91; NE]	1,25 [0,61; 2,56] 0,549
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,431)					
Ja	11/23 (47,8)	6,8 [2,14; NE]	5/14 (35,7)	8,8 [0,72; NE]	0,93 [0,32; 2,74] 0,912
Nein	20/44 (45,5)	5,6 [2,73; NE]	10/23 (43,5)	NE [1,45; NE]	1,13 [0,53; 2,42] 0,751

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	20/48 (41,7)	19,5 [5,65; NE]	16/36 (44,4)	7,0 [1,81; NE]	0,58 [0,30; 1,12] 0,100
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,742)					
Ja	5/16 (31,3)	NE [3,65; NE]	2/13 (15,4)	NE [1,91; NE]	0,99 [0,19; 5,15] 0,994
Nein	46/98 (46,9)	8,6 [4,37; 21,45]	29/60 (48,3)	7,0 [1,81; NE]	0,82 [0,51; 1,31] 0,411
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,122)					
TPS <50%	21/48 (43,8)	11,2 [5,55; NE]	12/27 (44,4)	24,4 [1,81; NE]	0,92 [0,45; 1,88] 0,821
TPS ≥50%	9/19 (47,4)	19,5 [2,73; NE]	7/13 (53,8)	1,1 [0,72; 7,23]	0,33 [0,11; 0,95] 0,032
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,231)					
TPS <50%	21/48 (43,8)	11,2 [5,55; NE]	12/27 (44,4)	24,4 [1,81; NE]	0,92 [0,45; 1,88] 0,821
TPS ≥50%	9/19 (47,4)	19,5 [2,73; NE]	7/13 (53,8)	1,1 [0,72; 7,23]	0,33 [0,11; 0,95] 0,032
Unbekannt	21/48 (43,8)	19,4 [2,79; NE]	12/33 (36,4)	9,9 [6,08; NE]	1,03 [0,51; 2,10] 0,938
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,368)					
Negativ	9/26 (34,6)	NE [5,62; NE]	7/12 (58,3)	1,8 [0,89; NE]	0,47 [0,17; 1,27] 0,131
Positiv	25/49 (51,0)	8,6 [3,65; 21,45]	13/34 (38,2)	8,8 [1,45; NE]	1,00 [0,51; 1,96] 0,995
Unbekannt	17/40 (42,5)	19,4 [2,20; NE]	11/27 (40,7)	7,0 [2,37; NE]	0,96 [0,45; 2,06] 0,906
Krankheitsstatus (p-Wert des Interaktionsterms: 0,964)					
III	3/6 (50,0)	19,5 [2,07; NE]	4/6 (66,7)	5,9 [1,45; NE]	0,42 [0,07; 2,35] 0,308
IVA	21/44 (47,7)	5,6 [3,52; NE]	15/33 (45,5)	7,2 [0,89; NE]	0,95 [0,49; 1,85] 0,903

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	27/65 (41,5)	19,4 [5,65; NE]	12/34 (35,3)	24,4 [2,37; NE]	0,83 [0,42; 1,64] 0,584
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,309)					
Asiatisch	29/66 (43,9)	19,4 [4,67; NE]	18/35 (51,4)	6,7 [1,28; NE]	0,67 [0,37; 1,21] 0,181
Nicht asiatisch	22/49 (44,9)	8,6 [4,21; NE]	11/34 (32,4)	NE [1,91; NE]	1,14 [0,55; 2,36] 0,726
RET-Probenart (p-Wert des Interaktionsterms: 0,479)					
Blut	6/9 (66,7)	4,0 [0,76; NE]	3/10 (30,0)	7,0 [0,72; NE]	1,38 [0,34; 5,57] 0,659
Gewebe	45/106 (42,5)	19,4 [5,62; NE]	28/63 (44,4)	8,8 [1,91; NE]	0,77 [0,48; 1,24] 0,281
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,585)					
CCDC6	5/9 (55,6)	14,1 [0,76; NE]	3/6 (50,0)	7,2 [1,84; NE]	1,15 [0,27; 4,86] 0,862
KIF5B	24/50 (48,0)	19,4 [4,93; NE]	14/36 (38,9)	7,0 [0,89; NE]	0,66 [0,34; 1,31] 0,239
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10pf2_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 72: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Funktionsskala Rollenfunktion (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab			HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,082)					
<65 Jahre	36/76 (47,4)	9,2 [4,30; 22,57]	25/45 (55,6)	4,0 [1,54; 6,21]	0,50 [0,29; 0,84] 0,008
≥65 Jahre	24/39 (61,5)	4,0 [1,54; 6,34]	15/28 (53,6)	3,0 [1,45; NE]	1,08 [0,57; 2,07] 0,813
Baseline ECOG (p-Wert des Interaktionsterms: 0,405)					
0	25/41 (61,0)	4,9 [2,79; 15,31]	17/25 (68,0)	2,0 [0,79; 5,39]	0,53 [0,28; 0,99] 0,044
1	35/74 (47,3)	9,2 [4,04; NE]	23/48 (47,9)	5,4 [1,64; NE]	0,75 [0,44; 1,27] 0,275
Geschlecht (p-Wert des Interaktionsterms: 0,109)					
Männlich	36/61 (59,0)	5,0 [2,96; 13,93]	19/34 (55,9)	4,2 [1,81; NE]	0,89 [0,51; 1,55] 0,671
Weiblich	24/54 (44,4)	8,2 [3,52; NE]	21/39 (53,8)	1,8 [0,82; 6,37]	0,49 [0,27; 0,88] 0,016
Geografische Region (p-Wert des Interaktionsterms: 0,980)					
Ostasiatisch	34/65 (52,3)	7,3 [3,29; 19,35]	20/35 (57,1)	1,8 [1,28; NE]	0,68 [0,39; 1,19] 0,171
Nicht-Ostasiatisch	26/50 (52,0)	5,7 [2,96; 21,45]	20/38 (52,6)	4,0 [1,54; 6,37]	0,63 [0,35; 1,16] 0,135
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,967)					
Ja	12/23 (52,2)	8,2 [2,83; 21,45]	7/14 (50,0)	2,8 [0,72; NE]	0,54 [0,20; 1,44] 0,219
Nein	22/44 (50,0)	6,3 [2,96; NE]	15/23 (65,2)	4,2 [0,99; 9,46]	0,71 [0,37; 1,38] 0,303
Unbekannt	26/48 (54,2)	5,7 [2,76; 22,57]	18/36 (50,0)	2,4 [1,54; NE]	0,65 [0,35; 1,20] 0,165
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,671)					
Negativ	12/26 (46,2)	15,3 [4,17; NE]	8/12 (66,7)	2,3 [0,89; NE]	0,52 [0,21; 1,29] 0,150

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Positiv	25/49 (51,0)	6,3 [3,52; NE]	17/34 (50,0)	2,8 [1,28; NE]	0,59 [0,32; 1,10] 0,096
Unbekannt	23/40 (57,5)	4,5 [1,54; 22,57]	15/27 (55,6)	5,4 [0,95; NE]	0,83 [0,43; 1,61] 0,581
Krankheitsstatus (p-Wert des Interaktionsterms: 0,903)					
III	3/6 (50,0)	5,4 [2,07; NE]	5/6 (83,3)	5,7 [1,45; NE]	0,77 [0,15; 3,86] 0,751
IVA	24/44 (54,5)	4,0 [1,54; 9,17]	21/33 (63,6)	2,4 [0,89; 5,36]	0,67 [0,37; 1,22] 0,185
IVB	33/65 (50,8)	13,9 [4,30; 19,35]	14/34 (41,2)	5,4 [1,54; NE]	0,72 [0,38; 1,36] 0,315
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,999)					
Asiatisch	35/66 (53,0)	6,3 [3,29; 19,35]	20/35 (57,1)	1,8 [1,28; NE]	0,71 [0,41; 1,23] 0,210
Nicht asiatisch	25/49 (51,0)	6,3 [2,96; 21,45]	17/34 (50,0)	4,2 [1,54; 6,37]	0,66 [0,35; 1,24] 0,191
RET-Probenart (p-Wert des Interaktionsterms: 0,174)					
Blut	6/9 (66,7)	4,2 [0,76; NE]	2/10 (20,0)	NE [0,72; NE]	1,95 [0,39; 9,69] 0,407
Gewebe	54/106 (50,9)	7,0 [4,17; 15,54]	38/63 (60,3)	2,4 [1,54; 5,39]	0,60 [0,39; 0,91] 0,015
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,845)					
CCDC6	5/9 (55,6)	5,0 [0,76; NE]	4/6 (66,7)	3,9 [1,84; NE]	0,70 [0,18; 2,67] 0,600
KIF5B	29/50 (58,0)	7,0 [2,83; 19,35]	15/36 (41,7)	4,2 [1,45; NE]	0,79 [0,42; 1,48] 0,462

Subgruppe	Selpercatinib	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	Mediane Ereigniszeit ^a [95% KI]	
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt.				
Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.				

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10rf_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 73: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Funktionsskala Emotionale Funktion (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,291)					
<65 Jahre	31/76 (40,8)	15,2 [4,63; NE]	18/45 (40,0)	6,5 [4,34; NE]	0,84 [0,47; 1,50] 0,550
≥65 Jahre	16/39 (41,0)	NE [4,50; NE]	8/28 (28,6)	NE [6,47; NE]	1,51 [0,65; 3,54] 0,337
Baseline ECOG (p-Wert des Interaktionsterms: 0,776)					
0	15/41 (36,6)	NE [3,29; NE]	9/25 (36,0)	NE [2,60; NE]	0,91 [0,40; 2,09] 0,826
1	32/74 (43,2)	9,1 [4,93; NE]	17/48 (35,4)	9,9 [4,40; NE]	1,08 [0,60; 1,94] 0,807
Geschlecht (p-Wert des Interaktionsterms: 0,647)					
Männlich	25/61 (41,0)	NE [5,03; NE]	13/34 (38,2)	9,9 [4,44; NE]	0,94 [0,48; 1,83] 0,846
Weiblich	22/54 (40,7)	15,2 [4,30; NE]	13/39 (33,3)	NE [4,34; NE]	1,16 [0,58; 2,30] 0,673
Geografische Region (p-Wert des Interaktionsterms: 0,595)					
Ostasiatisch	28/65 (43,1)	NE [4,34; NE]	15/35 (42,9)	7,4 [3,58; NE]	0,93 [0,50; 1,75] 0,823
Nicht-Ostasiatisch	19/50 (38,0)	15,2 [5,09; NE]	11/38 (28,9)	NE [5,03; NE]	1,16 [0,55; 2,44] 0,692
Raucherstatus (p-Wert des Interaktionsterms: 0,512)					
Nie	29/72 (40,3)	NE [5,03; NE]	18/50 (36,0)	9,9 [4,34; NE]	0,91 [0,51; 1,64] 0,758
Ehemals/Aktuell	18/43 (41,9)	9,1 [4,21; NE]	8/23 (34,8)	NE [4,44; NE]	1,29 [0,56; 2,96] 0,560
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,556)					
Ja	8/23 (34,8)	NE [1,48; NE]	3/14 (21,4)	NE [1,41; NE]	1,65 [0,44; 6,21] 0,460
Nein	21/44 (47,7)	6,2 [3,52; NE]	10/23 (43,5)	6,5 [2,83; NE]	1,20 [0,57; 2,55] 0,632

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	18/48 (37,5)	NE [5,09; NE]	13/36 (36,1)	9,9 [3,58; NE]	0,76 [0,37; 1,55] 0,441
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,934)					
Ja	3/16 (18,8)	NE [5,03; NE]	1/13 (7,7)	NE [2,14; NE]	1,24 [0,13; 12,04] 0,855
Nein	44/98 (44,9)	8,8 [4,50; NE]	25/60 (41,7)	7,4 [4,40; NE]	1,09 [0,67; 1,78] 0,738
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,060)					
TPS <50%	22/48 (45,8)	8,0 [4,21; NE]	7/27 (25,9)	NE [5,03; NE]	1,96 [0,84; 4,59] 0,115
TPS ≥50%	6/19 (31,6)	NE [2,73; NE]	6/13 (46,2)	5,5 [0,72; NE]	0,50 [0,16; 1,55] 0,218
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,123)					
TPS <50%	22/48 (45,8)	8,0 [4,21; NE]	7/27 (25,9)	NE [5,03; NE]	1,96 [0,84; 4,59] 0,115
TPS ≥50%	6/19 (31,6)	NE [2,73; NE]	6/13 (46,2)	5,5 [0,72; NE]	0,50 [0,16; 1,55] 0,218
Unbekannt	19/48 (39,6)	NE [4,93; NE]	13/33 (39,4)	7,4 [2,83; NE]	0,79 [0,39; 1,62] 0,518
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,286)					
Negativ	11/26 (42,3)	8,8 [4,21; NE]	2/12 (16,7)	NE [5,03; NE]	3,07 [0,68; 13,84] 0,125
Positiv	19/49 (38,8)	NE [4,34; NE]	12/34 (35,3)	6,5 [3,58; NE]	0,88 [0,43; 1,82] 0,731
Unbekannt	17/40 (42,5)	15,2 [4,50; NE]	12/27 (44,4)	7,4 [1,94; NE]	0,84 [0,40; 1,78] 0,650
Krankheitsstatus (p-Wert des Interaktionsterms: 0,821)					
III	3/6 (50,0)	NE [0,76; NE]	5/6 (83,3)	4,5 [1,45; NE]	1,28 [0,26; 6,43] 0,786
IVA	21/44 (47,7)	6,2 [3,52; NE]	12/33 (36,4)	NE [4,34; NE]	1,32 [0,65; 2,69] 0,438

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	23/65 (35,4)	NE [7,95; NE]	9/34 (26,5)	NE [5,03; NE]	1,02 [0,47; 2,20] 0,966
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,790)					
Asiatisch	29/66 (43,9)	NE [4,34; NE]	15/35 (42,9)	7,4 [3,58; NE]	0,94 [0,50; 1,76] 0,850
Nicht asiatisch	18/49 (36,7)	15,2 [5,09; NE]	10/34 (29,4)	NE [4,44; NE]	1,04 [0,48; 2,25] 0,927
RET-Probenart (p-Wert des Interaktionsterms: 0,635)					
Blut	5/9 (55,6)	4,7 [0,72; NE]	4/10 (40,0)	4,3 [0,72; NE]	0,84 [0,22; 3,19] 0,793
Gewebe	42/106 (39,6)	NE [5,09; NE]	22/63 (34,9)	NE [6,47; NE]	1,08 [0,64; 1,81] 0,772
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,610)					
CCDC6	4/9 (44,4)	NE [1,54; NE]	3/6 (50,0)	4,4 [2,60; NE]	0,96 [0,22; 4,31] 0,961
KIF5B	23/50 (46,0)	9,1 [4,73; NE]	11/36 (30,6)	NE [5,03; NE]	1,27 [0,62; 2,60] 0,522
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10ef_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 74: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Funktionsskala Kognitive Funktion (≥10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,394)					
<65 Jahre	50/76 (65,8)	3,3 [2,30; 5,59]	21/45 (46,7)	4,2 [1,68; NE]	1,14 [0,68; 1,90] 0,616
≥65 Jahre	27/39 (69,2)	3,8 [2,14; 5,59]	13/28 (46,4)	9,7 [2,07; NE]	1,63 [0,84; 3,17] 0,146
Baseline ECOG (p-Wert des Interaktionsterms: 0,101)					
0	24/41 (58,5)	5,6 [2,17; 11,10]	14/25 (56,0)	3,3 [1,68; 7,23]	0,84 [0,43; 1,62] 0,589
1	53/74 (71,6)	3,5 [2,20; 4,37]	20/48 (41,7)	9,7 [2,27; NE]	1,70 [1,02; 2,85] 0,040
Geschlecht (p-Wert des Interaktionsterms: 0,287)					
Männlich	40/61 (65,6)	4,2 [2,73; 5,59]	19/34 (55,9)	4,5 [1,81; 11,30]	1,07 [0,62; 1,85] 0,817
Weiblich	37/54 (68,5)	3,3 [2,17; 5,32]	15/39 (38,5)	4,2 [2,07; NE]	1,64 [0,90; 2,98] 0,105
Geografische Region (p-Wert des Interaktionsterms: 0,744)					
Ostasiatisch	48/65 (73,8)	3,0 [2,14; 4,01]	18/35 (51,4)	3,0 [1,68; NE]	1,33 [0,77; 2,30] 0,298
Nicht-Ostasiatisch	29/50 (58,0)	5,6 [2,79; 7,82]	16/38 (42,1)	5,0 [3,06; NE]	1,15 [0,62; 2,12] 0,666
Raucherstatus (p-Wert des Interaktionsterms: 0,135)					
Nie	49/72 (68,1)	4,4 [3,29; 6,28]	24/50 (48,0)	4,0 [2,07; 11,30]	1,01 [0,62; 1,66] 0,961
Ehemals/Aktuell	28/43 (65,1)	2,3 [2,10; 4,24]	10/23 (43,5)	9,7 [1,61; NE]	1,90 [0,92; 3,93] 0,079
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,185)					
Ja	15/23 (65,2)	3,1 [1,45; 6,28]	4/14 (28,6)	9,7 [4,04; NE]	3,61 [1,19; 10,97] 0,016
Nein	29/44 (65,9)	4,3 [2,14; 6,28]	13/23 (56,5)	3,1 [1,68; NE]	1,10 [0,57; 2,12] 0,765

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	33/48 (68,8)	3,7 [2,20; 5,59]	17/36 (47,2)	3,2 [1,54; NE]	1,02 [0,57; 1,84] 0,946
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,983)					
Ja*	10/16 (62,5)	5,0 [1,45; NE]	0/13 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,013
Nein	67/98 (68,4)	3,3 [2,20; 4,99]	34/60 (56,7)	3,3 [1,94; 7,23]	1,16 [0,77; 1,75] 0,493
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,218)					
TPS <50%	31/48 (64,6)	4,1 [2,14; 6,28]	15/27 (55,6)	3,1 [1,45; NE]	1,09 [0,59; 2,02] 0,787
TPS ≥50%	12/19 (63,2)	3,5 [2,17; 6,37]	4/13 (30,8)	NE [4,04; NE]	2,93 [0,93; 9,28] 0,055
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,449)					
TPS <50%	31/48 (64,6)	4,1 [2,14; 6,28]	15/27 (55,6)	3,1 [1,45; NE]	1,09 [0,59; 2,02] 0,787
TPS ≥50%	12/19 (63,2)	3,5 [2,17; 6,37]	4/13 (30,8)	NE [4,04; NE]	2,93 [0,93; 9,28] 0,055
Unbekannt	34/48 (70,8)	3,5 [2,17; 5,59]	15/33 (45,5)	4,5 [1,68; NE]	1,22 [0,66; 2,24] 0,528
Krankheitsstatus (p-Wert des Interaktionsterms: 0,219)					
III	3/6 (50,0)	2,3 [1,02; NE]	5/6 (83,3)	2,4 [0,85; NE]	0,69 [0,15; 3,14] 0,633
IVA	27/44 (61,4)	4,0 [2,20; 7,26]	17/33 (51,5)	4,2 [1,68; NE]	1,03 [0,56; 1,89] 0,927
IVB	47/65 (72,3)	3,5 [2,17; 5,49]	12/34 (35,3)	9,7 [3,02; NE]	1,94 [1,03; 3,65] 0,038
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,739)					
Asiatisch	49/66 (74,2)	3,0 [2,14; 4,01]	18/35 (51,4)	3,0 [1,68; NE]	1,33 [0,77; 2,29] 0,300
Nicht asiatisch	28/49 (57,1)	5,6 [2,73; 11,10]	14/34 (41,2)	5,0 [2,30; NE]	1,13 [0,59; 2,16] 0,713
RET-Probenart (p-Wert des Interaktionsterms: 0,843)					

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Blut	7/9 (77,8)	5,6 [1,45; NE]	3/10 (30,0)	4,2 [0,76; NE]	0,96 [0,23; 3,92] 0,954
Gewebe	70/106 (66,0)	3,5 [2,33; 4,99]	31/63 (49,2)	4,2 [2,27; 11,30]	1,33 [0,87; 2,03] 0,186
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,868)					
CCDC6	7/9 (77,8)	2,8 [0,76; NE]	4/6 (66,7)	5,3 [0,76; NE]	1,27 [0,37; 4,41] 0,699
KIF5B	38/50 (76,0)	3,5 [2,17; 5,59]	15/36 (41,7)	4,2 [1,61; NE]	1,43 [0,79; 2,61] 0,240
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. * SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10cf_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba
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Tabelle 75: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung der EORTC QLQ-C30 Funktionsskala Soziale Funktion (≥ 10 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,301)					
<65 Jahre	43/76 (56,6)	4,3 [2,73; 14,52]	25/45 (55,6)	1,7 [1,28; 6,31]	0,67 [0,41; 1,11] 0,115
≥65 Jahre	23/39 (59,0)	4,9 [2,37; 9,89]	15/28 (53,6)	4,0 [1,61; NE]	0,99 [0,51; 1,92] 0,970
Baseline ECOG (p-Wert des Interaktionsterms: 0,830)					
0	20/41 (48,8)	4,3 [2,73; NE]	12/25 (48,0)	4,2 [0,95; NE]	0,85 [0,41; 1,74] 0,656
1	46/74 (62,2)	4,3 [2,37; 7,66]	28/48 (58,3)	2,8 [1,48; 6,67]	0,73 [0,45; 1,18] 0,200
Geschlecht (p-Wert des Interaktionsterms: 0,939)					
Männlich	36/61 (59,0)	4,9 [2,73; 9,89]	20/34 (58,8)	2,8 [1,54; 10,74]	0,78 [0,45; 1,36] 0,378
Weiblich	30/54 (55,6)	4,0 [2,37; 16,72]	20/39 (51,3)	4,0 [0,95; 6,67]	0,82 [0,46; 1,44] 0,495
Geografische Region (p-Wert des Interaktionsterms: 0,499)					
Ostasiatisch	41/65 (63,1)	3,5 [2,14; 12,02]	20/35 (57,1)	1,7 [0,89; NE]	0,89 [0,52; 1,52] 0,664
Nicht-Ostasiatisch	25/50 (50,0)	5,0 [3,52; NE]	20/38 (52,6)	4,0 [1,58; 10,74]	0,68 [0,38; 1,23] 0,200
Raucherstatus (p-Wert des Interaktionsterms: 0,171)					
Nie	40/72 (55,6)	5,7 [3,52; 14,52]	27/50 (54,0)	1,8 [1,45; 6,31]	0,63 [0,39; 1,04] 0,071
Ehemals/Aktuell	26/43 (60,5)	3,5 [1,64; 6,34]	13/23 (56,5)	4,0 [0,89; NE]	1,14 [0,59; 2,22] 0,704
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,802)					
Ja	14/23 (60,9)	3,7 [1,45; 12,02]	6/14 (42,9)	4,2 [0,72; NE]	1,06 [0,40; 2,80] 0,914
Nein	26/44 (59,1)	3,5 [1,91; 7,10]	16/23 (69,6)	1,7 [0,85; 10,74]	0,76 [0,41; 1,42] 0,392

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	26/48 (54,2)	5,0 [2,37; 24,61]	18/36 (50,0)	4,4 [1,48; 6,67]	0,73 [0,40; 1,34] 0,298
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,448)					
Ja	8/16 (50,0)	6,0 [1,45; NE]	3/13 (23,1)	NE [0,85; NE]	1,36 [0,36; 5,15] 0,649
Nein	58/98 (59,2)	4,0 [2,79; 7,16]	37/60 (61,7)	2,2 [1,51; 5,68]	0,76 [0,50; 1,15] 0,197
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,658)					
TPS <50%	25/48 (52,1)	7,1 [4,30; 16,72]	17/27 (63,0)	2,8 [1,48; 14,00]	0,64 [0,35; 1,20] 0,163
TPS ≥50%	9/19 (47,4)	4,0 [1,41; NE]	7/13 (53,8)	3,2 [0,72; 4,63]	0,61 [0,23; 1,64] 0,300
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,382)					
TPS <50%	25/48 (52,1)	7,1 [4,30; 16,72]	17/27 (63,0)	2,8 [1,48; 14,00]	0,64 [0,35; 1,20] 0,163
TPS ≥50%	9/19 (47,4)	4,0 [1,41; NE]	7/13 (53,8)	3,2 [0,72; 4,63]	0,61 [0,23; 1,64] 0,300
Unbekannt	32/48 (66,7)	2,6 [1,91; 3,84]	16/33 (48,5)	3,1 [0,89; NE]	1,04 [0,56; 1,91] 0,918
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,193)					
Negativ	12/26 (46,2)	7,2 [3,55; NE]	10/12 (83,3)	1,7 [0,79; 14,00]	0,42 [0,18; 0,97] 0,037
Positiv	26/49 (53,1)	5,7 [3,06; 16,72]	15/34 (44,1)	4,6 [1,58; NE]	0,85 [0,45; 1,61] 0,615
Unbekannt	28/40 (70,0)	2,2 [1,54; 3,52]	15/27 (55,6)	1,5 [0,89; 10,74]	0,99 [0,52; 1,87] 0,963
Krankheitsstatus (p-Wert des Interaktionsterms: 0,690)					
III	3/6 (50,0)	NE [0,76; NE]	5/6 (83,3)	1,7 [0,92; NE]	0,54 [0,13; 2,28] 0,388
IVA	25/44 (56,8)	3,5 [2,17; 14,52]	20/33 (60,6)	4,0 [0,89; 10,74]	0,75 [0,41; 1,35] 0,330

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	38/65 (58,5)	4,9 [3,52; 12,02]	15/34 (44,1)	4,2 [1,48; NE]	0,97 [0,53; 1,76] 0,896
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,342)					
Asiatisch	42/66 (63,6)	3,4 [1,91; 12,02]	20/35 (57,1)	1,7 [0,89; NE]	0,91 [0,53; 1,56] 0,739
Nicht asiatisch	24/49 (49,0)	5,0 [3,52; NE]	18/34 (52,9)	4,0 [1,54; 5,68]	0,63 [0,34; 1,16] 0,132
RET-Probenart (p-Wert des Interaktionsterms: 0,260)					
Blut	7/9 (77,8)	3,5 [1,45; NE]	3/10 (30,0)	NE [0,76; NE]	1,75 [0,45; 6,82] 0,423
Gewebe	59/106 (55,7)	4,9 [3,06; 12,02]	37/63 (58,7)	2,2 [1,54; 5,68]	0,74 [0,49; 1,11] 0,142
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,817)					
CCDC6	6/9 (66,7)	12,0 [0,76; NE]	4/6 (66,7)	4,4 [0,76; NE]	0,81 [0,23; 2,91] 0,732
KIF5B	30/50 (60,0)	4,3 [2,79; 16,72]	18/36 (50,0)	4,0 [0,92; 6,31]	0,77 [0,42; 1,39] 0,368
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EORTC: European Organisation for Research and Treatment of Cancer; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; QLQ-C30: Quality of Life Questionnaire Core 30; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. ***** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw10sf_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 76: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung für Gesundheitszustand EQ-5D VAS (≥15 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,223)					
<65 Jahre	25/76 (32,9)	18,7 [16,76; NE]	7/45 (15,6)	NE [12,02; NE]	1,73 [0,75; 4,03] 0,195
≥65 Jahre	16/39 (41,0)	12,6 [5,03; NE]	11/28 (39,3)	11,3 [1,68; NE]	0,94 [0,44; 2,02] 0,869
Baseline ECOG (p-Wert des Interaktionsterms: 0,853)					
0	13/41 (31,7)	NE [10,35; NE]	5/25 (20,0)	NE [6,21; NE]	1,41 [0,50; 3,95] 0,517
1	28/74 (37,8)	18,0 [7,66; NE]	13/48 (27,1)	NE [11,30; NE]	1,19 [0,62; 2,31] 0,605
Geschlecht (p-Wert des Interaktionsterms: 0,888)					
Männlich	26/61 (42,6)	18,7 [6,28; NE]	10/34 (29,4)	NE [11,30; NE]	1,23 [0,59; 2,58] 0,581
Weiblich	15/54 (27,8)	NE [12,62; NE]	8/39 (20,5)	NE [8,41; NE]	1,16 [0,49; 2,74] 0,727
Geografische Region (p-Wert des Interaktionsterms: 0,583)					
Ostasiatisch	24/65 (36,9)	18,2 [13,31; NE]	11/35 (31,4)	NE [8,41; NE]	1,06 [0,52; 2,17] 0,875
Nicht-Ostasiatisch	17/50 (34,0)	NE [6,93; NE]	7/38 (18,4)	NE [12,02; NE]	1,50 [0,62; 3,64] 0,363
Raucherstatus (p-Wert des Interaktionsterms: 0,657)					
Nie	22/72 (30,6)	NE [13,31; NE]	11/50 (22,0)	NE [11,30; NE]	1,09 [0,53; 2,25] 0,817
Ehemals/Aktuell	19/43 (44,2)	16,8 [4,27; NE]	7/23 (30,4)	NE [5,39; NE]	1,43 [0,60; 3,43] 0,418
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,475)					
Ja	6/23 (26,1)	NE [7,66; NE]	3/14 (21,4)	NE [0,82; NE]	0,95 [0,23; 3,97] 0,937
Nein	18/44 (40,9)	13,3 [5,03; NE]	5/23 (21,7)	NE [5,39; NE]	2,06 [0,76; 5,56] 0,142

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	17/48 (35,4)	NE [12,62; NE]	10/36 (27,8)	NE [8,41; NE]	0,94 [0,43; 2,06] 0,878
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,464)					
Ja	4/16 (25,0)	NE [6,93; NE]	2/13 (15,4)	NE [0,82; NE]	0,64 [0,12; 3,58] 0,598
Nein	37/98 (37,8)	18,7 [12,62; NE]	16/60 (26,7)	NE [12,02; NE]	1,34 [0,75; 2,42] 0,325
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,573)					
TPS <50%	17/48 (35,4)	NE [6,28; NE]	6/27 (22,2)	NE [NE; NE]	1,47 [0,58; 3,75] 0,413
TPS ≥50%	8/19 (42,1)	12,6 [5,03; NE]	2/13 (15,4)	NE [0,76; NE]	2,57 [0,54; 12,22] 0,220
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,543)					
TPS <50%	17/48 (35,4)	NE [6,28; NE]	6/27 (22,2)	NE [NE; NE]	1,47 [0,58; 3,75] 0,413
TPS ≥50%	8/19 (42,1)	12,6 [5,03; NE]	2/13 (15,4)	NE [0,76; NE]	2,57 [0,54; 12,22] 0,220
Unbekannt	16/48 (33,3)	NE [7,20; NE]	10/33 (30,3)	NE [5,39; NE]	0,93 [0,42; 2,06] 0,863
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,714)					
Negativ	6/26 (23,1)	NE [5,55; NE]	3/12 (25,0)	NE [0,79; NE]	0,85 [0,21; 3,42] 0,833
Positiv	20/49 (40,8)	16,8 [6,93; NE]	7/34 (20,6)	NE [8,41; NE]	1,48 [0,62; 3,52] 0,369
Unbekannt	15/40 (37,5)	NE [5,03; NE]	8/27 (29,6)	NE [5,39; NE]	1,19 [0,50; 2,81] 0,695
Krankheitsstatus (p-Wert des Interaktionsterms: 0,192)					
III	2/6 (33,3)	16,8 [1,38; NE]	3/6 (50,0)	11,3 [0,76; NE]	0,28 [0,03; 2,72] 0,240
IVA	16/44 (36,4)	18,2 [7,20; NE]	11/33 (33,3)	NE [1,68; NE]	0,87 [0,40; 1,89] 0,729

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	23/65 (35,4)	NE [7,66; NE]	4/34 (11,8)	NE [NE; NE]	2,67 [0,92; 7,71] 0,061
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,475)					
Asiatisch	25/66 (37,9)	18,2 [7,66; NE]	11/35 (31,4)	NE [8,41; NE]	1,09 [0,54; 2,23] 0,810
Nicht asiatisch	16/49 (32,7)	NE [6,93; NE]	5/34 (14,7)	NE [12,02; NE]	1,75 [0,64; 4,82] 0,267
RET-Probenart (p-Wert des Interaktionsterms: 0,583)					
Blut	5/9 (55,6)	7,7 [0,76; NE]	2/10 (20,0)	12,0 [0,85; NE]	1,96 [0,38; 10,20] 0,422
Gewebe	36/106 (34,0)	NE [16,76; NE]	16/63 (25,4)	NE [11,30; NE]	1,19 [0,66; 2,14] 0,568
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,882)					
CCDC6	4/9 (44,4)	18,0 [3,45; NE]	2/6 (33,3)	NE [0,76; NE]	0,97 [0,16; 5,79] 0,970
KIF5B	21/50 (42,0)	18,7 [5,55; NE]	8/36 (22,2)	NE [11,30; NE]	1,31 [0,58; 2,99] 0,517
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; EQ-5D: Fragebogen der EuroQol-Gruppe zur Lebensqualität auf 5 Dimensionen; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection; VAS: Visuelle Analogskala. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw15vas_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 77: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des NSCLC-SAQ, Gesamtwertung (≥3 Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,481)					
0	12/41 (29,3)	14,6 [10,78; NE]	14/25 (56,0)	1,5 [0,36; 3,71]	0,30 [0,13; 0,70] 0,003
1	26/74 (35,1)	20,5 [7,62; NE]	22/48 (45,8)	0,8 [0,36; NE]	0,43 [0,23; 0,77] 0,004
Geschlecht (p-Wert des Interaktionsterms: 0,748)					
Männlich	21/61 (34,4)	11,1 [2,37; NE]	15/34 (44,1)	1,2 [0,36; 7,00]	0,43 [0,20; 0,89] 0,021
Weiblich	17/54 (31,5)	15,5 [12,91; NE]	21/39 (53,8)	1,0 [0,33; 8,51]	0,30 [0,15; 0,61] <0,001
Geografische Region (p-Wert des Interaktionsterms: 0,726)					
Ostasiatisch	24/65 (36,9)	20,5 [9,72; NE]	22/35 (62,9)	1,0 [0,36; 8,51]	0,34 [0,18; 0,61] <0,001
Nicht-Ostasiatisch	14/50 (28,0)	14,6 [6,70; 16,82]	14/38 (36,8)	1,8 [0,36; 7,00]	0,40 [0,18; 0,89] 0,020
Raucherstatus (p-Wert des Interaktionsterms: 0,081)					
Nie	20/72 (27,8)	16,8 [10,78; NE]	29/50 (58,0)	0,5 [0,36; 3,71]	0,27 [0,15; 0,49] <0,001
Ehemals/Aktuell	18/43 (41,9)	11,1 [4,24; 23,03]	7/23 (30,4)	7,0 [0,33; NE]	0,65 [0,26; 1,64] 0,376
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,084)					
Ja	7/23 (30,4)	15,5 [5,82; NE]	6/14 (42,9)	3,7 [0,33; NE]	0,32 [0,09; 1,18] 0,075
Nein	16/44 (36,4)	12,9 [2,17; NE]	11/23 (47,8)	3,9 [0,36; NE]	0,67 [0,31; 1,47] 0,320
Unbekannt	15/48 (31,3)	23,0 [6,70; NE]	19/36 (52,8)	0,4 [0,33; 1,02]	0,23 [0,11; 0,47] <0,001
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,947)					
Ja	2/16 (12,5)	NE [7,66; NE]	2/13 (15,4)	NE [0,33; NE]	0,71 [0,09; 5,45] 0,738

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	36/98 (36,7)	14,6 [7,62; 20,50]	34/60 (56,7)	0,8 [0,36; 3,71]	0,37 [0,22; 0,61] <0,001
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,793)					
TPS <50%	18/48 (37,5)	15,5 [1,68; NE]	14/27 (51,9)	0,5 [0,33; 3,94]	0,29 [0,12; 0,66] 0,003
TPS ≥50%	5/19 (26,3)	12,9 [6,77; NE]	6/13 (46,2)	5,4 [0,30; NE]	0,33 [0,08; 1,36] 0,108
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,855)					
TPS <50%	18/48 (37,5)	15,5 [1,68; NE]	14/27 (51,9)	0,5 [0,33; 3,94]	0,29 [0,12; 0,66] 0,003
TPS ≥50%	5/19 (26,3)	12,9 [6,77; NE]	6/13 (46,2)	5,4 [0,30; NE]	0,33 [0,08; 1,36] 0,108
Unbekannt	15/48 (31,3)	14,6 [6,70; NE]	16/33 (48,5)	1,2 [0,36; NE]	0,28 [0,12; 0,62] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,858)					
Negativ	9/26 (34,6)	15,5 [0,59; NE]	6/12 (50,0)	0,5 [0,33; NE]	0,38 [0,12; 1,22] 0,086
Positiv	16/49 (32,7)	16,7 [6,51; NE]	15/34 (44,1)	3,7 [0,33; 8,51]	0,43 [0,20; 0,93] 0,031
Unbekannt	13/40 (32,5)	14,6 [10,78; NE]	15/27 (55,6)	0,7 [0,33; NE]	0,27 [0,12; 0,63] 0,001
Krankheitsstatus (p-Wert des Interaktionsterms: 0,726)					
III	2/6 (33,3)	10,8 [2,37; NE]	4/6 (66,7)	0,4 [0,26; NE]	0,47 [0,06; 3,62] 0,460
IVA	19/44 (43,2)	12,9 [6,70; 20,50]	16/33 (48,5)	0,6 [0,36; 6,18]	0,36 [0,17; 0,75] 0,005
IVB	17/65 (26,2)	16,8 [14,59; NE]	16/34 (47,1)	2,4 [0,36; NE]	0,34 [0,16; 0,72] 0,003
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,749)					
Asiatisch	24/66 (36,4)	20,5 [10,78; NE]	22/35 (62,9)	1,0 [0,36; 8,51]	0,34 [0,18; 0,61] <0,001

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	14/49 (28,6)	14,6 [6,70; 16,82]	12/34 (35,3)	1,2 [0,33; NE]	0,40 [0,17; 0,91] 0,024
RET-Probenart (p-Wert des Interaktionsterms: 0,716)					
Blut	2/9 (22,2)	NE [5,82; NE]	2/10 (20,0)	NE [0,33; NE]	1,00 [0,00; NE] NE
Gewebe	36/106 (34,0)	15,5 [10,78; 23,03]	34/63 (54,0)	0,8 [0,36; 2,60]	0,34 [0,21; 0,57] <0,001
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,312)					
CCDC6	3/9 (33,3)	NE [0,53; NE]	1/6 (16,7)	NE [0,30; NE]	0,45 [0,02; 8,98] 0,593
KIF5B	16/50 (32,0)	16,8 [7,66; NE]	16/36 (44,4)	3,7 [0,43; NE]	0,34 [0,16; 0,74] 0,004
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; IWRS: Interactive Web Response System; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection; vs.: versus. a: In Monaten. b: Aus dem stratifizierten Log-rank-Test. Das HR wurde mit einem stratifizierten Cox-Modell mit Behandlung als Kovariable und mit geografischer Region (ostasiatisch vs. nicht ostasiatisch; laut IWRS), Hirnmetastasenstatus zu Baseline (vorhanden vs. nicht vorhanden/unbekannt; laut IWRS) sowie Absicht des Prüfers, mit Pembrolizumab zu behandeln (Ja/Nein; laut IWRS) als Stratifizierungsvariablen geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 78: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des NSCLC-SAQ, Husten (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,108)					
<65 Jahre	23/76 (30,3)	14,6 [11,30; NE]	17/45 (37,8)	8,0 [0,76; NE]	0,57 [0,29; 1,09] 0,091
≥65 Jahre	17/39 (43,6)	6,7 [0,72; 21,68]	10/28 (35,7)	5,2 [2,40; NE]	1,21 [0,54; 2,71] 0,653
Baseline ECOG (p-Wert des Interaktionsterms: 0,127)					
0	12/41 (29,3)	14,6 [1,71; NE]	12/25 (48,0)	2,8 [0,76; NE]	0,45 [0,19; 1,07] 0,065
1	28/74 (37,8)	15,7 [8,12; 21,68]	15/48 (31,3)	24,0 [2,20; NE]	0,96 [0,50; 1,82] 0,896
Geschlecht (p-Wert des Interaktionsterms: 0,434)					
Männlich	18/61 (29,5)	16,6 [11,10; NE]	11/34 (32,4)	5,2 [1,58; NE]	0,65 [0,29; 1,48] 0,299
Weiblich	22/54 (40,7)	11,3 [6,74; 16,20]	16/39 (41,0)	17,5 [0,99; NE]	0,95 [0,50; 1,84] 0,914
Geografische Region (p-Wert des Interaktionsterms: 0,862)					
Ostasiatisch	26/65 (40,0)	15,7 [10,05; NE]	15/35 (42,9)	17,5 [2,20; NE]	0,80 [0,42; 1,53] 0,515
Nicht-Ostasiatisch	14/50 (28,0)	12,7 [1,68; 16,20]	12/38 (31,6)	3,7 [0,76; NE]	0,74 [0,34; 1,61] 0,446
Raucherstatus (p-Wert des Interaktionsterms: 0,641)					
Nie	23/72 (31,9)	14,6 [10,05; NE]	21/50 (42,0)	8,0 [1,74; 23,98]	0,67 [0,36; 1,25] 0,214
Ehemals/Aktuell	17/43 (39,5)	15,5 [6,77; 20,30]	6/23 (26,1)	5,2 [0,76; NE]	0,62 [0,23; 1,70] 0,351
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,316)					
Ja	9/23 (39,1)	12,7 [3,06; 21,68]	5/14 (35,7)	3,7 [0,76; NE]	0,97 [0,31; 3,04] 0,990
Nein	15/44 (34,1)	15,7 [1,71; NE]	7/23 (30,4)	17,5 [2,83; NE]	1,32 [0,53; 3,25] 0,549

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	16/48 (33,3)	14,6 [4,01; NE]	15/36 (41,7)	2,4 [0,56; 23,98]	0,53 [0,26; 1,09] 0,079
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,569)					
Ja	5/16 (31,3)	NE [0,53; NE]	2/13 (15,4)	NE [1,74; NE]	1,19 [0,20; 6,98] 0,848
Nein	35/98 (35,7)	15,5 [10,18; 20,30]	25/60 (41,7)	5,2 [1,74; 23,98]	0,72 [0,43; 1,23] 0,233
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,340)					
TPS <50%	20/48 (41,7)	15,5 [1,18; 20,30]	9/27 (33,3)	3,9 [0,99; NE]	0,82 [0,34; 1,98] 0,660
TPS ≥50%	4/19 (21,1)	12,7 [6,74; NE]	5/13 (38,5)	6,6 [0,33; NE]	0,52 [0,13; 2,02] 0,336
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,545)					
TPS <50%	20/48 (41,7)	15,5 [1,18; 20,30]	9/27 (33,3)	3,9 [0,99; NE]	0,82 [0,34; 1,98] 0,660
TPS ≥50%	4/19 (21,1)	12,7 [6,74; NE]	5/13 (38,5)	6,6 [0,33; NE]	0,52 [0,13; 2,02] 0,336
Unbekannt	16/48 (33,3)	14,6 [8,12; NE]	13/33 (39,4)	17,5 [0,76; NE]	0,63 [0,29; 1,37] 0,235
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,348)					
Negativ	10/26 (38,5)	15,5 [0,59; NE]	3/12 (25,0)	NE [0,99; NE]	1,21 [0,31; 4,74] 0,792
Positiv	14/49 (28,6)	21,7 [10,18; NE]	13/34 (38,2)	3,9 [1,74; NE]	0,51 [0,22; 1,15] 0,105
Unbekannt	16/40 (40,0)	11,3 [4,01; NE]	11/27 (40,7)	17,5 [0,59; NE]	0,84 [0,37; 1,90] 0,682
Krankheitsstatus (p-Wert des Interaktionsterms: 0,654)					
III*	0/6 (0,0)	NE [NE; NE]	3/6 (50,0)	3,9 [0,72; NE]	0,00 [0,00; NE] 0,248
IVA	19/44 (43,2)	10,2 [1,68; 20,30]	11/33 (33,3)	NE [0,59; NE]	1,05 [0,47; 2,34] 0,902

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	21/65 (32,3)	15,5 [12,68; 21,68]	13/34 (38,2)	8,0 [2,20; NE]	0,59 [0,29; 1,24] 0,160
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,817)					
Asiatisch	26/66 (39,4)	15,7 [10,05; NE]	15/35 (42,9)	17,5 [2,20; NE]	0,80 [0,42; 1,53] 0,515
Nicht asiatisch	14/49 (28,6)	12,7 [1,68; 16,20]	9/34 (26,5)	3,7 [0,72; NE]	0,91 [0,39; 2,12] 0,827
RET-Probenart (p-Wert des Interaktionsterms: 0,926)					
Blut	2/9 (22,2)	NE [0,53; NE]	2/10 (20,0)	NE [0,33; NE]	>100 [0,00; NE] 0,655
Gewebe	38/106 (35,8)	14,6 [10,18; 20,30]	25/63 (39,7)	5,2 [1,74; 23,98]	0,78 [0,47; 1,31] 0,351
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,493)					
CCDC6	3/9 (33,3)	NE [0,33; NE]	1/6 (16,7)	NE [2,83; NE]	0,93 [0,09; 9,20] 0,953
KIF5B	16/50 (32,0)	15,5 [6,77; NE]	13/36 (36,1)	3,9 [1,58; NE]	0,64 [0,30; 1,36] 0,259
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; IWRS: Interactive Web Response System; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection; vs.: versus. a: In Monaten. b: Aus dem stratifizierten Log-rank-Test. Das HR wurde mit einem stratifizierten Cox-Modell mit Behandlung als Kovariable und mit geografischer Region (ostasiatisch vs. nicht ostasiatisch; laut IWRS), Hirnmetastasenstatus zu Baseline (vorhanden vs. nicht vorhanden/unbekannt; laut IWRS) sowie Absicht des Prüfers, mit Pembrolizumab zu behandeln (Ja/Nein; laut IWRS) als Stratifizierungsvariablen geschätzt. * SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

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Tabelle 79: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des NSCLC-SAQ, Schmerz (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,936)					
0	15/41 (36,6)	6,3 [1,22; 14,46]	12/25 (48,0)	0,8 [0,53; 8,15]	0,65 [0,30; 1,43] 0,330
1	33/74 (44,6)	3,5 [0,76; NE]	24/48 (50,0)	0,9 [0,43; 4,70]	0,68 [0,40; 1,16] 0,150
Geschlecht (p-Wert des Interaktionsterms: 0,766)					
Männlich	24/61 (39,3)	1,9 [0,76; 14,46]	16/34 (47,1)	0,8 [0,39; 9,26]	0,61 [0,31; 1,20] 0,139
Weiblich	24/54 (44,4)	4,9 [0,82; NE]	20/39 (51,3)	0,9 [0,53; 8,15]	0,71 [0,39; 1,30] 0,281
Geografische Region (p-Wert des Interaktionsterms: 0,851)					
Ostasiatisch	34/65 (52,3)	3,5 [1,02; 14,46]	22/35 (62,9)	0,8 [0,43; 4,70]	0,64 [0,37; 1,10] 0,111
Nicht-Ostasiatisch	14/50 (28,0)	6,3 [0,72; NE]	14/38 (36,8)	1,3 [0,36; 9,26]	0,70 [0,33; 1,49] 0,352
Raucherstatus (p-Wert des Interaktionsterms: 0,702)					
Nie	30/72 (41,7)	4,5 [0,82; 14,46]	26/50 (52,0)	0,6 [0,39; 4,70]	0,67 [0,39; 1,15] 0,156
Ehemals/Aktuell	18/43 (41,9)	3,5 [0,76; NE]	10/23 (43,5)	1,7 [0,53; 9,26]	0,88 [0,37; 2,11] 0,759
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,636)					
Ja	8/23 (34,8)	4,9 [0,79; NE]	6/14 (42,9)	9,3 [0,36; NE]	1,08 [0,35; 3,39] 0,891
Nein	22/44 (50,0)	1,6 [0,56; 14,09]	12/23 (52,2)	0,5 [0,33; NE]	0,76 [0,37; 1,59] 0,502
Unbekannt	18/48 (37,5)	4,4 [0,72; NE]	18/36 (50,0)	0,9 [0,39; 1,71]	0,51 [0,26; 0,99] 0,038
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,464)					
Ja	3/16 (18,8)	NE [0,76; NE]	3/13 (23,1)	NE [0,43; NE]	0,56 [0,10; 2,97] 0,489

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	45/98 (45,9)	3,4 [1,02; 6,77]	33/60 (55,0)	0,8 [0,43; 3,29]	0,72 [0,45; 1,14] 0,167
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,423)					
TPS <50%	21/48 (43,8)	1,7 [0,76; NE]	13/27 (48,1)	0,7 [0,43; 9,26]	0,62 [0,29; 1,34] 0,247
TPS ≥50%	7/19 (36,8)	7,9 [0,79; NE]	7/13 (53,8)	1,3 [0,26; 6,08]	0,34 [0,10; 1,15] 0,072
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,465)					
TPS <50%	21/48 (43,8)	1,7 [0,76; NE]	13/27 (48,1)	0,7 [0,43; 9,26]	0,62 [0,29; 1,34] 0,247
TPS ≥50%	7/19 (36,8)	7,9 [0,79; NE]	7/13 (53,8)	1,3 [0,26; 6,08]	0,34 [0,10; 1,15] 0,072
Unbekannt	20/48 (41,7)	4,4 [0,53; NE]	16/33 (48,5)	1,0 [0,39; NE]	0,77 [0,40; 1,52] 0,440
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,486)					
Negativ	12/26 (46,2)	1,2 [0,53; NE]	6/12 (50,0)	0,8 [0,43; NE]	1,17 [0,41; 3,38] 0,766
Positiv	20/49 (40,8)	6,3 [0,79; NE]	16/34 (47,1)	0,9 [0,36; 8,15]	0,47 [0,22; 0,99] 0,052
Unbekannt	16/40 (40,0)	4,9 [0,56; NE]	14/27 (51,9)	0,9 [0,36; 4,70]	0,70 [0,33; 1,45] 0,328
Krankheitsstatus (p-Wert des Interaktionsterms: 0,825)					
III	3/6 (50,0)	14,5 [0,76; NE]	3/6 (50,0)	0,5 [0,26; NE]	0,33 [0,04; 2,45] 0,257
IVA	21/44 (47,7)	4,0 [0,59; 6,77]	18/33 (54,5)	0,6 [0,39; 3,29]	0,51 [0,27; 0,97] 0,040
IVB	24/65 (36,9)	4,1 [0,79; NE]	15/34 (44,1)	1,0 [0,53; NE]	0,75 [0,39; 1,46] 0,388
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,670)					
Asiatisch	34/66 (51,5)	4,0 [1,02; 14,46]	22/35 (62,9)	0,8 [0,43; 4,70]	0,64 [0,37; 1,10] 0,111

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	14/49 (28,6)	6,3 [0,72; NE]	12/34 (35,3)	1,0 [0,36; 9,26]	0,79 [0,36; 1,76] 0,566
RET-Probenart (p-Wert des Interaktionsterms: 0,090)					
Blut	3/9 (33,3)	NE [0,53; NE]	5/10 (50,0)	0,4 [0,26; NE]	0,00 [0,00; NE] 0,025
Gewebe	45/106 (42,5)	3,5 [1,18; 14,09]	31/63 (49,2)	1,0 [0,53; 6,08]	0,74 [0,46; 1,18] 0,216
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,534)					
CCDC6	3/9 (33,3)	NE [0,53; NE]	1/6 (16,7)	NE [0,53; NE]	0,80 [0,06; 11,50] 1,000
KIF5B	23/50 (46,0)	3,8 [0,79; NE]	19/36 (52,8)	0,8 [0,43; 6,08]	0,60 [0,32; 1,12] 0,105
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; IWRS: Interactive Web Response System; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection; vs.: versus. a: In Monaten. b: Aus dem stratifizierten Log-rank-Test. Das HR wurde mit einem stratifizierten Cox-Modell mit Behandlung als Kovariable und mit geografischer Region (ostasiatisch vs. nicht ostasiatisch; laut IWRS), Hirnmetastasenstatus zu Baseline (vorhanden vs. nicht vorhanden/unbekannt; laut IWRS) sowie Absicht des Prüfers, mit Pembrolizumab zu behandeln (Ja/Nein; laut IWRS) als Stratifizierungsvariablen geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fwspai_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 80: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des NSCLC-SAQ, Dyspnoe (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,074)					
<65 Jahre	30/76 (39,5)	7,7 [2,43; NE]	25/45 (55,6)	0,5 [0,36; 1,02]	0,42 [0,24; 0,74] 0,002
≥65 Jahre	22/39 (56,4)	1,9 [0,79; 4,17]	15/28 (53,6)	1,1 [0,39; 1,74]	0,73 [0,37; 1,46] 0,373
Baseline ECOG (p-Wert des Interaktionsterms: 0,377)					
0	16/41 (39,0)	5,6 [1,94; 15,51]	14/25 (56,0)	0,5 [0,33; 1,64]	0,38 [0,17; 0,84] 0,014
1	36/74 (48,6)	3,7 [1,87; 12,02]	26/48 (54,2)	0,6 [0,36; 1,18]	0,56 [0,33; 0,93] 0,026
Geografische Region (p-Wert des Interaktionsterms: 0,582)					
Ostasiatisch	33/65 (50,8)	3,3 [1,68; 14,09]	25/35 (71,4)	0,5 [0,36; 1,02]	0,46 [0,27; 0,78] 0,004
Nicht-Ostasiatisch	19/50 (38,0)	4,5 [2,10; 7,69]	15/38 (39,5)	1,1 [0,36; 3,71]	0,59 [0,29; 1,18] 0,136
Raucherstatus (p-Wert des Interaktionsterms: 0,558)					
Nie	32/72 (44,4)	2,8 [1,05; 14,09]	29/50 (58,0)	0,6 [0,36; 1,64]	0,54 [0,33; 0,91] 0,020
Ehemals/Aktuell	20/43 (46,5)	6,1 [2,10; 12,91]	11/23 (47,8)	0,6 [0,33; 1,64]	0,30 [0,12; 0,72] 0,005
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,468)					
Ja	10/23 (43,5)	7,7 [0,53; 15,51]	9/14 (64,3)	1,7 [0,33; 3,71]	0,54 [0,20; 1,47] 0,210
Nein	21/44 (47,7)	2,8 [1,91; 12,91]	13/23 (56,5)	1,0 [0,33; 6,18]	0,63 [0,31; 1,29] 0,201
Unbekannt	21/48 (43,8)	4,5 [1,64; NE]	18/36 (50,0)	0,4 [0,33; 0,56]	0,37 [0,19; 0,74] 0,004
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,797)					
Ja	7/16 (43,8)	4,5 [0,99; NE]	5/13 (38,5)	1,3 [0,33; NE]	0,12 [0,01; 1,09] 0,030

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	45/98 (45,9)	4,4 [1,94; 12,02]	35/60 (58,3)	0,6 [0,36; 1,08]	0,52 [0,33; 0,82] 0,005
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,465)					
TPS <50%	22/48 (45,8)	2,4 [1,91; 15,51]	12/27 (44,4)	0,7 [0,43; NE]	0,71 [0,34; 1,51] 0,390
TPS ≥50%	9/19 (47,4)	5,1 [0,99; NE]	6/13 (46,2)	0,5 [0,30; NE]	0,65 [0,22; 1,96] 0,471
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,177)					
TPS <50%	22/48 (45,8)	2,4 [1,91; 15,51]	12/27 (44,4)	0,7 [0,43; NE]	0,71 [0,34; 1,51] 0,390
TPS ≥50%	9/19 (47,4)	5,1 [0,99; NE]	6/13 (46,2)	0,5 [0,30; NE]	0,65 [0,22; 1,96] 0,471
Unbekannt	21/48 (43,8)	6,1 [0,79; 14,09]	22/33 (66,7)	0,4 [0,33; 1,64]	0,28 [0,14; 0,57] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,096)					
Negativ	13/26 (50,0)	2,1 [0,76; 3,71]	5/12 (41,7)	3,4 [0,36; NE]	1,19 [0,40; 3,53] 0,758
Positiv	21/49 (42,9)	5,3 [2,37; NE]	18/34 (52,9)	0,8 [0,36; 1,91]	0,52 [0,26; 1,03] 0,063
Unbekannt	18/40 (45,0)	2,8 [0,66; NE]	17/27 (63,0)	0,4 [0,33; 1,08]	0,39 [0,19; 0,82] 0,011
Krankheitsstatus (p-Wert des Interaktionsterms: 0,393)					
III	3/6 (50,0)	4,4 [0,66; NE]	5/6 (83,3)	0,5 [0,26; NE]	0,11 [0,01; 1,05] 0,022
IVA	21/44 (47,7)	4,2 [1,64; 12,91]	19/33 (57,6)	0,4 [0,33; 1,08]	0,47 [0,24; 0,93] 0,030
IVB	28/65 (43,1)	4,5 [1,91; 14,09]	16/34 (47,1)	0,9 [0,36; 3,71]	0,59 [0,31; 1,12] 0,104
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,433)					
Asiatisch	34/66 (51,5)	3,3 [1,68; 14,09]	25/35 (71,4)	0,5 [0,36; 1,02]	0,46 [0,27; 0,78] 0,004

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	18/49 (36,7)	5,1 [2,10; 7,69]	12/34 (35,3)	1,2 [0,36; NE]	0,67 [0,32; 1,42] 0,298
RET-Probenart (p-Wert des Interaktionsterms: 0,066)					
Blut	4/9 (44,4)	5,3 [0,30; NE]	2/10 (20,0)	NE [0,89; NE]	0,51 [0,05; 5,74] 0,583
Gewebe	48/106 (45,3)	4,2 [1,94; 7,69]	38/63 (60,3)	0,5 [0,36; 1,02]	0,40 [0,25; 0,63] <0,001
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,250)					
CCDC6	4/9 (44,4)	10,3 [0,30; NE]	1/6 (16,7)	NE [0,53; NE]	0,79 [0,06; 10,15] 0,857
KIF5B	24/50 (48,0)	4,5 [2,43; 15,51]	18/36 (50,0)	1,0 [0,39; 3,71]	0,59 [0,31; 1,10] 0,097
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; IWRS: Interactive Web Response System; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection; vs.: versus. a: In Monaten. b: Aus dem stratifizierten Log-rank-Test. Das HR wurde mit einem stratifizierten Cox-Modell mit Behandlung als Kovariable und mit geografischer Region (ostasiatisch vs. nicht ostasiatisch; laut IWRS), Hirnmetastasenstatus zu Baseline (vorhanden vs. nicht vorhanden/unbekannt; laut IWRS) sowie Absicht des Prüfers, mit Pembrolizumab zu behandeln (Ja/Nein; laut IWRS) als Stratifizierungsvariablen geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fwdsys_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 81: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des NSCLC-SAQ, Müdigkeit ($\geq 0,6$ Punkte) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,128)					
<65 Jahre	28/76 (36,8)	11,1 [3,48; NE]	26/45 (57,8)	0,4 [0,36; 0,79]	0,28 [0,15; 0,50] <0,001
≥65 Jahre	17/39 (43,6)	1,9 [0,76; 13,90]	13/28 (46,4)	0,6 [0,33; 1,64]	0,61 [0,29; 1,30] 0,164
Baseline ECOG (p-Wert des Interaktionsterms: 0,778)					
0	15/41 (36,6)	3,5 [1,22; NE]	13/25 (52,0)	0,5 [0,33; 1,22]	0,32 [0,14; 0,72] 0,004
1	30/74 (40,5)	10,3 [2,43; NE]	26/48 (54,2)	0,4 [0,36; 1,02]	0,43 [0,25; 0,75] 0,002
Geschlecht (p-Wert des Interaktionsterms: 0,727)					
Männlich	27/61 (44,3)	1,9 [0,99; 11,10]	19/34 (55,9)	0,4 [0,33; 0,79]	0,29 [0,15; 0,60] <0,001
Weiblich	18/54 (33,3)	14,6 [4,47; NE]	20/39 (51,3)	0,5 [0,33; 1,91]	0,38 [0,20; 0,72] 0,003
Geografische Region (p-Wert des Interaktionsterms: 0,643)					
Ostasiatisch	30/65 (46,2)	10,3 [1,71; NE]	24/35 (68,6)	0,5 [0,36; 0,79]	0,35 [0,20; 0,62] <0,001
Nicht-Ostasiatisch	15/50 (30,0)	5,6 [1,22; NE]	15/38 (39,5)	0,5 [0,33; 2,43]	0,44 [0,21; 0,91] 0,024
Raucherstatus (p-Wert des Interaktionsterms: 0,183)					
Nie	24/72 (33,3)	14,6 [3,48; NE]	30/50 (60,0)	0,5 [0,36; 0,79]	0,28 [0,16; 0,51] <0,001
Ehemals/Aktuell	21/43 (48,8)	2,6 [0,99; 11,10]	9/23 (39,1)	0,5 [0,33; NE]	0,52 [0,22; 1,23] 0,143
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,566)					
Ja	7/23 (30,4)	6,0 [1,22; NE]	5/14 (35,7)	NE [0,30; NE]	0,80 [0,25; 2,54] 0,697
Nein	19/44 (43,2)	6,8 [1,18; NE]	15/23 (65,2)	0,5 [0,33; 1,22]	0,33 [0,16; 0,70] 0,003

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	19/48 (39,6)	11,1 [0,99; NE]	19/36 (52,8)	0,4 [0,33; 0,79]	0,34 [0,17; 0,67] 0,001
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,070)					
Ja	2/16 (12,5)	NE [1,22; NE]	4/13 (30,8)	0,8 [0,33; NE]	0,29 [0,05; 1,74] 0,158
Nein	43/98 (43,9)	4,5 [1,68; 13,90]	35/60 (58,3)	0,5 [0,36; 0,79]	0,45 [0,28; 0,72] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,510)					
Negativ	11/26 (42,3)	2,4 [0,76; NE]	6/12 (50,0)	0,5 [0,33; NE]	0,42 [0,13; 1,36] 0,140
Positiv	18/49 (36,7)	13,9 [1,68; NE]	15/34 (44,1)	0,8 [0,33; NE]	0,46 [0,22; 0,96] 0,034
Unbekannt	16/40 (40,0)	10,8 [1,22; NE]	18/27 (66,7)	0,4 [0,33; 0,79]	0,32 [0,15; 0,67] 0,001
Krankheitsstatus (p-Wert des Interaktionsterms: 0,373)					
III	2/6 (33,3)	10,8 [4,44; NE]	5/6 (83,3)	0,4 [0,26; NE]	0,00 [0,00; NE] 0,004
IVA	21/44 (47,7)	3,7 [1,22; 14,59]	18/33 (54,5)	0,4 [0,33; 1,05]	0,33 [0,16; 0,66] 0,002
IVB	22/65 (33,8)	13,9 [1,08; NE]	16/34 (47,1)	0,5 [0,36; 1,91]	0,51 [0,26; 0,98] 0,033
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,393)					
Asiatisch	30/66 (45,5)	10,8 [1,71; NE]	24/35 (68,6)	0,5 [0,36; 0,79]	0,35 [0,20; 0,62] <0,001
Nicht asiatisch	15/49 (30,6)	4,5 [1,22; 14,59]	12/34 (35,3)	0,6 [0,30; NE]	0,54 [0,25; 1,16] 0,110
RET-Probenart (p-Wert des Interaktionsterms: 0,195)					
Blut	4/9 (44,4)	6,0 [0,53; NE]	3/10 (30,0)	NE [0,33; NE]	>100 [0,00; NE] 0,405
Gewebe	41/106 (38,7)	10,3 [1,94; 16,69]	36/63 (57,1)	0,5 [0,36; 0,79]	0,33 [0,21; 0,54] <0,001

Subgruppe	Selpercatinib	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	Mediane Ereigniszeit ^a [95% KI]	
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; IWRS: Interactive Web Response System; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection; vs.: versus. a: In Monaten. b: Aus dem stratifizierten Log-rank-Test. Das HR wurde mit einem stratifizierten Cox-Modell mit Behandlung als Kovariable und mit geografischer Region (ostasiatisch vs. nicht ostasiatisch; laut IWRS), Hirnmetastasenstatus zu Baseline (vorhanden vs. nicht vorhanden/unbekannt; laut IWRS) sowie Absicht des Prüfers, mit Pembrolizumab zu behandeln (Ja/Nein; laut IWRS) als Stratifizierungsvariablen geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.				

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fwnsfat_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 82: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des NSCLC-SAQ, Verminderter Appetit (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,283)					
<65 Jahre	31/76 (40,8)	6,2 [2,37; 14,59]	29/45 (64,4)	0,4 [0,33; 0,56]	0,24 [0,14; 0,43] <0,001
≥65 Jahre	17/39 (43,6)	1,2 [0,76; 11,10]	15/28 (53,6)	0,5 [0,33; 1,87]	0,43 [0,20; 0,93] 0,028
Baseline ECOG (p-Wert des Interaktionsterms: 0,754)					
0	13/41 (31,7)	4,9 [0,99; NE]	15/25 (60,0)	0,5 [0,33; 1,87]	0,28 [0,12; 0,63] 0,001
1	35/74 (47,3)	5,1 [1,51; 11,10]	29/48 (60,4)	0,4 [0,33; 0,49]	0,37 [0,22; 0,62] <0,001
Geografische Region (p-Wert des Interaktionsterms: 0,806)					
Ostasiatisch	33/65 (50,8)	4,9 [1,22; 14,55]	26/35 (74,3)	0,4 [0,33; 0,66]	0,35 [0,21; 0,59] <0,001
Nicht-Ostasiatisch	15/50 (30,0)	5,1 [1,18; NE]	18/38 (47,4)	0,4 [0,33; 1,87]	0,31 [0,15; 0,64] <0,001
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,415)					
Ja	9/23 (39,1)	5,1 [1,22; NE]	10/14 (71,4)	0,4 [0,33; 2,37]	0,25 [0,09; 0,71] 0,005
Nein	19/44 (43,2)	2,4 [0,85; NE]	14/23 (60,9)	0,5 [0,33; 1,87]	0,42 [0,20; 0,87] 0,018
Unbekannt	20/48 (41,7)	6,2 [0,99; NE]	20/36 (55,6)	0,4 [0,33; 0,43]	0,27 [0,14; 0,52] <0,001
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,069)					
Ja	3/16 (18,8)	NE [5,09; NE]	5/13 (38,5)	0,4 [0,33; NE]	0,13 [0,01; 1,15] 0,032
Nein	45/98 (45,9)	4,0 [1,22; 11,10]	39/60 (65,0)	0,4 [0,36; 0,66]	0,39 [0,25; 0,60] <0,001
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,200)					
TPS <50%	21/48 (43,8)	2,4 [0,76; NE]	15/27 (55,6)	0,5 [0,33; 0,99]	0,41 [0,20; 0,83] 0,012

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
TPS ≥50%	4/19 (21,1)	NE [4,86; NE]	7/13 (53,8)	1,5 [0,30; 3,78]	0,15 [0,03; 0,74] 0,009
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,312)					
TPS <50%	21/48 (43,8)	2,4 [0,76; NE]	15/27 (55,6)	0,5 [0,33; 0,99]	0,41 [0,20; 0,83] 0,012
TPS ≥50%	4/19 (21,1)	NE [4,86; NE]	7/13 (53,8)	1,5 [0,30; 3,78]	0,15 [0,03; 0,74] 0,009
Unbekannt	23/48 (47,9)	4,0 [0,99; 14,55]	22/33 (66,7)	0,4 [0,33; 0,99]	0,36 [0,19; 0,67] 0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,880)					
Negativ	10/26 (38,5)	5,1 [0,59; NE]	7/12 (58,3)	0,5 [0,30; 0,66]	0,27 [0,08; 0,87] 0,018
Positiv	18/49 (36,7)	6,8 [0,95; NE]	20/34 (58,8)	0,5 [0,33; 1,91]	0,39 [0,20; 0,76] 0,004
Unbekannt	20/40 (50,0)	4,9 [0,99; 14,55]	17/27 (63,0)	0,4 [0,33; 1,02]	0,40 [0,20; 0,80] 0,010
Krankheitsstatus (p-Wert des Interaktionsterms: 0,925)					
III	2/6 (33,3)	NE [0,43; NE]	4/6 (66,7)	1,6 [0,30; NE]	0,33 [0,04; 2,45] 0,257
IVA	22/44 (50,0)	4,0 [0,99; 11,10]	20/33 (60,6)	0,4 [0,33; 0,53]	0,34 [0,17; 0,66] 0,001
IVB	24/65 (36,9)	6,2 [1,22; NE]	20/34 (58,8)	0,4 [0,33; 1,87]	0,30 [0,16; 0,58] <0,001
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,964)					
Asiatisch	33/66 (50,0)	6,2 [1,22; 14,55]	26/35 (74,3)	0,4 [0,33; 0,66]	0,35 [0,21; 0,59] <0,001
Nicht asiatisch	15/49 (30,6)	5,1 [1,18; NE]	15/34 (44,1)	0,4 [0,30; 1,87]	0,34 [0,16; 0,73] 0,004
RET-Probenart (p-Wert des Interaktionsterms: 0,113)					
Blut	3/9 (33,3)	7,4 [0,76; NE]	5/10 (50,0)	0,4 [0,26; NE]	0,00 [0,00; NE] 0,013

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Gewebe	45/106 (42,5)	4,9 [1,74; 11,10]	39/63 (61,9)	0,4 [0,36; 0,66]	0,36 [0,23; 0,56] <0,001
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; IWRS: Interactive Web Response System; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; NSCLC-SAQ: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection; vs.: versus. a: In Monaten. b: Aus dem stratifizierten Log-rank-Test. Das HR wurde mit einem stratifizierten Cox-Modell mit Behandlung als Kovariable und mit geografischer Region (ostasiatisch vs. nicht ostasiatisch; laut IWRS), Hirnmetastasenstatus zu Baseline (vorhanden vs. nicht vorhanden/unbekannt; laut IWRS) sowie Absicht des Prüfers, mit Pembrolizumab zu behandeln (Ja/Nein; laut IWRS) als Stratifizierungsvariablen geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fwnsapp_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 83: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung für FACT-G Nebenwirkungen (≥15 % der Spanne) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,196)					
<65 Jahre	44/76 (57,9)	1,0 [0,76; 2,14]	29/45 (64,4)	0,4 [0,33; 0,43]	0,32 [0,19; 0,52] <0,001
≥65 Jahre	22/39 (56,4)	0,8 [0,72; 0,99]	17/28 (60,7)	0,3 [0,30; 0,49]	0,58 [0,30; 1,11] 0,106
Baseline ECOG (p-Wert des Interaktionsterms: 0,161)					
0	19/41 (46,3)	1,0 [0,76; 2,04]	15/25 (60,0)	0,3 [0,30; 0,49]	0,25 [0,12; 0,52] <0,001
1	47/74 (63,5)	1,0 [0,76; 1,48]	31/48 (64,6)	0,4 [0,33; 0,43]	0,44 [0,28; 0,70] <0,001
Geschlecht (p-Wert des Interaktionsterms: 0,886)					
Männlich	33/61 (54,1)	1,0 [0,76; 1,45]	20/34 (58,8)	0,4 [0,33; 0,49]	0,38 [0,21; 0,67] <0,001
Weiblich	33/54 (61,1)	1,0 [0,76; 2,14]	26/39 (66,7)	0,3 [0,33; 0,36]	0,39 [0,23; 0,67] <0,001
Geografische Region (p-Wert des Interaktionsterms: 0,216)					
Ostasiatisch	46/65 (70,8)	1,0 [0,76; 1,68]	28/35 (80,0)	0,4 [0,33; 0,49]	0,44 [0,28; 0,72] <0,001
Nicht-Ostasiatisch	20/50 (40,0)	0,9 [0,72; 0,99]	18/38 (47,4)	0,3 [0,30; 0,39]	0,25 [0,12; 0,51] <0,001
Raucherstatus (p-Wert des Interaktionsterms: 0,081)					
Nie	41/72 (56,9)	0,9 [0,76; 1,68]	35/50 (70,0)	0,3 [0,33; 0,36]	0,31 [0,19; 0,50] <0,001
Ehemals/Aktuell	25/43 (58,1)	1,0 [0,76; 1,45]	11/23 (47,8)	0,5 [0,33; 1,12]	0,64 [0,31; 1,32] 0,209
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,112)					
Ja	13/23 (56,5)	1,4 [0,76; 2,60]	11/14 (78,6)	0,3 [0,30; 0,36]	0,17 [0,06; 0,46] <0,001
Nein	25/44 (56,8)	1,0 [0,76; 1,97]	15/23 (65,2)	0,4 [0,30; 0,49]	0,21 [0,10; 0,43] <0,001

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	28/48 (58,3)	0,9 [0,59; 1,45]	20/36 (55,6)	0,4 [0,33; 0,53]	0,56 [0,31; 1,00] 0,058
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,112)					
Ja	9/16 (56,3)	0,8 [0,49; 0,95]	5/13 (38,5)	0,4 [0,33; NE]	0,83 [0,27; 2,60] 0,677
Nein	57/98 (58,2)	1,0 [0,76; 1,68]	41/60 (68,3)	0,3 [0,33; 0,39]	0,34 [0,23; 0,52] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,193)					
Negativ	12/26 (46,2)	1,0 [0,72; 1,97]	8/12 (66,7)	0,4 [0,30; 0,53]	0,05 [0,01; 0,24] <0,001
Positiv	31/49 (63,3)	0,8 [0,76; 0,99]	22/34 (64,7)	0,3 [0,30; 0,36]	0,30 [0,17; 0,53] <0,001
Unbekannt	23/40 (57,5)	1,0 [0,56; 2,37]	16/27 (59,3)	0,4 [0,33; 0,79]	0,58 [0,30; 1,10] 0,101
Krankheitsstatus (p-Wert des Interaktionsterms: 0,735)					
III	3/6 (50,0)	2,0 [0,56; NE]	4/6 (66,7)	0,3 [0,26; NE]	0,29 [0,06; 1,37] 0,100
IVA	29/44 (65,9)	0,9 [0,72; 1,02]	23/33 (69,7)	0,4 [0,33; 0,43]	0,38 [0,21; 0,68] <0,001
IVB	34/65 (52,3)	1,0 [0,76; 2,17]	19/34 (55,9)	0,3 [0,33; 0,49]	0,41 [0,23; 0,73] 0,002
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,469)					
Asiatisch	46/66 (69,7)	1,0 [0,76; 1,97]	28/35 (80,0)	0,4 [0,33; 0,49]	0,43 [0,27; 0,69] <0,001
Nicht asiatisch	20/49 (40,8)	0,8 [0,72; 0,95]	15/34 (44,1)	0,3 [0,30; 0,39]	0,29 [0,14; 0,61] <0,001
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,169)					
CCDC6	5/9 (55,6)	4,3 [0,76; NE]	3/6 (50,0)	0,3 [0,30; NE]	0,09 [0,01; 0,87] 0,012
KIF5B	32/50 (64,0)	0,8 [0,72; 0,95]	23/36 (63,9)	0,3 [0,30; 0,43]	0,45 [0,26; 0,77] 0,003

Subgruppe	Selpercatinib	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	Mediane Ereigniszeit ^a [95% KI]	
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt.				
Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.				

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_fw15pfact_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteqol_gba

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Tabelle 84: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Geschwollene Arme oder Beine - Häufigkeit (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,528)					
<65 Jahre	41/76 (53,9)	2,2 [1,25; 5,65]	22/45 (48,9)	1,4 [1,02; 5,16]	0,90 [0,53; 1,51] 0,682
≥65 Jahre	23/39 (59,0)	2,1 [0,95; 5,16]	13/28 (46,4)	1,7 [0,72; 7,49]	1,13 [0,57; 2,25] 0,737
Baseline ECOG (p-Wert des Interaktionsterms: 0,149)					
0	17/41 (41,5)	3,1 [1,22; 9,26]	12/25 (48,0)	1,5 [0,53; 4,01]	0,48 [0,22; 1,09] 0,072
1	47/74 (63,5)	2,1 [1,22; 5,16]	23/48 (47,9)	1,5 [1,02; 7,23]	1,17 [0,71; 1,93] 0,550
Geschlecht (p-Wert des Interaktionsterms: 0,517)					
Männlich	29/61 (47,5)	5,2 [1,94; 7,95]	14/34 (41,2)	1,7 [1,02; NE]	0,83 [0,43; 1,59] 0,565
Weiblich	35/54 (64,8)	1,6 [0,76; 3,32]	21/39 (53,8)	1,3 [0,95; 4,73]	1,12 [0,65; 1,93] 0,673
Geografische Region (p-Wert des Interaktionsterms: 0,276)					
Ostasiatisch	46/65 (70,8)	2,2 [1,25; 5,16]	23/35 (65,7)	1,2 [0,95; 2,37]	0,80 [0,48; 1,33] 0,384
Nicht-Ostasiatisch	18/50 (36,0)	1,4 [0,72; 6,01]	12/38 (31,6)	3,8 [1,41; 7,49]	1,31 [0,63; 2,74] 0,477
Raucherstatus (p-Wert des Interaktionsterms: 0,188)					
Nie	41/72 (56,9)	2,1 [1,22; 5,16]	25/50 (50,0)	1,7 [1,22; 5,16]	1,14 [0,69; 1,88] 0,614
Ehemals/Aktuell	23/43 (53,5)	2,2 [1,22; 7,43]	10/23 (43,5)	1,2 [0,36; 4,01]	0,65 [0,30; 1,38] 0,251
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,413)					
Ja	12/23 (52,2)	2,0 [0,53; 12,48]	6/14 (42,9)	4,7 [1,68; NE]	1,30 [0,45; 3,74] 0,636
Nein	25/44 (56,8)	3,3 [1,22; 5,65]	13/23 (56,5)	1,2 [0,72; 2,37]	0,73 [0,37; 1,44] 0,371

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	27/48 (56,3)	2,1 [1,18; 5,36]	16/36 (44,4)	1,3 [0,62; 7,49]	0,96 [0,52; 1,79] 0,909
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,810)					
Ja	8/16 (50,0)	5,2 [0,99; NE]	3/13 (23,1)	7,2 [0,62; NE]	0,79 [0,21; 3,02] 0,731
Nein	56/98 (57,1)	2,2 [1,22; 4,40]	32/60 (53,3)	1,5 [1,02; 3,81]	1,01 [0,65; 1,56] 0,968
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,583)					
TPS <50%	26/48 (54,2)	3,8 [1,18; 5,65]	12/27 (44,4)	1,3 [0,72; NE]	0,97 [0,49; 1,94] 0,916
TPS ≥50%	10/19 (52,6)	2,6 [0,59; NE]	6/13 (46,2)	3,7 [0,33; 4,73]	0,70 [0,25; 2,00] 0,498
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,810)					
TPS <50%	26/48 (54,2)	3,8 [1,18; 5,65]	12/27 (44,4)	1,3 [0,72; NE]	0,97 [0,49; 1,94] 0,916
TPS ≥50%	10/19 (52,6)	2,6 [0,59; NE]	6/13 (46,2)	3,7 [0,33; 4,73]	0,70 [0,25; 2,00] 0,498
Unbekannt	28/48 (58,3)	2,1 [1,22; 6,01]	17/33 (51,5)	1,6 [0,95; 5,16]	1,10 [0,60; 2,02] 0,766
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,726)					
Negativ	13/26 (50,0)	2,1 [0,53; 5,65]	6/12 (50,0)	1,3 [0,43; NE]	1,13 [0,43; 3,00] 0,805
Positiv	27/49 (55,1)	3,8 [1,25; 5,36]	15/34 (44,1)	1,7 [0,89; NE]	0,70 [0,36; 1,35] 0,279
Unbekannt	24/40 (60,0)	1,9 [0,76; 6,01]	14/27 (51,9)	1,5 [0,95; 5,16]	1,12 [0,58; 2,17] 0,750
Krankheitsstatus (p-Wert des Interaktionsterms: 0,480)					
III	2/6 (33,3)	8,7 [2,60; NE]	4/6 (66,7)	1,4 [0,72; NE]	0,35 [0,06; 1,95] 0,211
IVA	26/44 (59,1)	1,4 [1,22; 5,65]	17/33 (51,5)	1,5 [1,02; 4,01]	1,05 [0,57; 1,96] 0,865

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	36/65 (55,4)	2,2 [0,99; 5,16]	14/34 (41,2)	1,7 [0,62; 7,23]	0,99 [0,53; 1,84] 0,949
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,114)					
Asiatisch	46/66 (69,7)	2,6 [1,25; 5,16]	23/35 (65,7)	1,2 [0,95; 2,37]	0,78 [0,47; 1,29] 0,321
Nicht asiatisch	18/49 (36,7)	1,4 [0,72; 6,01]	10/34 (29,4)	4,0 [1,41; NE]	1,63 [0,74; 3,55] 0,219
RET-Probenart (p-Wert des Interaktionsterms: 0,714)					
Blut	6/9 (66,7)	1,0 [0,53; 3,06]	4/10 (40,0)	1,0 [0,36; NE]	1,34 [0,38; 4,78] 0,663
Gewebe	58/106 (54,7)	2,6 [1,25; 5,36]	31/63 (49,2)	1,7 [1,22; 4,01]	0,95 [0,61; 1,47] 0,794
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,272)					
CCDC6	6/9 (66,7)	3,8 [1,22; NE]	1/6 (16,7)	NE [1,22; NE]	2,23 [0,26; 19,17] 0,432
KIF5B	30/50 (60,0)	2,0 [0,99; 5,16]	19/36 (52,8)	1,5 [0,79; 3,75]	0,83 [0,47; 1,49] 0,527
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01alsf_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 85: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Schüttelfrost - Häufigkeit (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,160)					
0	14/41 (34,1)	6,2 [0,99; 21,26]	11/25 (44,0)	1,0 [0,33; NE]	0,54 [0,24; 1,21] 0,135
1	41/74 (55,4)	1,9 [0,99; 5,88]	21/48 (43,8)	2,0 [0,95; NE]	1,14 [0,67; 1,93] 0,630
Geschlecht (p-Wert des Interaktionsterms: 0,117)					
Männlich	27/61 (44,3)	2,3 [0,76; 6,05]	11/34 (32,4)	7,2 [0,95; NE]	1,39 [0,69; 2,81] 0,371
Weiblich	28/54 (51,9)	3,3 [0,99; 9,72]	21/39 (53,8)	1,0 [0,33; 2,56]	0,66 [0,37; 1,17] 0,167
Geografische Region (p-Wert des Interaktionsterms: 0,855)					
Ostasiatisch	37/65 (56,9)	3,1 [1,45; 6,05]	19/35 (54,3)	1,5 [0,72; NE]	0,97 [0,56; 1,69] 0,918
Nicht-Ostasiatisch	18/50 (36,0)	3,2 [0,72; 9,07]	13/38 (34,2)	1,6 [0,79; 7,20]	0,84 [0,40; 1,75] 0,602
Raucherstatus (p-Wert des Interaktionsterms: 0,784)					
Nie	35/72 (48,6)	3,0 [0,99; 5,88]	25/50 (50,0)	1,1 [0,82; 7,20]	0,89 [0,53; 1,50] 0,680
Ehemals/Aktuell	20/43 (46,5)	3,3 [0,99; 9,07]	7/23 (30,4)	3,6 [0,33; NE]	1,02 [0,43; 2,43] 0,986
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,704)					
Ja	11/23 (47,8)	1,8 [0,30; 13,86]	7/14 (50,0)	1,2 [0,33; NE]	0,91 [0,34; 2,46] 0,835
Nein	20/44 (45,5)	5,4 [0,76; 15,21]	9/23 (39,1)	2,6 [0,43; NE]	1,14 [0,52; 2,51] 0,742
Unbekannt	24/48 (50,0)	3,0 [0,99; 8,12]	16/36 (44,4)	1,5 [0,33; 5,82]	0,78 [0,41; 1,48] 0,474
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,958)					
Ja	6/16 (37,5)	5,4 [0,59; NE]	2/13 (15,4)	NE [0,33; NE]	1,09 [0,22; 5,46] 0,918

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	49/98 (50,0)	3,1 [1,22; 6,05]	30/60 (50,0)	1,3 [0,82; 5,82]	0,93 [0,59; 1,46] 0,741
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,576)					
Negativ	10/26 (38,5)	1,7 [0,53; NE]	5/12 (41,7)	9,2 [0,30; NE]	1,17 [0,40; 3,43] 0,775
Positiv	24/49 (49,0)	3,0 [0,76; 6,77]	16/34 (47,1)	1,0 [0,33; 5,82]	0,67 [0,35; 1,28] 0,235
Unbekannt	21/40 (52,5)	5,4 [0,99; 9,72]	11/27 (40,7)	2,0 [0,95; NE]	1,03 [0,49; 2,17] 0,923
Krankheitsstatus (p-Wert des Interaktionsterms: 0,918)					
III	2/6 (33,3)	NE [1,45; NE]	2/6 (33,3)	NE [0,95; NE]	0,85 [0,12; 6,11] 0,876
IVA	22/44 (50,0)	2,6 [0,72; 6,77]	16/33 (48,5)	1,2 [0,72; 15,70]	0,97 [0,51; 1,86] 0,929
IVB	31/65 (47,7)	3,3 [0,99; 9,07]	14/34 (41,2)	1,0 [0,33; 7,20]	0,76 [0,40; 1,46] 0,422
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,843)					
Asiatisch	38/66 (57,6)	3,3 [1,45; 6,05]	19/35 (54,3)	1,5 [0,72; NE]	0,97 [0,56; 1,68] 0,921
Nicht asiatisch	17/49 (34,7)	3,0 [0,72; 9,07]	11/34 (32,4)	1,2 [0,33; 7,20]	0,86 [0,39; 1,87] 0,647
RET-Probenart (p-Wert des Interaktionsterms: 0,150)					
Blut	5/9 (55,6)	1,7 [0,30; NE]	5/10 (50,0)	0,4 [0,26; NE]	0,46 [0,13; 1,63] 0,226
Gewebe	50/106 (47,2)	3,3 [1,22; 6,51]	27/63 (42,9)	2,1 [0,99; 15,70]	1,00 [0,63; 1,61] 0,995
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,601)					
CCDC6	4/9 (44,4)	10,2 [0,30; NE]	1/6 (16,7)	NE [0,30; NE]	0,48 [0,03; 7,63] 0,593
KIF5B	27/50 (54,0)	2,7 [1,22; 6,77]	20/36 (55,6)	0,8 [0,33; 1,48]	0,57 [0,32; 1,02] 0,058

Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab			
Subgruppe	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	HR [95% KI] p-Wert ^b
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte.					
Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01chif_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba
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Tabelle 86: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Schüttelfrost - Ausprägung (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,448)					
0	2/41 (4,9)	12,5 [5,59; NE]	3/25 (12,0)	1,0 [0,30; NE]	0,00 [0,00; NE] 0,036
1	6/74 (8,1)	3,2 [0,30; NE]	5/48 (10,4)	0,9 [0,33; NE]	0,32 [0,08; 1,26] 0,092
Geografische Region (p-Wert des Interaktionsterms: 0,979)					
Ostasiatisch	4/65 (6,2)	2,6 [0,30; NE]	7/35 (20,0)	0,9 [0,30; NE]	0,21 [0,04; 1,05] 0,040
Nicht-Ostasiatisch	4/50 (8,0)	19,4 [0,49; NE]	1/38 (2,6)	2,0 [NE; NE]	0,34 [0,03; 3,74] 0,353
Raucherstatus (p-Wert des Interaktionsterms: 0,494)					
Nie	5/72 (6,9)	3,7 [0,49; NE]	7/50 (14,0)	1,0 [0,30; 1,87]	0,17 [0,04; 0,66] 0,005
Ehemals/Aktuell	3/43 (7,0)	5,6 [0,30; NE]	1/23 (4,3)	NE [0,82; NE]	0,82 [0,05; 13,24] 0,886
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,274)					
Ja	2/16 (12,5)	1,7 [0,53; NE]	1/13 (7,7)	NE [1,02; NE]	0,82 [0,05; 13,24] 0,886
Nein	6/98 (6,1)	5,6 [0,30; NE]	7/60 (11,7)	0,8 [0,30; 1,87]	0,12 [0,02; 0,59] 0,002
Krankheitsstatus (p-Wert des Interaktionsterms: 0,321)					
III*	0/6 (0,0)	NE [NE; NE]	0/6 (0,0)	NE [NE; NE]	NE
IVA	3/44 (6,8)	2,6 [0,49; NE]	3/33 (9,1)	1,0 [0,30; NE]	0,25 [0,03; 2,43] 0,197
IVB	5/65 (7,7)	19,4 [0,30; NE]	5/34 (14,7)	0,9 [0,33; NE]	0,22 [0,05; 0,98] 0,033
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,979)					
Asiatisch	4/66 (6,1)	2,6 [0,30; NE]	7/35 (20,0)	0,9 [0,30; NE]	0,21 [0,04; 1,05] 0,040

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	4/49 (8,2)	19,4 [0,49; NE]	1/34 (2,9)	2,0 [NE; NE]	0,34 [0,03; 3,74] 0,353
RET-Probenart (p-Wert des Interaktionsterms: 0,091)					
Blut	2/9 (22,2)	1,7 [0,49; NE]	1/10 (10,0)	NE [0,82; NE]	0,82 [0,05; 13,24] 0,886
Gewebe	6/106 (5,7)	12,5 [0,30; NE]	7/63 (11,1)	1,0 [0,30; 1,87]	0,11 [0,02; 0,57] 0,002
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. * SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01chis_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 87: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Verstopfung - Ausprägung (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,120)					
<65 Jahre	41/76 (53,9)	1,8 [0,72; 2,37]	28/45 (62,2)	0,5 [0,33; 1,02]	0,52 [0,32; 0,85] 0,010
≥65 Jahre	21/39 (53,8)	0,8 [0,30; 2,37]	15/28 (53,6)	0,8 [0,30; 2,40]	1,06 [0,54; 2,05] 0,846
Baseline ECOG (p-Wert des Interaktionsterms: 0,579)					
0	20/41 (48,8)	1,6 [0,53; 2,37]	13/25 (52,0)	0,7 [0,33; 2,40]	0,68 [0,33; 1,39] 0,294
1	42/74 (56,8)	1,2 [0,62; 2,23]	30/48 (62,5)	0,7 [0,33; 0,95]	0,64 [0,40; 1,03] 0,059
Geschlecht (p-Wert des Interaktionsterms: 0,421)					
Männlich	30/61 (49,2)	1,6 [0,62; 3,32]	17/34 (50,0)	0,8 [0,36; 2,40]	0,79 [0,44; 1,44] 0,441
Weiblich	32/54 (59,3)	1,1 [0,59; 2,17]	26/39 (66,7)	0,5 [0,33; 0,95]	0,58 [0,34; 0,99] 0,043
Geografische Region (p-Wert des Interaktionsterms: 0,707)					
Ostasiatisch	45/65 (69,2)	1,2 [0,76; 2,23]	26/35 (74,3)	0,5 [0,33; 1,02]	0,69 [0,43; 1,13] 0,148
Nicht-Ostasiatisch	17/50 (34,0)	1,2 [0,30; 6,70]	17/38 (44,7)	0,7 [0,33; 1,68]	0,59 [0,29; 1,19] 0,127
Raucherstatus (p-Wert des Interaktionsterms: 0,363)					
Nie	39/72 (54,2)	1,4 [0,72; 2,23]	34/50 (68,0)	0,5 [0,33; 1,02]	0,59 [0,37; 0,94] 0,026
Ehemals/Aktuell	23/43 (53,5)	1,0 [0,53; 3,52]	9/23 (39,1)	0,8 [0,30; 2,40]	0,92 [0,43; 2,01] 0,851
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,151)					
Ja	12/23 (52,2)	0,7 [0,30; 1,71]	8/14 (57,1)	2,3 [0,30; NE]	1,25 [0,50; 3,14] 0,711
Nein	24/44 (54,5)	1,9 [1,25; 4,01]	14/23 (60,9)	0,4 [0,30; 0,79]	0,44 [0,22; 0,85] 0,013

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	26/48 (54,2)	0,9 [0,53; 3,32]	21/36 (58,3)	0,8 [0,33; 1,05]	0,65 [0,36; 1,18] 0,157
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,247)					
Ja	7/16 (43,8)	5,2 [0,30; NE]	2/13 (15,4)	9,1 [0,33; NE]	1,32 [0,26; 6,63] 0,745
Nein	55/98 (56,1)	1,2 [0,72; 1,91]	41/60 (68,3)	0,5 [0,33; 0,82]	0,60 [0,40; 0,90] 0,013
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,078)					
TPS <50%	25/48 (52,1)	1,7 [0,76; 2,37]	17/27 (63,0)	0,6 [0,33; 0,82]	0,30 [0,14; 0,61] <0,001
TPS ≥50%	13/19 (68,4)	0,5 [0,30; 2,23]	7/13 (53,8)	0,4 [0,30; 2,40]	0,89 [0,34; 2,32] 0,811
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,274)					
TPS <50%	25/48 (52,1)	1,7 [0,76; 2,37]	17/27 (63,0)	0,6 [0,33; 0,82]	0,30 [0,14; 0,61] <0,001
TPS ≥50%	13/19 (68,4)	0,5 [0,30; 2,23]	7/13 (53,8)	0,4 [0,30; 2,40]	0,89 [0,34; 2,32] 0,811
Unbekannt	24/48 (50,0)	1,8 [0,53; 9,26]	19/33 (57,6)	0,8 [0,33; 7,43]	0,69 [0,38; 1,27] 0,247
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,424)					
Negativ	12/26 (46,2)	1,5 [0,53; 2,37]	8/12 (66,7)	0,6 [0,30; 0,79]	0,16 [0,05; 0,55] 0,001
Positiv	29/49 (59,2)	0,8 [0,36; 2,37]	19/34 (55,9)	0,9 [0,33; 2,33]	0,76 [0,42; 1,37] 0,344
Unbekannt	21/40 (52,5)	1,8 [0,53; 9,92]	16/27 (59,3)	0,5 [0,33; 2,69]	0,62 [0,32; 1,20] 0,170
Krankheitsstatus (p-Wert des Interaktionsterms: 0,692)					
III	4/6 (66,7)	3,5 [0,39; NE]	4/6 (66,7)	0,8 [0,26; NE]	0,63 [0,15; 2,58] 0,513
IVA	24/44 (54,5)	1,2 [0,53; 2,17]	21/33 (63,6)	0,4 [0,33; 0,79]	0,57 [0,31; 1,04] 0,070

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	34/65 (52,3)	1,2 [0,62; 3,32]	18/34 (52,9)	0,8 [0,36; 2,40]	0,77 [0,43; 1,36] 0,342
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,636)					
Asiatisch	45/66 (68,2)	1,5 [0,76; 2,37]	26/35 (74,3)	0,5 [0,33; 1,02]	0,67 [0,41; 1,09] 0,113
Nicht asiatisch	17/49 (34,7)	1,0 [0,30; 4,70]	15/34 (44,1)	0,5 [0,30; 1,05]	0,56 [0,27; 1,14] 0,097
RET-Probenart (p-Wert des Interaktionsterms: 0,067)					
Blut	6/9 (66,7)	0,5 [0,26; 1,22]	4/10 (40,0)	1,4 [0,33; NE]	1,72 [0,48; 6,17] 0,379
Gewebe	56/106 (52,8)	1,7 [0,76; 2,37]	39/63 (61,9)	0,7 [0,33; 0,95]	0,57 [0,38; 0,87] 0,009
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01cons_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 88: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Appetitmangel - Beeinträchtigung (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,947)					
<65 Jahre	11/76 (14,5)	6,2 [0,72; NE]	14/45 (31,1)	0,5 [0,33; 1,02]	0,21 [0,08; 0,52] <0,001
≥65 Jahre	5/39 (12,8)	2,2 [0,76; NE]	7/28 (25,0)	0,4 [0,30; 1,64]	0,24 [0,07; 0,84] 0,014
Geschlecht (p-Wert des Interaktionsterms: 0,131)					
Männlich	8/61 (13,1)	2,3 [0,53; 6,24]	4/34 (11,8)	0,4 [0,33; NE]	0,33 [0,09; 1,26] 0,098
Weiblich	8/54 (14,8)	NE [0,99; NE]	17/39 (43,6)	0,5 [0,33; 1,02]	0,17 [0,07; 0,42] <0,001
Geografische Region (p-Wert des Interaktionsterms: 0,853)					
Ostasiatisch	8/65 (12,3)	6,2 [0,53; NE]	18/35 (51,4)	0,5 [0,33; 1,02]	0,26 [0,11; 0,64] 0,002
Nicht-Ostasiatisch	8/50 (16,0)	4,6 [0,99; NE]	3/38 (7,9)	0,4 [0,30; NE]	0,17 [0,04; 0,76] 0,009
Raucherstatus (p-Wert des Interaktionsterms: 0,108)					
Nie	10/72 (13,9)	6,0 [0,99; NE]	15/50 (30,0)	0,5 [0,33; 0,99]	0,16 [0,06; 0,39] <0,001
Ehemals/Aktuell	6/43 (14,0)	2,2 [0,53; 6,70]	6/23 (26,1)	0,4 [0,30; NE]	0,39 [0,11; 1,40] 0,134
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,283)					
Ja	6/23 (26,1)	1,3 [0,53; NE]	4/14 (28,6)	1,0 [0,30; NE]	0,62 [0,17; 2,24] 0,406
Nein	4/44 (9,1)	6,0 [0,76; NE]	6/23 (26,1)	0,5 [0,33; NE]	0,08 [0,02; 0,44] <0,001
Unbekannt	6/48 (12,5)	6,7 [0,72; NE]	11/36 (30,6)	0,4 [0,33; 1,02]	0,19 [0,06; 0,62] 0,003
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,827)					
Ja	3/16 (18,8)	NE [0,53; NE]	1/13 (7,7)	NE [0,33; NE]	0,24 [0,01; 3,93] 0,275

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	13/98 (13,3)	3,3 [0,76; NE]	20/60 (33,3)	0,5 [0,33; 1,02]	0,23 [0,11; 0,49] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,393)					
Negativ	1/26 (3,8)	NE [3,25; NE]	2/12 (16,7)	0,4 [0,33; NE]	0,00 [0,00; NE] 0,039
Positiv	5/49 (10,2)	NE [0,76; NE]	10/34 (29,4)	1,0 [0,33; 2,37]	0,27 [0,09; 0,79] 0,012
Unbekannt	10/40 (25,0)	2,2 [0,53; 6,70]	9/27 (33,3)	0,4 [0,33; 1,02]	0,22 [0,08; 0,64] 0,002
Krankheitsstatus (p-Wert des Interaktionsterms: 0,689)					
III*	0/6 (0,0)	NE [NE; NE]	1/6 (16,7)	1,6 [NE; NE]	1,00 [1,00; 1,00] NE
IVA	6/44 (13,6)	3,3 [0,72; NE]	9/33 (27,3)	0,4 [0,30; 0,99]	0,16 [0,05; 0,53] <0,001
IVB	10/65 (15,4)	6,0 [0,76; NE]	11/34 (32,4)	0,5 [0,33; 1,05]	0,22 [0,09; 0,58] <0,001
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,794)					
Asiatisch	9/66 (13,6)	6,0 [0,53; NE]	18/35 (51,4)	0,5 [0,33; 1,02]	0,24 [0,10; 0,59] <0,001
Nicht asiatisch	7/49 (14,3)	3,3 [0,99; NE]	3/34 (8,8)	0,4 [0,30; NE]	0,18 [0,04; 0,84] 0,015
RET-Probenart (p-Wert des Interaktionsterms: 0,901)					
Blut	2/9 (22,2)	NE [0,53; NE]	3/10 (30,0)	0,3 [0,33; NE]	0,32 [0,05; 2,05] 0,180
Gewebe	14/106 (13,2)	6,0 [0,99; NE]	18/63 (28,6)	0,5 [0,33; 1,02]	0,20 [0,09; 0,44] <0,001

Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab			
Subgruppe	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	HR [95% KI] p-Wert ^b
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte.					
* SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01deai_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 89: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Appetitmangel - Ausprägung (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,322)					
0	16/41 (39,0)	1,0 [0,59; 14,36]	13/25 (52,0)	0,7 [0,33; 3,71]	0,52 [0,25; 1,10] 0,082
1	37/74 (50,0)	4,4 [1,71; 8,08]	31/48 (64,6)	0,4 [0,33; 0,43]	0,32 [0,19; 0,52] <0,001
Geschlecht (p-Wert des Interaktionsterms: 0,090)					
Männlich	26/61 (42,6)	2,0 [0,95; 5,36]	18/34 (52,9)	0,8 [0,36; 3,71]	0,54 [0,29; 1,00] 0,042
Weiblich	27/54 (50,0)	4,9 [1,22; 14,36]	26/39 (66,7)	0,3 [0,33; 0,49]	0,27 [0,15; 0,49] <0,001
Geografische Region (p-Wert des Interaktionsterms: 0,841)					
Ostasiatisch	37/65 (56,9)	2,9 [0,99; 14,52]	28/35 (80,0)	0,4 [0,33; 0,99]	0,34 [0,21; 0,57] <0,001
Nicht-Ostasiatisch	16/50 (32,0)	4,5 [0,79; 14,36]	16/38 (42,1)	0,4 [0,30; 0,99]	0,41 [0,20; 0,84] 0,013
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,220)					
Ja	10/23 (43,5)	3,7 [0,53; 18,00]	9/14 (64,3)	1,0 [0,33; 3,71]	0,59 [0,23; 1,50] 0,258
Nein	21/44 (47,7)	2,0 [0,85; 6,77]	13/23 (56,5)	0,4 [0,30; 0,72]	0,42 [0,21; 0,86] 0,015
Unbekannt	22/48 (45,8)	5,1 [1,22; 22,80]	22/36 (61,1)	0,3 [0,33; 0,43]	0,25 [0,13; 0,48] <0,001
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,942)					
Ja	5/16 (31,3)	NE [0,53; NE]	4/13 (30,8)	1,1 [0,33; NE]	0,43 [0,11; 1,63] 0,190
Nein	48/98 (49,0)	3,1 [0,99; 5,36]	40/60 (66,7)	0,4 [0,33; 0,72]	0,36 [0,24; 0,56] <0,001
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,098)					
TPS <50%	24/48 (50,0)	1,0 [0,76; 3,48]	16/27 (59,3)	0,3 [0,30; 0,53]	0,40 [0,21; 0,77] 0,004

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
TPS ≥50%	5/19 (26,3)	NE [0,76; NE]	7/13 (53,8)	0,3 [0,30; 3,71]	0,11 [0,03; 0,43] <0,001
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,125)					
TPS <50%	24/48 (50,0)	1,0 [0,76; 3,48]	16/27 (59,3)	0,3 [0,30; 0,53]	0,40 [0,21; 0,77] 0,004
TPS ≥50%	5/19 (26,3)	NE [0,76; NE]	7/13 (53,8)	0,3 [0,30; 3,71]	0,11 [0,03; 0,43] <0,001
Unbekannt	24/48 (50,0)	4,2 [1,22; 14,36]	21/33 (63,6)	0,6 [0,33; 1,12]	0,41 [0,22; 0,76] 0,004
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,556)					
Negativ	12/26 (46,2)	1,7 [0,53; 5,13]	7/12 (58,3)	0,4 [0,30; 0,79]	0,39 [0,15; 1,04] 0,053
Positiv	20/49 (40,8)	4,0 [0,76; NE]	21/34 (61,8)	0,3 [0,33; 0,99]	0,31 [0,17; 0,58] <0,001
Unbekannt	21/40 (52,5)	4,4 [1,22; 14,36]	16/27 (59,3)	0,4 [0,33; 1,28]	0,41 [0,21; 0,80] 0,009
Krankheitsstatus (p-Wert des Interaktionsterms: 0,788)					
III	3/6 (50,0)	2,4 [0,43; NE]	4/6 (66,7)	0,4 [0,26; NE]	0,50 [0,11; 2,29] 0,366
IVA	23/44 (52,3)	3,7 [0,99; 6,77]	21/33 (63,6)	0,4 [0,33; 0,43]	0,30 [0,16; 0,56] <0,001
IVB	27/65 (41,5)	4,4 [0,95; 22,80]	19/34 (55,9)	1,0 [0,33; 1,28]	0,42 [0,23; 0,76] 0,004
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,672)					
Asiatisch	37/66 (56,1)	3,1 [0,99; 14,52]	28/35 (80,0)	0,4 [0,33; 0,99]	0,33 [0,20; 0,55] <0,001
Nicht asiatisch	16/49 (32,7)	4,2 [0,79; 8,08]	13/34 (38,2)	0,4 [0,30; 0,99]	0,46 [0,21; 0,98] 0,041
RET-Probenart (p-Wert des Interaktionsterms: 0,913)					
Blut	5/9 (55,6)	3,1 [0,26; NE]	6/10 (60,0)	0,7 [0,26; NE]	0,38 [0,10; 1,37] 0,115

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Gewebe	48/106 (45,3)	4,0 [1,22; 7,46]	38/63 (60,3)	0,4 [0,33; 0,72]	0,37 [0,24; 0,57] <0,001
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01deas_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 90: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Diarrhö - Häufigkeit (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,905)					
<65 Jahre	42/76 (55,3)	1,3 [0,76; 2,37]	23/45 (51,1)	2,6 [0,79; 5,32]	1,31 [0,78; 2,19] 0,314
≥65 Jahre	24/39 (61,5)	1,2 [0,59; 2,14]	13/28 (46,4)	0,6 [0,36; 7,43]	1,21 [0,61; 2,39] 0,575
Baseline ECOG (p-Wert des Interaktionsterms: 0,733)					
0	19/41 (46,3)	1,0 [0,53; 1,54]	11/25 (44,0)	1,0 [0,33; 6,51]	1,39 [0,65; 2,96] 0,403
1	47/74 (63,5)	1,6 [0,82; 2,63]	25/48 (52,1)	2,3 [0,56; 4,70]	1,26 [0,77; 2,07] 0,361
Geschlecht (p-Wert des Interaktionsterms: 0,320)					
Männlich	33/61 (54,1)	1,3 [0,76; 2,14]	16/34 (47,1)	0,6 [0,39; 2,86]	0,97 [0,53; 1,78] 0,926
Weiblich	33/54 (61,1)	1,2 [0,76; 2,37]	20/39 (51,3)	2,6 [0,99; 7,43]	1,53 [0,87; 2,69] 0,143
Geografische Region (p-Wert des Interaktionsterms: 0,484)					
Ostasiatisch	48/65 (73,8)	1,1 [0,76; 1,68]	23/35 (65,7)	2,4 [0,62; 4,70]	1,42 [0,86; 2,36] 0,179
Nicht-Ostasiatisch	18/50 (36,0)	1,4 [0,76; 4,40]	13/38 (34,2)	0,9 [0,36; 7,43]	1,04 [0,51; 2,14] 0,910
Raucherstatus (p-Wert des Interaktionsterms: 0,821)					
Nie	40/72 (55,6)	1,5 [0,76; 3,09]	26/50 (52,0)	2,4 [0,99; 4,70]	1,26 [0,77; 2,08] 0,361
Ehemals/Aktuell	26/43 (60,5)	1,1 [0,76; 1,68]	10/23 (43,5)	0,6 [0,33; 6,51]	1,10 [0,51; 2,38] 0,796
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,833)					
Ja	11/23 (47,8)	1,9 [0,53; NE]	7/14 (50,0)	5,3 [0,30; NE]	1,46 [0,56; 3,84] 0,425
Nein	26/44 (59,1)	0,9 [0,53; 1,54]	13/23 (56,5)	1,0 [0,36; 2,33]	1,00 [0,51; 1,94] 0,978

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	29/48 (60,4)	1,4 [0,76; 3,29]	16/36 (44,4)	2,6 [0,56; NE]	1,34 [0,72; 2,51] 0,359
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,173)					
Ja	8/16 (50,0)	2,1 [0,36; NE]	4/13 (30,8)	0,6 [0,36; NE]	0,65 [0,19; 2,20] 0,489
Nein	58/98 (59,2)	1,2 [0,76; 1,71]	32/60 (53,3)	2,1 [0,56; 5,32]	1,43 [0,92; 2,22] 0,111
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,795)					
TPS <50%	29/48 (60,4)	1,4 [0,76; 2,14]	11/27 (40,7)	2,1 [0,56; NE]	1,96 [0,97; 3,97] 0,055
TPS ≥50%	12/19 (63,2)	1,2 [0,39; 5,39]	5/13 (38,5)	5,3 [0,33; NE]	1,62 [0,55; 4,81] 0,376
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,146)					
TPS <50%	29/48 (60,4)	1,4 [0,76; 2,14]	11/27 (40,7)	2,1 [0,56; NE]	1,96 [0,97; 3,97] 0,055
TPS ≥50%	12/19 (63,2)	1,2 [0,39; 5,39]	5/13 (38,5)	5,3 [0,33; NE]	1,62 [0,55; 4,81] 0,376
Unbekannt	25/48 (52,1)	1,0 [0,56; 4,93]	20/33 (60,6)	1,0 [0,36; 2,86]	0,81 [0,44; 1,47] 0,452
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,447)					
Negativ	14/26 (53,8)	1,4 [0,30; 2,37]	5/12 (41,7)	1,4 [0,43; NE]	1,77 [0,64; 4,95] 0,266
Positiv	30/49 (61,2)	1,3 [0,76; 2,60]	15/34 (44,1)	2,5 [0,43; 7,43]	1,41 [0,75; 2,65] 0,290
Unbekannt	22/40 (55,0)	0,8 [0,53; 6,28]	16/27 (59,3)	1,3 [0,36; 3,29]	0,95 [0,49; 1,84] 0,855
Krankheitsstatus (p-Wert des Interaktionsterms: 0,665)					
III	3/6 (50,0)	1,7 [0,33; NE]	3/6 (50,0)	2,3 [0,26; NE]	0,98 [0,20; 4,91] 0,982
IVA	26/44 (59,1)	1,0 [0,53; 2,14]	19/33 (57,6)	1,1 [0,39; 2,56]	1,07 [0,59; 1,93] 0,836

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	37/65 (56,9)	1,4 [0,82; 2,37]	14/34 (41,2)	4,7 [0,56; NE]	1,65 [0,87; 3,13] 0,119
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,951)					
Asiatisch	48/66 (72,7)	1,2 [0,76; 1,74]	23/35 (65,7)	2,4 [0,62; 4,70]	1,36 [0,82; 2,26] 0,236
Nicht asiatisch	18/49 (36,7)	1,4 [0,76; 4,40]	10/34 (29,4)	2,3 [0,30; NE]	1,42 [0,65; 3,10] 0,375
RET-Probenart (p-Wert des Interaktionsterms: 0,592)					
Blut	6/9 (66,7)	2,1 [0,53; NE]	5/10 (50,0)	2,6 [0,36; NE]	0,97 [0,27; 3,42] 0,961
Gewebe	60/106 (56,6)	1,2 [0,76; 1,71]	31/63 (49,2)	1,3 [0,56; 4,70]	1,33 [0,86; 2,07] 0,200
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,112)					
CCDC6	6/9 (66,7)	1,1 [0,53; NE]	1/6 (16,7)	NE [0,53; NE]	3,80 [0,45; 32,11] 0,177
KIF5B	30/50 (60,0)	1,6 [0,99; 3,09]	20/36 (55,6)	0,7 [0,36; 2,56]	0,81 [0,45; 1,43] 0,467
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01diaf_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 91: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Mundtrockenheit - Ausprägung (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,080)					
<65 Jahre	47/76 (61,8)	0,5 [0,39; 0,76]	28/45 (62,2)	0,7 [0,33; 1,91]	1,17 [0,73; 1,88] 0,530
≥65 Jahre	23/39 (59,0)	0,5 [0,30; 0,76]	12/28 (42,9)	1,5 [0,30; NE]	2,39 [1,14; 5,00] 0,015
Baseline ECOG (p-Wert des Interaktionsterms: 0,985)					
0	22/41 (53,7)	0,5 [0,33; 0,76]	13/25 (52,0)	0,4 [0,30; 1,02]	1,49 [0,71; 3,16] 0,279
1	48/74 (64,9)	0,6 [0,33; 0,95]	27/48 (56,3)	1,5 [0,43; 2,63]	1,53 [0,95; 2,46] 0,084
Geschlecht (p-Wert des Interaktionsterms: 0,511)					
Männlich	34/61 (55,7)	0,8 [0,43; 0,95]	17/34 (50,0)	0,9 [0,39; 2,63]	1,38 [0,77; 2,48] 0,307
Weiblich	36/54 (66,7)	0,5 [0,33; 0,59]	23/39 (59,0)	0,8 [0,33; 1,91]	1,65 [0,96; 2,84] 0,059
Geografische Region (p-Wert des Interaktionsterms: 0,812)					
Ostasiatisch	50/65 (76,9)	0,5 [0,36; 0,76]	26/35 (74,3)	1,0 [0,39; 2,63]	1,58 [0,97; 2,57] 0,065
Nicht-Ostasiatisch	20/50 (40,0)	0,5 [0,33; 0,95]	14/38 (36,8)	0,8 [0,33; 1,97]	1,41 [0,70; 2,84] 0,351
Raucherstatus (p-Wert des Interaktionsterms: 0,443)					
Nie	43/72 (59,7)	0,6 [0,39; 0,76]	31/50 (62,0)	0,9 [0,36; 1,97]	1,35 [0,84; 2,17] 0,209
Ehemals/Aktuell	27/43 (62,8)	0,5 [0,33; 0,76]	9/23 (39,1)	1,1 [0,33; 6,67]	1,98 [0,92; 4,24] 0,074
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,623)					
Ja	12/23 (52,2)	0,5 [0,30; 0,99]	8/14 (57,1)	0,6 [0,30; NE]	1,30 [0,53; 3,19] 0,630
Nein	27/44 (61,4)	0,7 [0,43; 0,95]	13/23 (56,5)	0,5 [0,30; 2,86]	1,25 [0,63; 2,49] 0,516

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	31/48 (64,6)	0,5 [0,30; 0,76]	19/36 (52,8)	1,5 [0,39; 2,17]	1,92 [1,08; 3,43] 0,024
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,676)					
Ja	9/16 (56,3)	0,5 [0,26; 1,71]	3/13 (23,1)	6,7 [0,33; NE]	1,87 [0,50; 6,96] 0,354
Nein	61/98 (62,2)	0,5 [0,39; 0,76]	37/60 (61,7)	0,8 [0,36; 1,91]	1,51 [1,00; 2,30] 0,053
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,449)					
Negativ	15/26 (57,7)	0,6 [0,30; 0,76]	6/12 (50,0)	0,8 [0,30; NE]	2,20 [0,84; 5,80] 0,108
Positiv	29/49 (59,2)	0,8 [0,49; 0,99]	17/34 (50,0)	1,0 [0,33; 2,37]	1,20 [0,65; 2,20] 0,556
Unbekannt	26/40 (65,0)	0,3 [0,30; 0,53]	17/27 (63,0)	0,6 [0,33; 2,86]	1,68 [0,89; 3,17] 0,108
Krankheitsstatus (p-Wert des Interaktionsterms: 0,521)					
III	4/6 (66,7)	0,4 [0,33; NE]	3/6 (50,0)	2,9 [0,26; NE]	1,83 [0,33; 10,14] 0,484
IVA	28/44 (63,6)	0,6 [0,33; 0,76]	20/33 (60,6)	0,5 [0,33; 1,02]	1,18 [0,66; 2,11] 0,581
IVB	38/65 (58,5)	0,5 [0,33; 0,95]	17/34 (50,0)	1,9 [0,36; 6,67]	1,89 [1,04; 3,43] 0,035
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,941)					
Asiatisch	50/66 (75,8)	0,5 [0,36; 0,76]	26/35 (74,3)	1,0 [0,39; 2,63]	1,50 [0,92; 2,43] 0,104
Nicht asiatisch	20/49 (40,8)	0,5 [0,33; 0,76]	12/34 (35,3)	0,8 [0,30; 1,97]	1,56 [0,74; 3,28] 0,248
RET-Probenart (p-Wert des Interaktionsterms: 0,272)					
Blut	7/9 (77,8)	0,5 [0,49; 1,22]	3/10 (30,0)	1,9 [0,26; NE]	2,97 [0,71; 12,37] 0,154
Gewebe	63/106 (59,4)	0,5 [0,33; 0,76]	37/63 (58,7)	0,8 [0,39; 1,91]	1,40 [0,93; 2,11] 0,118
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,299)					

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
CCDC6	6/9 (66,7)	0,6 [0,30; NE]	3/6 (50,0)	0,3 [0,30; NE]	0,73 [0,17; 3,15] 0,744
KIF5B	33/50 (66,0)	0,5 [0,49; 0,95]	17/36 (47,2)	1,0 [0,36; 6,70]	1,79 [0,99; 3,24] 0,054

Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg).
Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology
Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI:
Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n:
Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT:
Randomisierte kontrollierte Studie; RET: Rearranged during transfection.
a: In Monaten.
b: Aus dem unstratifizierten Log-rank-Test.
Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt.
Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in
wenigen Fällen zu Fehlern führte.

Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet
Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko,
Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine
*** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.
**** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben
unberücksichtigt.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01drms_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adttepae_gba

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Tabelle 92: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Müdigkeit, Erschöpfung oder fehlende Energie - Beeinträchtigung (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,059)					
0	5/41 (12,2)	NE [0,30; NE]	7/25 (28,0)	0,4 [0,26; 0,72]	0,19 [0,05; 0,69] 0,006
1	22/74 (29,7)	3,1 [0,76; 10,15]	19/48 (39,6)	0,5 [0,33; 1,91]	0,57 [0,31; 1,06] 0,077
Geschlecht (p-Wert des Interaktionsterms: 0,108)					
Männlich	14/61 (23,0)	0,8 [0,33; 4,27]	9/34 (26,5)	0,5 [0,26; 2,43]	0,74 [0,32; 1,73] 0,472
Weiblich	13/54 (24,1)	8,5 [1,45; NE]	17/39 (43,6)	0,4 [0,33; 0,99]	0,30 [0,14; 0,63] <0,001
Geografische Region (p-Wert des Interaktionsterms: 0,728)					
Ostasiatisch	19/65 (29,2)	3,1 [0,76; 10,18]	16/35 (45,7)	0,5 [0,33; 1,02]	0,45 [0,23; 0,89] 0,020
Nicht-Ostasiatisch	8/50 (16,0)	7,2 [0,72; NE]	10/38 (26,3)	0,4 [0,30; 6,01]	0,37 [0,14; 0,98] 0,036
Raucherstatus (p-Wert des Interaktionsterms: 0,078)					
Nie	17/72 (23,6)	7,2 [1,22; NE]	22/50 (44,0)	0,4 [0,33; 0,99]	0,30 [0,16; 0,58] <0,001
Ehemals/Aktuell	10/43 (23,3)	1,2 [0,30; NE]	4/23 (17,4)	1,3 [0,30; NE]	1,13 [0,35; 3,59] 0,857
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,319)					
Ja	7/23 (30,4)	1,0 [0,30; NE]	7/14 (50,0)	0,5 [0,26; 1,91]	0,55 [0,19; 1,60] 0,266
Nein	9/44 (20,5)	6,8 [0,76; NE]	6/23 (26,1)	2,4 [0,33; NE]	0,70 [0,25; 1,97] 0,488
Unbekannt	11/48 (22,9)	7,2 [0,53; NE]	13/36 (36,1)	0,3 [0,33; 0,43]	0,31 [0,13; 0,72] 0,005
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,377)					
Ja	5/16 (31,3)	2,2 [0,72; NE]	2/13 (15,4)	0,7 [0,36; NE]	0,57 [0,10; 3,18] 0,515

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	22/98 (22,4)	6,8 [0,76; NE]	24/60 (40,0)	0,4 [0,33; 0,99]	0,41 [0,23; 0,74] 0,002
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,057)					
TPS <50%	7/48 (14,6)	4,3 [0,56; NE]	8/27 (29,6)	0,4 [0,30; 0,99]	0,42 [0,15; 1,19] 0,092
TPS ≥50%	5/19 (26,3)	6,8 [0,53; NE]	5/13 (38,5)	0,3 [0,26; NE]	0,00 [0,00; NE] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,110)					
Negativ	2/26 (7,7)	NE [0,56; NE]	3/12 (25,0)	0,5 [0,36; NE]	0,26 [0,04; 1,62] 0,123
Positiv	11/49 (22,4)	6,8 [0,72; NE]	14/34 (41,2)	0,3 [0,30; 0,49]	0,23 [0,10; 0,56] <0,001
Unbekannt	14/40 (35,0)	2,1 [0,53; 10,18]	9/27 (33,3)	1,0 [0,33; NE]	0,78 [0,34; 1,80] 0,558
Krankheitsstatus (p-Wert des Interaktionsterms: 0,127)					
III	2/6 (33,3)	0,5 [0,43; NE]	2/6 (33,3)	6,0 [0,36; NE]	2,92 [0,26; 32,93] 0,364
IVA	11/44 (25,0)	6,8 [0,76; NE]	13/33 (39,4)	0,4 [0,33; 0,99]	0,38 [0,17; 0,86] 0,017
IVB	14/65 (21,5)	3,1 [0,72; NE]	11/34 (32,4)	0,4 [0,30; 1,02]	0,39 [0,17; 0,87] 0,018
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,887)					
Asiatisch	19/66 (28,8)	3,1 [0,76; 10,18]	16/35 (45,7)	0,5 [0,33; 1,02]	0,45 [0,23; 0,89] 0,020
Nicht asiatisch	8/49 (16,3)	7,2 [0,72; NE]	8/34 (23,5)	0,4 [0,26; 6,01]	0,41 [0,15; 1,14] 0,075
RET-Probenart (p-Wert des Interaktionsterms: 0,994)					
Blut	3/9 (33,3)	8,5 [0,53; NE]	3/10 (30,0)	0,5 [0,26; NE]	0,48 [0,09; 2,44] 0,365
Gewebe	24/106 (22,6)	4,3 [0,76; 10,18]	23/63 (36,5)	0,4 [0,33; 1,02]	0,44 [0,25; 0,79] 0,005
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,992)					

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
CCDC6*	2/9 (22,2)	6,4 [2,60; NE]	0/6 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,225
KIF5B	13/50 (26,0)	4,9 [0,72; NE]	13/36 (36,1)	0,4 [0,33; 0,66]	0,38 [0,18; 0,84] 0,015

Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg).
 Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology
 Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI:
 Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n:
 Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT:
 Randomisierte kontrollierte Studie; RET: Rearranged during transfection.
 a: In Monaten.
 b: Aus dem unstratifizierten Log-rank-Test.
 Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt.
 Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in
 wenigen Fällen zu Fehlern führte.

* SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events.
 Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet
 Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko,
 Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine
 * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS
 $\geq 50\%$ bzw <50% wurden nicht berücksichtigt.
 *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.
 **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben
 unberücksichtigt.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01fati_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 93: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Müdigkeit, Erschöpfung oder fehlende Energie - Ausprägung (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,209)					
0	18/41 (43,9)	0,8 [0,56; 3,09]	13/25 (52,0)	0,5 [0,30; 0,56]	0,39 [0,19; 0,81] 0,011
1	40/74 (54,1)	1,4 [0,76; 4,96]	26/48 (54,2)	0,6 [0,33; 1,91]	0,80 [0,49; 1,32] 0,401
Geschlecht (p-Wert des Interaktionsterms: 0,069)					
Männlich	32/61 (52,5)	1,0 [0,53; 1,48]	16/34 (47,1)	0,6 [0,39; 2,43]	1,04 [0,57; 1,89] 0,919
Weiblich	26/54 (48,1)	2,0 [0,76; 8,54]	23/39 (59,0)	0,4 [0,33; 0,59]	0,47 [0,26; 0,82] 0,008
Geografische Region (p-Wert des Interaktionsterms: 0,253)					
Ostasiatisch	42/65 (64,6)	1,2 [0,59; 3,09]	27/35 (77,1)	0,5 [0,33; 0,66]	0,55 [0,34; 0,90] 0,018
Nicht-Ostasiatisch	16/50 (32,0)	1,0 [0,72; 8,54]	12/38 (31,6)	0,6 [0,33; NE]	0,92 [0,43; 1,94] 0,825
Raucherstatus (p-Wert des Interaktionsterms: 0,199)					
Nie	35/72 (48,6)	2,2 [0,76; 5,59]	30/50 (60,0)	0,5 [0,33; 0,99]	0,55 [0,34; 0,90] 0,017
Ehemals/Aktuell	23/43 (53,5)	1,0 [0,53; 1,45]	9/23 (39,1)	0,6 [0,33; NE]	1,00 [0,46; 2,17] 0,989
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,746)					
Ja	9/23 (39,1)	1,0 [0,53; NE]	9/14 (64,3)	0,6 [0,30; 1,91]	0,58 [0,23; 1,46] 0,229
Nein	23/44 (52,3)	2,0 [0,72; 4,96]	11/23 (47,8)	0,5 [0,33; 2,86]	0,80 [0,39; 1,66] 0,555
Unbekannt	26/48 (54,2)	1,0 [0,53; 5,16]	19/36 (52,8)	0,4 [0,33; 0,79]	0,74 [0,41; 1,34] 0,346
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,746)					
Ja	8/16 (50,0)	1,2 [0,30; NE]	4/13 (30,8)	0,6 [0,33; NE]	0,58 [0,17; 2,04] 0,412

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	50/98 (51,0)	1,0 [0,76; 3,09]	35/60 (58,3)	0,5 [0,33; 0,99]	0,70 [0,45; 1,08] 0,119
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,347)					
Negativ	12/26 (46,2)	1,0 [0,30; 9,95]	5/12 (41,7)	0,5 [0,33; NE]	1,28 [0,45; 3,67] 0,642
Positiv	25/49 (51,0)	0,9 [0,59; 3,09]	19/34 (55,9)	0,4 [0,33; 0,66]	0,50 [0,27; 0,91] 0,025
Unbekannt	21/40 (52,5)	1,5 [0,53; 8,71]	15/27 (55,6)	0,6 [0,33; 2,43]	0,72 [0,37; 1,41] 0,339
Krankheitsstatus (p-Wert des Interaktionsterms: 0,401)					
III	4/6 (66,7)	3,1 [0,99; NE]	2/6 (33,3)	NE [0,30; NE]	2,30 [0,41; 12,77] 0,328
IVA	22/44 (50,0)	1,3 [0,76; 5,16]	19/33 (57,6)	0,4 [0,33; 0,79]	0,54 [0,29; 1,01] 0,053
IVB	32/65 (49,2)	0,8 [0,53; 1,45]	18/34 (52,9)	0,5 [0,33; 0,66]	0,65 [0,36; 1,17] 0,154
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,308)					
Asiatisch	43/66 (65,2)	1,2 [0,59; 3,09]	27/35 (77,1)	0,5 [0,33; 0,66]	0,57 [0,35; 0,93] 0,023
Nicht asiatisch	15/49 (30,6)	1,0 [0,72; 8,54]	10/34 (29,4)	0,6 [0,30; NE]	0,89 [0,40; 1,99] 0,787
RET-Probenart (p-Wert des Interaktionsterms: 0,358)					
Blut	7/9 (77,8)	0,5 [0,26; 5,59]	5/10 (50,0)	0,6 [0,33; NE]	1,07 [0,34; 3,39] 0,954
Gewebe	51/106 (48,1)	1,2 [0,76; 3,09]	34/63 (54,0)	0,5 [0,33; 0,79]	0,66 [0,42; 1,01] 0,060
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,686)					
CCDC6	4/9 (44,4)	0,6 [0,33; NE]	2/6 (33,3)	2,6 [0,30; NE]	1,08 [0,19; 6,05] 0,961
KIF5B	28/50 (56,0)	1,0 [0,53; 1,48]	18/36 (50,0)	0,5 [0,33; 0,79]	0,77 [0,43; 1,40] 0,432

Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab			
Subgruppe	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	HR [95% KI] p-Wert ^b
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte.					
Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01fats_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba
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Tabelle 94: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Kopfschmerzen - Häufigkeit (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Baseline ECOG (p-Wert des Interaktionsterms: 0,325)					
0	14/41 (34,1)	6,6 [0,99; NE]	11/25 (44,0)	1,0 [0,33; 6,34]	0,58 [0,26; 1,29] 0,183
1	47/74 (63,5)	1,0 [0,53; 1,64]	29/48 (60,4)	0,8 [0,49; 1,48]	0,94 [0,59; 1,50] 0,750
Geschlecht (p-Wert des Interaktionsterms: 0,054)					
Männlich	30/61 (49,2)	1,0 [0,72; 4,70]	15/34 (44,1)	2,9 [0,95; 7,26]	1,24 [0,67; 2,31] 0,529
Weiblich	31/54 (57,4)	1,3 [0,76; 3,71]	25/39 (64,1)	0,5 [0,36; 0,79]	0,57 [0,33; 0,97] 0,037
Geografische Region (p-Wert des Interaktionsterms: 0,628)					
Ostasiatisch	45/65 (69,2)	0,9 [0,56; 1,45]	26/35 (74,3)	0,8 [0,53; 2,86]	0,89 [0,54; 1,44] 0,578
Nicht-Ostasiatisch	16/50 (32,0)	4,3 [0,99; 8,15]	14/38 (36,8)	1,0 [0,39; 4,80]	0,68 [0,33; 1,40] 0,289
Raucherstatus (p-Wert des Interaktionsterms: 0,131)					
Nie	38/72 (52,8)	1,3 [0,76; 4,70]	32/50 (64,0)	0,8 [0,53; 1,05]	0,67 [0,41; 1,08] 0,094
Ehemals/Aktuell	23/43 (53,5)	1,2 [0,49; 2,60]	8/23 (34,8)	3,4 [0,33; NE]	1,45 [0,65; 3,26] 0,379
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,499)					
Ja	11/23 (47,8)	1,0 [0,30; 5,78]	8/14 (57,1)	1,0 [0,30; NE]	1,11 [0,45; 2,77] 0,833
Nein	25/44 (56,8)	1,2 [0,76; 2,23]	14/23 (60,9)	0,6 [0,30; 1,02]	0,56 [0,29; 1,10] 0,091
Unbekannt	25/48 (52,1)	1,2 [0,53; 7,46]	18/36 (50,0)	1,1 [0,53; 4,60]	0,90 [0,49; 1,66] 0,706
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,227)					
Ja	8/16 (50,0)	1,7 [0,49; NE]	5/13 (38,5)	0,6 [0,33; NE]	0,40 [0,13; 1,30] 0,116

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	53/98 (54,1)	1,2 [0,76; 2,23]	35/60 (58,3)	1,0 [0,53; 2,86]	0,90 [0,58; 1,38] 0,585
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,131)					
TPS <50%	27/48 (56,3)	0,8 [0,53; 1,25]	14/27 (51,9)	0,9 [0,53; 4,80]	1,25 [0,65; 2,39] 0,497
TPS ≥50%	9/19 (47,4)	4,9 [2,23; NE]	6/13 (46,2)	1,0 [0,30; 6,34]	0,51 [0,18; 1,46] 0,213
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,263)					
TPS <50%	27/48 (56,3)	0,8 [0,53; 1,25]	14/27 (51,9)	0,9 [0,53; 4,80]	1,25 [0,65; 2,39] 0,497
TPS ≥50%	9/19 (47,4)	4,9 [2,23; NE]	6/13 (46,2)	1,0 [0,30; 6,34]	0,51 [0,18; 1,46] 0,213
Unbekannt	25/48 (52,1)	1,0 [0,49; 1,68]	20/33 (60,6)	0,8 [0,43; 1,48]	0,78 [0,43; 1,42] 0,379
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,566)					
Negativ	13/26 (50,0)	1,0 [0,33; 2,60]	6/12 (50,0)	2,9 [0,43; NE]	1,35 [0,51; 3,56] 0,537
Positiv	25/49 (51,0)	2,2 [0,76; 5,78]	17/34 (50,0)	0,9 [0,43; 4,27]	0,75 [0,41; 1,40] 0,370
Unbekannt	23/40 (57,5)	0,8 [0,33; 1,45]	17/27 (63,0)	0,6 [0,36; 1,48]	0,79 [0,42; 1,50] 0,427
Krankheitsstatus (p-Wert des Interaktionsterms: 0,228)					
III	3/6 (50,0)	7,7 [1,25; NE]	5/6 (83,3)	0,8 [0,26; NE]	0,12 [0,01; 1,07] 0,025
IVA	25/44 (56,8)	1,1 [0,56; 2,23]	20/33 (60,6)	1,0 [0,43; 1,48]	0,82 [0,45; 1,48] 0,505
IVB	33/65 (50,8)	1,0 [0,76; 3,81]	15/34 (44,1)	1,0 [0,53; 6,34]	1,06 [0,58; 1,96] 0,892
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,576)					
Asiatisch	45/66 (68,2)	1,0 [0,56; 1,68]	26/35 (74,3)	0,8 [0,53; 2,86]	0,85 [0,52; 1,39] 0,485

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	16/49 (32,7)	3,7 [0,99; 7,46]	12/34 (35,3)	0,8 [0,30; 4,27]	0,65 [0,31; 1,38] 0,258
RET-Probenart (p-Wert des Interaktionsterms: 0,132)					
Blut	5/9 (55,6)	1,7 [0,30; NE]	6/10 (60,0)	0,5 [0,33; NE]	0,34 [0,09; 1,23] 0,086
Gewebe	56/106 (52,8)	1,2 [0,76; 2,23]	34/63 (54,0)	1,0 [0,56; 3,38]	0,90 [0,59; 1,38] 0,606
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,246)					
CCDC6	4/9 (44,4)	1,0 [0,30; NE]	3/6 (50,0)	0,5 [0,49; NE]	0,20 [0,03; 1,29] 0,075
KIF5B	28/50 (56,0)	1,7 [0,76; 4,93]	20/36 (55,6)	1,0 [0,43; 3,38]	0,76 [0,43; 1,35] 0,340
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01head_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 95: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Kopfschmerzen - Beeinträchtigung (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,411)					
<65 Jahre	9/76 (11,8)	7,2 [0,99; NE]	10/45 (22,2)	0,5 [0,30; 2,43]	0,31 [0,12; 0,79] 0,009
≥65 Jahre	6/39 (15,4)	0,3 [0,26; 4,17]	3/28 (10,7)	0,4 [0,30; NE]	0,84 [0,20; 3,56] 0,747
Baseline ECOG (p-Wert des Interaktionsterms: 0,533)					
0	5/41 (12,2)	14,4 [0,26; NE]	3/25 (12,0)	8,0 [0,30; NE]	0,54 [0,12; 2,42] 0,389
1	10/74 (13,5)	1,2 [0,30; 4,17]	10/48 (20,8)	0,4 [0,26; 0,79]	0,39 [0,15; 1,02] 0,039
Geschlecht (p-Wert des Interaktionsterms: 0,345)					
Männlich	4/61 (6,6)	7,2 [0,30; NE]	3/34 (8,8)	0,4 [0,26; NE]	0,26 [0,05; 1,33] 0,084
Weiblich	11/54 (20,4)	4,0 [0,30; 14,36]	10/39 (25,6)	0,5 [0,30; 3,25]	0,52 [0,22; 1,27] 0,144
Geografische Region (p-Wert des Interaktionsterms: 0,092)					
Ostasiatisch	7/65 (10,8)	1,7 [0,30; NE]	10/35 (28,6)	0,8 [0,33; 3,25]	0,54 [0,20; 1,43] 0,196
Nicht-Ostasiatisch	8/50 (16,0)	5,7 [0,26; 14,36]	3/38 (7,9)	0,3 [0,26; NE]	0,14 [0,02; 0,84] 0,013
Raucherstatus (p-Wert des Interaktionsterms: 0,109)					
Nie	10/72 (13,9)	1,7 [0,30; 14,36]	11/50 (22,0)	0,6 [0,30; 3,25]	0,54 [0,22; 1,31] 0,165
Ehemals/Aktuell	5/43 (11,6)	5,6 [0,30; NE]	2/23 (8,7)	0,3 [0,30; NE]	0,10 [0,01; 1,07] 0,019
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,212)					
Ja	3/23 (13,0)	1,7 [0,30; NE]	2/14 (14,3)	0,3 [NE; NE]	0,13 [0,01; 1,46] 0,074
Nein	3/44 (6,8)	7,2 [0,26; NE]	5/23 (21,7)	1,9 [0,26; NE]	0,55 [0,12; 2,53] 0,434

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	9/48 (18,8)	4,0 [0,76; 14,36]	6/36 (16,7)	0,4 [0,33; 2,43]	0,47 [0,16; 1,39] 0,161
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,418)					
TPS <50%	4/48 (8,3)	7,2 [0,30; NE]	4/27 (14,8)	2,4 [0,30; NE]	0,99 [0,22; 4,45] 0,972
TPS ≥50%	4/19 (21,1)	4,2 [0,30; NE]	3/13 (23,1)	0,3 [0,30; NE]	0,16 [0,02; 1,55] 0,064
Unbekannt	7/48 (14,6)	1,4 [0,26; NE]	6/33 (18,2)	0,4 [0,26; NE]	0,26 [0,08; 0,85] 0,016
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,236)					
Negativ	2/26 (7,7)	0,7 [0,30; NE]	2/12 (16,7)	7,6 [2,43; NE]	2,27 [0,19; 26,53] 0,502
Positiv	7/49 (14,3)	4,2 [0,26; NE]	6/34 (17,6)	0,5 [0,30; 1,94]	0,54 [0,18; 1,67] 0,246
Unbekannt	6/40 (15,0)	1,7 [0,76; NE]	5/27 (18,5)	0,4 [0,26; NE]	0,22 [0,06; 0,80] 0,011
Krankheitsstatus (p-Wert des Interaktionsterms: 0,744)					
III*	0/6 (0,0)	NE [NE; NE]	2/6 (33,3)	1,3 [0,26; NE]	1,00 [1,00; 1,00] NE
IVA	6/44 (13,6)	7,2 [0,26; NE]	7/33 (21,2)	0,4 [0,30; NE]	0,36 [0,11; 1,17] 0,073
IVB	9/65 (13,8)	1,2 [0,30; NE]	4/34 (11,8)	0,6 [0,33; NE]	0,53 [0,16; 1,78] 0,258
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,092)					
Asiatisch	7/66 (10,6)	1,7 [0,30; NE]	10/35 (28,6)	0,8 [0,33; 3,25]	0,54 [0,20; 1,43] 0,196
Nicht asiatisch	8/49 (16,3)	5,7 [0,26; 14,36]	3/34 (8,8)	0,3 [0,26; NE]	0,14 [0,02; 0,84] 0,013
RET-Probenart (p-Wert des Interaktionsterms: 0,587)					
Blut	2/9 (22,2)	4,2 [1,68; NE]	3/10 (30,0)	0,4 [0,33; NE]	0,18 [0,02; 1,84] 0,110

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Gewebe	13/106 (12,3)	4,0 [0,72; 14,36]	10/63 (15,9)	0,5 [0,30; 3,25]	0,49 [0,21; 1,14] 0,079
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. * SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01heai_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 96: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Kopfschmerzen - Ausprägung (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,542)					
<65 Jahre	9/76 (11,8)	4,4 [0,30; NE]	10/45 (22,2)	0,4 [0,30; 1,02]	0,44 [0,17; 1,15] 0,077
≥65 Jahre	5/39 (12,8)	1,2 [0,26; NE]	3/28 (10,7)	1,3 [0,30; NE]	0,74 [0,16; 3,36] 0,706
Baseline ECOG (p-Wert des Interaktionsterms: 0,588)					
0	6/41 (14,6)	5,8 [0,26; NE]	3/25 (12,0)	1,8 [0,30; NE]	0,64 [0,15; 2,68] 0,550
1	8/74 (10,8)	1,7 [0,30; NE]	10/48 (20,8)	0,4 [0,30; 1,02]	0,48 [0,18; 1,26] 0,115
Geschlecht (p-Wert des Interaktionsterms: 0,450)					
Männlich	5/61 (8,2)	0,7 [0,30; NE]	3/34 (8,8)	0,4 [0,26; NE]	0,83 [0,20; 3,52] 0,725
Weiblich	9/54 (16,7)	3,0 [0,30; NE]	10/39 (25,6)	0,5 [0,30; 1,28]	0,38 [0,14; 0,99] 0,040
Geografische Region (p-Wert des Interaktionsterms: 0,098)					
Ostasiatisch	7/65 (10,8)	1,7 [0,30; NE]	9/35 (25,7)	0,8 [0,33; 3,02]	0,71 [0,26; 1,93] 0,450
Nicht-Ostasiatisch	7/50 (14,0)	3,0 [0,26; NE]	4/38 (10,5)	0,3 [0,26; NE]	0,15 [0,03; 0,83] 0,010
Raucherstatus (p-Wert des Interaktionsterms: 0,719)					
Nie	9/72 (12,5)	1,7 [0,30; NE]	11/50 (22,0)	0,5 [0,33; 1,02]	0,50 [0,20; 1,27] 0,135
Ehemals/Aktuell	5/43 (11,6)	3,0 [0,30; NE]	2/23 (8,7)	0,8 [0,30; NE]	0,36 [0,06; 2,13] 0,192
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,291)					
Ja	4/23 (17,4)	1,7 [0,26; NE]	2/14 (14,3)	0,3 [NE; NE]	0,35 [0,05; 2,54] 0,358
Nein	3/44 (6,8)	5,8 [0,26; NE]	6/23 (26,1)	0,5 [0,26; NE]	0,20 [0,04; 1,05] 0,038

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	7/48 (14,6)	1,2 [0,30; NE]	5/36 (13,9)	1,0 [0,33; NE]	0,79 [0,24; 2,61] 0,677
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,089)					
TPS <50%	5/48 (10,4)	0,7 [0,26; NE]	3/27 (11,1)	1,0 [0,30; NE]	1,67 [0,40; 7,05] 0,481
TPS ≥50%	3/19 (15,8)	3,3 [1,18; NE]	3/13 (23,1)	0,3 [0,30; NE]	0,00 [0,00; NE] 0,004
Unbekannt	6/48 (12,5)	1,7 [0,26; NE]	7/33 (21,2)	0,4 [0,26; 1,28]	0,35 [0,11; 1,13] 0,062
Krankheitsstatus (p-Wert des Interaktionsterms: 0,964)					
III*	0/6 (0,0)	NE [NE; NE]	1/6 (16,7)	NE [0,26; NE]	1,00 [1,00; 1,00] NE
IVA	7/44 (15,9)	3,0 [0,26; 14,36]	8/33 (24,2)	0,4 [0,30; 0,79]	0,41 [0,13; 1,23] 0,101
IVB	7/65 (10,8)	3,3 [0,30; NE]	4/34 (11,8)	1,1 [0,33; NE]	0,49 [0,14; 1,75] 0,231
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,098)					
Asiatisch	7/66 (10,6)	1,7 [0,30; NE]	9/35 (25,7)	0,8 [0,33; 3,02]	0,71 [0,26; 1,93] 0,450
Nicht asiatisch	7/49 (14,3)	3,0 [0,26; NE]	4/34 (11,8)	0,3 [0,26; NE]	0,15 [0,03; 0,83] 0,010
RET-Probenart (p-Wert des Interaktionsterms: 0,411)					
Blut	3/9 (33,3)	1,2 [0,30; NE]	3/10 (30,0)	0,8 [0,33; NE]	0,62 [0,10; 3,83] 0,607
Gewebe	11/106 (10,4)	3,3 [0,30; NE]	10/63 (15,9)	0,4 [0,30; 3,02]	0,47 [0,19; 1,15] 0,085

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte.					
* SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01heas_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba
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Tabelle 97: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Juckreiz - Ausprägung (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,732)					
<65 Jahre	41/76 (53,9)	2,9 [1,94; 4,67]	23/45 (51,1)	1,0 [0,59; 2,56]	0,74 [0,44; 1,23] 0,244
≥65 Jahre	19/39 (48,7)	2,2 [0,99; 4,47]	14/28 (50,0)	0,5 [0,33; 9,72]	0,66 [0,33; 1,33] 0,253
Baseline ECOG (p-Wert des Interaktionsterms: 0,593)					
0	18/41 (43,9)	3,4 [0,76; 7,00]	11/25 (44,0)	1,8 [0,33; 9,72]	0,93 [0,43; 2,00] 0,895
1	42/74 (56,8)	2,8 [1,87; 3,94]	26/48 (54,2)	1,0 [0,56; 1,71]	0,68 [0,41; 1,11] 0,121
Geschlecht (p-Wert des Interaktionsterms: 0,387)					
Männlich	33/61 (54,1)	2,8 [1,22; 3,29]	16/34 (47,1)	1,5 [0,53; 2,56]	0,83 [0,46; 1,52] 0,540
Weiblich	27/54 (50,0)	3,5 [1,45; 7,00]	21/39 (53,8)	0,9 [0,53; 1,91]	0,62 [0,35; 1,10] 0,104
Geografische Region (p-Wert des Interaktionsterms: 0,141)					
Ostasiatisch	42/65 (64,6)	2,9 [1,68; 4,47]	26/35 (74,3)	1,0 [0,56; 1,71]	0,55 [0,34; 0,90] 0,016
Nicht-Ostasiatisch	18/50 (36,0)	2,7 [0,72; 7,00]	11/38 (28,9)	1,8 [0,33; NE]	1,13 [0,53; 2,43] 0,736
Raucherstatus (p-Wert des Interaktionsterms: 0,060)					
Nie	35/72 (48,6)	2,8 [1,31; 4,01]	26/50 (52,0)	1,0 [0,59; 2,83]	0,82 [0,49; 1,36] 0,447
Ehemals/Aktuell	25/43 (58,1)	3,2 [1,87; 6,05]	11/23 (47,8)	0,6 [0,30; 1,48]	0,26 [0,12; 0,58] <0,001
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,200)					
Ja	9/23 (39,1)	7,4 [0,76; NE]	7/14 (50,0)	2,6 [0,30; NE]	0,78 [0,29; 2,14] 0,653
Nein	24/44 (54,5)	1,9 [0,95; 2,86]	10/23 (43,5)	1,0 [0,33; NE]	1,08 [0,51; 2,27] 0,831

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	27/48 (56,3)	3,2 [1,68; 4,47]	20/36 (55,6)	1,0 [0,43; 1,48]	0,46 [0,25; 0,83] 0,008
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,477)					
Ja	6/16 (37,5)	4,7 [0,79; NE]	2/13 (15,4)	4,8 [1,02; NE]	1,36 [0,27; 6,79] 0,704
Nein	54/98 (55,1)	2,8 [1,68; 3,94]	35/60 (58,3)	1,0 [0,53; 1,71]	0,69 [0,45; 1,06] 0,086
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,547)					
TPS <50%	24/48 (50,0)	2,9 [0,99; 6,05]	14/27 (51,9)	0,9 [0,43; 2,43]	0,51 [0,26; 1,00] 0,044
TPS ≥50%	9/19 (47,4)	2,8 [0,79; NE]	6/13 (46,2)	0,3 [0,30; 2,56]	0,33 [0,11; 0,94] 0,036
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,154)					
TPS <50%	24/48 (50,0)	2,9 [0,99; 6,05]	14/27 (51,9)	0,9 [0,43; 2,43]	0,51 [0,26; 1,00] 0,044
TPS ≥50%	9/19 (47,4)	2,8 [0,79; NE]	6/13 (46,2)	0,3 [0,30; 2,56]	0,33 [0,11; 0,94] 0,036
Unbekannt	27/48 (56,3)	2,2 [0,99; 4,47]	17/33 (51,5)	1,2 [0,62; 9,72]	1,05 [0,57; 1,93] 0,877
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,349)					
Negativ	11/26 (42,3)	2,9 [0,76; 8,38]	7/12 (58,3)	1,1 [0,30; NE]	0,31 [0,11; 0,90] 0,023
Positiv	26/49 (53,1)	2,8 [1,87; 5,32]	16/34 (47,1)	0,7 [0,33; 9,72]	0,67 [0,36; 1,25] 0,213
Unbekannt	23/40 (57,5)	3,1 [0,99; 5,82]	14/27 (51,9)	1,2 [0,62; 13,37]	0,96 [0,49; 1,87] 0,917
Krankheitsstatus (p-Wert des Interaktionsterms: 0,496)					
III	3/6 (50,0)	4,0 [0,33; NE]	3/6 (50,0)	2,4 [0,53; NE]	0,82 [0,16; 4,16] 0,815
IVA	24/44 (54,5)	2,9 [1,22; 5,32]	18/33 (54,5)	0,5 [0,33; 1,25]	0,54 [0,29; 1,00] 0,049

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	33/65 (50,8)	2,8 [1,45; 4,01]	16/34 (47,1)	1,7 [0,79; 9,72]	0,90 [0,49; 1,65] 0,744
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,147)					
Asiatisch	43/66 (65,2)	2,9 [1,45; 4,01]	26/35 (74,3)	1,0 [0,56; 1,71]	0,57 [0,35; 0,93] 0,022
Nicht asiatisch	17/49 (34,7)	2,8 [1,22; 7,00]	9/34 (26,5)	2,6 [0,30; NE]	1,18 [0,52; 2,68] 0,691
RET-Probenart (p-Wert des Interaktionsterms: 0,780)					
Blut	5/9 (55,6)	3,5 [0,53; NE]	4/10 (40,0)	1,8 [0,33; NE]	0,67 [0,17; 2,54] 0,549
Gewebe	55/106 (51,9)	2,9 [1,87; 4,01]	33/63 (52,4)	1,0 [0,53; 1,91]	0,73 [0,48; 1,13] 0,162
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,589)					
CCDC6	4/9 (44,4)	6,1 [0,53; NE]	2/6 (33,3)	0,5 [0,30; NE]	0,31 [0,04; 2,25] 0,226
KIF5B	28/50 (56,0)	2,4 [0,99; 4,47]	18/36 (50,0)	0,6 [0,33; 2,56]	0,67 [0,37; 1,24] 0,212
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01itcs_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 98: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Übelkeit - Häufigkeit (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,698)					
<65 Jahre	29/76 (38,2)	9,3 [2,40; NE]	29/45 (64,4)	0,4 [0,33; 0,53]	0,20 [0,11; 0,35] <0,001
≥65 Jahre	16/39 (41,0)	7,9 [3,29; NE]	17/28 (60,7)	0,4 [0,30; 1,74]	0,15 [0,06; 0,34] <0,001
Geschlecht (p-Wert des Interaktionsterms: 0,115)					
Männlich	22/61 (36,1)	11,1 [1,68; NE]	18/34 (52,9)	0,4 [0,36; 1,91]	0,26 [0,13; 0,51] <0,001
Weiblich	23/54 (42,6)	5,2 [2,40; 22,77]	28/39 (71,8)	0,3 [0,33; 0,49]	0,11 [0,05; 0,22] <0,001
Geografische Region (p-Wert des Interaktionsterms: 0,152)					
Ostasiatisch	30/65 (46,2)	11,1 [3,61; 22,77]	30/35 (85,7)	0,4 [0,33; 0,53]	0,13 [0,07; 0,24] <0,001
Nicht-Ostasiatisch	15/50 (30,0)	4,3 [0,99; 15,28]	16/38 (42,1)	0,4 [0,33; 0,99]	0,34 [0,16; 0,72] 0,003
Raucherstatus (p-Wert des Interaktionsterms: 0,572)					
Nie	27/72 (37,5)	7,4 [3,29; NE]	35/50 (70,0)	0,4 [0,33; 0,53]	0,17 [0,10; 0,30] <0,001
Ehemals/Aktuell	18/43 (41,9)	9,3 [1,68; 15,28]	11/23 (47,8)	0,4 [0,33; 1,91]	0,22 [0,10; 0,52] <0,001
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,162)					
Ja	10/23 (43,5)	5,2 [0,30; 15,28]	10/14 (71,4)	0,4 [0,33; 1,91]	0,35 [0,13; 0,94] 0,028
Nein	18/44 (40,9)	4,9 [1,71; 16,20]	14/23 (60,9)	0,4 [0,30; 0,49]	0,12 [0,05; 0,28] <0,001
Unbekannt	17/48 (35,4)	12,9 [3,32; NE]	22/36 (61,1)	0,4 [0,33; 0,59]	0,15 [0,07; 0,31] <0,001
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,623)					
Ja	4/16 (25,0)	NE [0,59; NE]	4/13 (30,8)	0,4 [0,33; NE]	0,19 [0,04; 0,89] 0,022

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	41/98 (41,8)	7,9 [3,02; 12,94]	42/60 (70,0)	0,4 [0,33; 0,53]	0,18 [0,11; 0,30] <0,001
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,646)					
TPS <50%	20/48 (41,7)	7,4 [1,68; 16,20]	17/27 (63,0)	0,5 [0,33; 0,99]	0,16 [0,07; 0,35] <0,001
TPS ≥50%	6/19 (31,6)	NE [0,76; NE]	6/13 (46,2)	0,3 [0,30; 0,36]	0,20 [0,06; 0,67] 0,007
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,815)					
TPS <50%	20/48 (41,7)	7,4 [1,68; 16,20]	17/27 (63,0)	0,5 [0,33; 0,99]	0,16 [0,07; 0,35] <0,001
TPS ≥50%	6/19 (31,6)	NE [0,76; NE]	6/13 (46,2)	0,3 [0,30; 0,36]	0,20 [0,06; 0,67] 0,007
Unbekannt	19/48 (39,6)	9,3 [2,14; NE]	23/33 (69,7)	0,4 [0,33; 0,49]	0,19 [0,09; 0,37] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,393)					
Negativ	7/26 (26,9)	16,2 [1,22; NE]	7/12 (58,3)	0,8 [0,30; NE]	0,11 [0,03; 0,45] <0,001
Positiv	22/49 (44,9)	3,3 [1,68; 12,94]	21/34 (61,8)	0,4 [0,33; 0,99]	0,25 [0,13; 0,48] <0,001
Unbekannt	16/40 (40,0)	11,1 [2,14; NE]	18/27 (66,7)	0,4 [0,33; 0,49]	0,16 [0,07; 0,34] <0,001
Krankheitsstatus (p-Wert des Interaktionsterms: 0,283)					
III	3/6 (50,0)	5,2 [0,66; NE]	5/6 (83,3)	1,1 [0,26; NE]	0,29 [0,06; 1,52] 0,120
IVA	17/44 (38,6)	5,6 [2,40; NE]	22/33 (66,7)	0,4 [0,33; 0,43]	0,11 [0,05; 0,24] <0,001
IVB	25/65 (38,5)	12,3 [3,02; 16,20]	19/34 (55,9)	0,4 [0,33; 0,99]	0,22 [0,11; 0,42] <0,001
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,118)					
Asiatisch	31/66 (47,0)	9,3 [3,61; 22,77]	30/35 (85,7)	0,4 [0,33; 0,53]	0,13 [0,07; 0,24] <0,001

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	14/49 (28,6)	3,7 [0,99; NE]	13/34 (38,2)	0,4 [0,30; 1,74]	0,38 [0,17; 0,84] 0,014
RET-Probenart (p-Wert des Interaktionsterms: 0,770)					
Blut	4/9 (44,4)	7,4 [0,30; NE]	5/10 (50,0)	0,3 [0,26; NE]	0,26 [0,06; 1,18] 0,067
Gewebe	41/106 (38,7)	9,3 [3,61; 16,20]	41/63 (65,1)	0,4 [0,33; 0,53]	0,17 [0,10; 0,28] <0,001
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01nauf_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 99: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Übelkeit - Ausprägung (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,478)					
<65 Jahre	4/76 (5,3)	NE [0,59; NE]	9/45 (20,0)	0,5 [0,26; 1,38]	0,19 [0,06; 0,65] 0,004
≥65 Jahre	3/39 (7,7)	4,7 [0,30; NE]	2/28 (7,1)	0,3 [0,30; NE]	0,13 [0,01; 1,46] 0,049
Baseline ECOG (p-Wert des Interaktionsterms: 0,228)					
0	1/41 (2,4)	NE [3,29; NE]	1/25 (4,0)	0,3 [NE; NE]	0,00 [0,00; NE] 0,157
1	6/74 (8,1)	4,7 [3,06; NE]	10/48 (20,8)	0,4 [0,30; 1,38]	0,22 [0,07; 0,63] 0,002
Geschlecht (p-Wert des Interaktionsterms: 0,775)					
Männlich	2/61 (3,3)	4,7 [0,30; NE]	3/34 (8,8)	0,4 [0,26; NE]	0,23 [0,02; 2,26] 0,171
Weiblich	5/54 (9,3)	4,4 [3,06; NE]	8/39 (20,5)	0,4 [0,30; 2,40]	0,19 [0,06; 0,60] 0,002
Raucherstatus (p-Wert des Interaktionsterms: 0,792)					
Nie	4/72 (5,6)	4,4 [3,06; NE]	8/50 (16,0)	0,4 [0,26; 2,40]	0,17 [0,05; 0,59] 0,002
Ehemals/Aktuell	3/43 (7,0)	4,7 [0,30; NE]	3/23 (13,0)	0,4 [0,30; NE]	0,28 [0,05; 1,72] 0,137
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,352)					
Ja	2/23 (8,7)	NE [3,06; NE]	3/14 (21,4)	0,5 [0,30; NE]	0,32 [0,05; 2,05] 0,223
Nein	1/44 (2,3)	3,3 [NE; NE]	2/23 (8,7)	0,3 [0,26; NE]	0,00 [0,00; NE] 0,018
Unbekannt	4/48 (8,3)	4,7 [0,30; NE]	6/36 (16,7)	0,7 [0,33; NE]	0,18 [0,03; 0,93] 0,024
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,062)					
Ja	2/16 (12,5)	4,4 [0,59; NE]	1/13 (7,7)	NE [0,66; NE]	1,10 [0,10; 12,24] 0,936

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	5/98 (5,1)	4,7 [3,06; NE]	10/60 (16,7)	0,3 [0,26; 0,99]	0,04 [0,00; 0,33] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,610)					
Negativ*	1/26 (3,8)	NE [4,67; NE]	0/12 (0,0)	NE [NE; NE]	1,00 [1,00; 1,00] NE
Positiv	4/49 (8,2)	3,3 [0,30; NE]	7/34 (20,6)	0,3 [0,30; 1,38]	0,25 [0,05; 1,26] 0,067
Unbekannt	2/40 (5,0)	NE [3,06; NE]	4/27 (14,8)	0,4 [0,26; NE]	0,17 [0,03; 0,98] 0,027
RET-Probenart (p-Wert des Interaktionsterms: 0,764)					
Blut	2/9 (22,2)	4,4 [3,06; NE]	3/10 (30,0)	0,4 [0,33; NE]	0,00 [0,00; NE] 0,025
Gewebe	5/106 (4,7)	4,7 [0,59; NE]	8/63 (12,7)	0,4 [0,26; 2,40]	0,23 [0,07; 0,71] 0,006
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. * SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01naus_sub_mitt_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 100: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Erbrechen - Häufigkeit (≥1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,366)					
<65 Jahre	19/76 (25,0)	NE [11,10; NE]	24/45 (53,3)	1,1 [0,33; 4,04]	0,21 [0,11; 0,40] <0,001
≥65 Jahre	8/39 (20,5)	NE [8,61; NE]	10/28 (35,7)	4,4 [1,05; NE]	0,37 [0,14; 0,95] 0,033
Baseline ECOG (p-Wert des Interaktionsterms: 0,126)					
0	9/41 (22,0)	16,4 [6,24; NE]	8/25 (32,0)	3,3 [0,33; NE]	0,46 [0,18; 1,20] 0,108
1	18/74 (24,3)	NE [18,23; NE]	26/48 (54,2)	1,9 [0,43; 4,40]	0,20 [0,10; 0,37] <0,001
Geschlecht (p-Wert des Interaktionsterms: 0,743)					
Männlich	12/61 (19,7)	NE [11,10; NE]	12/34 (35,3)	4,1 [0,43; NE]	0,27 [0,12; 0,63] 0,001
Weiblich	15/54 (27,8)	22,8 [8,77; NE]	22/39 (56,4)	1,6 [0,33; 3,29]	0,25 [0,12; 0,50] <0,001
Raucherstatus (p-Wert des Interaktionsterms: 0,662)					
Nie	17/72 (23,6)	22,8 [16,36; NE]	27/50 (54,0)	2,1 [0,95; 5,19]	0,23 [0,12; 0,44] <0,001
Ehemals/Aktuell	10/43 (23,3)	NE [8,77; NE]	7/23 (30,4)	2,6 [0,33; NE]	0,33 [0,12; 0,88] 0,021
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,134)					
Ja	7/23 (30,4)	18,2 [1,41; NE]	6/14 (42,9)	6,5 [0,33; NE]	0,63 [0,20; 1,96] 0,411
Nein	7/44 (15,9)	NE [8,77; NE]	12/23 (52,2)	1,9 [0,39; 4,40]	0,14 [0,05; 0,36] <0,001
Unbekannt	13/48 (27,1)	22,8 [11,10; NE]	16/36 (44,4)	2,0 [0,33; 8,51]	0,28 [0,13; 0,59] <0,001
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,966)					
Ja	3/16 (18,8)	NE [1,41; NE]	3/13 (23,1)	8,6 [0,33; NE]	0,28 [0,06; 1,43] 0,103

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	24/98 (24,5)	22,8 [11,33; NE]	31/60 (51,7)	2,0 [0,95; 4,40]	0,27 [0,16; 0,46] <0,001
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,576)					
TPS <50%	8/48 (16,7)	NE [16,36; NE]	11/27 (40,7)	4,0 [0,53; NE]	0,26 [0,10; 0,67] 0,002
TPS ≥50%	4/19 (21,1)	NE [5,78; NE]	4/13 (30,8)	8,5 [0,33; NE]	0,44 [0,11; 1,77] 0,235
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,648)					
TPS <50%	8/48 (16,7)	NE [16,36; NE]	11/27 (40,7)	4,0 [0,53; NE]	0,26 [0,10; 0,67] 0,002
TPS ≥50%	4/19 (21,1)	NE [5,78; NE]	4/13 (30,8)	8,5 [0,33; NE]	0,44 [0,11; 1,77] 0,235
Unbekannt	15/48 (31,3)	18,2 [8,61; NE]	19/33 (57,6)	1,2 [0,33; 5,19]	0,20 [0,09; 0,43] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,741)					
Negativ	4/26 (15,4)	NE [3,29; NE]	4/12 (33,3)	4,1 [0,43; NE]	0,37 [0,09; 1,50] 0,148
Positiv	10/49 (20,4)	NE [16,36; NE]	14/34 (41,2)	3,8 [0,43; NE]	0,29 [0,13; 0,65] 0,002
Unbekannt	13/40 (32,5)	18,2 [8,61; NE]	16/27 (59,3)	1,0 [0,33; 2,00]	0,18 [0,08; 0,42] <0,001
Krankheitsstatus (p-Wert des Interaktionsterms: 0,808)					
III	2/6 (33,3)	7,8 [1,22; NE]	4/6 (66,7)	4,0 [0,95; NE]	0,45 [0,08; 2,46] 0,343
IVA	12/44 (27,3)	NE [8,61; NE]	17/33 (51,5)	1,3 [0,33; 4,11]	0,26 [0,12; 0,55] <0,001
IVB	13/65 (20,0)	NE [18,23; NE]	13/34 (38,2)	6,5 [0,43; NE]	0,28 [0,13; 0,62] <0,001
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,057)					
Asiatisch	18/66 (27,3)	NE [11,33; NE]	24/35 (68,6)	1,1 [0,33; 3,29]	0,16 [0,08; 0,30] <0,001

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	9/49 (18,4)	NE [5,78; NE]	9/34 (26,5)	5,2 [0,95; NE]	0,50 [0,20; 1,28] 0,140
RET-Probenart (p-Wert des Interaktionsterms: 0,248)					
Blut	2/9 (22,2)	NE [0,30; NE]	5/10 (50,0)	0,4 [0,26; NE]	0,19 [0,04; 1,06] 0,040
Gewebe	25/106 (23,6)	22,8 [16,36; NE]	29/63 (46,0)	3,3 [1,02; 6,51]	0,29 [0,17; 0,50] <0,001
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,496)					
CCDC6	4/9 (44,4)	14,2 [0,76; NE]	2/6 (33,3)	2,1 [0,26; NE]	0,53 [0,09; 3,23] 0,499
KIF5B	13/50 (26,0)	NE [8,77; NE]	16/36 (44,4)	1,9 [0,39; 6,51]	0,30 [0,14; 0,64] 0,001
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw. <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw. <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01vomf_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 101: Subgruppen für die Zeit bis zur erstmaligen Verschlechterung des PRO-CTCAE Tränende Augen - Ausprägung (≥ 1 Punkt) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,879)					
<65 Jahre	30/76 (39,5)	7,9 [2,60; NE]	25/45 (55,6)	1,2 [0,82; 1,97]	0,41 [0,24; 0,70] <0,001
≥65 Jahre	17/39 (43,6)	2,2 [1,22; 4,44]	16/28 (57,1)	1,1 [0,49; 1,48]	0,36 [0,17; 0,73] 0,003
Baseline ECOG (p-Wert des Interaktionsterms: 0,551)					
0	11/41 (26,8)	10,9 [1,22; NE]	12/25 (48,0)	1,4 [0,79; 2,79]	0,32 [0,14; 0,75] 0,006
1	36/74 (48,6)	3,3 [1,97; 8,84]	29/48 (60,4)	1,0 [0,82; 1,48]	0,42 [0,25; 0,70] <0,001
Geschlecht (p-Wert des Interaktionsterms: 0,478)					
Männlich	21/61 (34,4)	9,3 [2,60; NE]	17/34 (50,0)	1,2 [0,82; 2,04]	0,34 [0,17; 0,66] <0,001
Weiblich	26/54 (48,1)	2,6 [1,68; 4,44]	24/39 (61,5)	1,1 [0,79; 1,68]	0,47 [0,27; 0,82] 0,007
Geografische Region (p-Wert des Interaktionsterms: 0,841)					
Ostasiatisch	33/65 (50,8)	5,7 [2,17; 16,69]	24/35 (68,6)	1,2 [0,82; 1,68]	0,40 [0,23; 0,69] <0,001
Nicht-Ostasiatisch	14/50 (28,0)	3,8 [1,02; NE]	17/38 (44,7)	1,0 [0,79; 1,45]	0,42 [0,20; 0,85] 0,014
Raucherstatus (p-Wert des Interaktionsterms: 0,599)					
Nie	30/72 (41,7)	4,0 [1,97; 16,69]	32/50 (64,0)	1,1 [0,82; 1,48]	0,36 [0,21; 0,60] <0,001
Ehemals/Aktuell	17/43 (39,5)	4,5 [1,22; NE]	9/23 (39,1)	1,2 [0,79; 1,74]	0,52 [0,23; 1,19] 0,120
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,502)					
Ja	9/23 (39,1)	4,2 [2,37; NE]	7/14 (50,0)	1,4 [0,99; NE]	0,54 [0,20; 1,50] 0,231
Nein	16/44 (36,4)	8,8 [1,64; NE]	13/23 (56,5)	0,8 [0,39; 1,68]	0,33 [0,16; 0,70] 0,003

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	22/48 (45,8)	2,8 [1,22; 10,91]	21/36 (58,3)	1,0 [0,82; 1,48]	0,36 [0,19; 0,68] 0,001
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,956)					
Ja	7/16 (43,8)	4,2 [1,71; NE]	3/13 (23,1)	1,1 [0,56; NE]	0,19 [0,03; 1,21] 0,052
Nein	40/98 (40,8)	3,3 [1,91; 10,91]	38/60 (63,3)	1,2 [0,82; 1,48]	0,41 [0,26; 0,65] <0,001
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,870)					
TPS <50%	19/48 (39,6)	5,7 [1,74; 16,69]	14/27 (51,9)	1,4 [0,79; 2,04]	0,46 [0,23; 0,93] 0,027
TPS ≥50%	10/19 (52,6)	1,8 [0,79; 4,44]	7/13 (53,8)	0,9 [0,79; 2,79]	0,53 [0,20; 1,42] 0,220
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,622)					
TPS <50%	19/48 (39,6)	5,7 [1,74; 16,69]	14/27 (51,9)	1,4 [0,79; 2,04]	0,46 [0,23; 0,93] 0,027
TPS ≥50%	10/19 (52,6)	1,8 [0,79; 4,44]	7/13 (53,8)	0,9 [0,79; 2,79]	0,53 [0,20; 1,42] 0,220
Unbekannt	18/48 (37,5)	9,3 [2,14; NE]	20/33 (60,6)	1,0 [0,72; 1,68]	0,32 [0,16; 0,62] <0,001
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,931)					
Negativ	10/26 (38,5)	3,5 [0,82; NE]	7/12 (58,3)	1,1 [0,43; 2,04]	0,48 [0,18; 1,29] 0,139
Positiv	19/49 (38,8)	5,7 [1,71; NE]	18/34 (52,9)	1,2 [0,79; 1,48]	0,36 [0,18; 0,71] 0,002
Unbekannt	18/40 (45,0)	3,3 [1,22; NE]	16/27 (59,3)	1,0 [0,56; 1,74]	0,40 [0,20; 0,80] 0,008
Krankheitsstatus (p-Wert des Interaktionsterms: 0,872)					
III	2/6 (33,3)	NE [0,89; NE]	4/6 (66,7)	1,0 [0,26; NE]	0,31 [0,05; 1,72] 0,156
IVA	21/44 (47,7)	1,7 [0,95; 7,89]	21/33 (63,6)	1,1 [0,79; 1,48]	0,48 [0,25; 0,90] 0,019

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	24/65 (36,9)	5,7 [3,29; NE]	16/34 (47,1)	1,4 [0,82; 2,79]	0,38 [0,20; 0,73] 0,002
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,775)					
Asiatisch	33/66 (50,0)	5,7 [2,37; 16,69]	24/35 (68,6)	1,2 [0,82; 1,68]	0,39 [0,23; 0,68] <0,001
Nicht asiatisch	14/49 (28,6)	3,5 [1,02; NE]	14/34 (41,2)	1,2 [0,76; 2,79]	0,50 [0,24; 1,06] 0,064
RET-Probenart (p-Wert des Interaktionsterms: 0,440)					
Blut	3/9 (33,3)	NE [0,49; NE]	5/10 (50,0)	1,4 [0,56; NE]	0,09 [0,01; 0,84] 0,011
Gewebe	44/106 (41,5)	3,5 [1,97; 9,26]	36/63 (57,1)	1,1 [0,82; 1,48]	0,42 [0,27; 0,66] <0,001
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,490)					
CCDC6	5/9 (55,6)	8,6 [0,76; NE]	3/6 (50,0)	1,2 [0,53; NE]	0,11 [0,01; 1,09] 0,024
KIF5B	23/50 (46,0)	3,3 [1,71; NE]	21/36 (58,3)	1,1 [0,79; 1,48]	0,37 [0,20; 0,68] 0,001
Datenschnitt: 01. Mai 2023; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; PRO: Patient Reported Outcome; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Die Cox-Modell-Likelihood-Funktion wurde mit der Efron-Methode statt der exakten Methode gerechnet, da letztere in wenigen Fällen zu Fehlern führte. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_uw01wats_sub_mitt_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttepae_gba

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Tabelle 102: Subgruppen für die Zeit bis zum ersten unerwünschten Ereignis (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,726)					
<65 Jahre	76/76 (100,0)	0,3 [0,16; 0,30]	44/45 (97,8)	0,1 [0,07; 0,16]	0,89 [0,61; 1,30] 0,584
≥65 Jahre	39/39 (100,0)	0,3 [0,23; 0,36]	27/27 (100,0)	0,1 [0,07; 0,16]	0,76 [0,45; 1,28] 0,287
Baseline ECOG (p-Wert des Interaktionsterms: 0,765)					
0	41/41 (100,0)	0,3 [0,16; 0,39]	24/25 (96,0)	0,1 [0,03; 0,13]	0,79 [0,47; 1,33] 0,446
1	74/74 (100,0)	0,3 [0,20; 0,26]	47/47 (100,0)	0,1 [0,10; 0,20]	0,89 [0,61; 1,31] 0,545
Geografische Region (p-Wert des Interaktionsterms: 0,641)					
Ostasiatisch	65/65 (100,0)	0,2 [0,13; 0,26]	35/35 (100,0)	0,1 [0,07; 0,20]	0,89 [0,58; 1,36] 0,593
Nicht-Ostasiatisch	50/50 (100,0)	0,4 [0,26; 0,49]	36/37 (97,3)	0,1 [0,10; 0,16]	0,80 [0,51; 1,25] 0,350
Raucherstatus (p-Wert des Interaktionsterms: 0,305)					
Nie	72/72 (100,0)	0,3 [0,23; 0,33]	48/49 (98,0)	0,1 [0,07; 0,13]	0,75 [0,51; 1,09] 0,162
Ehemals/Aktuell	43/43 (100,0)	0,3 [0,10; 0,26]	23/23 (100,0)	0,1 [0,07; 0,23]	1,05 [0,61; 1,81] 0,900
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,913)					
Ja	23/23 (100,0)	0,4 [0,23; 0,56]	13/14 (92,9)	0,1 [0,03; 0,30]	0,79 [0,38; 1,61] 0,434
Nein	44/44 (100,0)	0,3 [0,16; 0,36]	23/23 (100,0)	0,1 [0,03; 0,13]	0,97 [0,56; 1,68] 0,918
Unbekannt	48/48 (100,0)	0,2 [0,10; 0,26]	35/35 (100,0)	0,1 [0,10; 0,16]	0,79 [0,50; 1,22] 0,288
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,805)					
Ja	16/16 (100,0)	0,3 [0,20; 0,72]	13/13 (100,0)	0,3 [0,03; 0,43]	0,76 [0,35; 1,63] 0,441

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nein	98/98 (100,0)	0,3 [0,20; 0,26]	58/59 (98,3)	0,1 [0,07; 0,13]	0,84 [0,60; 1,18] 0,345
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,732)					
TPS <50%	48/48 (100,0)	0,3 [0,20; 0,33]	27/27 (100,0)	0,1 [0,03; 0,26]	0,77 [0,47; 1,25] 0,326
TPS ≥50%	19/19 (100,0)	0,2 [0,03; 0,39]	12/13 (92,3)	0,1 [0,03; 0,13]	0,79 [0,38; 1,66] 0,564
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,836)					
TPS <50%	48/48 (100,0)	0,3 [0,20; 0,33]	27/27 (100,0)	0,1 [0,03; 0,26]	0,77 [0,47; 1,25] 0,326
TPS ≥50%	19/19 (100,0)	0,2 [0,03; 0,39]	12/13 (92,3)	0,1 [0,03; 0,13]	0,79 [0,38; 1,66] 0,564
Unbekannt	48/48 (100,0)	0,3 [0,13; 0,36]	32/32 (100,0)	0,1 [0,07; 0,26]	0,93 [0,58; 1,49] 0,786
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,441)					
Negativ	26/26 (100,0)	0,3 [0,20; 0,49]	12/12 (100,0)	0,1 [0,03; 0,26]	0,60 [0,29; 1,20] 0,160
Positiv	49/49 (100,0)	0,3 [0,13; 0,26]	33/34 (97,1)	0,1 [0,07; 0,13]	0,95 [0,60; 1,51] 0,854
Unbekannt	40/40 (100,0)	0,2 [0,13; 0,26]	26/26 (100,0)	0,1 [0,07; 0,23]	0,91 [0,54; 1,54] 0,729
Krankheitsstatus (p-Wert des Interaktionsterms: 0,523)					
III	6/6 (100,0)	0,3 [0,03; NE]	6/6 (100,0)	0,2 [0,03; NE]	0,85 [0,25; 2,94] 0,802
IVA	44/44 (100,0)	0,2 [0,13; 0,26]	32/32 (100,0)	0,1 [0,03; 0,13]	0,64 [0,40; 1,04] 0,079
IVB	65/65 (100,0)	0,3 [0,20; 0,39]	33/34 (97,1)	0,1 [0,10; 0,26]	1,02 [0,67; 1,58] 0,921
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,818)					
Asiatisch	66/66 (100,0)	0,2 [0,13; 0,26]	35/35 (100,0)	0,1 [0,07; 0,20]	0,90 [0,59; 1,37] 0,612

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Nicht asiatisch	49/49 (100,0)	0,4 [0,26; 0,49]	32/33 (97,0)	0,1 [0,10; 0,16]	0,87 [0,55; 1,39] 0,592
RET-Probenart (p-Wert des Interaktionsterms: 0,527)					
Blut	9/9 (100,0)	0,3 [0,03; 0,69]	9/10 (90,0)	0,1 [0,03; 0,43]	0,88 [0,35; 2,26] 0,777
Gewebe	106/106 (100,0)	0,3 [0,20; 0,26]	62/62 (100,0)	0,1 [0,07; 0,13]	0,80 [0,58; 1,11] 0,197
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,433)					
CCDC6	9/9 (100,0)	0,3 [0,03; 0,72]	6/6 (100,0)	0,1 [0,03; NE]	0,45 [0,14; 1,38] 0,159
KIF5B	50/50 (100,0)	0,3 [0,20; 0,39]	35/36 (97,2)	0,1 [0,07; 0,23]	0,88 [0,56; 1,38] 0,596
Datenschnitt: 01. Mai 2023; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_tte_sub_msaf_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adtteae_gba

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Tabelle 103: Subgruppen für die Zeit bis zum ersten schwerwiegenden unerwünschten Ereignis aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit* [95% KI]	n/N (%)	Mediane Ereigniszeit* [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,106)					
<65 Jahre	25/76 (32,9)	NE [21,42; NE]	8/45 (17,8)	NE [NE; NE]	1,64 [0,74; 3,65] 0,218
≥65 Jahre	15/39 (38,5)	NE [10,68; NE]	12/27 (44,4)	NE [2,86; NE]	0,70 [0,33; 1,50] 0,357
Baseline ECOG (p-Wert des Interaktionsterms: 0,432)					
0	11/41 (26,8)	NE [21,49; NE]	7/25 (28,0)	NE [NE; NE]	0,80 [0,31; 2,08] 0,654
1	29/74 (39,2)	NE [14,06; NE]	13/47 (27,7)	NE [NE; NE]	1,22 [0,63; 2,36] 0,549
Geschlecht (p-Wert des Interaktionsterms: 0,713)					
Männlich	21/61 (34,4)	NE [21,42; NE]	10/34 (29,4)	NE [NE; NE]	0,96 [0,45; 2,05] 0,918
Weiblich	19/54 (35,2)	NE [13,40; NE]	10/38 (26,3)	NE [NE; NE]	1,19 [0,55; 2,57] 0,652
Geografische Region (p-Wert des Interaktionsterms: 0,257)					
Ostasiatisch	24/65 (36,9)	NE [14,06; NE]	13/35 (37,1)	NE [5,13; NE]	0,80 [0,41; 1,58] 0,525
Nicht-Ostasiatisch	16/50 (32,0)	NE [21,49; NE]	7/37 (18,9)	NE [NE; NE]	1,54 [0,63; 3,77] 0,335
Raucherstatus (p-Wert des Interaktionsterms: 0,326)					
Nie	24/72 (33,3)	NE [17,31; NE]	11/49 (22,4)	NE [NE; NE]	1,30 [0,64; 2,66] 0,472
Ehemals/Aktuell	16/43 (37,2)	NE [12,16; NE]	9/23 (39,1)	NE [2,86; NE]	0,78 [0,35; 1,77] 0,557
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,945)					
Ja	8/23 (34,8)	NE [7,69; NE]	4/14 (28,6)	NE [2,43; NE]	0,94 [0,28; 3,17] 0,925
Nein	16/44 (36,4)	NE [14,06; NE]	8/23 (34,8)	NE [3,42; NE]	0,95 [0,41; 2,22] 0,909

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	16/48 (33,3)	NE [22,14; NE]	8/35 (22,9)	NE [NE; NE]	1,16 [0,50; 2,72] 0,731
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,681)					
Ja	8/16 (50,0)	21,4 [6,01; NE]	5/13 (38,5)	NE [0,46; NE]	0,78 [0,24; 2,52] 0,683
Nein	32/98 (32,7)	NE [22,14; NE]	15/59 (25,4)	NE [NE; NE]	1,17 [0,63; 2,16] 0,622
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,368)					
TPS <50%	20/48 (41,7)	22,1 [14,06; NE]	5/27 (18,5)	NE [NE; NE]	1,87 [0,70; 5,01] 0,204
TPS ≥50%	6/19 (31,6)	NE [11,24; NE]	4/13 (30,8)	NE [1,41; NE]	0,87 [0,25; 3,11] 0,835
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,274)					
TPS <50%	20/48 (41,7)	22,1 [14,06; NE]	5/27 (18,5)	NE [NE; NE]	1,87 [0,70; 5,01] 0,204
TPS ≥50%	6/19 (31,6)	NE [11,24; NE]	4/13 (30,8)	NE [1,41; NE]	0,87 [0,25; 3,11] 0,835
Unbekannt	14/48 (29,2)	NE [NE; NE]	11/32 (34,4)	NE [5,78; NE]	0,74 [0,33; 1,63] 0,452
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,593)					
Negativ	8/26 (30,8)	NE [14,85; NE]	3/12 (25,0)	NE [1,28; NE]	0,86 [0,22; 3,31] 0,829
Positiv	21/49 (42,9)	21,5 [11,24; NE]	9/34 (26,5)	NE [NE; NE]	1,43 [0,65; 3,13] 0,365
Unbekannt	11/40 (27,5)	NE [NE; NE]	8/26 (30,8)	NE [12,62; NE]	0,81 [0,33; 2,02] 0,655
Krankheitsstatus (p-Wert des Interaktionsterms: 0,789)					
III	2/6 (33,3)	NE [1,31; NE]	2/6 (33,3)	NE [1,12; NE]	1,01 [0,14; 7,21] 0,992
IVA	14/44 (31,8)	NE [17,31; NE]	7/32 (21,9)	NE [NE; NE]	1,36 [0,55; 3,36] 0,510

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	24/65 (36,9)	NE [14,42; NE]	11/34 (32,4)	NE [5,78; NE]	0,85 [0,41; 1,74] 0,651
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,330)					
Asiatisch	24/66 (36,4)	NE [17,31; NE]	13/35 (37,1)	NE [5,13; NE]	0,79 [0,40; 1,56] 0,499
Nicht asiatisch	16/49 (32,7)	NE [21,49; NE]	7/33 (21,2)	NE [NE; NE]	1,39 [0,57; 3,40] 0,464
RET-Probenart (p-Wert des Interaktionsterms: 0,318)					
Blut	2/9 (22,2)	NE [7,06; NE]	3/10 (30,0)	NE [0,03; NE]	0,51 [0,08; 3,12] 0,458
Gewebe	38/106 (35,8)	NE [21,42; NE]	17/62 (27,4)	NE [NE; NE]	1,18 [0,66; 2,09] 0,574
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,774)					
CCDC6	1/9 (11,1)	NE [22,14; NE]	1/6 (16,7)	NE [1,12; NE]	0,00 [0,00; NE] 0,221
KIF5B	17/50 (34,0)	NE [13,40; NE]	12/36 (33,3)	NE [7,16; NE]	0,72 [0,34; 1,53] 0,394
Datenschnitt: 01. Mai 2023; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht erchenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50% wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS >1% ohne weitere Spezifizierung in TPS ≥50% bzw <50%. **** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. ***** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas
 Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_sae_sub_msa_f_a.rtf
 Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba
 /lillyce/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adtteae_gba
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Tabelle 104: Subgruppen für die Zeit bis zum ersten unerwünschten Ereignis CTCAE Grad ≥ 3 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,059)					
<65 Jahre	51/76 (67,1)	2,9 [1,71; 11,56]	22/45 (48,9)	13,9 [3,12; NE]	1,63 [0,99; 2,69] 0,055
≥65 Jahre	28/39 (71,8)	7,0 [1,15; 13,86]	21/27 (77,8)	4,8 [0,49; 7,16]	0,71 [0,40; 1,26] 0,236
Baseline ECOG (p-Wert des Interaktionsterms: 0,134)					
0	22/41 (53,7)	15,2 [2,10; NE]	15/25 (60,0)	7,2 [2,17; NE]	0,82 [0,42; 1,58] 0,551
1	57/74 (77,0)	2,8 [1,41; 7,03]	28/47 (59,6)	7,0 [2,76; 17,38]	1,44 [0,92; 2,27] 0,111
Geschlecht (p-Wert des Interaktionsterms: 0,738)					
Männlich	42/61 (68,9)	6,9 [2,07; 14,42]	19/34 (55,9)	7,2 [2,43; NE]	1,25 [0,73; 2,16] 0,417
Weiblich	37/54 (68,5)	3,4 [1,45; 8,35]	24/38 (63,2)	5,5 [2,27; 17,38]	1,14 [0,68; 1,91] 0,622
Geografische Region (p-Wert des Interaktionsterms: 0,233)					
Ostasiatisch	50/65 (76,9)	2,1 [1,31; 5,85]	21/35 (60,0)	5,1 [2,04; NE]	1,42 [0,85; 2,37] 0,176
Nicht-Ostasiatisch	29/50 (58,0)	14,0 [4,04; 24,90]	22/37 (59,5)	7,2 [4,76; 17,38]	0,89 [0,51; 1,57] 0,693
Raucherstatus (p-Wert des Interaktionsterms: 0,764)					
Nie	51/72 (70,8)	3,2 [1,45; 6,93]	30/49 (61,2)	7,0 [2,76; 17,38]	1,27 [0,81; 1,99] 0,307
Ehemals/Aktuell	28/43 (65,1)	10,9 [2,07; 23,59]	13/23 (56,5)	13,9 [0,99; NE]	1,08 [0,56; 2,09] 0,815
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,833)					
Ja	15/23 (65,2)	8,3 [1,15; 24,90]	9/14 (64,3)	5,1 [2,17; NE]	0,83 [0,35; 1,98] 0,681
Nein	31/44 (70,5)	2,8 [1,18; 14,03]	15/23 (65,2)	7,0 [2,30; 16,79]	1,30 [0,70; 2,41] 0,409

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	33/48 (68,8)	6,3 [1,45; 15,21]	19/35 (54,3)	12,7 [2,04; NE]	1,21 [0,69; 2,14] 0,500
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,571)					
Ja	12/16 (75,0)	7,3 [0,82; NE]	9/13 (69,2)	4,8 [0,46; NE]	0,79 [0,32; 1,93] 0,590
Nein	67/98 (68,4)	3,5 [2,07; 9,36]	34/59 (57,6)	12,7 [2,86; 17,38]	1,27 [0,84; 1,93] 0,250
PD-L1 Expression - SG-Analyse 1 * (p-Wert des Interaktionsterms: 0,344)					
TPS <50%	34/48 (70,8)	6,4 [2,10; 16,26]	13/27 (48,1)	16,0 [2,92; NE]	1,53 [0,80; 2,90] 0,194
TPS ≥50%	13/19 (68,4)	6,8 [1,45; 14,03]	9/13 (69,2)	3,1 [0,49; NE]	0,91 [0,39; 2,14] 0,837
PD-L1 Expression - SG-Analyse 2 ** (p-Wert des Interaktionsterms: 0,544)					
TPS <50%	34/48 (70,8)	6,4 [2,10; 16,26]	13/27 (48,1)	16,0 [2,92; NE]	1,53 [0,80; 2,90] 0,194
TPS ≥50%	13/19 (68,4)	6,8 [1,45; 14,03]	9/13 (69,2)	3,1 [0,49; NE]	0,91 [0,39; 2,14] 0,837
Unbekannt	32/48 (66,7)	2,1 [1,15; 13,86]	21/32 (65,6)	5,1 [2,04; 16,79]	1,11 [0,64; 1,92] 0,732
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,658)					
Negativ	16/26 (61,5)	15,2 [2,43; NE]	6/12 (50,0)	16,0 [0,16; NE]	0,91 [0,35; 2,35] 0,840
Positiv	37/49 (75,5)	5,7 [1,71; 7,69]	20/34 (58,8)	7,2 [3,12; NE]	1,47 [0,85; 2,54] 0,163
Unbekannt	26/40 (65,0)	2,1 [1,15; 10,91]	17/26 (65,4)	3,8 [1,35; 16,79]	1,10 [0,60; 2,03] 0,770
Krankheitsstatus (p-Wert des Interaktionsterms: 0,322)					
III	6/6 (100,0)	1,4 [0,79; NE]	3/6 (50,0)	NE [0,26; NE]	2,82 [0,67; 11,96] 0,145
IVA	31/44 (70,5)	2,5 [1,15; 14,03]	19/32 (59,4)	12,7 [2,04; NE]	1,27 [0,72; 2,26] 0,406

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
IVB	42/65 (64,6)	7,7 [2,43; 15,21]	21/34 (61,8)	5,5 [2,30; NE]	1,00 [0,59; 1,69] 0,986
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,215)					
Asiatisch	51/66 (77,3)	2,2 [1,31; 5,68]	21/35 (60,0)	5,1 [2,04; NE]	1,42 [0,86; 2,37] 0,171
Nicht asiatisch	28/49 (57,1)	14,0 [2,86; 24,90]	20/33 (60,6)	7,2 [4,76; 17,38]	0,87 [0,49; 1,56] 0,640
RET-Probenart (p-Wert des Interaktionsterms: 0,274)					
Blut	6/9 (66,7)	7,7 [0,26; NE]	8/10 (80,0)	3,9 [0,16; NE]	0,66 [0,23; 1,92] 0,439
Gewebe	73/106 (68,9)	3,6 [2,07; 10,91]	35/62 (56,5)	7,2 [2,76; NE]	1,29 [0,86; 1,93] 0,216
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,138)					
CCDC6	6/9 (66,7)	2,4 [0,85; NE]	3/6 (50,0)	16,0 [0,59; NE]	1,44 [0,34; 6,13] 0,622
KIF5B	31/50 (62,0)	10,9 [4,04; 24,90]	25/36 (69,4)	3,9 [1,41; 7,23]	0,60 [0,35; 1,03] 0,061
Datenschnitt: 01. Mai 2023; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine * Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$ wurden nicht berücksichtigt. ** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status und Patienten mit TPS $>1\%$ ohne weitere Spezifizierung in TPS $\geq 50\%$ bzw $<50\%$. *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. ***** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/ttte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aegr3_sub_msaf_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/csr1/data/analysis/restricted/adtteae_gba

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Tabelle 105: Subgruppen für die Zeit bis zum Behandlungsabbruch aufgrund unerwünschter Ereignisse aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
RET-Probenart (p-Wert des Interaktionsterms: 0,992)					
Blut*	0/9 (0,0)	NE [NE; NE]	1/10 (10,0)	NE [6,24; NE]	0,00 [0,00; NE] 0,248
Gewebe	10/106 (9,4)	NE [NE; NE]	1/62 (1,6)	NE [NE; NE]	5,46 [0,70; 42,75] 0,069
Datenschnitt: 01. Mai 2023; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt.					
* SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc230501.sas

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Anhang 4-G4.2: Subgruppen – UE nach SOC und PT - Übersicht über Interaktions-p-Werte

Table 112: Interaction term results of the subgroup analysis for adverse events according to SOC/PT - study LIBRETTO-431, mSAF

SOC/Preferred term	Subgroup													
	Age	Baseline ECOG	Sex	Geographic region	Smoking Status	Brain Metastases at Baseline (CRF)	Liver Metastasis - BICR	PD-L1 Expression - SG-Analysis 1	PD-L1 Expression - SG-Analysis 2	PD-L1 Expression - SG-Analysis 3	Disease Stage	Race	RET Specimen Type	RET Fusion Result
Time to first occurrence of adverse event														
Investigations														
Aspartate aminotransferase increased	0,145	0,880	0,028	0,828	0,020	0,255	0,763	0,556	0,640	0,406	0,568	0,772	0,658	0,926
Alanine aminotransferase increased	0,342	0,516	0,062	0,646	0,135	0,352	0,548	0,846	0,721	0,230	0,525	0,721	0,605	0,632
Blood bilirubin increased*	1,000	1,000	1,000	0,999	1,000	1,000	0,999	1,000	1,000	1,000	1,000	0,999	1,000	1,000
Electrocardiogram QT prolonged	0,993	0,992	0,993	0,990	0,991	1,000	0,991	NE	NE	1,000	1,000	0,990	0,993	1,000
Bilirubin conjugated increased	0,991	0,993	0,990	0,993	0,992	NE	0,999	NE	1,000	NE	1,000	0,993	0,993	NE
Gastrointestinal disorders														
Diarrhoea	0,702	0,929	0,039	0,031	0,504	0,062	0,892	0,674	0,136	0,082	0,595	0,073	0,764	0,120
Dry mouth	0,511	0,248	0,674	0,276	0,068	0,968	0,605	0,419	0,731	0,783	0,354	0,304	0,949	0,702
Constipation	0,978	0,145	0,909	0,144	0,266	0,666	0,694	0,354	0,547	0,607	0,948	0,089	0,733	0,972
Nausea	0,824	0,898	0,153	0,459	0,650	0,771	0,999	0,742	0,686	0,185	0,666	0,582	0,349	0,713
Vomiting	0,049	0,428	0,245	0,680	0,212	0,475	0,985	0,071	0,170	0,825	0,807	0,655	0,316	0,798
General disorders and administration site conditions	0,425	0,666	0,343	0,476	0,137	0,741	0,139	0,352	0,443	0,285	0,456	0,672	0,010	0,839
Asthenia	0,588	0,745	0,462	0,049	0,584	0,295	0,710	0,010	0,020	0,180	0,520	0,024	0,508	0,465
Pyrexia	0,701	0,477	0,207	0,411	0,724	0,985	0,245	1,000	0,764	0,400	0,927	0,412	0,600	0,864
Metabolism and nutrition disorders														
Decreased appetite	0,359	0,502	0,862	0,264	0,026	0,562	0,760	0,105	0,219	0,577	0,985	0,377	0,606	0,153
Hypocalcaemia*	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	0,998	NE
Hyperglycaemia	NE	0,992	NE	0,994	NE	NE	0,991	NE	NE	NE	NE	0,993	0,993	NE
Skin and subcutaneous tissue disorders														

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SOC/Preferred term	Subgroup													
	Age	Baseline ECOG	Sex	Geographic region	Smoking Status	Brain Metastases at Baseline (CRF)	Liver Metastasis - BICR	PD-L1 Expression - SC-Analyses 1	PD-L1 Expression - SC-Analyses 2	PD-L1 Expression - SC-Analyses 3	Disease Stage	Race	RET Specimen Type	RET Fusion Result
Pruritus	0,809	0,967	0,958	0,764	0,990	0,221	0,990	0,991	0,348	0,099	0,803	0,616	0,974	0,993
Vascular disorders	0,328	0,248	0,839	0,047	0,378	0,094	0,138	0,070	0,040	0,268	0,985	0,069	0,975	0,989
Hypertension	0,983	0,649	0,632	0,833	0,621	0,782	0,107	0,645	0,819	0,905	0,946	0,780	0,892	0,992
Respiratory, thoracic and mediastinal disorders														
Dyspnoea	NE	NE	NE	NE	NE	NE	0,992	NE	NE	NE	NE	NE	0,993	NE
Blood and lymphatic system disorders	0,049	0,418	0,436	0,570	0,713	0,678	0,316	0,872	0,991	0,846	0,501	0,686	0,207	0,309
Anaemia	0,065	0,128	0,017	0,999	0,064	0,364	0,848	0,941	0,434	0,261	0,649	0,866	0,308	0,059
Neutropenia	0,990	NE	0,295	0,237	0,993	0,559	1,000	NE	NE	0,906	1,000	0,323	1,000	0,996
Eye disorders														
Lacrimation increased	NE	NE	NE	NE	NE	NE	0,993	NE	NE	NE	NE	NE	0,999	NE
Reproductive system and breast disorders	0,992	NE	0,991	NE	NE	NE	0,993	NE	NE	NE	NE	NE	0,994	NE
Time to first occurrence of serious adverse event														
Investigations	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Time to first occurrence of adverse event with CTCAE grade ≥3														
Investigations	0,180	0,835	0,844	0,693	0,848	0,374	0,655	0,725	0,690	0,337	0,954	0,621	0,374	0,565
Alanine aminotransferase increased*	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	NE
Aspartate aminotransferase increased*	1,000	NE	NE	1,000	1,000	NE	1,000	NE	NE	NE	NE	1,000	0,998	NE
Electrocardiogram QT prolonged*	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Neutrophil count decreased	NE	NE	NE	0,993	NE	NE	0,993	NE	NE	NE	NE	0,994	NE	NE
Vascular disorders	0,989	0,590	0,987	0,988	0,990	0,905	0,989	0,689	0,924	1,000	1,000	0,988	0,338	0,994
Hypertension	0,989	0,544	0,987	0,988	0,990	0,860	0,989	0,619	0,882	1,000	1,000	0,989	0,382	0,994
Blood and lymphatic system disorders	0,993	0,993	0,991	0,993	0,993	NE	0,994	NE	NE	NE	NE	0,994	0,999	0,994

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SOC/Preferred term	Subgroup													
	Age	Baseline ECOG	Sex	Geographic region	Smoking Status	Brain Metastases at Baseline (CRF)	Liver Metastasis - BICR	PD-L1 Expression - SC-Analyses 1	PD-L1 Expression - SC-Analyses 2	PD-L1 Expression - SC-Analyses 3	Disease Stage	Race	RET Specimen Type	RET Fusion Result
Anaemia	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE
Neutropenia*	NE	NE	NE	NE	NE	NE	0,998	NE	NE	NE	NE	NE	0,999	NE
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection; SOC: System Organ Class. Only endpoints with p-value <0.05 in main model are taken into account. The interaction test is only performed if each subgroup category comprises at least 10 patients and at least 10 events have occurred in one of the subgroup categories. The table shows p-values of the interaction term of subgroup factor and treatment group from the unstratified Cox proportional hazards model.														

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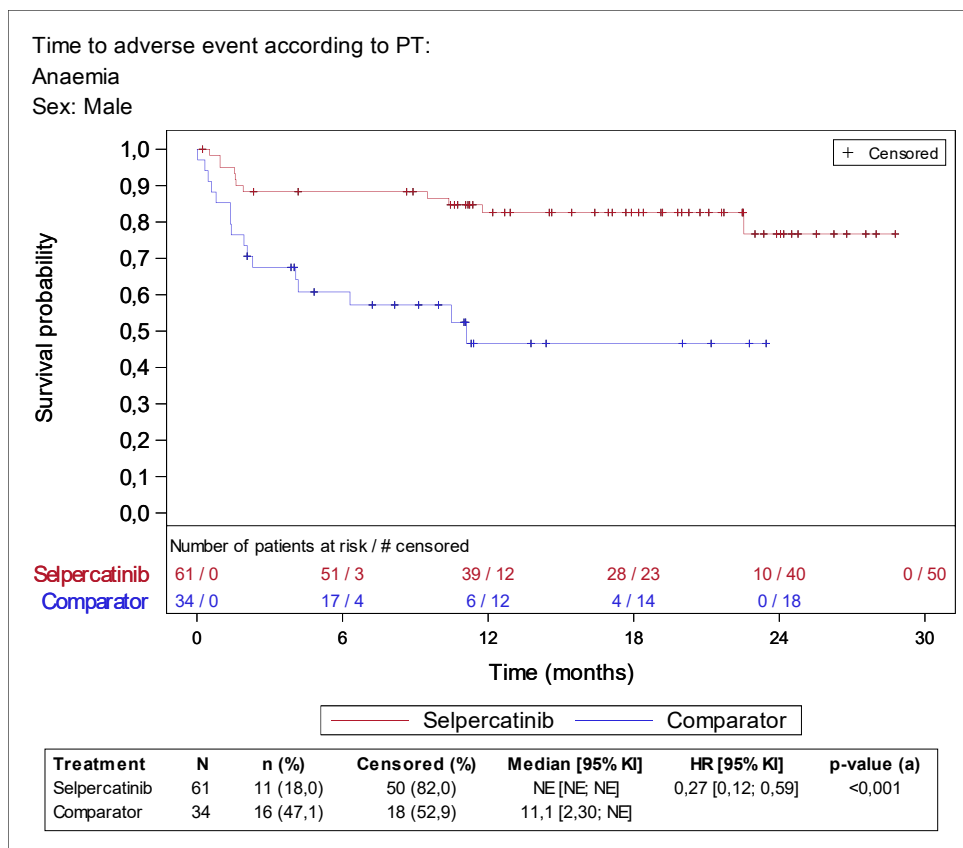
Anhang 4-G4.3: Subgruppen – UE nach SOC und PT signifikant

Table 113: Interacting Subgroups: Time to adverse event according to PT: Blood and lymphatic system disorders/Anaemia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Sex (p-value of the interaction term: 0,017)					
Male	11/61 (18,0)	NE [NE; NE]	16/34 (47,1)	11,1 [2,30; NE]	0,27 [0,12; 0,59] <0,001
Female	3/54 (5,6)	NE [NE; NE]	24/38 (63,2)	2,5 [1,35; NE]	0,05 [0,02; 0,17] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					

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Figure 85: Kaplan-Meier Plot - Time to adverse event according to PT: Anaemia, subgroup analysis for Sex: Male - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

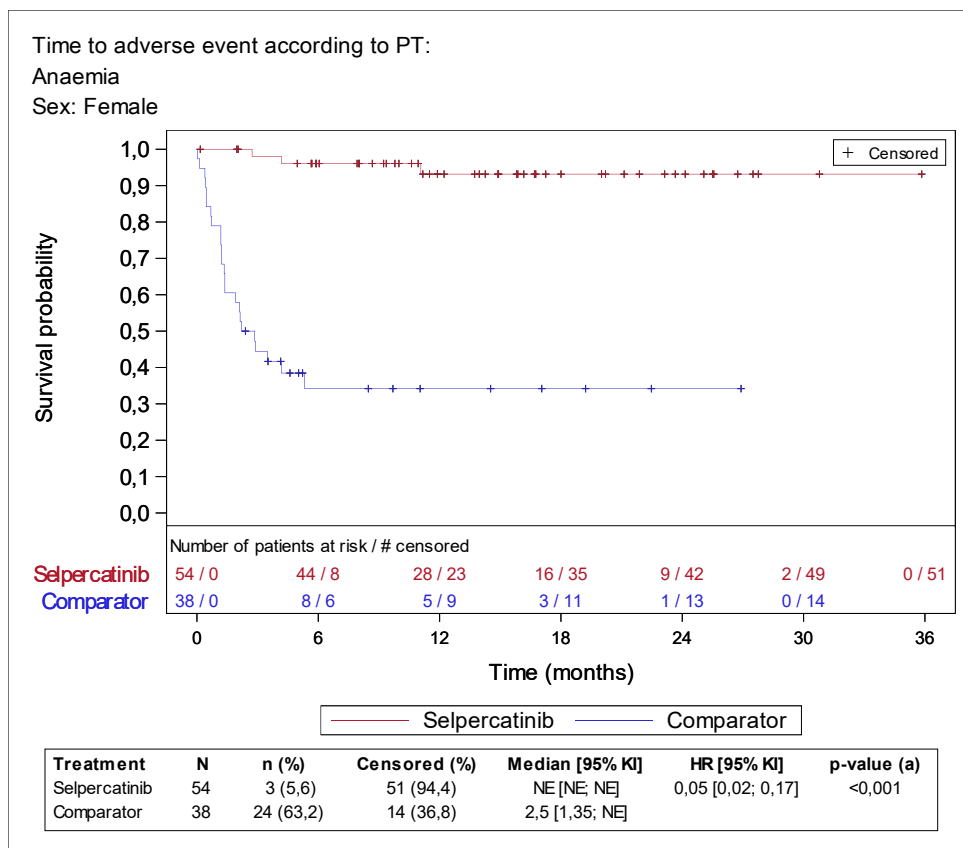
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Figure 86: Kaplan-Meier Plot - Time to adverse event according to PT: Anaemia, subgroup analysis for Sex: Female - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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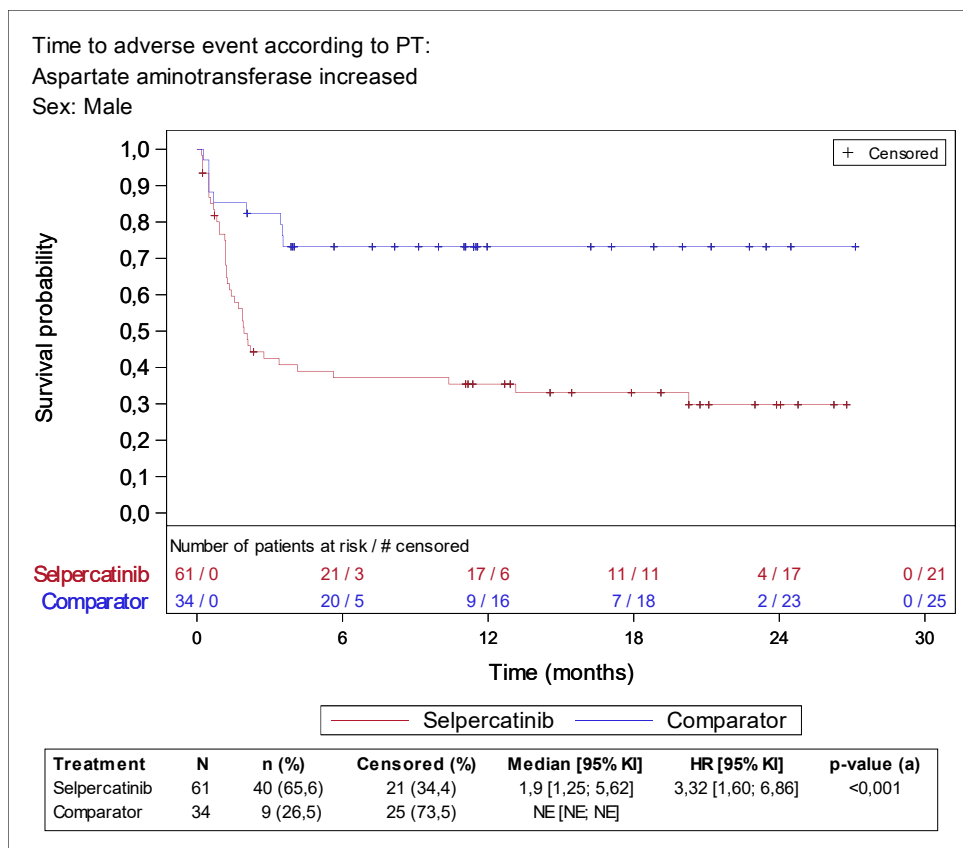
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**Table 114: Interacting Subgroups: Time to adverse event according to PT:
Investigations/Aspartate aminotransferase increased - study LIBRETTO-431, mSAF**

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Sex (p-value of the interaction term: 0,028)					
Male	40/61 (65,6)	1,9 [1,25; 5,62]	9/34 (26,5)	NE [NE; NE]	3,32 [1,60; 6,86] <0,001
Female	31/54 (57,4)	2,1 [1,41; NE]	21/38 (55,3)	5,3 [2,50; NE]	1,18 [0,68; 2,07] 0,554
Smoking Status (p-value of the interaction term: 0,020)					
Never	45/72 (62,5)	1,9 [1,28; 13,14]	27/49 (55,1)	5,0 [3,45; NE]	1,33 [0,82; 2,15] 0,246
Former/Current	26/43 (60,5)	2,2 [1,41; NE]	3/23 (13,0)	NE [NE; NE]	6,17 [1,86; 20,44] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					

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Figure 87: Kaplan-Meier Plot - Time to adverse event according to PT: Aspartate aminotransferase increased, subgroup analysis for Sex: Male - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

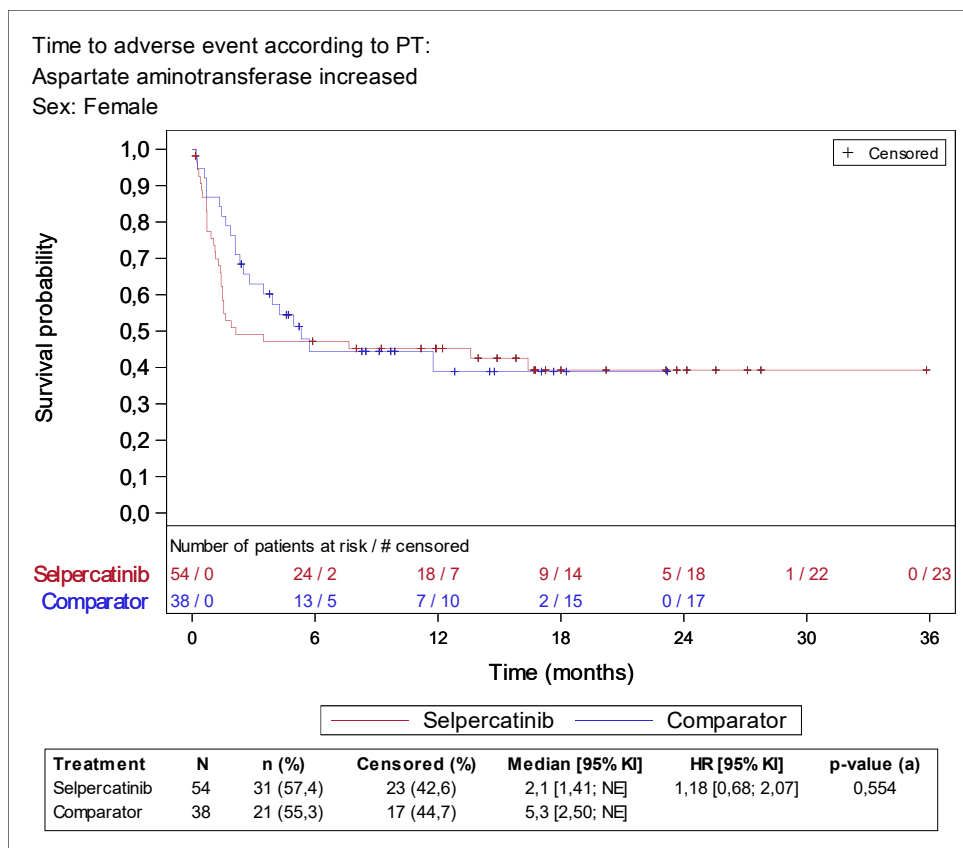
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Figure 88: Kaplan-Meier Plot - Time to adverse event according to PT: Aspartate aminotransferase increased, subgroup analysis for Sex: Female - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

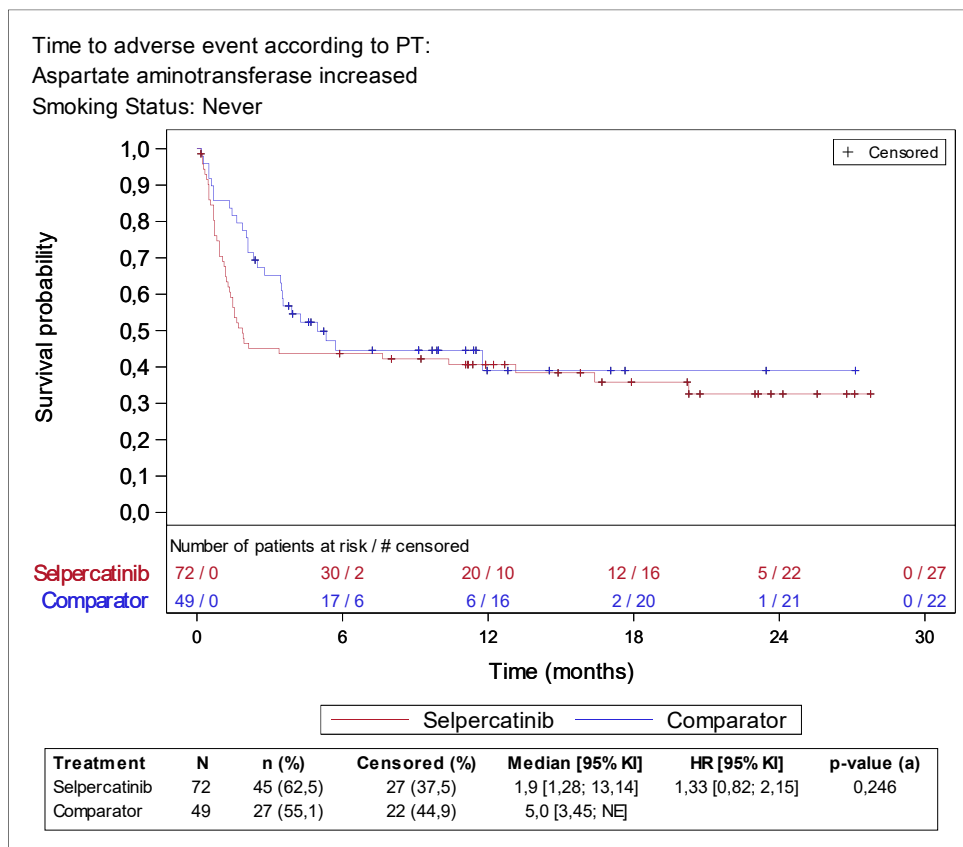
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Figure 89: Kaplan-Meier Plot - Time to adverse event according to PT: Aspartate aminotransferase increased, subgroup analysis for Smoking Status: Never - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

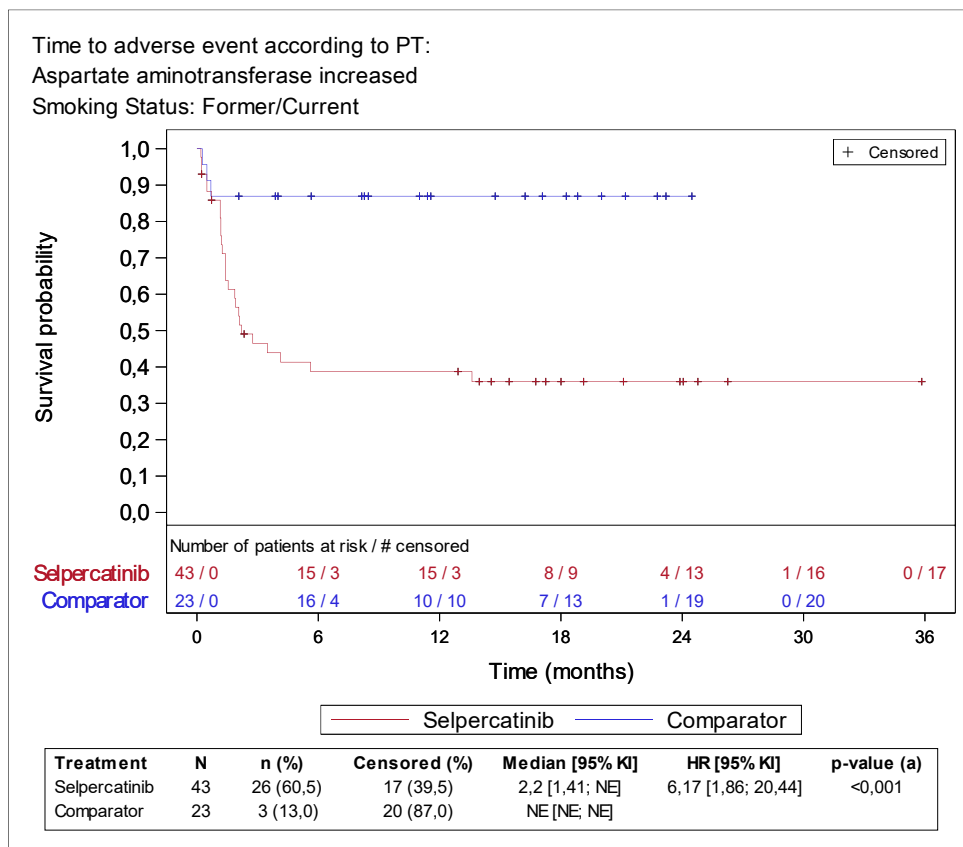
HR is based on the unstratified Cox proportional hazards model.

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Figure 90: Kaplan-Meier Plot - Time to adverse event according to PT: Aspartate aminotransferase increased, subgroup analysis for Smoking Status: Former/Current - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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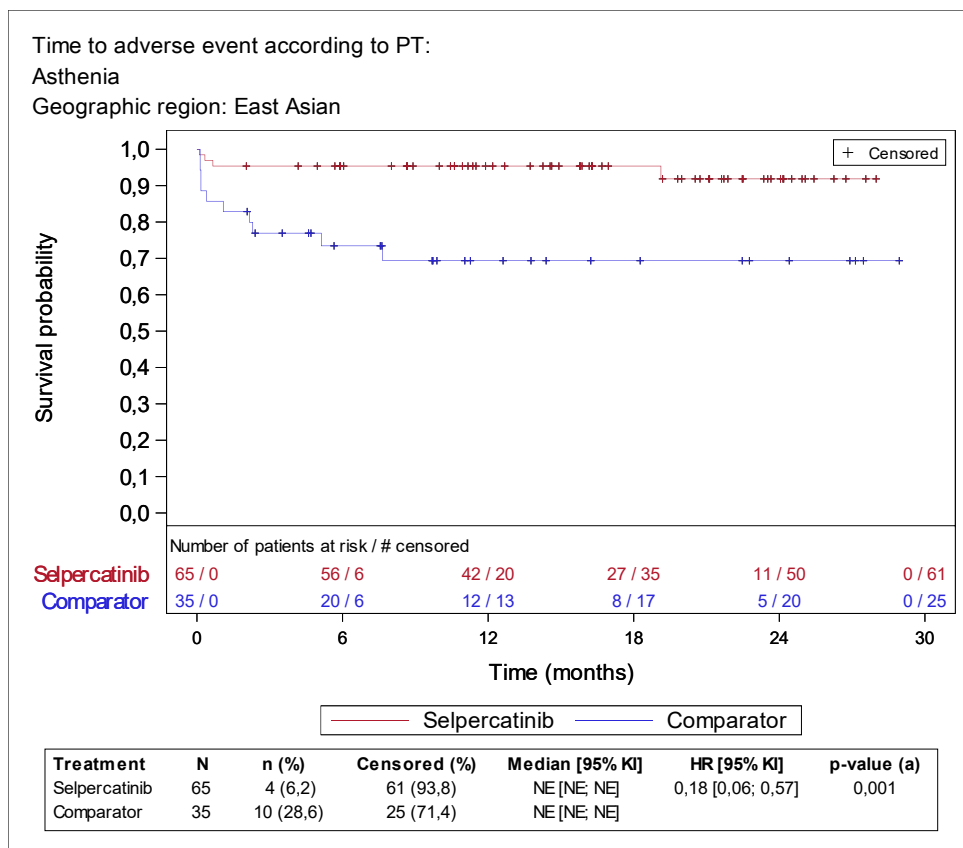
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Table 115: Interacting Subgroups: Time to adverse event according to PT: General disorders and administration site conditions/Asthenia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Geographic region (p-value of the interaction term: 0,049)					
East Asian	4/65 (6,2)	NE [NE; NE]	10/35 (28,6)	NE [NE; NE]	0,18 [0,06; 0,57] 0,001
Non-EastAsian	12/50 (24,0)	NE [NE; NE]	11/37 (29,7)	NE [13,83; NE]	0,71 [0,31; 1,62] 0,416
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,010)					
TPS <50%	5/48 (10,4)	NE [NE; NE]	9/27 (33,3)	NE [10,12; NE]	0,21 [0,07; 0,65] 0,003
TPS ≥50%	7/19 (36,8)	NE [0,66; NE]	2/13 (15,4)	NE [6,93; NE]	2,77 [0,58; 13,38] 0,184
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,020)					
TPS <50%	5/48 (10,4)	NE [NE; NE]	9/27 (33,3)	NE [10,12; NE]	0,21 [0,07; 0,65] 0,003
TPS ≥50%	7/19 (36,8)	NE [0,66; NE]	2/13 (15,4)	NE [6,93; NE]	2,77 [0,58; 13,38] 0,184
Unknown	4/48 (8,3)	NE [NE; NE]	10/32 (31,3)	NE [7,66; NE]	0,23 [0,07; 0,73] 0,006
Race (p-value of the interaction term: 0,024)					
Asian	4/66 (6,1)	NE [NE; NE]	10/35 (28,6)	NE [NE; NE]	0,18 [0,05; 0,56] 0,001
Non-Asian	12/49 (24,5)	NE [NE; NE]	8/33 (24,2)	NE [13,83; NE]	0,91 [0,37; 2,23] 0,836
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively					

*Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
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Figure 91: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for Geographic region: East Asian - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

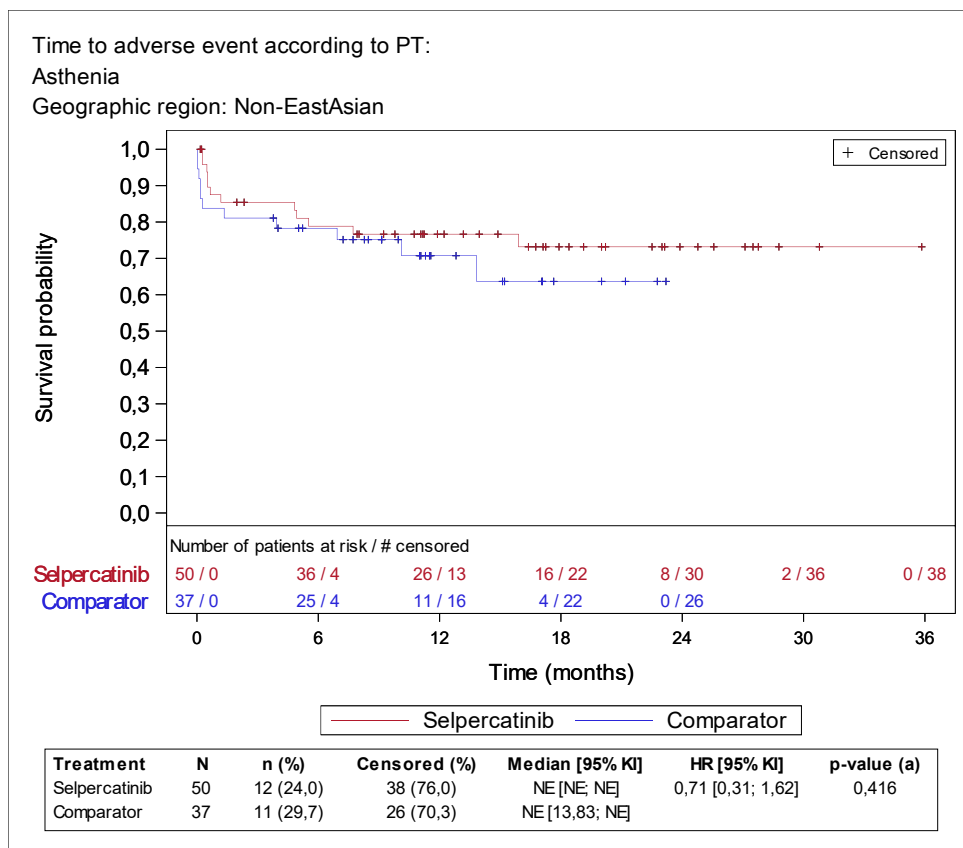
Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine

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Figure 92: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for Geographic region: Non-EastAsian - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine

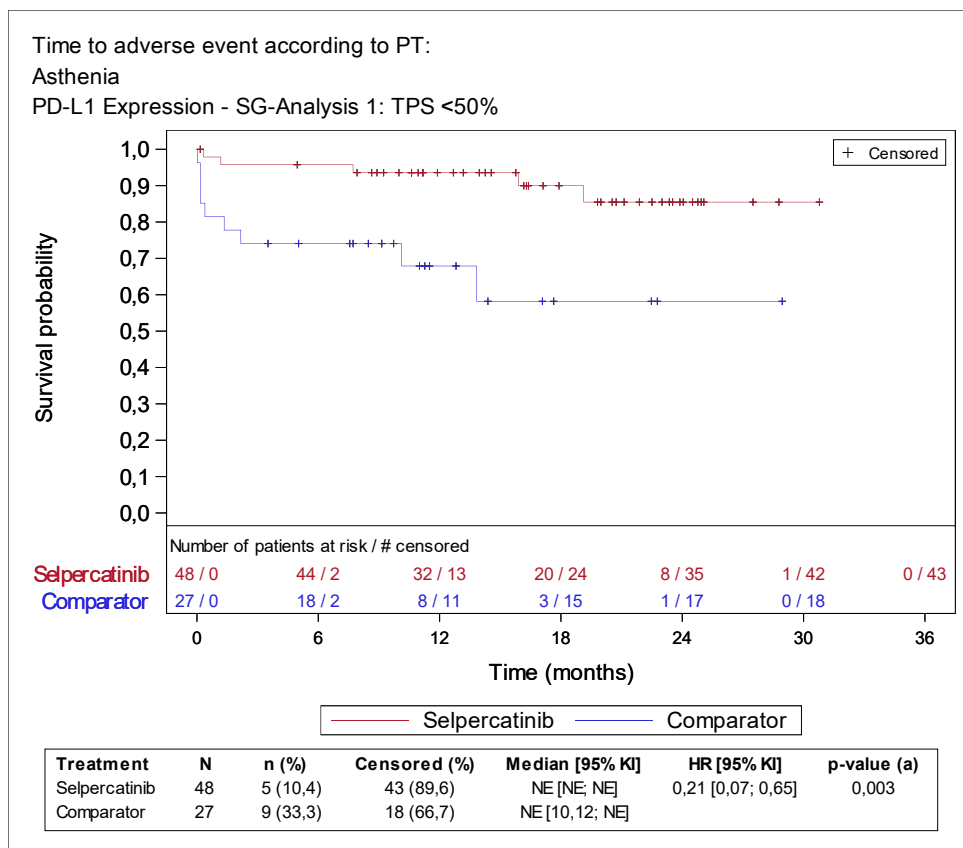
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Figure 93: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for PD-L1 Expression - SG-Analysis 1: TPS <50% - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

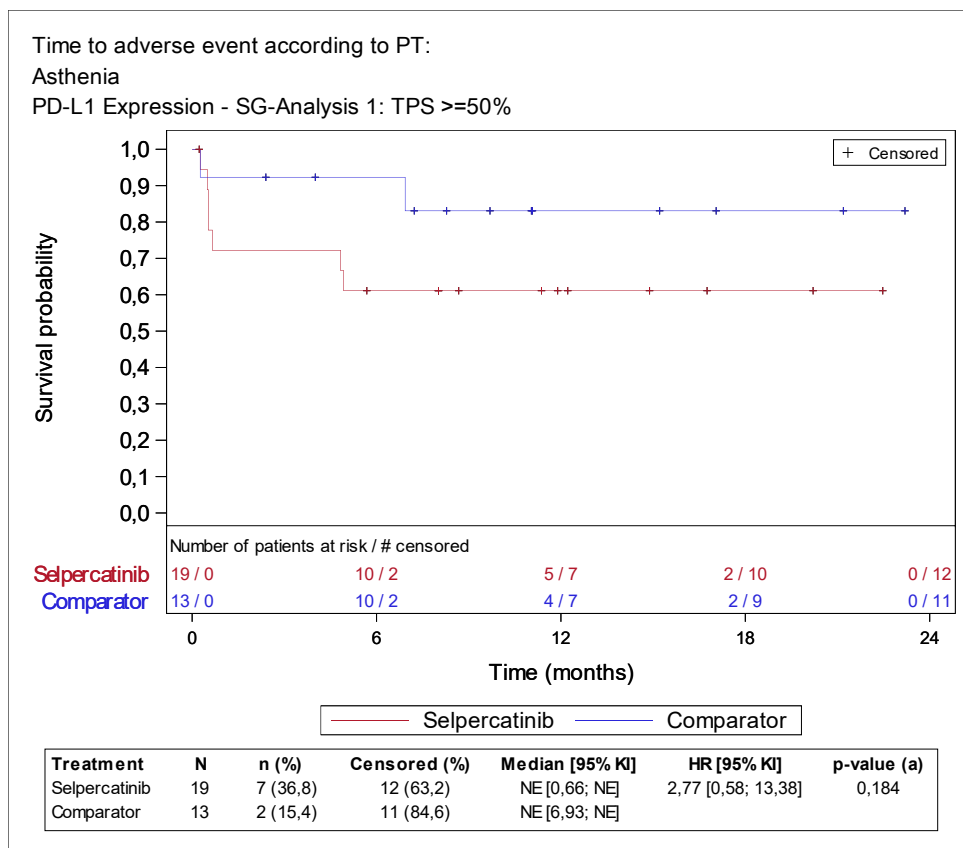
Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS $\geq 50\%$ or <50%, respectively, have not been taken into account.

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Figure 94: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for PD-L1 Expression - SG-Analysis 1: TPS $\geq 50\%$ - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

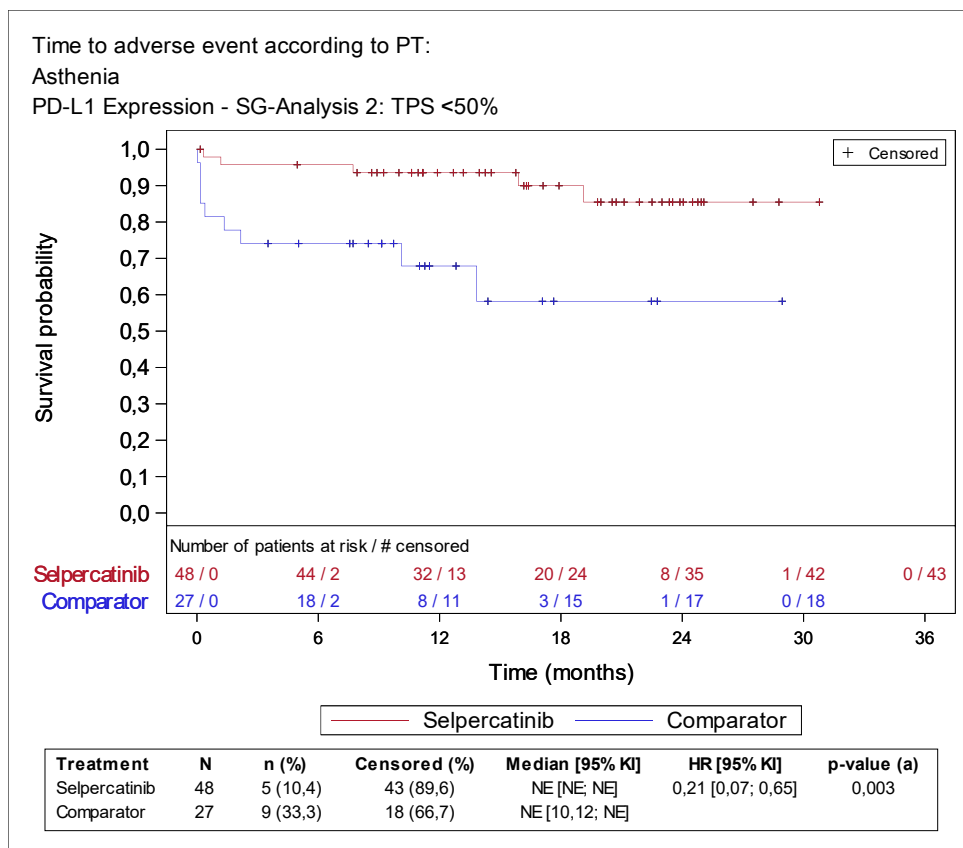
Patients with missing status for PD-L1 Expression and patients with TPS $>1\%$ without further specification in TPS $\geq 50\%$ or $<50\%$, respectively, have not been taken into account.

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Figure 95: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for PD-L1 Expression - SG-Analysis 2: TPS <50% - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

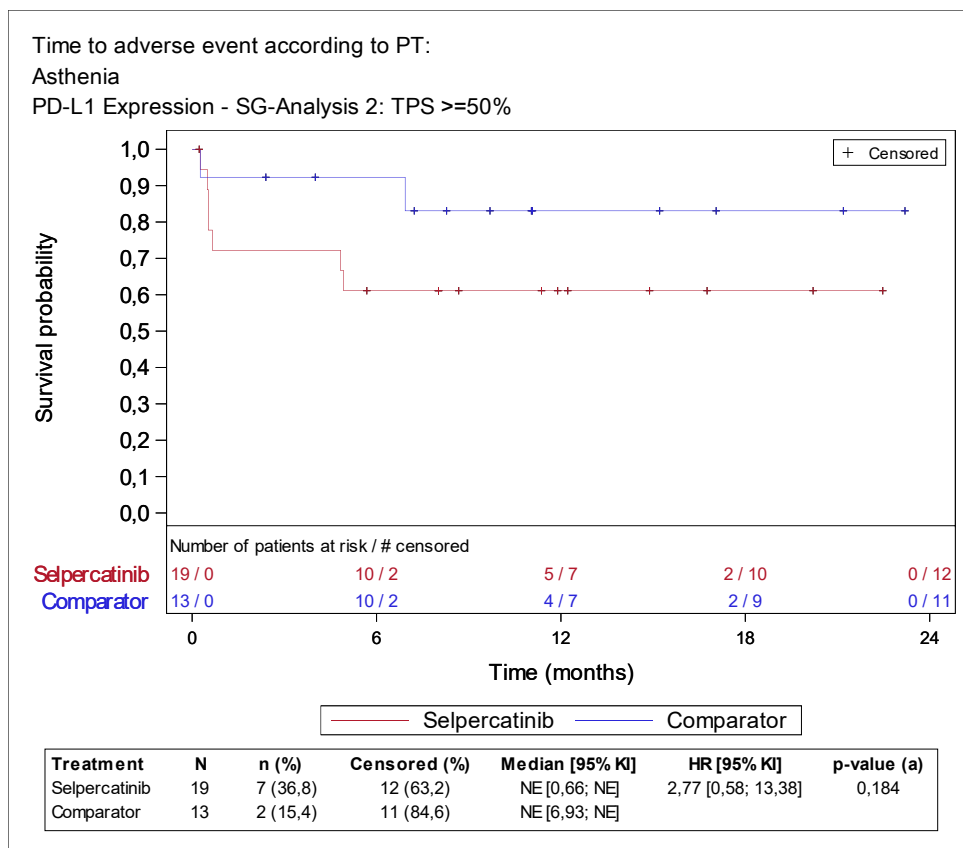
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Figure 96: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for PD-L1 Expression - SG-Analysis 2: TPS $\geq 50\%$ - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

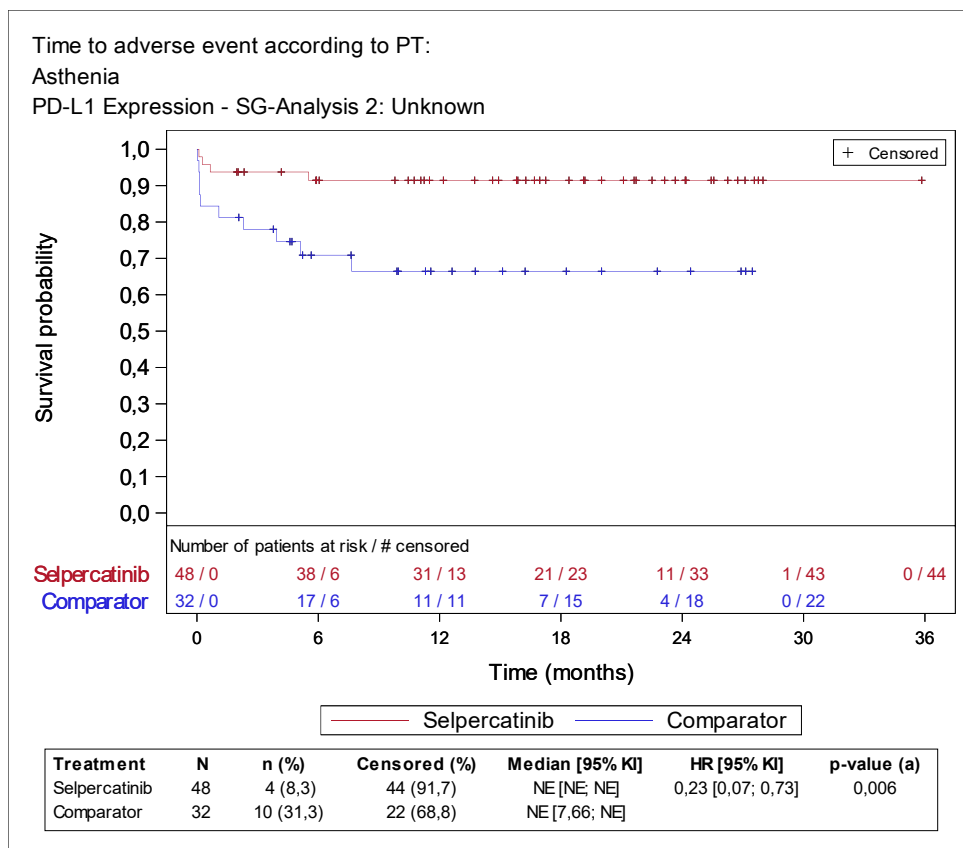
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Figure 97: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for PD-L1 Expression - SG-Analysis 2: Unknown - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

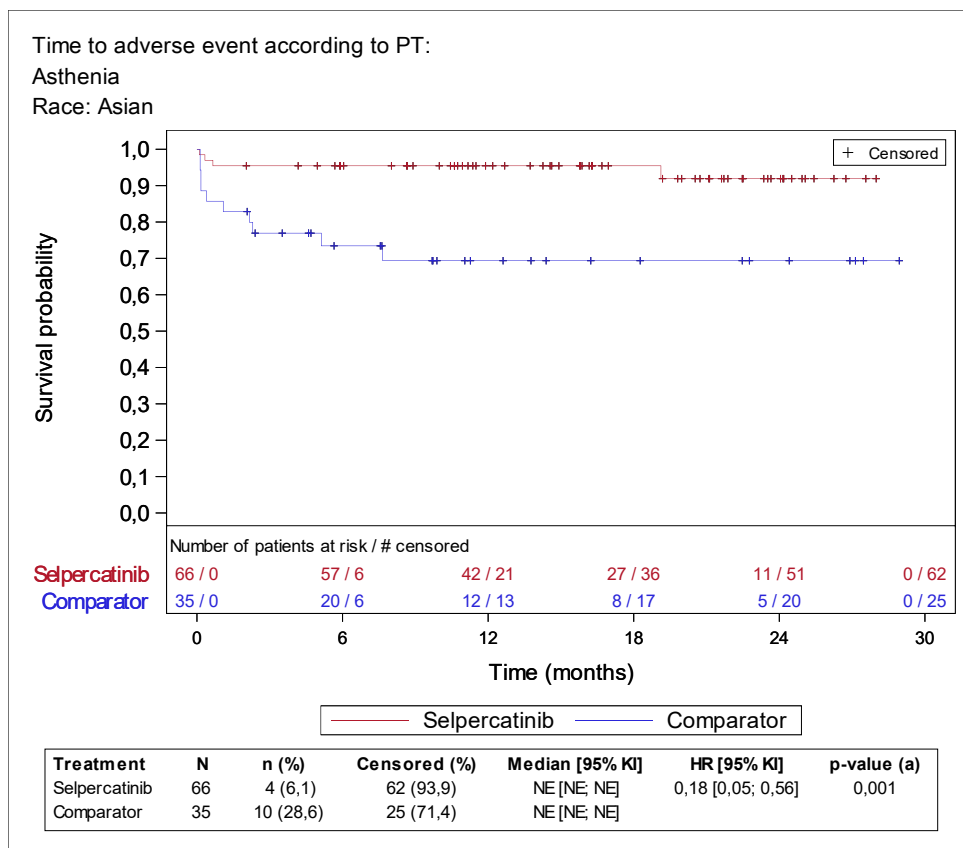
The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS $>1\%$ without further specification in TPS $\geq 50\%$ or $<50\%$., respectively

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Figure 98: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for Race: Asian - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

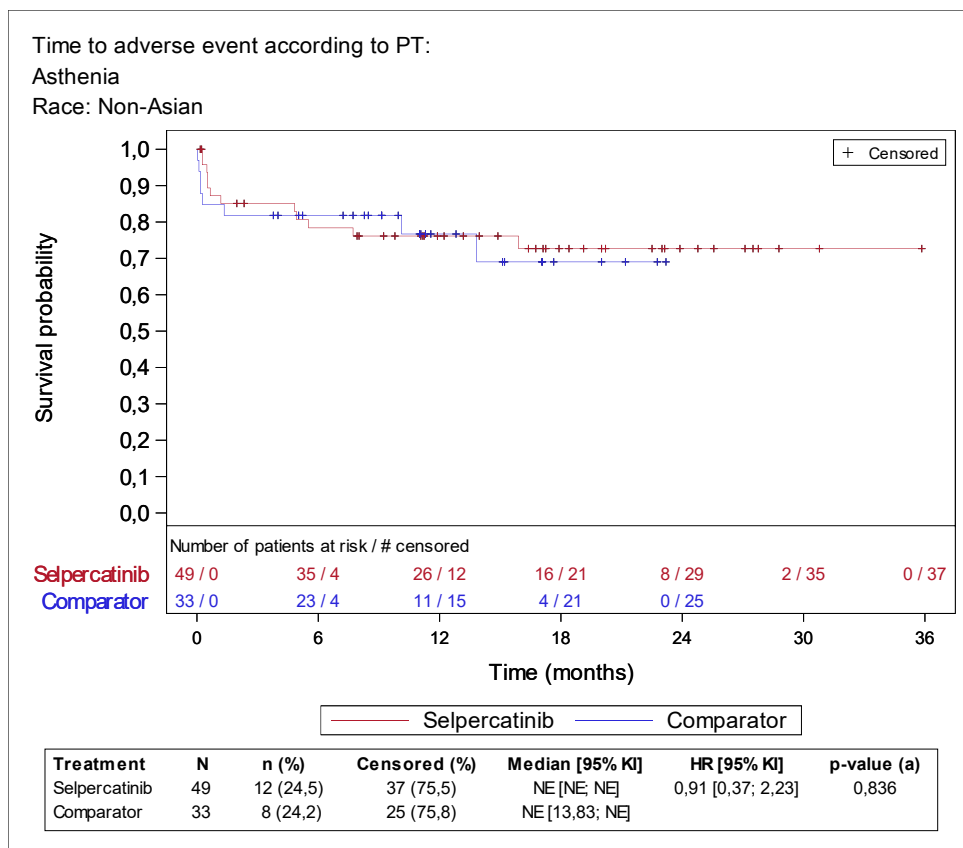
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Figure 99: Kaplan-Meier Plot - Time to adverse event according to PT: Asthenia, subgroup analysis for Race: Non-Asian - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_km_aespt_sub_dc230501.sas

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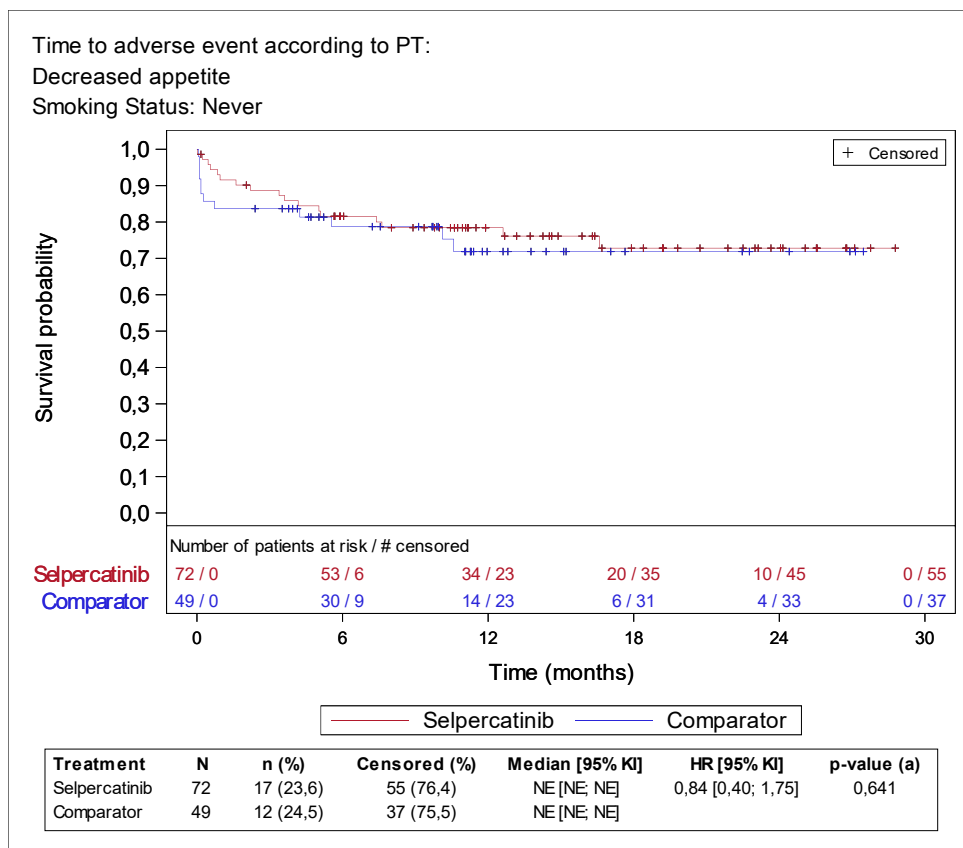
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Table 116: Interacting Subgroups: Time to adverse event according to PT: Metabolism and nutrition disorders/Decreased appetite - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Smoking Status (p-value of the interaction term: 0,026)					
Never	17/72 (23,6)	NE [NE; NE]	12/49 (24,5)	NE [NE; NE]	0,84 [0,40; 1,75] 0,641
Former/Current	3/43 (7,0)	NE [NE; NE]	8/23 (34,8)	NE [7,06; NE]	0,15 [0,04; 0,57] 0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					

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Figure 100: Kaplan-Meier Plot - Time to adverse event according to PT: Decreased appetite, subgroup analysis for Smoking Status: Never - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

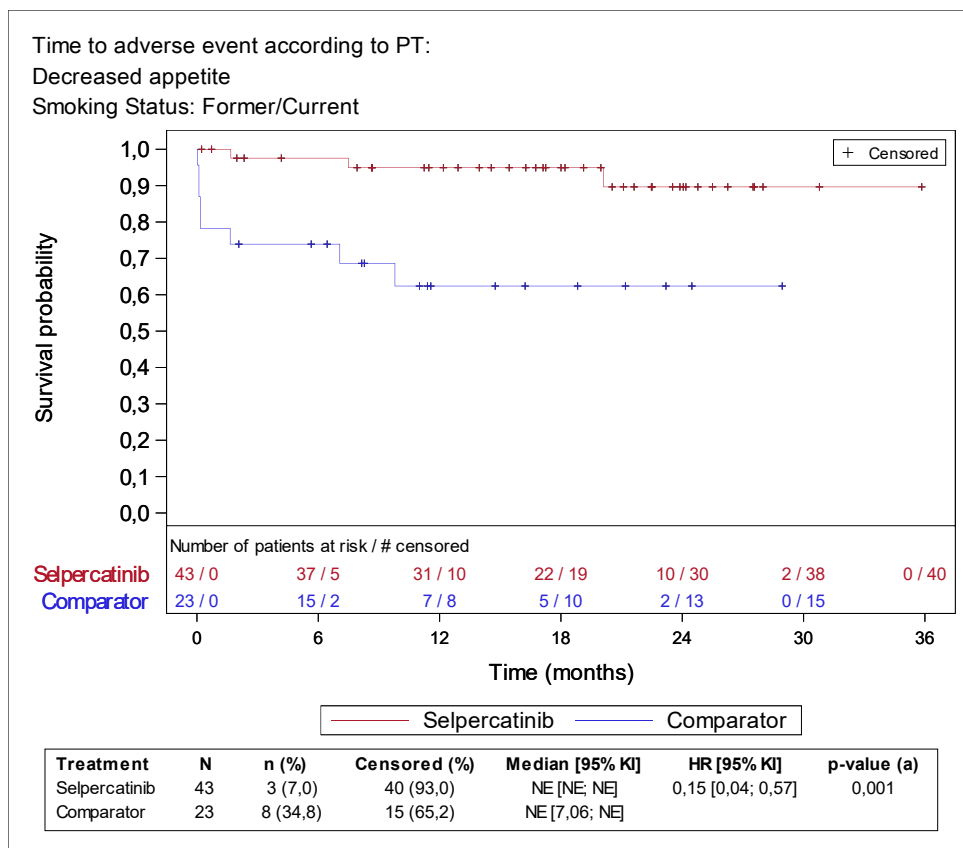
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Figure 101: Kaplan-Meier Plot - Time to adverse event according to PT: Decreased appetite, subgroup analysis for Smoking Status: Former/Current - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_km_aespt_sub_dc230501.sas

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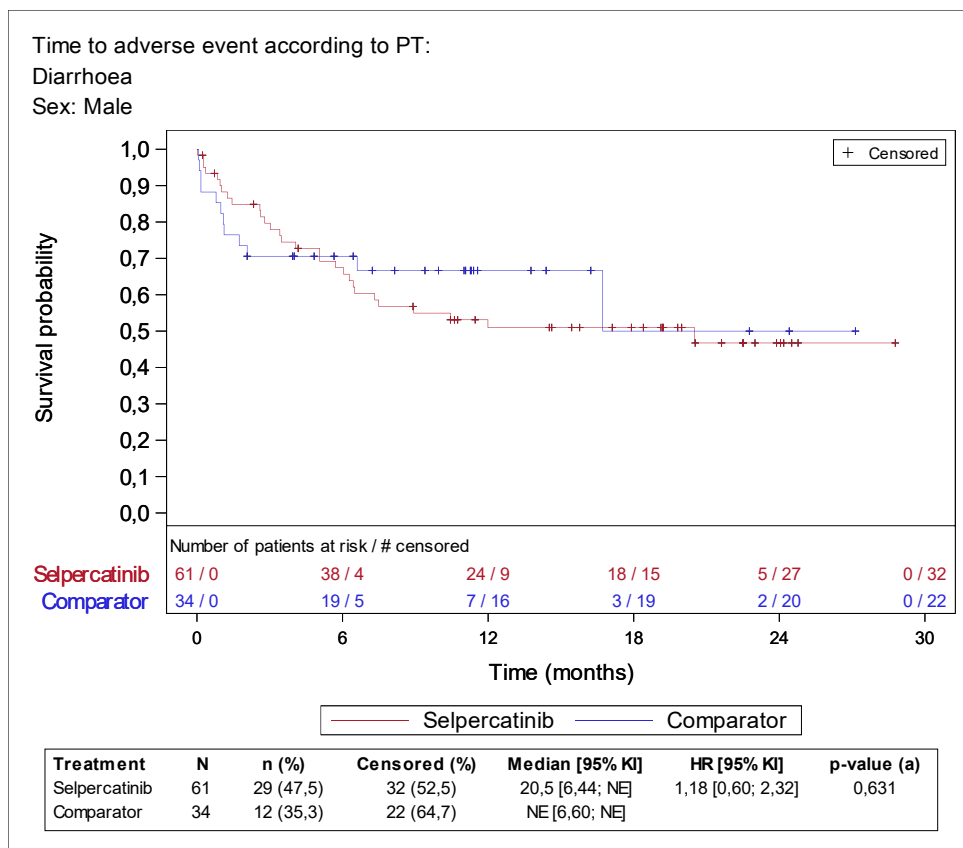
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Table 117: Interacting Subgroups: Time to adverse event according to PT: Gastrointestinal disorders/Diarrhoea - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Sex (p-value of the interaction term: 0,039)					
Male	29/61 (47,5)	20,5 [6,44; NE]	12/34 (35,3)	NE [6,60; NE]	1,18 [0,60; 2,32] 0,631
Female	28/54 (51,9)	7,5 [4,90; NE]	7/38 (18,4)	NE [16,03; NE]	3,63 [1,58; 8,32] 0,001
Geographic region (p-value of the interaction term: 0,031)					
East Asian	32/65 (49,2)	10,4 [6,44; NE]	4/35 (11,4)	NE [NE; NE]	4,84 [1,71; 13,70] 0,001
Non-EastAsian	25/50 (50,0)	9,8 [4,04; NE]	15/37 (40,5)	15,5 [6,60; NE]	1,23 [0,65; 2,34] 0,523
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine					

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Figure 102: Kaplan-Meier Plot - Time to adverse event according to PT: Diarrhoea, subgroup analysis for Sex: Male - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

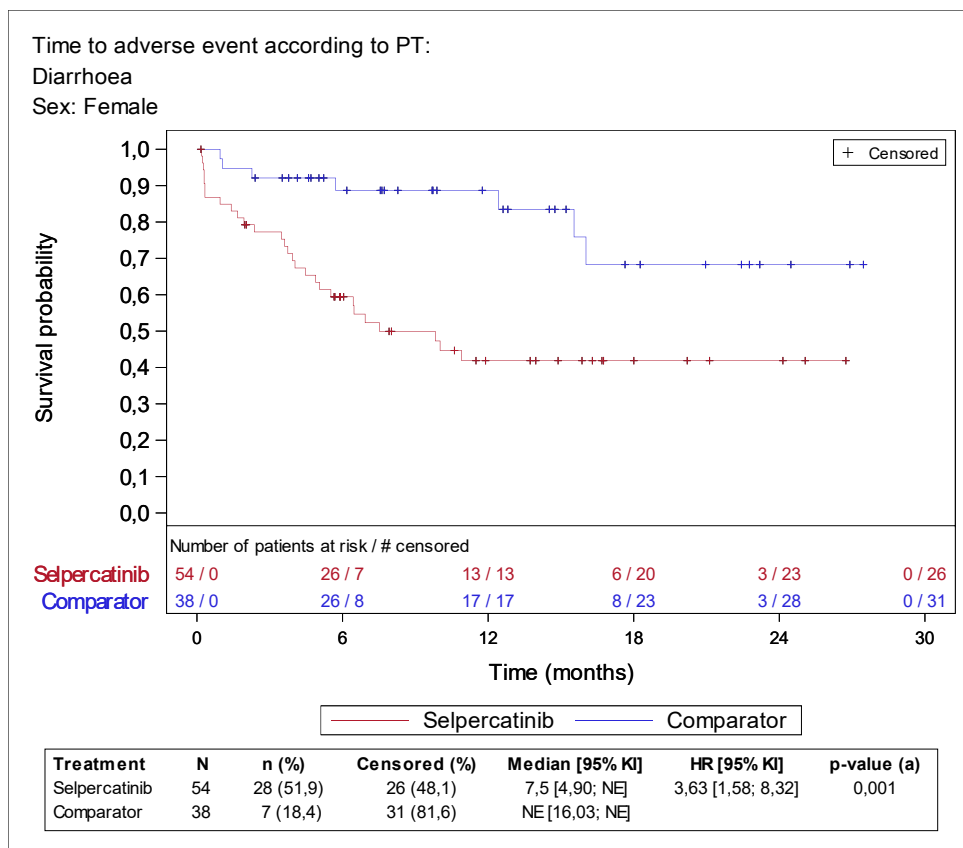
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Figure 103: Kaplan-Meier Plot - Time to adverse event according to PT: Diarrhoea, subgroup analysis for Sex: Female - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

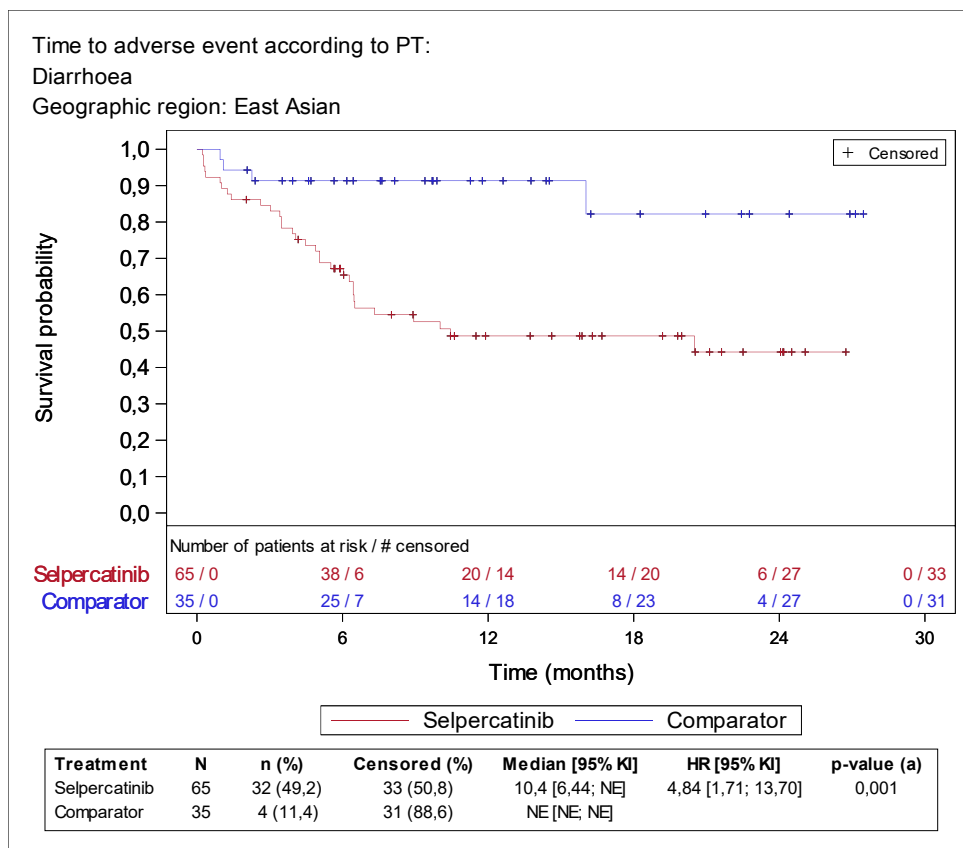
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Figure 104: Kaplan-Meier Plot - Time to adverse event according to PT: Diarrhoea, subgroup analysis for Geographic region: East Asian - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine

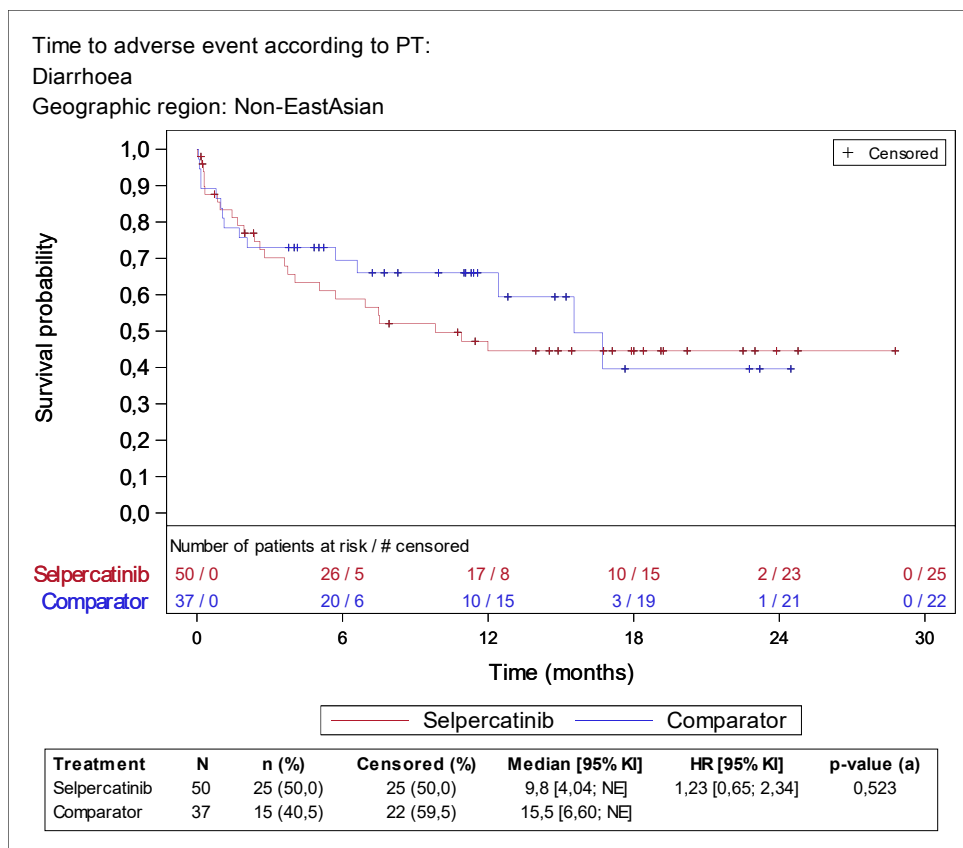
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Figure 105: Kaplan-Meier Plot - Time to adverse event according to PT: Diarrhoea, subgroup analysis for Geographic region: Non-EastAsian - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine

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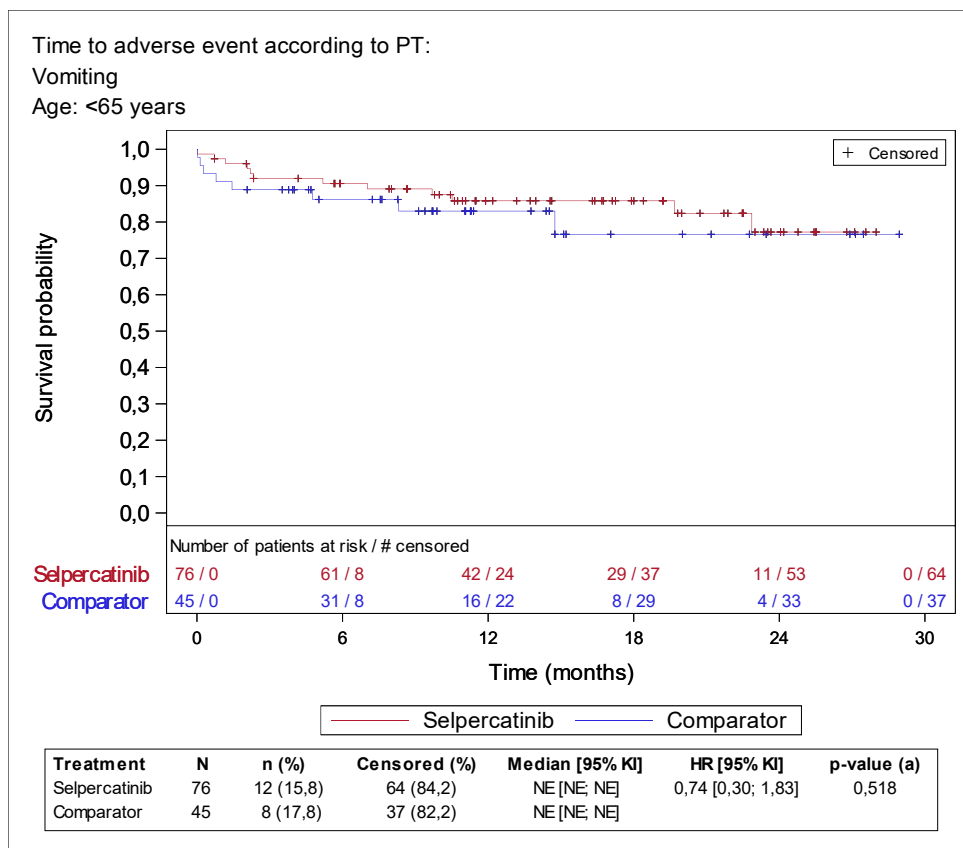
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Table 118: Interacting Subgroups: Time to adverse event according to PT: Gastrointestinal disorders/Vomiting - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,049)					
<65 years	12/76 (15,8)	NE [NE; NE]	8/45 (17,8)	NE [NE; NE]	0,74 [0,30; 1,83] 0,518
≥65 years	3/39 (7,7)	NE [NE; NE]	10/27 (37,0)	NE [2,14; NE]	0,18 [0,05; 0,64] 0,003
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					

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Figure 106: Kaplan-Meier Plot - Time to adverse event according to PT: Vomiting, subgroup analysis for Age: <65 years - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

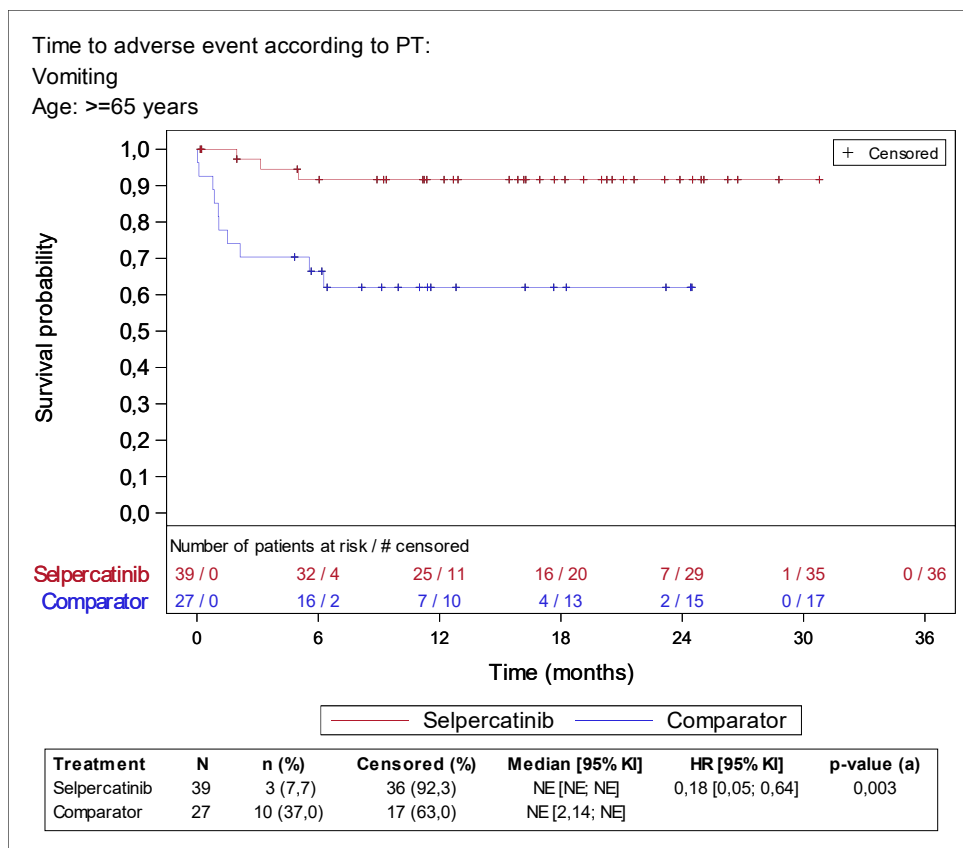
HR is based on the unstratified Cox proportional hazards model.

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Figure 107: Kaplan-Meier Plot - Time to adverse event according to PT: Vomiting, subgroup analysis for Age: ≥ 65 years - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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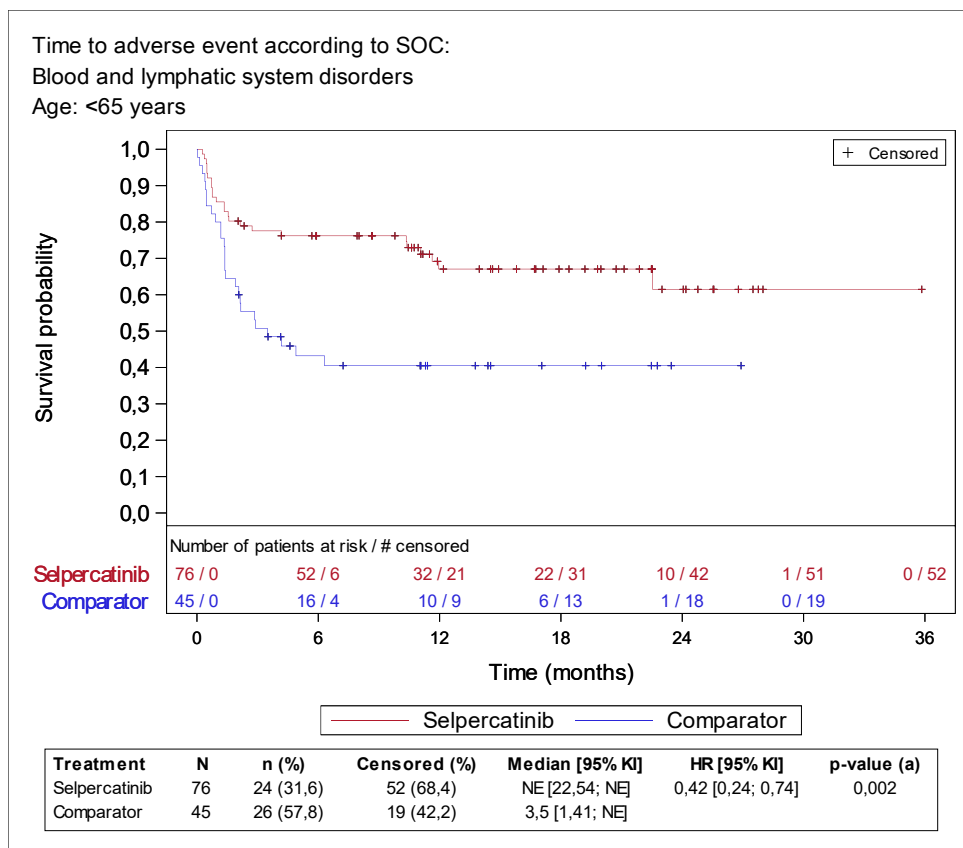
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Table 119: Interacting Subgroups: Time to adverse event according to SOC: Blood and lymphatic system disorders - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,049)					
<65 years	24/76 (31,6)	NE [22,54; NE]	26/45 (57,8)	3,5 [1,41; NE]	0,42 [0,24; 0,74] 0,002
≥65 years	8/39 (20,5)	NE [NE; NE]	21/27 (77,8)	1,8 [0,69; 4,17]	0,16 [0,07; 0,37] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					

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Figure 108: Kaplan-Meier Plot - Time to adverse event according to SOC: Blood and lymphatic system disorders, subgroup analysis for Age: <65 years - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

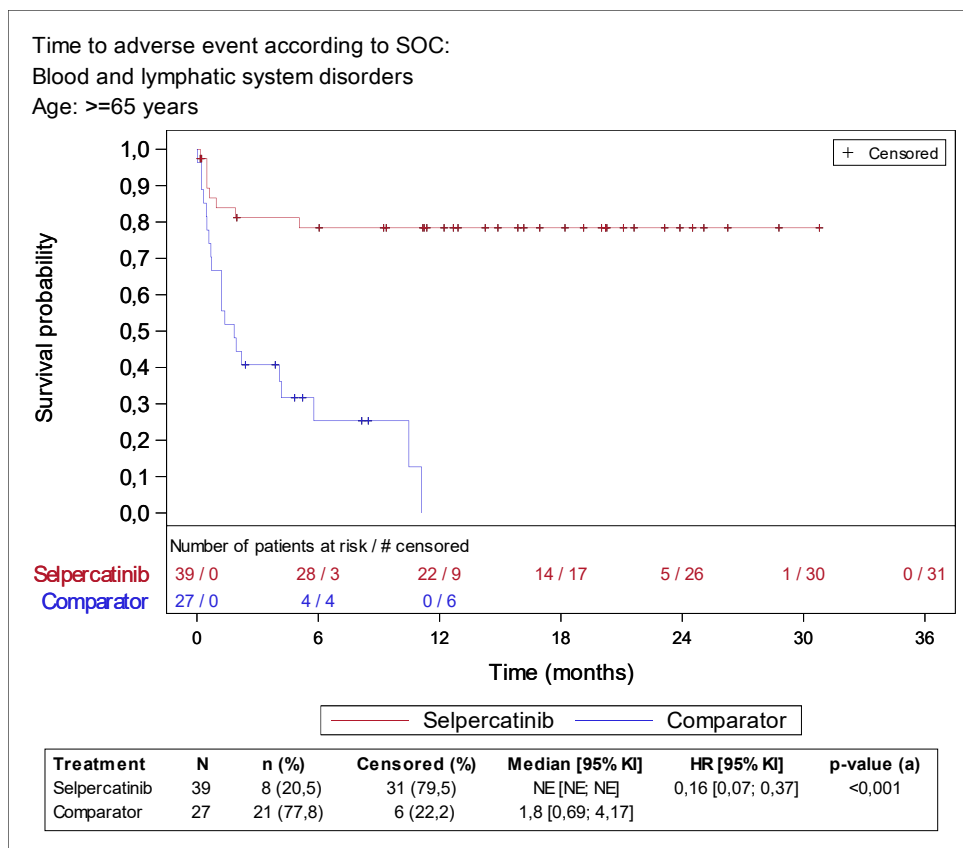
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Figure 109: Kaplan-Meier Plot - Time to adverse event according to SOC: Blood and lymphatic system disorders, subgroup analysis for Age: ≥ 65 years - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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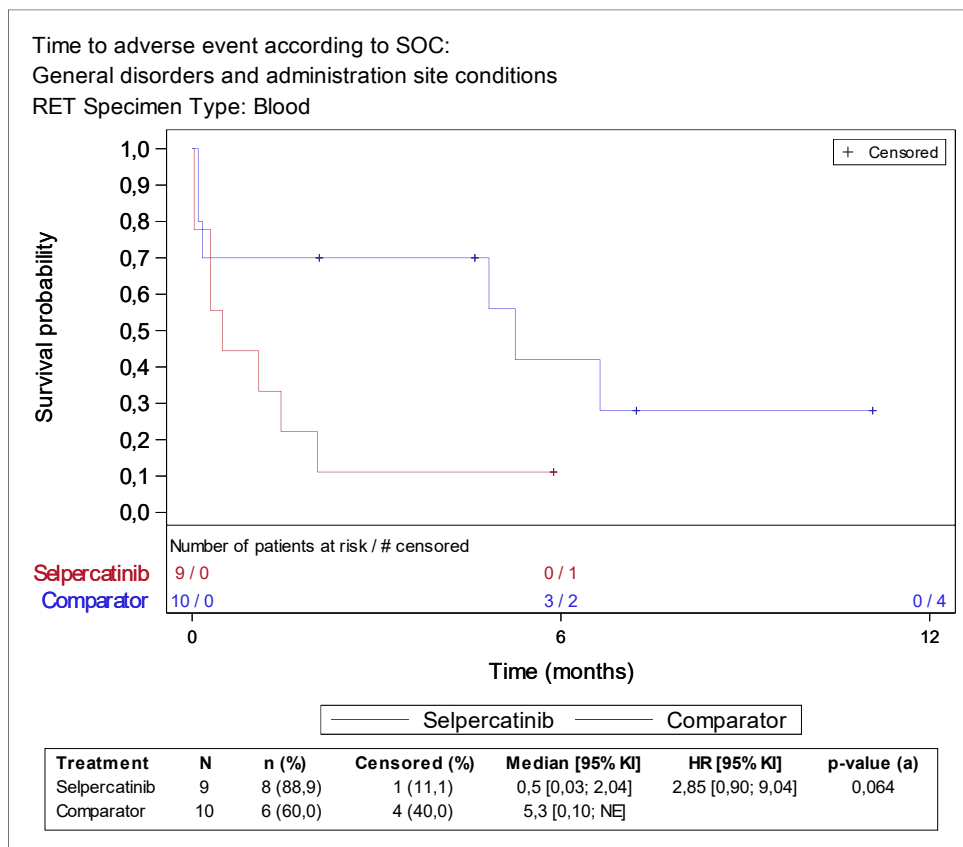
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Table 120: Interacting Subgroups: Time to adverse event according to SOC: General disorders and administration site conditions - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
RET Specimen Type (p-value of the interaction term: 0,010)					
Blood	8/9 (88,9)	0,5 [0,03; 2,04]	6/10 (60,0)	5,3 [0,10; NE]	2,85 [0,90; 9,04] 0,064
Tissue	63/106 (59,4)	5,9 [2,83; 9,69]	44/62 (71,0)	1,3 [0,26; 2,89]	0,59 [0,40; 0,86] 0,007
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					

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Figure 110: Kaplan-Meier Plot - Time to adverse event according to SOC: General disorders and administration site conditions, subgroup analysis for RET Specimen Type: Blood - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

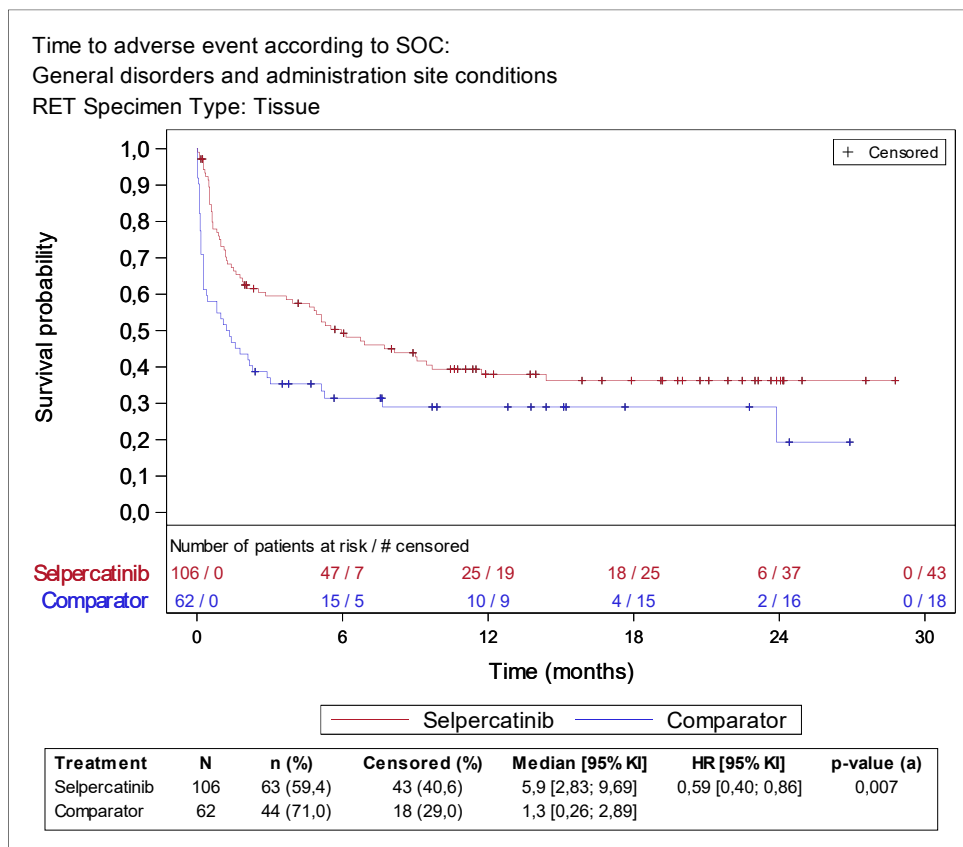
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Figure 111: Kaplan-Meier Plot - Time to adverse event according to SOC: General disorders and administration site conditions, subgroup analysis for RET Specimen Type: Tissue - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; RET: Rearranged during transfection; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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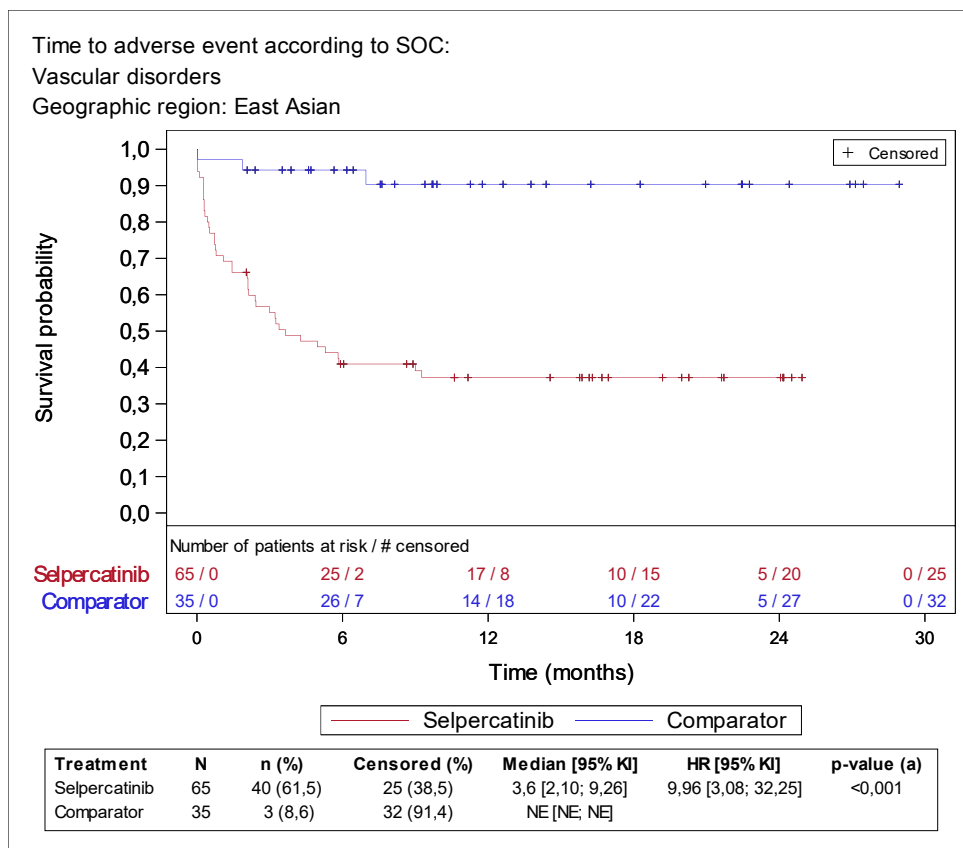
Table 121: Interacting Subgroups: Time to adverse event according to SOC: Vascular disorders - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Geographic region (p-value of the interaction term: 0,047)					
East Asian	40/65 (61,5)	3,6 [2,10; 9,26]	3/35 (8,6)	NE [NE; NE]	9,96 [3,08; 32,25] <0,001
Non-EastAsian	19/50 (38,0)	NE [6,93; NE]	7/37 (18,9)	NE [18,40; NE]	2,22 [0,93; 5,31] 0,066
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,040)					
TPS <50%	22/48 (45,8)	23,3 [2,86; NE]	2/27 (7,4)	NE [NE; NE]	7,44 [1,74; 31,72] 0,001
TPS ≥50%	12/19 (63,2)	3,0 [1,45; NE]	6/13 (46,2)	7,0 [0,53; NE]	1,53 [0,57; 4,09] 0,394
Unknown	25/48 (52,1)	9,0 [2,40; NE]	2/32 (6,3)	NE [NE; NE]	11,41 [2,70; 48,22] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively					

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Figure 112: Kaplan-Meier Plot - Time to adverse event according to SOC: Vascular disorders, subgroup analysis for Geographic region: East Asian - study LIBRETTO-431, mSAF

Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine

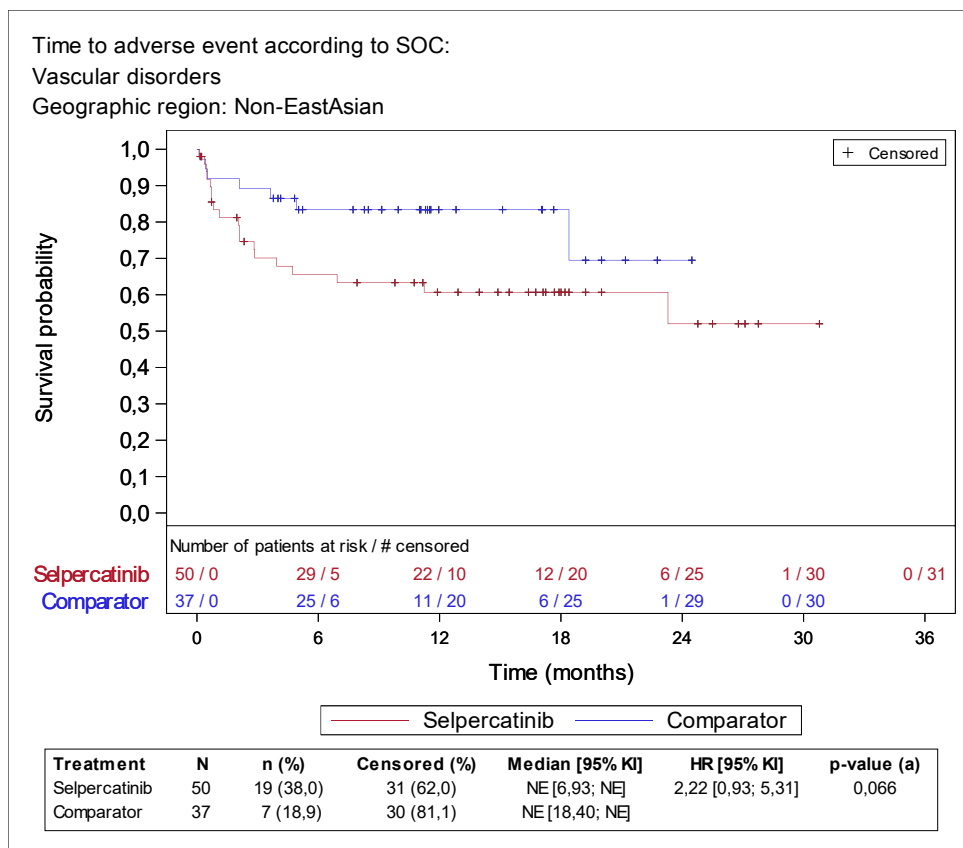
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Figure 113: Kaplan-Meier Plot - Time to adverse event according to SOC: Vascular disorders, subgroup analysis for Geographic region: Non-EastAsian - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

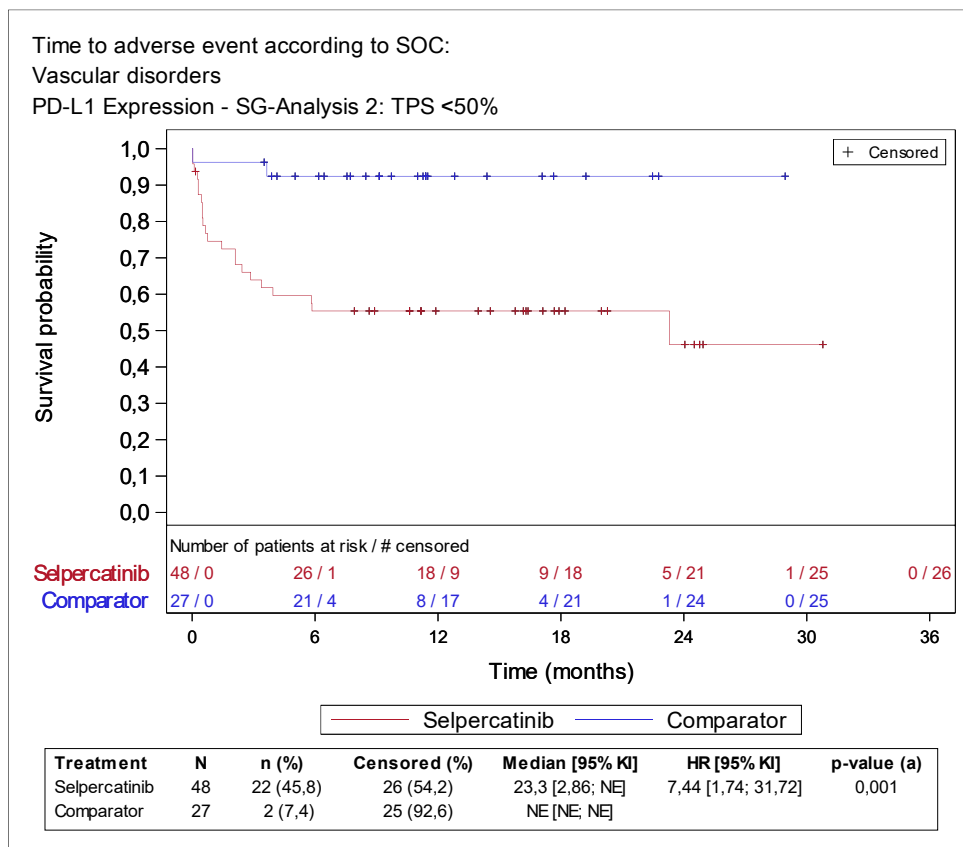
Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine

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Figure 114: Kaplan-Meier Plot - Time to adverse event according to SOC: Vascular disorders, subgroup analysis for PD-L1 Expression - SG-Analysis 2: TPS <50% - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

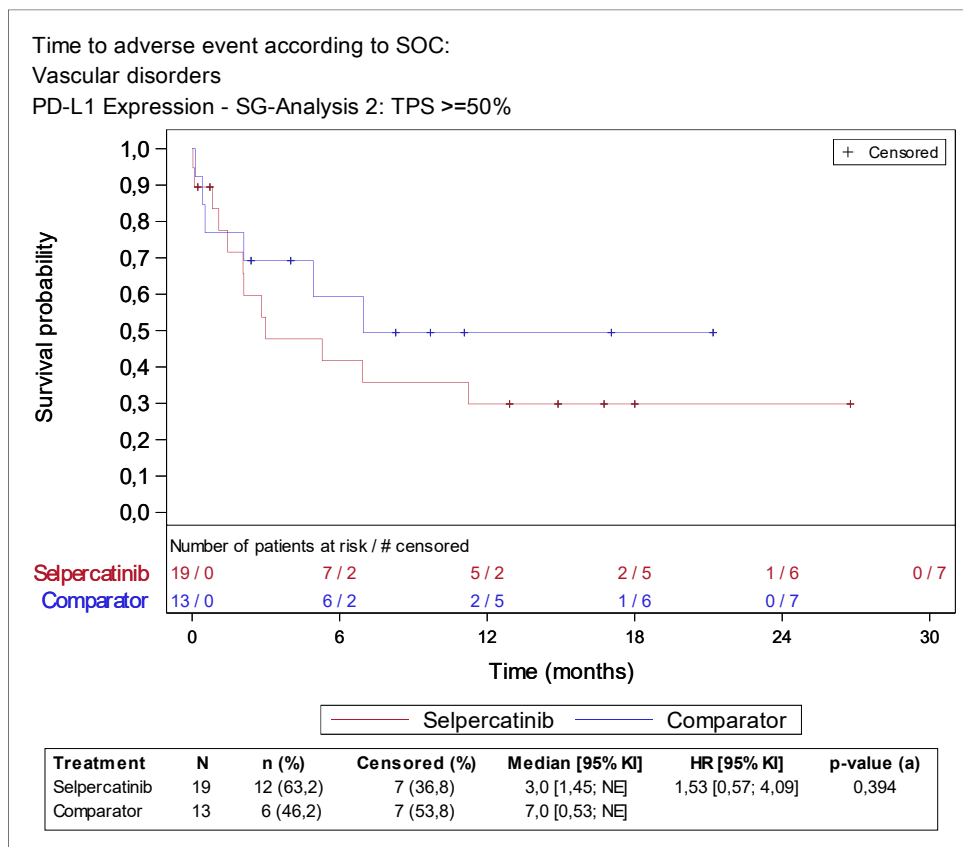
Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_km_aespt_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aespx019sg_pdl1sg21_msaf.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba

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Figure 115: Kaplan-Meier Plot - Time to adverse event according to SOC: Vascular disorders, subgroup analysis for PD-L1 Expression - SG-Analysis 2: TPS $\geq 50\%$ - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

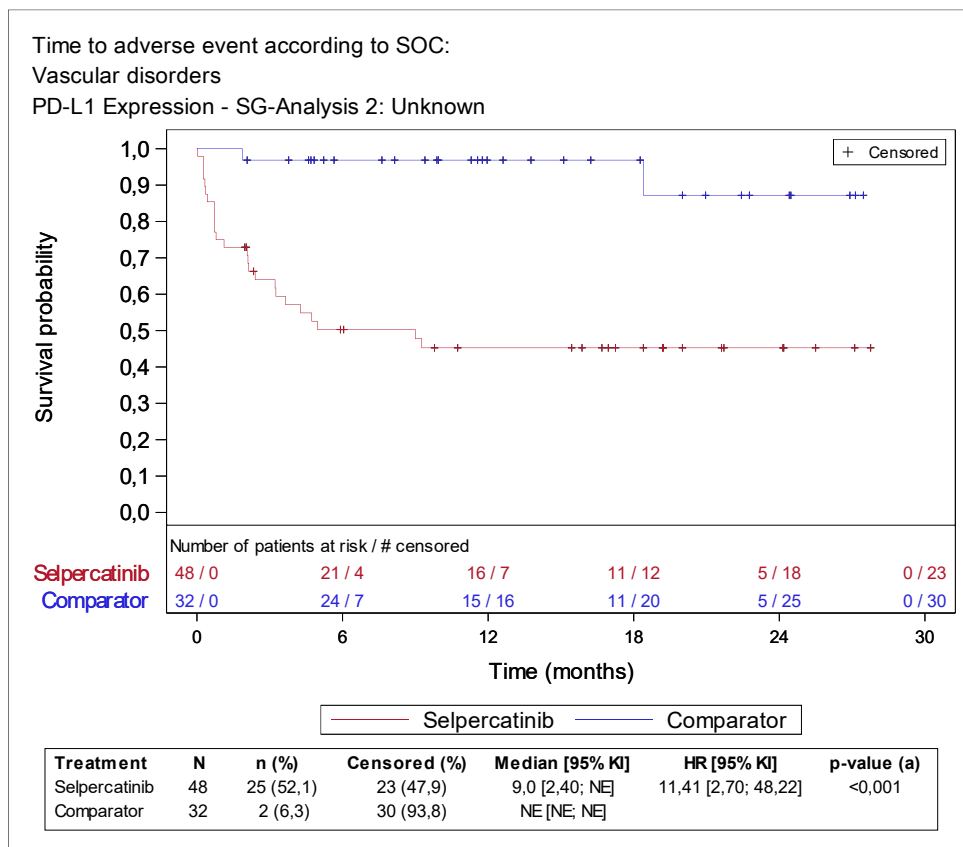
Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_km_aespt_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aespx019sg_pdl1sg22_msaf.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba

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Figure 116: Kaplan-Meier Plot - Time to adverse event according to SOC: Vascular disorders, subgroup analysis for PD-L1 Expression - SG-Analysis 2: Unknown - study LIBRETTO-431, mSAF



Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from 2-sided unstratified Log-rank-Test.

The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS $>1\%$ without further specification in TPS $\geq 50\%$ or $<50\%$, respectively

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_km_aespt_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/f_aespx019sg_pdl1sg23_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba

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Anhang 4-G4.4: Subgruppen – UE nach SOC und PT nicht signifikant

Table 122: Subgroups: Time to adverse event according to PT: Investigations/Alanine aminotransferase increased - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,342)					
<65 years	48/76 (63,2)	2,8 [1,48; 13,14]	21/45 (46,7)	11,8 [3,48; NE]	1,47 [0,88; 2,46] 0,138
≥65 years	20/39 (51,3)	2,2 [1,12; NE]	8/27 (29,6)	NE [7,16; NE]	2,15 [0,95; 4,90] 0,062
Baseline ECOG (p-value of the interaction term: 0,516)					
0	23/41 (56,1)	4,1 [1,71; NE]	11/25 (44,0)	17,5 [4,37; NE]	1,43 [0,69; 2,93] 0,333
1	45/74 (60,8)	1,9 [1,35; 8,51]	18/47 (38,3)	NE [4,17; NE]	1,92 [1,11; 3,33] 0,017
Sex (p-value of the interaction term: 0,062)					
Male	39/61 (63,9)	2,8 [1,41; 10,38]	10/34 (29,4)	NE [7,16; NE]	2,79 [1,39; 5,60] 0,003
Female	29/54 (53,7)	3,5 [1,38; NE]	19/38 (50,0)	11,8 [3,48; NE]	1,15 [0,64; 2,06] 0,637
Geographic region (p-value of the interaction term: 0,646)					
East Asian	46/65 (70,8)	1,5 [1,18; 2,79]	17/35 (48,6)	11,8 [3,45; NE]	1,77 [1,01; 3,09] 0,042
Non-EastAsian	22/50 (44,0)	NE [3,48; NE]	12/37 (32,4)	NE [7,16; NE]	1,48 [0,73; 2,99] 0,277
Smoking Status (p-value of the interaction term: 0,135)					
Never	43/72 (59,7)	1,9 [1,31; 13,14]	24/49 (49,0)	11,8 [3,84; NE]	1,40 [0,85; 2,31] 0,188
Former/Current	25/43 (58,1)	4,1 [1,41; NE]	5/23 (21,7)	NE [NE; NE]	3,18 [1,21; 8,36] 0,013
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,352)					
Yes	14/23 (60,9)	3,5 [1,15; NE]	5/14 (35,7)	NE [0,69; NE]	1,90 [0,68; 5,28] 0,213
No	28/44 (63,6)	1,3 [0,79; 4,14]	10/23 (43,5)	17,5 [4,37; NE]	2,44 [1,18; 5,06] 0,013

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	26/48 (54,2)	13,1 [2,20; NE]	14/35 (40,0)	NE [3,48; NE]	1,22 [0,63; 2,34] 0,553
Liver Metastasis - BICR (p-value of the interaction term: 0,548)					
Yes	8/16 (50,0)	13,1 [1,15; NE]	5/13 (38,5)	8,0 [4,17; NE]	0,99 [0,31; 3,17] 0,997
No	60/98 (61,2)	2,1 [1,41; 8,51]	24/59 (40,7)	NE [6,87; NE]	1,83 [1,14; 2,94] 0,012
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,846)					
TPS <50%	32/48 (66,7)	1,7 [0,72; 5,62]	12/27 (44,4)	11,8 [3,48; NE]	1,87 [0,96; 3,64] 0,061
TPS ≥50%	6/19 (31,6)	NE [1,48; NE]	2/13 (15,4)	NE [NE; NE]	2,32 [0,47; 11,52] 0,292
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,721)					
TPS <50%	32/48 (66,7)	1,7 [0,72; 5,62]	12/27 (44,4)	11,8 [3,48; NE]	1,87 [0,96; 3,64] 0,061
TPS ≥50%	6/19 (31,6)	NE [1,48; NE]	2/13 (15,4)	NE [NE; NE]	2,32 [0,47; 11,52] 0,292
Unknown	30/48 (62,5)	2,8 [1,35; 25,49]	15/32 (46,9)	17,5 [3,45; NE]	1,45 [0,78; 2,70] 0,242
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,230)					
Negative	17/26 (65,4)	1,9 [0,56; NE]	3/12 (25,0)	NE [0,33; NE]	3,27 [0,95; 11,21] 0,045
Positive	27/49 (55,1)	5,6 [1,41; NE]	12/34 (35,3)	NE [4,37; NE]	1,83 [0,92; 3,61] 0,080
Unknown	24/40 (60,0)	2,8 [1,38; NE]	14/26 (53,8)	7,2 [2,10; NE]	1,16 [0,60; 2,26] 0,662
Disease Stage (p-value of the interaction term: 0,525)					
III	5/6 (83,3)	1,4 [0,26; NE]	4/6 (66,7)	2,7 [0,20; NE]	1,55 [0,40; 5,95] 0,515
IVA	27/44 (61,4)	1,9 [1,25; NE]	11/32 (34,4)	NE [6,87; NE]	2,44 [1,21; 4,93] 0,010

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB	36/65 (55,4)	8,5 [1,41; NE]	14/34 (41,2)	17,5 [4,37; NE]	1,34 [0,72; 2,50] 0,354
Race (p-value of the interaction term: 0,721)					
Asian	47/66 (71,2)	1,5 [1,18; 2,76]	17/35 (48,6)	11,8 [3,45; NE]	1,78 [1,02; 3,12] 0,038
Non-Asian	21/49 (42,9)	NE [3,48; NE]	10/33 (30,3)	NE [7,16; NE]	1,53 [0,72; 3,27] 0,264
RET Specimen Type (p-value of the interaction term: 0,605)					
Blood	4/9 (44,4)	NE [0,72; NE]	2/10 (20,0)	NE [1,97; NE]	2,67 [0,49; 14,59] 0,240
Tissue	64/106 (60,4)	2,8 [1,48; 10,38]	27/62 (43,5)	17,5 [6,87; NE]	1,59 [1,01; 2,50] 0,042
RET Fusion Result **** (p-value of the interaction term: 0,632)					
CCDC6	6/9 (66,7)	4,1 [0,49; NE]	2/6 (33,3)	NE [0,20; NE]	2,65 [0,52; 13,37] 0,223
KIF5B	25/50 (50,0)	25,5 [1,87; NE]	6/36 (16,7)	NE [NE; NE]	3,45 [1,41; 8,46] 0,004
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 123: Subgroups: Time to adverse event according to PT: Blood and lymphatic system disorders/Anaemia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,065)					
<65 years	11/76 (14,5)	NE [NE; NE]	21/45 (46,7)	NE [2,86; NE]	0,22 [0,10; 0,46] <0,001
≥65 years	3/39 (7,7)	NE [NE; NE]	19/27 (70,4)	2,2 [0,79; 10,48]	0,05 [0,01; 0,19] <0,001
Baseline ECOG (p-value of the interaction term: 0,128)					
0	2/41 (4,9)	NE [NE; NE]	14/25 (56,0)	5,3 [1,22; NE]	0,06 [0,01; 0,26] <0,001
1	12/74 (16,2)	NE [NE; NE]	26/47 (55,3)	4,2 [1,94; NE]	0,19 [0,09; 0,38] <0,001
Geographic region (p-value of the interaction term: 0,999)					
East Asian	9/65 (13,8)	NE [NE; NE]	21/35 (60,0)	2,2 [1,38; NE]	0,14 [0,06; 0,31] <0,001
Non-EastAsian	5/50 (10,0)	NE [NE; NE]	19/37 (51,4)	10,5 [2,89; NE]	0,13 [0,05; 0,36] <0,001
Smoking Status (p-value of the interaction term: 0,064)					
Never	5/72 (6,9)	NE [NE; NE]	27/49 (55,1)	3,5 [1,41; NE]	0,08 [0,03; 0,22] <0,001
Former/Current	9/43 (20,9)	NE [NE; NE]	13/23 (56,5)	6,3 [2,20; NE]	0,23 [0,10; 0,55] <0,001
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,364)					
Yes	4/23 (17,4)	NE [NE; NE]	6/14 (42,9)	NE [1,38; NE]	0,28 [0,08; 1,01] 0,038
No	3/44 (6,8)	NE [NE; NE]	14/23 (60,9)	4,2 [1,22; NE]	0,08 [0,02; 0,27] <0,001
Unknown	7/48 (14,6)	NE [NE; NE]	20/35 (57,1)	4,1 [1,94; NE]	0,15 [0,06; 0,37] <0,001
Liver Metastasis - BICR (p-value of the interaction term: 0,848)					
Yes	1/16 (6,3)	NE [NE; NE]	5/13 (38,5)	10,5 [4,17; NE]	0,07 [0,01; 0,74] 0,007

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
No	13/98 (13,3)	NE [NE; NE]	35/59 (59,3)	2,9 [1,91; NE]	0,14 [0,08; 0,28] <0,001
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,941)					
TPS <50%	7/48 (14,6)	NE [NE; NE]	14/27 (51,9)	11,1 [2,30; NE]	0,18 [0,07; 0,45] <0,001
TPS ≥50%	2/19 (10,5)	NE [NE; NE]	5/13 (38,5)	NE [2,10; NE]	0,21 [0,04; 1,08] 0,040
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,434)					
TPS <50%	7/48 (14,6)	NE [NE; NE]	14/27 (51,9)	11,1 [2,30; NE]	0,18 [0,07; 0,45] <0,001
TPS ≥50%	2/19 (10,5)	NE [NE; NE]	5/13 (38,5)	NE [2,10; NE]	0,21 [0,04; 1,08] 0,040
Unknown	5/48 (10,4)	NE [NE; NE]	21/32 (65,6)	2,0 [1,18; 10,48]	0,09 [0,04; 0,25] <0,001
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,261)					
Negative	3/26 (11,5)	NE [NE; NE]	5/12 (41,7)	NE [0,33; NE]	0,16 [0,04; 0,70] 0,006
Positive	7/49 (14,3)	NE [22,54; NE]	16/34 (47,1)	5,3 [2,89; NE]	0,22 [0,09; 0,55] <0,001
Unknown	4/40 (10,0)	NE [NE; NE]	19/26 (73,1)	1,6 [0,79; 6,31]	0,08 [0,03; 0,23] <0,001
Disease Stage (p-value of the interaction term: 0,649)					
III*	0/6 (0,0)	NE [NE; NE]	4/6 (66,7)	3,1 [1,22; NE]	0,00 [0,00; NE] 0,018
IVA	4/44 (9,1)	NE [NE; NE]	17/32 (53,1)	6,6 [1,18; NE]	0,10 [0,03; 0,31] <0,001
IVB	10/65 (15,4)	NE [NE; NE]	19/34 (55,9)	5,3 [2,30; NE]	0,18 [0,08; 0,39] <0,001
Race (p-value of the interaction term: 0,866)					
Asian	9/66 (13,6)	NE [NE; NE]	21/35 (60,0)	2,2 [1,38; NE]	0,14 [0,06; 0,31] <0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Non-Asian	5/49 (10,2)	NE [NE; NE]	16/33 (48,5)	11,1 [2,89; NE]	0,15 [0,05; 0,41] <0,001
RET Specimen Type (p-value of the interaction term: 0,308)					
Blood	1/9 (11,1)	NE [2,73; NE]	2/10 (20,0)	NE [2,20; NE]	0,48 [0,04; 5,30] 0,541
Tissue	13/106 (12,3)	NE [NE; NE]	38/62 (61,3)	3,5 [1,41; 11,10]	0,12 [0,07; 0,23] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,059)					
CCDC6	4/9 (44,4)	22,5 [0,95; NE]	4/6 (66,7)	7,0 [0,46; NE]	0,41 [0,09; 1,83] 0,226
KIF5B	4/50 (8,0)	NE [NE; NE]	18/36 (50,0)	5,3 [2,07; NE]	0,08 [0,03; 0,26] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

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Table 124: Subgroups: Time to adverse event according to PT: Investigations/Aspartate aminotransferase increased - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,145)					
<65 years	49/76 (64,5)	2,1 [1,48; 10,38]	23/45 (51,1)	5,7 [3,48; NE]	1,49 [0,91; 2,45] 0,114
≥65 years	22/39 (56,4)	1,9 [1,15; NE]	7/27 (25,9)	NE [NE; NE]	2,90 [1,24; 6,82] 0,010
Baseline ECOG (p-value of the interaction term: 0,880)					
0	23/41 (56,1)	10,4 [1,71; NE]	9/25 (36,0)	NE [5,32; NE]	1,72 [0,79; 3,73] 0,164
1	48/74 (64,9)	1,6 [1,28; 2,76]	21/47 (44,7)	NE [3,52; NE]	1,96 [1,17; 3,29] 0,009
Geographic region (p-value of the interaction term: 0,828)					
East Asian	50/65 (76,9)	1,4 [1,12; 1,87]	20/35 (57,1)	3,9 [2,50; NE]	1,91 [1,13; 3,22] 0,014
Non-EastAsian	21/50 (42,0)	20,3 [7,66; NE]	10/37 (27,0)	NE [NE; NE]	1,66 [0,78; 3,53] 0,183
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,255)					
Yes	14/23 (60,9)	2,1 [1,15; NE]	5/14 (35,7)	NE [1,87; NE]	2,17 [0,78; 6,05] 0,126
No	29/44 (65,9)	1,5 [0,92; 2,07]	9/23 (39,1)	NE [3,52; NE]	2,79 [1,31; 5,94] 0,005
Unknown	28/48 (58,3)	10,4 [1,71; NE]	16/35 (45,7)	NE [2,79; NE]	1,25 [0,67; 2,32] 0,472
Liver Metastasis - BICR (p-value of the interaction term: 0,763)					
Yes	8/16 (50,0)	13,1 [0,92; NE]	3/13 (23,1)	NE [5,72; NE]	1,93 [0,51; 7,39] 0,315
No	63/98 (64,3)	1,9 [1,41; 3,48]	27/59 (45,8)	NE [3,55; NE]	1,86 [1,18; 2,92] 0,007
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,556)					
TPS <50%	34/48 (70,8)	1,6 [0,72; 5,62]	13/27 (48,1)	11,8 [2,10; NE]	1,85 [0,97; 3,51] 0,059

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
TPS ≥50%	7/19 (36,8)	NE [1,54; NE]	2/13 (15,4)	NE [5,32; NE]	3,06 [0,64; 14,78] 0,142
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,640)					
TPS <50%	34/48 (70,8)	1,6 [0,72; 5,62]	13/27 (48,1)	11,8 [2,10; NE]	1,85 [0,97; 3,51] 0,059
TPS ≥50%	7/19 (36,8)	NE [1,54; NE]	2/13 (15,4)	NE [5,32; NE]	3,06 [0,64; 14,78] 0,142
Unknown	30/48 (62,5)	2,0 [1,35; NE]	15/32 (46,9)	NE [2,33; NE]	1,63 [0,87; 3,03] 0,121
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,406)					
Negative	17/26 (65,4)	1,8 [0,72; NE]	4/12 (33,3)	NE [0,69; NE]	2,52 [0,84; 7,52] 0,087
Positive	29/49 (59,2)	5,6 [1,41; 16,39]	12/34 (35,3)	NE [4,96; NE]	2,09 [1,07; 4,11] 0,028
Unknown	25/40 (62,5)	2,0 [1,35; NE]	14/26 (53,8)	3,9 [2,10; NE]	1,44 [0,75; 2,77] 0,276
Disease Stage (p-value of the interaction term: 0,568)					
III	5/6 (83,3)	1,3 [0,72; NE]	5/6 (83,3)	2,7 [0,20; NE]	1,26 [0,35; 4,50] 0,718
IVA	29/44 (65,9)	1,9 [1,25; 7,66]	13/32 (40,6)	NE [3,52; NE]	2,24 [1,16; 4,32] 0,013
IVB	37/65 (56,9)	2,2 [1,41; NE]	12/34 (35,3)	NE [4,96; NE]	1,91 [0,99; 3,68] 0,048
Race (p-value of the interaction term: 0,772)					
Asian	51/66 (77,3)	1,4 [1,12; 1,87]	20/35 (57,1)	3,9 [2,50; NE]	1,92 [1,14; 3,24] 0,013
Non-Asian	20/49 (40,8)	NE [7,66; NE]	9/33 (27,3)	NE [NE; NE]	1,58 [0,72; 3,49] 0,247
RET Specimen Type (p-value of the interaction term: 0,658)					
Blood	4/9 (44,4)	NE [0,72; NE]	2/10 (20,0)	NE [4,27; NE]	2,68 [0,49; 14,69] 0,237

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Tissue	67/106 (63,2)	1,9 [1,41; 7,66]	28/62 (45,2)	NE [3,52; NE]	1,73 [1,11; 2,70] 0,013
RET Fusion Result **** (p-value of the interaction term: 0,926)					
CCDC6	6/9 (66,7)	4,1 [0,49; NE]	2/6 (33,3)	NE [0,20; NE]	2,45 [0,49; 12,26] 0,261
KIF5B	25/50 (50,0)	16,4 [1,91; NE]	8/36 (22,2)	NE [NE; NE]	2,61 [1,17; 5,81] 0,015
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx006_sub_msaf_a.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
14OCT2025 / 07:23

Table 125: Subgroups: Time to adverse event according to PT: General disorders and administration site conditions/Asthenia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,588)					
<65 years	10/76 (13,2)	NE [NE; NE]	11/45 (24,4)	NE [NE; NE]	0,47 [0,20; 1,11] 0,078
≥65 years	6/39 (15,4)	NE [NE; NE]	10/27 (37,0)	NE [3,94; NE]	0,31 [0,11; 0,86] 0,019
Baseline ECOG (p-value of the interaction term: 0,745)					
0	7/41 (17,1)	NE [NE; NE]	8/25 (32,0)	NE [6,93; NE]	0,47 [0,17; 1,31] 0,138
1	9/74 (12,2)	NE [NE; NE]	13/47 (27,7)	NE [13,83; NE]	0,35 [0,15; 0,82] 0,012
Sex (p-value of the interaction term: 0,462)					
Male	12/61 (19,7)	NE [NE; NE]	12/34 (35,3)	NE [7,66; NE]	0,44 [0,20; 1,00] 0,044
Female	4/54 (7,4)	NE [NE; NE]	9/38 (23,7)	NE [NE; NE]	0,28 [0,09; 0,90] 0,023
Smoking Status (p-value of the interaction term: 0,584)					
Never	8/72 (11,1)	NE [NE; NE]	13/49 (26,5)	NE [NE; NE]	0,33 [0,14; 0,81] 0,011
Former/Current	8/43 (18,6)	NE [NE; NE]	8/23 (34,8)	NE [6,93; NE]	0,50 [0,19; 1,33] 0,159
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,295)					
Yes	3/23 (13,0)	NE [NE; NE]	7/14 (50,0)	10,1 [0,26; NE]	0,20 [0,05; 0,79] 0,011
No	8/44 (18,2)	NE [19,12; NE]	5/23 (21,7)	NE [NE; NE]	0,70 [0,23; 2,18] 0,539
Unknown	5/48 (10,4)	NE [NE; NE]	9/35 (25,7)	NE [13,83; NE]	0,33 [0,11; 1,00] 0,039
Liver Metastasis - BICR (p-value of the interaction term: 0,710)					
Yes	3/16 (18,8)	NE [NE; NE]	6/13 (46,2)	13,8 [2,30; NE]	0,30 [0,07; 1,24] 0,080

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
No	13/98 (13,3)	NE [NE; NE]	15/59 (25,4)	NE [NE; NE]	0,45 [0,21; 0,94] 0,029
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,180)					
Negative	3/26 (11,5)	NE [NE; NE]	4/12 (33,3)	NE [0,16; NE]	0,21 [0,05; 1,01] 0,035
Positive	11/49 (22,4)	NE [NE; NE]	10/34 (29,4)	NE [10,12; NE]	0,69 [0,29; 1,62] 0,388
Unknown	2/40 (5,0)	NE [NE; NE]	7/26 (26,9)	NE [7,66; NE]	0,17 [0,03; 0,80] 0,011
Disease Stage (p-value of the interaction term: 0,520)					
III*	0/6 (0,0)	NE [NE; NE]	1/6 (16,7)	NE [0,39; NE]	0,00 [0,00; NE] 0,317
IVA	4/44 (9,1)	NE [NE; NE]	10/32 (31,3)	NE [10,12; NE]	0,24 [0,07; 0,75] 0,008
IVB	12/65 (18,5)	NE [NE; NE]	10/34 (29,4)	NE [13,83; NE]	0,55 [0,23; 1,27] 0,154
RET Specimen Type (p-value of the interaction term: 0,508)					
Blood	1/9 (11,1)	NE [0,49; NE]	1/10 (10,0)	NE [0,16; NE]	1,05 [0,07; 16,87] 0,970
Tissue	15/106 (14,2)	NE [NE; NE]	20/62 (32,3)	NE [13,83; NE]	0,36 [0,19; 0,71] 0,002
RET Fusion Result **** (p-value of the interaction term: 0,465)					
CCDC6	2/9 (22,2)	NE [4,83; NE]	1/6 (16,7)	NE [0,39; NE]	1,23 [0,11; 13,58] 0,866
KIF5B	7/50 (14,0)	NE [NE; NE]	8/36 (22,2)	NE [NE; NE]	0,45 [0,16; 1,27] 0,122
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

*Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx007_sub_msaf_a.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
14OCT2025 / 07:23*

Table 126: Subgroups: Time to adverse event according to PT: Investigations/Bilirubin conjugated increased - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,991)					
<65 years	11/76 (14,5)	NE [NE; NE]	1/45 (2,2)	NE [NE; NE]	6,52 [0,84; 50,56] 0,038
≥65 years*	6/39 (15,4)	NE [NE; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,031
Baseline ECOG (p-value of the interaction term: 0,993)					
0*	3/41 (7,3)	NE [NE; NE]	0/25 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,165
1	14/74 (18,9)	NE [NE; NE]	1/47 (2,1)	NE [NE; NE]	9,08 [1,19; 69,13] 0,010
Sex (p-value of the interaction term: 0,990)					
Male*	10/61 (16,4)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,021
Female	7/54 (13,0)	NE [NE; NE]	1/38 (2,6)	NE [NE; NE]	5,23 [0,64; 42,54] 0,083
Geographic region (p-value of the interaction term: 0,993)					
East Asian	16/65 (24,6)	NE [NE; NE]	1/35 (2,9)	NE [NE; NE]	9,02 [1,20; 68,01] 0,010
Non-EastAsian*	1/50 (2,0)	NE [NE; NE]	0/37 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,375
Smoking Status (p-value of the interaction term: 0,992)					
Never	10/72 (13,9)	NE [NE; NE]	1/49 (2,0)	NE [NE; NE]	7,16 [0,92; 55,97] 0,028
Former/Current*	7/43 (16,3)	NE [NE; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,054
Liver Metastasis - BICR (p-value of the interaction term: 0,999)					
Yes*	0/16 (0,0)	NE [NE; NE]	0/13 (0,0)	NE [NE; NE]	NE
No	17/98 (17,3)	NE [NE; NE]	1/59 (1,7)	NE [NE; NE]	10,98 [1,46; 82,52] 0,003
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 1,000)					

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
TPS <50%	7/48 (14,6)	NE [NE; NE]	1/27 (3,7)	NE [NE; NE]	4,21 [0,52; 34,19] 0,143
TPS ≥50%*	0/19 (0,0)	NE [NE; NE]	0/13 (0,0)	NE [NE; NE]	NE
Unknown*	10/48 (20,8)	NE [NE; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,009
Disease Stage (p-value of the interaction term: 1,000)					
III*	0/6 (0,0)	NE [NE; NE]	0/6 (0,0)	NE [NE; NE]	NE
IVA*	7/44 (15,9)	NE [NE; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,019
IVB	10/65 (15,4)	NE [NE; NE]	1/34 (2,9)	NE [NE; NE]	5,12 [0,65; 40,07] 0,082
Race (p-value of the interaction term: 0,993)					
Asian	16/66 (24,2)	NE [NE; NE]	1/35 (2,9)	NE [NE; NE]	8,88 [1,18; 66,95] 0,010
Non-Asian*	1/49 (2,0)	NE [NE; NE]	0/33 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,397
RET Specimen Type (p-value of the interaction term: 0,993)					
Blood*	1/9 (11,1)	NE [1,87; NE]	0/10 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,292
Tissue	16/106 (15,1)	NE [NE; NE]	1/62 (1,6)	NE [NE; NE]	9,76 [1,29; 73,64] 0,006
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx009_sub_msaf_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
14OCT2025 / 07:23

Table 127: Subgroups: Time to adverse event according to PT: Investigations/Blood bilirubin increased - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 1,000)					
<65 years*	30/76 (39,5)	NE [11,60; NE]	0/45 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
≥65 years*	17/39 (43,6)	16,6 [2,10; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Baseline ECOG (p-value of the interaction term: 1,000)					
0*	12/41 (29,3)	NE [NE; NE]	0/25 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
1*	35/74 (47,3)	16,6 [5,52; NE]	0/47 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Sex (p-value of the interaction term: 1,000)					
Male*	25/61 (41,0)	NE [9,86; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Female*	22/54 (40,7)	NE [3,22; NE]	0/38 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Geographic region (p-value of the interaction term: 0,999)					
East Asian*	39/65 (60,0)	5,6 [1,45; 16,59]	0/35 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Non-EastAsian*	8/50 (16,0)	NE [NE; NE]	0/37 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,009
Smoking Status (p-value of the interaction term: 1,000)					
Never*	32/72 (44,4)	NE [2,14; NE]	0/49 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Former/Current*	15/43 (34,9)	NE [11,60; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,002
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 1,000)					
Yes*	7/23 (30,4)	NE [2,10; NE]	0/14 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,027
No*	22/44 (50,0)	5,0 [1,18; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown*	18/48 (37,5)	NE [11,96; NE]	0/35 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Liver Metastasis - BICR (p-value of the interaction term: 0,999)					
Yes*	2/16 (12,5)	NE [NE; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,247
No*	45/98 (45,9)	NE [5,03; NE]	0/59 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 1,000)					
TPS <50%*	21/48 (43,8)	NE [2,10; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
TPS ≥50%*	7/19 (36,8)	NE [1,48; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,013
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 1,000)					
TPS <50%*	21/48 (43,8)	NE [2,10; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
TPS ≥50%*	7/19 (36,8)	NE [1,48; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,013
Unknown*	19/48 (39,6)	NE [5,59; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 1,000)					
Negative*	9/26 (34,6)	NE [2,10; NE]	0/12 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,032
Positive*	22/49 (44,9)	NE [3,22; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Unknown*	16/40 (40,0)	NE [5,52; NE]	0/26 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Disease Stage (p-value of the interaction term: 1,000)					
III*	5/6 (83,3)	3,4 [1,18; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,008
IVA*	18/44 (40,9)	NE [1,45; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB*	24/65 (36,9)	NE [11,96; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Race (p-value of the interaction term: 0,999)					
Asian*	39/66 (59,1)	5,6 [1,45; 16,59]	0/35 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Non-Asian*	8/49 (16,3)	NE [NE; NE]	0/33 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,012
RET Specimen Type (p-value of the interaction term: 1,000)					
Blood*	2/9 (22,2)	NE [0,69; NE]	0/10 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,161
Tissue*	45/106 (42,5)	NE [9,86; NE]	0/62 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
RET Fusion Result **** (p-value of the interaction term: 1,000)					
CCDC6*	3/9 (33,3)	NE [0,53; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,132
KIF5B*	17/50 (34,0)	NE [16,59; NE]	0/36 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx011_sub_msaf_a.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 128: Subgroups: Time to adverse event according to PT: Gastrointestinal disorders/Constipation - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,978)					
<65 years	16/76 (21,1)	NE [NE; NE]	18/45 (40,0)	NE [2,43; NE]	0,43 [0,22; 0,84] 0,011
≥65 years	8/39 (20,5)	NE [NE; NE]	11/27 (40,7)	NE [0,79; NE]	0,41 [0,16; 1,01] 0,047
Baseline ECOG (p-value of the interaction term: 0,145)					
0	13/41 (31,7)	NE [12,48; NE]	10/25 (40,0)	NE [0,79; NE]	0,67 [0,29; 1,54] 0,348
1	11/74 (14,9)	NE [NE; NE]	19/47 (40,4)	NE [2,43; NE]	0,29 [0,14; 0,62] <0,001
Sex (p-value of the interaction term: 0,909)					
Male	13/61 (21,3)	NE [NE; NE]	14/34 (41,2)	NE [1,58; NE]	0,44 [0,21; 0,94] 0,029
Female	11/54 (20,4)	NE [NE; NE]	15/38 (39,5)	NE [1,41; NE]	0,41 [0,19; 0,90] 0,022
Geographic region (p-value of the interaction term: 0,144)					
East Asian	9/65 (13,8)	NE [NE; NE]	14/35 (40,0)	NE [2,43; NE]	0,28 [0,12; 0,65] 0,002
Non-EastAsian	15/50 (30,0)	NE [NE; NE]	15/37 (40,5)	NE [1,41; NE]	0,62 [0,30; 1,26] 0,183
Smoking Status (p-value of the interaction term: 0,266)					
Never	11/72 (15,3)	NE [NE; NE]	19/49 (38,8)	NE [2,43; NE]	0,33 [0,16; 0,69] 0,002
Former/Current	13/43 (30,2)	NE [12,48; NE]	10/23 (43,5)	NE [1,58; NE]	0,55 [0,24; 1,25] 0,147
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,666)					
Yes	6/23 (26,1)	NE [12,48; NE]	7/14 (50,0)	NE [0,07; NE]	0,34 [0,11; 1,03] 0,047
No	10/44 (22,7)	NE [NE; NE]	8/23 (34,8)	NE [1,58; NE]	0,59 [0,23; 1,49] 0,256

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	8/48 (16,7)	NE [NE; NE]	14/35 (40,0)	NE [2,43; NE]	0,34 [0,14; 0,82] 0,012
Liver Metastasis - BICR (p-value of the interaction term: 0,694)					
Yes	3/16 (18,8)	NE [6,24; NE]	6/13 (46,2)	7,9 [0,72; NE]	0,32 [0,08; 1,30] 0,097
No	21/98 (21,4)	NE [NE; NE]	23/59 (39,0)	NE [2,79; NE]	0,45 [0,25; 0,81] 0,007
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,354)					
TPS <50%	10/48 (20,8)	NE [NE; NE]	12/27 (44,4)	NE [0,49; NE]	0,40 [0,17; 0,92] 0,027
TPS ≥50%	5/19 (26,3)	NE [6,24; NE]	4/13 (30,8)	NE [1,58; NE]	0,85 [0,23; 3,16] 0,796
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,547)					
TPS <50%	10/48 (20,8)	NE [NE; NE]	12/27 (44,4)	NE [0,49; NE]	0,40 [0,17; 0,92] 0,027
TPS ≥50%	5/19 (26,3)	NE [6,24; NE]	4/13 (30,8)	NE [1,58; NE]	0,85 [0,23; 3,16] 0,796
Unknown	9/48 (18,8)	NE [NE; NE]	13/32 (40,6)	NE [0,82; NE]	0,35 [0,15; 0,82] 0,012
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,607)					
Negative	4/26 (15,4)	NE [NE; NE]	6/12 (50,0)	NE [0,13; NE]	0,27 [0,08; 0,96] 0,029
Positive	13/49 (26,5)	NE [NE; NE]	15/34 (44,1)	NE [0,79; NE]	0,49 [0,23; 1,03] 0,056
Unknown	7/40 (17,5)	NE [NE; NE]	8/26 (30,8)	NE [7,92; NE]	0,48 [0,17; 1,33] 0,150
Disease Stage (p-value of the interaction term: 0,948)					
III	1/6 (16,7)	NE [5,65; NE]	2/6 (33,3)	NE [0,10; NE]	0,44 [0,04; 4,82] 0,486
IVA	11/44 (25,0)	NE [NE; NE]	14/32 (43,8)	NE [0,72; NE]	0,47 [0,21; 1,04] 0,057

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB	12/65 (18,5)	NE [NE; NE]	13/34 (38,2)	NE [2,43; NE]	0,37 [0,17; 0,82] 0,011
Race (p-value of the interaction term: 0,089)					
Asian	9/66 (13,6)	NE [NE; NE]	14/35 (40,0)	NE [2,43; NE]	0,28 [0,12; 0,64] 0,001
Non-Asian	15/49 (30,6)	NE [12,48; NE]	12/33 (36,4)	NE [1,41; NE]	0,71 [0,33; 1,53] 0,385
RET Specimen Type (p-value of the interaction term: 0,733)					
Blood	2/9 (22,2)	NE [3,71; NE]	5/10 (50,0)	NE [0,26; NE]	0,29 [0,06; 1,52] 0,121
Tissue	22/106 (20,8)	NE [NE; NE]	24/62 (38,7)	NE [2,89; NE]	0,44 [0,25; 0,79] 0,005
RET Fusion Result **** (p-value of the interaction term: 0,972)					
CCDC6	3/9 (33,3)	NE [1,38; NE]	3/6 (50,0)	NE [0,10; NE]	0,42 [0,08; 2,14] 0,285
KIF5B	13/50 (26,0)	NE [NE; NE]	16/36 (44,4)	NE [1,41; NE]	0,45 [0,21; 0,93] 0,029
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx014_sub_msa_f_a.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 129: Subgroups: Time to adverse event according to PT: Metabolism and nutrition disorders/Decreased appetite - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,359)					
<65 years	8/76 (10,5)	NE [NE; NE]	10/45 (22,2)	NE [NE; NE]	0,40 [0,16; 1,01] 0,047
≥65 years	12/39 (30,8)	NE [16,59; NE]	10/27 (37,0)	NE [4,24; NE]	0,69 [0,30; 1,60] 0,385
Baseline ECOG (p-value of the interaction term: 0,502)					
0	5/41 (12,2)	NE [NE; NE]	7/25 (28,0)	NE [10,58; NE]	0,39 [0,12; 1,23] 0,097
1	15/74 (20,3)	NE [NE; NE]	13/47 (27,7)	NE [10,12; NE]	0,58 [0,27; 1,22] 0,148
Sex (p-value of the interaction term: 0,862)					
Male	10/61 (16,4)	NE [NE; NE]	9/34 (26,5)	NE [NE; NE]	0,48 [0,19; 1,19] 0,110
Female	10/54 (18,5)	NE [NE; NE]	11/38 (28,9)	NE [10,58; NE]	0,56 [0,24; 1,31] 0,173
Geographic region (p-value of the interaction term: 0,264)					
East Asian	14/65 (21,5)	NE [NE; NE]	9/35 (25,7)	NE [10,58; NE]	0,68 [0,30; 1,59] 0,383
Non-EastAsian	6/50 (12,0)	NE [NE; NE]	11/37 (29,7)	NE [10,12; NE]	0,34 [0,12; 0,92] 0,027
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,562)					
Yes	4/23 (17,4)	NE [12,62; NE]	2/14 (14,3)	NE [10,12; NE]	1,05 [0,19; 5,77] 0,959
No	10/44 (22,7)	NE [NE; NE]	9/23 (39,1)	NE [0,26; NE]	0,49 [0,20; 1,20] 0,112
Unknown	6/48 (12,5)	NE [NE; NE]	9/35 (25,7)	NE [10,58; NE]	0,38 [0,13; 1,06] 0,056
Liver Metastasis - BICR (p-value of the interaction term: 0,760)					
Yes	3/16 (18,8)	NE [7,62; NE]	4/13 (30,8)	NE [0,72; NE]	0,40 [0,09; 1,82] 0,220

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
No	17/98 (17,3)	NE [NE; NE]	16/59 (27,1)	NE [NE; NE]	0,55 [0,28; 1,08] 0,081
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,105)					
TPS <50%	10/48 (20,8)	NE [NE; NE]	10/27 (37,0)	NE [9,79; NE]	0,41 [0,17; 1,00] 0,043
TPS ≥50%	4/19 (21,1)	NE [7,62; NE]	1/13 (7,7)	NE [NE; NE]	2,91 [0,33; 26,08] 0,317
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,219)					
TPS <50%	10/48 (20,8)	NE [NE; NE]	10/27 (37,0)	NE [9,79; NE]	0,41 [0,17; 1,00] 0,043
TPS ≥50%	4/19 (21,1)	NE [7,62; NE]	1/13 (7,7)	NE [NE; NE]	2,91 [0,33; 26,08] 0,317
Unknown	6/48 (12,5)	NE [NE; NE]	9/32 (28,1)	NE [7,06; NE]	0,37 [0,13; 1,04] 0,050
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,577)					
Negative	5/26 (19,2)	NE [20,11; NE]	3/12 (25,0)	NE [0,16; NE]	0,54 [0,13; 2,33] 0,403
Positive	10/49 (20,4)	NE [NE; NE]	9/34 (26,5)	NE [10,58; NE]	0,68 [0,28; 1,68] 0,409
Unknown	5/40 (12,5)	NE [NE; NE]	8/26 (30,8)	NE [5,55; NE]	0,33 [0,11; 1,02] 0,044
Disease Stage (p-value of the interaction term: 0,985)					
III	1/6 (16,7)	NE [0,23; NE]	2/6 (33,3)	NE [0,26; NE]	0,57 [0,05; 6,32] 0,644
IVA	9/44 (20,5)	NE [NE; NE]	10/32 (31,3)	NE [10,12; NE]	0,55 [0,22; 1,35] 0,186
IVB	10/65 (15,4)	NE [NE; NE]	8/34 (23,5)	NE [NE; NE]	0,51 [0,20; 1,31] 0,163
Race (p-value of the interaction term: 0,377)					
Asian	14/66 (21,2)	NE [NE; NE]	9/35 (25,7)	NE [10,58; NE]	0,67 [0,29; 1,56] 0,363

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Non-Asian	6/49 (12,2)	NE [NE; NE]	9/33 (27,3)	NE [10,12; NE]	0,38 [0,13; 1,07] 0,060
RET Specimen Type (p-value of the interaction term: 0,606)					
Blood	4/9 (44,4)	12,6 [0,03; NE]	4/10 (40,0)	NE [0,10; NE]	0,60 [0,13; 2,80] 0,524
Tissue	16/106 (15,1)	NE [NE; NE]	16/62 (25,8)	NE [NE; NE]	0,50 [0,25; 1,00] 0,047
RET Fusion Result **** (p-value of the interaction term: 0,153)					
CCDC6	2/9 (22,2)	NE [0,85; NE]	4/6 (66,7)	5,0 [0,10; NE]	0,23 [0,04; 1,24] 0,065
KIF5B	12/50 (24,0)	NE [NE; NE]	8/36 (22,2)	NE [NE; NE]	0,85 [0,34; 2,09] 0,721
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx016_sub_msaf_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteae_gba

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Table 130: Subgroups: Time to adverse event according to PT: Gastrointestinal disorders/Diarrhoea - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,702)					
<65 years	35/76 (46,1)	12,0 [7,33; NE]	11/45 (24,4)	NE [15,54; NE]	1,85 [0,94; 3,65] 0,070
≥65 years	22/39 (56,4)	6,4 [3,48; NE]	8/27 (29,6)	NE [6,60; NE]	2,26 [1,01; 5,09] 0,043
Baseline ECOG (p-value of the interaction term: 0,929)					
0	22/41 (53,7)	9,8 [3,48; NE]	8/25 (32,0)	NE [15,54; NE]	1,90 [0,85; 4,28] 0,113
1	35/74 (47,3)	10,4 [6,44; NE]	11/47 (23,4)	NE [16,72; NE]	2,04 [1,04; 4,02] 0,035
Smoking Status (p-value of the interaction term: 0,504)					
Never	35/72 (48,6)	10,9 [6,44; NE]	11/49 (22,4)	NE [15,54; NE]	2,26 [1,15; 4,44] 0,016
Former/Current	22/43 (51,2)	7,3 [5,72; NE]	8/23 (34,8)	16,7 [6,60; NE]	1,57 [0,70; 3,54] 0,272
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,062)					
Yes	14/23 (60,9)	6,5 [4,90; NE]	2/14 (14,3)	NE [12,42; NE]	5,20 [1,18; 22,95] 0,015
No	20/44 (45,5)	20,5 [3,61; NE]	11/23 (47,8)	15,5 [2,07; NE]	0,93 [0,45; 1,95] 0,849
Unknown	23/48 (47,9)	12,0 [6,51; NE]	6/35 (17,1)	NE [NE; NE]	2,89 [1,18; 7,10] 0,015
Liver Metastasis - BICR (p-value of the interaction term: 0,892)					
Yes	9/16 (56,3)	5,5 [1,68; NE]	3/13 (23,1)	NE [1,08; NE]	2,31 [0,62; 8,54] 0,197
No	48/98 (49,0)	10,9 [6,51; NE]	16/59 (27,1)	NE [16,03; NE]	1,99 [1,13; 3,51] 0,015
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,674)					
TPS <50%	25/48 (52,1)	7,5 [4,47; NE]	11/27 (40,7)	16,0 [5,72; NE]	1,23 [0,60; 2,50] 0,577

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
TPS ≥50%	8/19 (42,1)	NE [2,37; NE]	4/13 (30,8)	15,5 [6,60; NE]	1,68 [0,51; 5,60] 0,392
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,136)					
TPS <50%	25/48 (52,1)	7,5 [4,47; NE]	11/27 (40,7)	16,0 [5,72; NE]	1,23 [0,60; 2,50] 0,577
TPS ≥50%	8/19 (42,1)	NE [2,37; NE]	4/13 (30,8)	15,5 [6,60; NE]	1,68 [0,51; 5,60] 0,392
Unknown	24/48 (50,0)	10,4 [6,47; NE]	4/32 (12,5)	NE [NE; NE]	4,46 [1,55; 12,87] 0,002
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,082)					
Negative	14/26 (53,8)	9,8 [4,04; NE]	6/12 (50,0)	16,7 [0,16; NE]	0,86 [0,33; 2,26] 0,767
Positive	23/49 (46,9)	7,5 [5,06; NE]	10/34 (29,4)	16,0 [12,42; NE]	1,75 [0,83; 3,69] 0,136
Unknown	20/40 (50,0)	10,4 [6,44; NE]	3/26 (11,5)	NE [NE; NE]	5,18 [1,54; 17,50] 0,003
Disease Stage (p-value of the interaction term: 0,595)					
III	3/6 (50,0)	20,5 [3,42; NE]	2/6 (33,3)	NE [1,12; NE]	1,43 [0,24; 8,63] 0,694
IVA	20/44 (45,5)	10,4 [3,94; NE]	10/32 (31,3)	NE [12,42; NE]	1,52 [0,71; 3,24] 0,277
IVB	34/65 (52,3)	8,9 [6,05; NE]	7/34 (20,6)	NE [15,54; NE]	2,70 [1,19; 6,08] 0,013
Race (p-value of the interaction term: 0,073)					
Asian	32/66 (48,5)	10,4 [6,44; NE]	4/35 (11,4)	NE [NE; NE]	4,74 [1,68; 13,41] 0,001
Non-Asian	25/49 (51,0)	9,8 [3,75; NE]	12/33 (36,4)	16,7 [12,42; NE]	1,47 [0,74; 2,93] 0,269
RET Specimen Type (p-value of the interaction term: 0,764)					
Blood	7/9 (77,8)	6,4 [0,03; 10,91]	3/10 (30,0)	NE [0,16; NE]	2,38 [0,61; 9,25] 0,196

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Tissue	50/106 (47,2)	12,0 [6,47; NE]	16/62 (25,8)	NE [16,03; NE]	1,98 [1,13; 3,48] 0,015
RET Fusion Result **** (p-value of the interaction term: 0,120)					
CCDC6	4/9 (44,4)	NE [0,36; NE]	3/6 (50,0)	16,7 [0,16; NE]	0,79 [0,17; 3,73] 0,765
KIF5B	34/50 (68,0)	5,3 [3,48; 10,02]	10/36 (27,8)	NE [15,54; NE]	2,65 [1,31; 5,38] 0,005
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx017_sub_msaf_a.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 131: Subgroups: Time to adverse event according to PT: Gastrointestinal disorders/Dry mouth - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,511)					
<65 years	31/76 (40,8)	NE [1,77; NE]	2/45 (4,4)	NE [NE; NE]	11,14 [2,66; 46,57] <0,001
≥65 years	15/39 (38,5)	NE [3,81; NE]	2/27 (7,4)	NE [NE; NE]	5,89 [1,34; 25,76] 0,008
Baseline ECOG (p-value of the interaction term: 0,248)					
0	20/41 (48,8)	NE [0,66; NE]	3/25 (12,0)	NE [NE; NE]	4,87 [1,44; 16,43] 0,005
1	26/74 (35,1)	NE [16,16; NE]	1/47 (2,1)	NE [NE; NE]	18,89 [2,56; 139,24] <0,001
Sex (p-value of the interaction term: 0,674)					
Male	22/61 (36,1)	NE [14,36; NE]	2/34 (5,9)	NE [NE; NE]	6,90 [1,62; 29,39] 0,002
Female	24/54 (44,4)	NE [0,72; NE]	2/38 (5,3)	NE [NE; NE]	10,59 [2,50; 44,90] <0,001
Geographic region (p-value of the interaction term: 0,276)					
East Asian	25/65 (38,5)	NE [10,48; NE]	3/35 (8,6)	NE [NE; NE]	4,98 [1,50; 16,51] 0,003
Non-EastAsian	21/50 (42,0)	NE [1,45; NE]	1/37 (2,7)	NE [NE; NE]	20,15 [2,71; 149,99] <0,001
Smoking Status (p-value of the interaction term: 0,068)					
Never	31/72 (43,1)	NE [2,56; NE]	1/49 (2,0)	NE [NE; NE]	26,07 [3,56; 191,05] <0,001
Former/Current	15/43 (34,9)	NE [5,78; NE]	3/23 (13,0)	NE [NE; NE]	2,92 [0,84; 10,10] 0,075
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,968)					
Yes*	10/23 (43,5)	NE [0,72; NE]	0/14 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,005
No	18/44 (40,9)	NE [1,48; NE]	2/23 (8,7)	NE [NE; NE]	5,49 [1,27; 23,70] 0,010

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	18/48 (37,5)	NE [3,81; NE]	2/35 (5,7)	NE [NE; NE]	7,48 [1,73; 32,28] 0,002
Liver Metastasis - BICR (p-value of the interaction term: 0,605)					
Yes	6/16 (37,5)	NE [0,69; NE]	1/13 (7,7)	NE [NE; NE]	4,61 [0,55; 38,85] 0,124
No	40/98 (40,8)	NE [5,78; NE]	3/59 (5,1)	NE [NE; NE]	9,79 [3,03; 31,67] <0,001
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,419)					
TPS <50%	16/48 (33,3)	NE [14,36; NE]	3/27 (11,1)	NE [NE; NE]	3,09 [0,90; 10,62] 0,059
TPS ≥50%	9/19 (47,4)	3,8 [0,39; NE]	1/13 (7,7)	NE [NE; NE]	7,96 [1,00; 63,05] 0,020
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,731)					
TPS <50%	16/48 (33,3)	NE [14,36; NE]	3/27 (11,1)	NE [NE; NE]	3,09 [0,90; 10,62] 0,059
TPS ≥50%	9/19 (47,4)	3,8 [0,39; NE]	1/13 (7,7)	NE [NE; NE]	7,96 [1,00; 63,05] 0,020
Unknown*	21/48 (43,8)	NE [0,72; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,783)					
Negative	6/26 (23,1)	NE [NE; NE]	1/12 (8,3)	NE [NE; NE]	2,62 [0,32; 21,84] 0,354
Positive	23/49 (46,9)	NE [0,72; NE]	3/34 (8,8)	NE [NE; NE]	6,54 [1,96; 21,82] <0,001
Unknown*	17/40 (42,5)	NE [0,59; NE]	0/26 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Disease Stage (p-value of the interaction term: 0,354)					
III	2/6 (33,3)	NE [0,23; NE]	1/6 (16,7)	NE [0,03; NE]	2,04 [0,18; 22,62] 0,554
IVA	21/44 (47,7)	16,2 [0,66; NE]	1/32 (3,1)	NE [NE; NE]	19,80 [2,66; 147,43] <0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB	23/65 (35,4)	NE [14,36; NE]	2/34 (5,9)	NE [NE; NE]	6,94 [1,63; 29,46] 0,002
Race (p-value of the interaction term: 0,304)					
Asian	25/66 (37,9)	NE [14,36; NE]	3/35 (8,6)	NE [NE; NE]	4,89 [1,48; 16,21] 0,004
Non-Asian	21/49 (42,9)	NE [1,45; NE]	1/33 (3,0)	NE [NE; NE]	18,42 [2,47; 137,17] <0,001
RET Specimen Type (p-value of the interaction term: 0,949)					
Blood	6/9 (66,7)	1,4 [0,03; NE]	1/10 (10,0)	NE [0,20; NE]	8,57 [1,03; 71,61] 0,017
Tissue	40/106 (37,7)	NE [16,16; NE]	3/62 (4,8)	NE [NE; NE]	9,17 [2,83; 29,64] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,702)					
CCDC6	6/9 (66,7)	0,7 [0,03; NE]	1/6 (16,7)	NE [0,03; NE]	4,88 [0,58; 40,88] 0,104
KIF5B	21/50 (42,0)	NE [1,77; NE]	2/36 (5,6)	NE [NE; NE]	8,60 [2,01; 36,69] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 132: Subgroups: Time to adverse event according to PT: Respiratory, thoracic and mediastinal disorders/Dyspnoea - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Liver Metastasis - BICR (p-value of the interaction term: 0,992)					
Yes*	0/16 (0,0)	NE [NE; NE]	2/13 (15,4)	NE [5,26; NE]	0,00 [0,00; NE] 0,060
No	4/98 (4,1)	NE [NE; NE]	6/59 (10,2)	NE [NE; NE]	0,35 [0,10; 1,24] 0,089
RET Specimen Type (p-value of the interaction term: 0,993)					
Blood*	0/9 (0,0)	NE [NE; NE]	1/10 (10,0)	NE [15,80; NE]	0,00 [0,00; NE] 0,157
Tissue	4/106 (3,8)	NE [NE; NE]	7/62 (11,3)	NE [NE; NE]	0,29 [0,08; 0,99] 0,035
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
 Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx019_sub_msaf_a.rtf
 Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteae_gba
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**Table 133: Subgroups: Time to adverse event according to PT:
Investigations/Electrocardiogram QT prolonged - study LIBRETTO-431, mSAF**

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,993)					
<65 years*	11/76 (14,5)	NE [NE; NE]	0/45 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,008
≥65 years	10/39 (25,6)	NE [NE; NE]	1/27 (3,7)	NE [NE; NE]	7,43 [0,95; 58,15] 0,025
Baseline ECOG (p-value of the interaction term: 0,992)					
0*	3/41 (7,3)	NE [NE; NE]	0/25 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,164
1	18/74 (24,3)	NE [NE; NE]	1/47 (2,1)	NE [NE; NE]	12,44 [1,66; 93,16] 0,002
Sex (p-value of the interaction term: 0,993)					
Male	12/61 (19,7)	NE [NE; NE]	1/34 (2,9)	NE [NE; NE]	7,26 [0,94; 55,94] 0,026
Female*	9/54 (16,7)	NE [NE; NE]	0/38 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,009
Geographic region (p-value of the interaction term: 0,990)					
East Asian	15/65 (23,1)	NE [NE; NE]	1/35 (2,9)	NE [NE; NE]	8,72 [1,15; 66,01] 0,011
Non-EastAsian*	6/50 (12,0)	NE [NE; NE]	0/37 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,030
Smoking Status (p-value of the interaction term: 0,991)					
Never*	16/72 (22,2)	NE [NE; NE]	0/49 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Former/Current	5/43 (11,6)	NE [NE; NE]	1/23 (4,3)	NE [NE; NE]	2,71 [0,32; 23,25] 0,345
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 1,000)					
Yes*	5/23 (21,7)	NE [14,29; NE]	0/14 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,078
No*	6/44 (13,6)	NE [NE; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,060

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	10/48 (20,8)	NE [NE; NE]	1/35 (2,9)	NE [NE; NE]	7,65 [0,98; 59,85] 0,022
Liver Metastasis - BICR (p-value of the interaction term: 0,991)					
Yes*	4/16 (25,0)	NE [14,29; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,099
No	17/98 (17,3)	NE [NE; NE]	1/59 (1,7)	NE [NE; NE]	11,33 [1,51; 85,15] 0,003
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 1,000)					
Negative	2/26 (7,7)	NE [NE; NE]	1/12 (8,3)	NE [NE; NE]	0,96 [0,09; 10,59] 0,974
Positive*	13/49 (26,5)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,002
Unknown*	6/40 (15,0)	NE [NE; NE]	0/26 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,038
Disease Stage (p-value of the interaction term: 1,000)					
III*	2/6 (33,3)	NE [0,26; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,138
IVA*	4/44 (9,1)	NE [NE; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,077
IVB	15/65 (23,1)	NE [NE; NE]	1/34 (2,9)	NE [NE; NE]	8,14 [1,07; 61,69] 0,016
Race (p-value of the interaction term: 0,990)					
Asian	15/66 (22,7)	NE [NE; NE]	1/35 (2,9)	NE [NE; NE]	8,57 [1,13; 64,93] 0,012
Non-Asian*	6/49 (12,2)	NE [NE; NE]	0/33 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,038
RET Specimen Type (p-value of the interaction term: 0,993)					
Blood*	4/9 (44,4)	NE [1,41; NE]	0/10 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,051
Tissue	17/106 (16,0)	NE [NE; NE]	1/62 (1,6)	NE [NE; NE]	10,89 [1,45; 81,82] 0,004
RET Fusion Result **** (p-value of the interaction term: 1,000)					

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
CCDC6*	1/9 (11,1)	NE [1,41; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,414
KIF5B*	10/50 (20,0)	NE [NE; NE]	0/36 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,010
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx020_sub_msaf_a.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 134: Subgroups: Time to adverse event according to PT: Metabolism and nutrition disorders/Hyperglycaemia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Baseline ECOG (p-value of the interaction term: 0,992)					
0*	0/41 (0,0)	NE [NE; NE]	1/25 (4,0)	NE [NE; NE]	0,00 [0,00; NE] 0,206
1	4/74 (5,4)	27,1 [27,07; NE]	8/47 (17,0)	NE [NE; NE]	0,27 [0,08; 0,92] 0,026
Geographic region (p-value of the interaction term: 0,994)					
East Asian	4/65 (6,2)	27,1 [27,07; NE]	6/35 (17,1)	NE [NE; NE]	0,34 [0,09; 1,22] 0,085
Non-EastAsian*	0/50 (0,0)	NE [NE; NE]	3/37 (8,1)	NE [NE; NE]	0,00 [0,00; NE] 0,048
Liver Metastasis - BICR (p-value of the interaction term: 0,991)					
Yes*	0/16 (0,0)	NE [NE; NE]	2/13 (15,4)	NE [NE; NE]	0,00 [0,00; NE] 0,109
No	4/98 (4,1)	NE [27,07; NE]	7/59 (11,9)	NE [NE; NE]	0,30 [0,09; 1,04] 0,045
Race (p-value of the interaction term: 0,993)					
Asian	4/66 (6,1)	27,1 [27,07; NE]	6/35 (17,1)	NE [NE; NE]	0,34 [0,09; 1,21] 0,080
Non-Asian*	0/49 (0,0)	NE [NE; NE]	3/33 (9,1)	NE [NE; NE]	0,00 [0,00; NE] 0,038
RET Specimen Type (p-value of the interaction term: 0,993)					
Blood*	0/9 (0,0)	NE [NE; NE]	1/10 (10,0)	NE [5,55; NE]	0,00 [0,00; NE] 0,221
Tissue	4/106 (3,8)	NE [27,07; NE]	8/62 (12,9)	NE [NE; NE]	0,26 [0,08; 0,87] 0,018

Subgroup	Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.				
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine				

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx024_sub_msaf_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba

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Table 135: Subgroups: Time to adverse event according to PT: Vascular disorders/Hypertension - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,983)					
<65 years	38/76 (50,0)	9,0 [2,86; NE]	5/45 (11,1)	NE [NE; NE]	5,87 [2,31; 14,94] <0,001
≥65 years*	16/39 (41,0)	NE [2,10; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Baseline ECOG (p-value of the interaction term: 0,649)					
0	17/41 (41,5)	NE [2,86; NE]	1/25 (4,0)	NE [NE; NE]	12,81 [1,70; 96,34] 0,001
1	37/74 (50,0)	5,8 [2,99; NE]	4/47 (8,5)	NE [NE; NE]	8,02 [2,85; 22,52] <0,001
Sex (p-value of the interaction term: 0,632)					
Male	29/61 (47,5)	NE [2,86; NE]	3/34 (8,8)	NE [18,40; NE]	7,08 [2,15; 23,26] <0,001
Female	25/54 (46,3)	NE [2,83; NE]	2/38 (5,3)	NE [NE; NE]	11,71 [2,77; 49,54] <0,001
Geographic region (p-value of the interaction term: 0,833)					
East Asian	38/65 (58,5)	4,3 [2,14; NE]	3/35 (8,6)	NE [NE; NE]	9,20 [2,84; 29,83] <0,001
Non-EastAsian	16/50 (32,0)	NE [NE; NE]	2/37 (5,4)	NE [18,40; NE]	7,55 [1,73; 32,89] 0,002
Smoking Status (p-value of the interaction term: 0,621)					
Never	35/72 (48,6)	NE [2,86; NE]	4/49 (8,2)	NE [NE; NE]	7,86 [2,79; 22,14] <0,001
Former/Current	19/43 (44,2)	NE [2,10; NE]	1/23 (4,3)	NE [NE; NE]	13,27 [1,78; 99,25] 0,001
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,782)					
Yes	9/23 (39,1)	NE [2,14; NE]	1/14 (7,1)	NE [NE; NE]	6,67 [0,84; 52,70] 0,038
No	18/44 (40,9)	NE [2,10; NE]	2/23 (8,7)	NE [18,40; NE]	6,36 [1,47; 27,48] 0,005

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	27/48 (56,3)	5,8 [2,83; NE]	2/35 (5,7)	NE [NE; NE]	12,86 [3,05; 54,12] <0,001
Liver Metastasis - BICR (p-value of the interaction term: 0,107)					
Yes	6/16 (37,5)	NE [1,08; NE]	2/13 (15,4)	NE [3,65; NE]	2,58 [0,52; 12,84] 0,230
No	48/98 (49,0)	9,3 [2,99; NE]	3/59 (5,1)	NE [NE; NE]	13,33 [4,15; 42,85] <0,001
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,645)					
TPS <50%	18/48 (37,5)	NE [3,38; NE]	2/27 (7,4)	NE [NE; NE]	6,11 [1,42; 26,37] 0,006
TPS ≥50%	11/19 (57,9)	3,0 [1,45; NE]	1/13 (7,7)	NE [NE; NE]	12,55 [1,61; 97,79] 0,002
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,819)					
TPS <50%	18/48 (37,5)	NE [3,38; NE]	2/27 (7,4)	NE [NE; NE]	6,11 [1,42; 26,37] 0,006
TPS ≥50%	11/19 (57,9)	3,0 [1,45; NE]	1/13 (7,7)	NE [NE; NE]	12,55 [1,61; 97,79] 0,002
Unknown	25/48 (52,1)	9,0 [2,40; NE]	2/32 (6,3)	NE [NE; NE]	11,41 [2,70; 48,22] <0,001
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,905)					
Negative*	10/26 (38,5)	NE [2,43; NE]	0/12 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,017
Positive	22/49 (44,9)	NE [2,83; NE]	3/34 (8,8)	NE [NE; NE]	6,59 [1,97; 22,03] <0,001
Unknown	22/40 (55,0)	5,0 [2,14; NE]	2/26 (7,7)	NE [NE; NE]	10,45 [2,45; 44,55] <0,001
Disease Stage (p-value of the interaction term: 0,946)					
III*	4/6 (66,7)	3,0 [0,26; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,018
IVA	20/44 (45,5)	NE [2,07; NE]	3/32 (9,4)	NE [NE; NE]	6,72 [1,99; 22,71] <0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB	30/65 (46,2)	NE [3,65; NE]	2/34 (5,9)	NE [NE; NE]	9,78 [2,34; 40,92] <0,001
Race (p-value of the interaction term: 0,780)					
Asian	38/66 (57,6)	4,3 [2,14; NE]	3/35 (8,6)	NE [NE; NE]	8,98 [2,77; 29,11] <0,001
Non-Asian	16/49 (32,7)	NE [6,93; NE]	2/33 (6,1)	NE [18,40; NE]	6,90 [1,58; 30,07] 0,003
RET Specimen Type (p-value of the interaction term: 0,892)					
Blood	6/9 (66,7)	1,4 [0,03; NE]	1/10 (10,0)	NE [6,97; NE]	9,95 [1,19; 83,27] 0,009
Tissue	48/106 (45,3)	NE [4,27; NE]	4/62 (6,5)	NE [NE; NE]	9,22 [3,32; 25,59] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,992)					
CCDC6*	7/9 (77,8)	2,4 [0,46; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,010
KIF5B	24/50 (48,0)	NE [2,14; NE]	2/36 (5,6)	NE [NE; NE]	10,56 [2,49; 44,71] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx025_sub_msaf_a.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 136: Subgroups: Time to adverse event according to PT: Metabolism and nutrition disorders/Hypocalcaemia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
RET Specimen Type (p-value of the interaction term: 0,998)					
Blood*	0/9 (0,0)	NE [NE; NE]	0/10 (0,0)	NE [NE; NE]	NE
Tissue*	10/106 (9,4)	NE [NE; NE]	0/62 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,015
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
 Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx027_sub_msaf_a.rtf
 Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 137: Subgroups: Time to adverse event according to PT: Eye disorders/Lacrimation increased - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Liver Metastasis - BICR (p-value of the interaction term: 0,993)					
Yes*	0/16 (0,0)	NE [NE; NE]	1/13 (7,7)	NE [NE; NE]	0,00 [0,00; NE] 0,283
No	2/98 (2,0)	NE [NE; NE]	8/59 (13,6)	NE [NE; NE]	0,14 [0,03; 0,65] 0,003
RET Specimen Type (p-value of the interaction term: 0,999)					
Blood*	0/9 (0,0)	NE [NE; NE]	0/10 (0,0)	NE [NE; NE]	NE
Tissue	2/106 (1,9)	NE [NE; NE]	9/62 (14,5)	NE [NE; NE]	0,12 [0,02; 0,53] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
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 Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 138: Subgroups: Time to adverse event according to PT: Gastrointestinal disorders/Nausea - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,824)					
<65 years	11/76 (14,5)	NE [NE; NE]	20/45 (44,4)	NE [0,49; NE]	0,23 [0,11; 0,48] <0,001
≥65 years	5/39 (12,8)	NE [NE; NE]	10/27 (37,0)	NE [0,26; NE]	0,27 [0,09; 0,78] 0,010
Baseline ECOG (p-value of the interaction term: 0,898)					
0	7/41 (17,1)	NE [NE; NE]	12/25 (48,0)	NE [0,16; NE]	0,25 [0,10; 0,65] 0,002
1	9/74 (12,2)	NE [NE; NE]	18/47 (38,3)	NE [1,48; NE]	0,23 [0,10; 0,52] <0,001
Sex (p-value of the interaction term: 0,153)					
Male	4/61 (6,6)	NE [NE; NE]	13/34 (38,2)	NE [1,48; NE]	0,13 [0,04; 0,40] <0,001
Female	12/54 (22,2)	NE [NE; NE]	17/38 (44,7)	NE [0,16; NE]	0,36 [0,17; 0,75] 0,005
Geographic region (p-value of the interaction term: 0,459)					
East Asian	7/65 (10,8)	NE [NE; NE]	9/35 (25,7)	NE [NE; NE]	0,33 [0,12; 0,89] 0,022
Non-EastAsian	9/50 (18,0)	NE [NE; NE]	21/37 (56,8)	1,5 [0,13; NE]	0,21 [0,09; 0,45] <0,001
Smoking Status (p-value of the interaction term: 0,650)					
Never	11/72 (15,3)	NE [NE; NE]	20/49 (40,8)	NE [1,48; NE]	0,27 [0,13; 0,57] <0,001
Former/Current	5/43 (11,6)	NE [NE; NE]	10/23 (43,5)	NE [0,26; NE]	0,20 [0,07; 0,58] 0,001
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,771)					
Yes	2/23 (8,7)	NE [NE; NE]	6/14 (42,9)	8,2 [0,72; NE]	0,14 [0,03; 0,70] 0,006
No	6/44 (13,6)	NE [NE; NE]	10/23 (43,5)	NE [0,13; NE]	0,22 [0,08; 0,61] 0,002

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	8/48 (16,7)	NE [NE; NE]	14/35 (40,0)	NE [0,16; NE]	0,31 [0,13; 0,74] 0,006
Liver Metastasis - BICR (p-value of the interaction term: 0,999)					
Yes	2/16 (12,5)	NE [NE; NE]	5/13 (38,5)	NE [0,49; NE]	0,25 [0,05; 1,31] 0,077
No	14/98 (14,3)	NE [NE; NE]	25/59 (42,4)	NE [0,72; NE]	0,25 [0,13; 0,47] <0,001
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,742)					
TPS <50%	7/48 (14,6)	NE [NE; NE]	11/27 (40,7)	NE [0,16; NE]	0,26 [0,10; 0,68] 0,003
TPS ≥50%	5/19 (26,3)	NE [9,95; NE]	7/13 (53,8)	1,6 [0,07; NE]	0,34 [0,11; 1,06] 0,055
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,686)					
TPS <50%	7/48 (14,6)	NE [NE; NE]	11/27 (40,7)	NE [0,16; NE]	0,26 [0,10; 0,68] 0,003
TPS ≥50%	5/19 (26,3)	NE [9,95; NE]	7/13 (53,8)	1,6 [0,07; NE]	0,34 [0,11; 1,06] 0,055
Unknown	4/48 (8,3)	NE [NE; NE]	12/32 (37,5)	NE [1,48; NE]	0,17 [0,06; 0,54] <0,001
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,185)					
Negative	1/26 (3,8)	NE [NE; NE]	5/12 (41,7)	NE [0,10; NE]	0,07 [0,01; 0,61] 0,002
Positive	11/49 (22,4)	NE [NE; NE]	14/34 (41,2)	NE [0,49; NE]	0,38 [0,17; 0,85] 0,015
Unknown	4/40 (10,0)	NE [NE; NE]	11/26 (42,3)	NE [0,13; NE]	0,18 [0,06; 0,57] 0,001
Disease Stage (p-value of the interaction term: 0,666)					
III*	0/6 (0,0)	NE [NE; NE]	1/6 (16,7)	NE [0,13; NE]	0,00 [0,00; NE] 0,317
IVA	6/44 (13,6)	NE [NE; NE]	16/32 (50,0)	NE [0,10; NE]	0,19 [0,07; 0,49] <0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB	10/65 (15,4)	NE [NE; NE]	13/34 (38,2)	NE [1,64; NE]	0,29 [0,13; 0,67] 0,002
Race (p-value of the interaction term: 0,582)					
Asian	7/66 (10,6)	NE [NE; NE]	9/35 (25,7)	NE [NE; NE]	0,33 [0,12; 0,88] 0,020
Non-Asian	9/49 (18,4)	NE [NE; NE]	18/33 (54,5)	1,6 [0,16; NE]	0,23 [0,10; 0,51] <0,001
RET Specimen Type (p-value of the interaction term: 0,349)					
Blood	1/9 (11,1)	NE [12,48; NE]	6/10 (60,0)	0,8 [0,03; NE]	0,09 [0,01; 0,85] 0,012
Tissue	15/106 (14,2)	NE [NE; NE]	24/62 (38,7)	NE [7,36; NE]	0,28 [0,14; 0,53] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,713)					
CCDC6	1/9 (11,1)	NE [0,53; NE]	2/6 (33,3)	NE [0,10; NE]	0,27 [0,02; 3,03] 0,272
KIF5B	11/50 (22,0)	NE [NE; NE]	14/36 (38,9)	NE [1,48; NE]	0,39 [0,18; 0,87] 0,018
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx031_sub_msaf_a.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 139: Subgroups: Time to adverse event according to PT: Blood and lymphatic system disorders/Neutropenia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,990)					
<65 years	4/76 (5,3)	NE [NE; NE]	8/45 (17,8)	NE [NE; NE]	0,28 [0,08; 0,94] 0,027
≥65 years*	0/39 (0,0)	NE [NE; NE]	6/27 (22,2)	NE [NE; NE]	0,00 [0,00; NE] 0,001
Sex (p-value of the interaction term: 0,295)					
Male	1/61 (1,6)	NE [NE; NE]	7/34 (20,6)	NE [NE; NE]	0,07 [0,01; 0,58] 0,001
Female	3/54 (5,6)	NE [NE; NE]	7/38 (18,4)	NE [NE; NE]	0,29 [0,07; 1,11] 0,053
Geographic region (p-value of the interaction term: 0,237)					
East Asian	2/65 (3,1)	NE [NE; NE]	2/35 (5,7)	NE [NE; NE]	0,54 [0,08; 3,83] 0,530
Non-EastAsian	2/50 (4,0)	NE [NE; NE]	12/37 (32,4)	NE [7,56; NE]	0,11 [0,02; 0,50] <0,001
Smoking Status (p-value of the interaction term: 0,993)					
Never	4/72 (5,6)	NE [NE; NE]	10/49 (20,4)	NE [NE; NE]	0,25 [0,08; 0,81] 0,012
Former/Current*	0/43 (0,0)	NE [NE; NE]	4/23 (17,4)	NE [NE; NE]	0,00 [0,00; NE] 0,005
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,559)					
Yes*	0/23 (0,0)	NE [NE; NE]	3/14 (21,4)	NE [7,23; NE]	0,00 [0,00; NE] 0,014
No	2/44 (4,5)	NE [NE; NE]	2/23 (8,7)	NE [NE; NE]	0,56 [0,08; 3,96] 0,554
Unknown	2/48 (4,2)	NE [NE; NE]	9/35 (25,7)	NE [NE; NE]	0,14 [0,03; 0,65] 0,003
Liver Metastasis - BICR (p-value of the interaction term: 1,000)					
Yes*	0/16 (0,0)	NE [NE; NE]	0/13 (0,0)	NE [NE; NE]	NE

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
No	4/98 (4,1)	NE [NE; NE]	14/59 (23,7)	NE [NE; NE]	0,16 [0,05; 0,49] <0,001
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,906)					
Negative	1/26 (3,8)	NE [NE; NE]	1/12 (8,3)	NE [NE; NE]	0,47 [0,03; 7,53] 0,585
Positive	3/49 (6,1)	NE [NE; NE]	9/34 (26,5)	NE [NE; NE]	0,21 [0,06; 0,78] 0,010
Unknown*	0/40 (0,0)	NE [NE; NE]	4/26 (15,4)	NE [NE; NE]	0,00 [0,00; NE] 0,011
Disease Stage (p-value of the interaction term: 1,000)					
III*	0/6 (0,0)	NE [NE; NE]	0/6 (0,0)	NE [NE; NE]	NE
IVA*	0/44 (0,0)	NE [NE; NE]	6/32 (18,8)	NE [NE; NE]	0,00 [0,00; NE] 0,003
IVB	4/65 (6,2)	NE [NE; NE]	8/34 (23,5)	NE [NE; NE]	0,24 [0,07; 0,79] 0,011
Race (p-value of the interaction term: 0,323)					
Asian	2/66 (3,0)	NE [NE; NE]	2/35 (5,7)	NE [NE; NE]	0,53 [0,07; 3,77] 0,520
Non-Asian	2/49 (4,1)	NE [NE; NE]	9/33 (27,3)	NE [NE; NE]	0,14 [0,03; 0,65] 0,004
RET Specimen Type (p-value of the interaction term: 1,000)					
Blood*	0/9 (0,0)	NE [NE; NE]	0/10 (0,0)	NE [NE; NE]	NE
Tissue	4/106 (3,8)	NE [NE; NE]	14/62 (22,6)	NE [NE; NE]	0,16 [0,05; 0,47] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,996)					
CCDC6*	0/9 (0,0)	NE [NE; NE]	1/6 (16,7)	NE [2,07; NE]	0,00 [0,00; NE] 0,221
KIF5B	1/50 (2,0)	NE [NE; NE]	9/36 (25,0)	NE [NE; NE]	0,06 [0,01; 0,50] <0,001

Subgroup	Selpercatinib	Median time to event ^a [95% CI]	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab	Median time to event ^a [95% CI]	HR [95% CI] p-value ^b
	n/N (%)		n/N (%)		
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx032_sub_msa_f_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 140: Subgroups: Time to adverse event according to PT: Skin and subcutaneous tissue disorders/Pruritus - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,809)					
<65 years	9/76 (11,8)	31,0 [NE; NE]	9/45 (20,0)	NE [NE; NE]	0,44 [0,17; 1,16] 0,088
≥65 years	4/39 (10,3)	NE [NE; NE]	7/27 (25,9)	NE [12,22; NE]	0,34 [0,10; 1,18] 0,076
Baseline ECOG (p-value of the interaction term: 0,967)					
0	7/41 (17,1)	31,0 [NE; NE]	8/25 (32,0)	NE [9,20; NE]	0,38 [0,13; 1,09] 0,062
1	6/74 (8,1)	NE [NE; NE]	8/47 (17,0)	NE [NE; NE]	0,42 [0,14; 1,20] 0,094
Sex (p-value of the interaction term: 0,958)					
Male	6/61 (9,8)	NE [NE; NE]	7/34 (20,6)	NE [12,22; NE]	0,39 [0,13; 1,17] 0,083
Female	7/54 (13,0)	31,0 [NE; NE]	9/38 (23,7)	NE [NE; NE]	0,41 [0,15; 1,15] 0,080
Geographic region (p-value of the interaction term: 0,764)					
East Asian	5/65 (7,7)	NE [NE; NE]	6/35 (17,1)	NE [NE; NE]	0,39 [0,12; 1,29] 0,112
Non-EastAsian	8/50 (16,0)	31,0 [NE; NE]	10/37 (27,0)	NE [12,22; NE]	0,44 [0,17; 1,15] 0,085
Smoking Status (p-value of the interaction term: 0,990)					
Never	7/72 (9,7)	NE [NE; NE]	10/49 (20,4)	NE [NE; NE]	0,40 [0,15; 1,07] 0,058
Former/Current	6/43 (14,0)	31,0 [NE; NE]	6/23 (26,1)	NE [12,22; NE]	0,37 [0,11; 1,23] 0,091
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,221)					
Yes	3/23 (13,0)	NE [NE; NE]	4/14 (28,6)	NE [6,90; NE]	0,31 [0,07; 1,45] 0,119
No	1/44 (2,3)	NE [NE; NE]	5/23 (21,7)	NE [NE; NE]	0,10 [0,01; 0,82] 0,008

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	9/48 (18,8)	31,0 [NE; NE]	7/35 (20,0)	NE [NE; NE]	0,72 [0,26; 1,98] 0,522
Liver Metastasis - BICR (p-value of the interaction term: 0,990)					
Yes*	0/16 (0,0)	NE [NE; NE]	2/13 (15,4)	NE [4,73; NE]	0,00 [0,00; NE] 0,073
No	13/98 (13,3)	31,0 [NE; NE]	14/59 (23,7)	NE [NE; NE]	0,45 [0,21; 0,98] 0,038
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,991)					
TPS <50%	6/48 (12,5)	NE [NE; NE]	9/27 (33,3)	NE [3,38; NE]	0,29 [0,10; 0,82] 0,013
TPS ≥50%*	0/19 (0,0)	NE [NE; NE]	3/13 (23,1)	NE [12,22; NE]	0,00 [0,00; NE] 0,031
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,348)					
TPS <50%	6/48 (12,5)	NE [NE; NE]	9/27 (33,3)	NE [3,38; NE]	0,29 [0,10; 0,82] 0,013
TPS ≥50%*	0/19 (0,0)	NE [NE; NE]	3/13 (23,1)	NE [12,22; NE]	0,00 [0,00; NE] 0,031
Unknown	7/48 (14,6)	31,0 [NE; NE]	4/32 (12,5)	NE [NE; NE]	0,91 [0,26; 3,24] 0,886
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,099)					
Negative	3/26 (11,5)	NE [NE; NE]	3/12 (25,0)	NE [3,02; NE]	0,37 [0,07; 1,84] 0,205
Positive	4/49 (8,2)	31,0 [NE; NE]	10/34 (29,4)	NE [12,22; NE]	0,17 [0,05; 0,61] 0,002
Unknown	6/40 (15,0)	NE [NE; NE]	3/26 (11,5)	NE [NE; NE]	1,25 [0,31; 5,00] 0,753
Disease Stage (p-value of the interaction term: 0,803)					
III*	0/6 (0,0)	NE [NE; NE]	1/6 (16,7)	NE [0,26; NE]	0,00 [0,00; NE] 0,317
IVA	4/44 (9,1)	31,0 [NE; NE]	7/32 (21,9)	NE [NE; NE]	0,28 [0,07; 1,09] 0,051

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB	9/65 (13,8)	NE [NE; NE]	8/34 (23,5)	NE [12,22; NE]	0,45 [0,17; 1,18] 0,095
Race (p-value of the interaction term: 0,616)					
Asian	5/66 (7,6)	NE [NE; NE]	6/35 (17,1)	NE [NE; NE]	0,39 [0,12; 1,27] 0,106
Non-Asian	8/49 (16,3)	31,0 [NE; NE]	8/33 (24,2)	NE [NE; NE]	0,51 [0,19; 1,42] 0,191
RET Specimen Type (p-value of the interaction term: 0,974)					
Blood	1/9 (11,1)	NE [1,12; NE]	2/10 (20,0)	NE [0,10; NE]	0,50 [0,04; 5,50] 0,561
Tissue	12/106 (11,3)	31,0 [NE; NE]	14/62 (22,6)	NE [NE; NE]	0,40 [0,18; 0,87] 0,018
RET Fusion Result **** (p-value of the interaction term: 0,993)					
CCDC6	1/9 (11,1)	31,0 [NE; NE]	2/6 (33,3)	NE [0,23; NE]	0,00 [0,00; NE] 0,070
KIF5B	5/50 (10,0)	NE [NE; NE]	7/36 (19,4)	NE [12,22; NE]	0,39 [0,12; 1,23] 0,095
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx036_sub_msaf_a.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 141: Subgroups: Time to adverse event according to PT: General disorders and administration site conditions/Pyrexia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,701)					
<65 years	9/76 (11,8)	NE [NE; NE]	9/45 (20,0)	NE [23,89; NE]	0,49 [0,19; 1,25] 0,128
≥65 years	6/39 (15,4)	NE [NE; NE]	9/27 (33,3)	NE [5,55; NE]	0,39 [0,14; 1,10] 0,066
Baseline ECOG (p-value of the interaction term: 0,477)					
0	5/41 (12,2)	NE [NE; NE]	8/25 (32,0)	NE [11,37; NE]	0,32 [0,11; 0,99] 0,038
1	10/74 (13,5)	NE [NE; NE]	10/47 (21,3)	NE [23,89; NE]	0,57 [0,23; 1,37] 0,198
Sex (p-value of the interaction term: 0,207)					
Male	11/61 (18,0)	NE [NE; NE]	8/34 (23,5)	NE [NE; NE]	0,64 [0,26; 1,61] 0,342
Female	4/54 (7,4)	NE [NE; NE]	10/38 (26,3)	23,9 [12,29; NE]	0,23 [0,07; 0,76] 0,008
Geographic region (p-value of the interaction term: 0,411)					
East Asian	9/65 (13,8)	NE [NE; NE]	7/35 (20,0)	NE [12,29; NE]	0,62 [0,23; 1,67] 0,335
Non-EastAsian	6/50 (12,0)	NE [NE; NE]	11/37 (29,7)	NE [11,37; NE]	0,34 [0,12; 0,93] 0,028
Smoking Status (p-value of the interaction term: 0,724)					
Never	9/72 (12,5)	NE [NE; NE]	13/49 (26,5)	NE [23,89; NE]	0,43 [0,18; 1,00] 0,044
Former/Current	6/43 (14,0)	NE [NE; NE]	5/23 (21,7)	NE [11,37; NE]	0,51 [0,15; 1,68] 0,256
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,985)					
Yes	3/23 (13,0)	NE [NE; NE]	3/14 (21,4)	NE [3,68; NE]	0,54 [0,11; 2,68] 0,441
No	5/44 (11,4)	NE [NE; NE]	6/23 (26,1)	NE [11,37; NE]	0,41 [0,12; 1,34] 0,126

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	7/48 (14,6)	NE [NE; NE]	9/35 (25,7)	NE [23,89; NE]	0,43 [0,16; 1,18] 0,091
Liver Metastasis - BICR (p-value of the interaction term: 0,245)					
Yes	1/16 (6,3)	NE [NE; NE]	4/13 (30,8)	NE [3,02; NE]	0,14 [0,02; 1,30] 0,047
No	13/98 (13,3)	NE [NE; NE]	14/59 (23,7)	NE [23,89; NE]	0,50 [0,24; 1,07] 0,071
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 1,000)					
TPS <50%	10/48 (20,8)	NE [NE; NE]	9/27 (33,3)	NE [7,39; NE]	0,52 [0,21; 1,30] 0,158
TPS ≥50%*	0/19 (0,0)	NE [NE; NE]	0/13 (0,0)	NE [NE; NE]	NE
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,764)					
TPS <50%	10/48 (20,8)	NE [NE; NE]	9/27 (33,3)	NE [7,39; NE]	0,52 [0,21; 1,30] 0,158
TPS ≥50%*	0/19 (0,0)	NE [NE; NE]	0/13 (0,0)	NE [NE; NE]	NE
Unknown	5/48 (10,4)	NE [NE; NE]	9/32 (28,1)	NE [12,29; NE]	0,29 [0,10; 0,86] 0,018
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,400)					
Negative	7/26 (26,9)	NE [14,39; NE]	3/12 (25,0)	NE [3,68; NE]	0,91 [0,23; 3,58] 0,897
Positive	4/49 (8,2)	NE [NE; NE]	8/34 (23,5)	NE [11,37; NE]	0,30 [0,09; 0,99] 0,037
Unknown	4/40 (10,0)	NE [NE; NE]	7/26 (26,9)	NE [12,29; NE]	0,31 [0,09; 1,06] 0,047
Disease Stage (p-value of the interaction term: 0,927)					
III*	0/6 (0,0)	NE [NE; NE]	0/6 (0,0)	NE [NE; NE]	NE
IVA	6/44 (13,6)	NE [NE; NE]	8/32 (25,0)	NE [11,37; NE]	0,48 [0,16; 1,38] 0,164
IVB	9/65 (13,8)	NE [NE; NE]	10/34 (29,4)	23,9 [7,39; NE]	0,37 [0,15; 0,93] 0,028
Race (p-value of the interaction term: 0,412)					

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Asian	9/66 (13,6)	NE [NE; NE]	7/35 (20,0)	NE [12,29; NE]	0,61 [0,23; 1,64] 0,321
Non-Asian	6/49 (12,2)	NE [NE; NE]	10/33 (30,3)	NE [11,37; NE]	0,34 [0,12; 0,94] 0,029
RET Specimen Type (p-value of the interaction term: 0,600)					
Blood	1/9 (11,1)	NE [0,30; NE]	1/10 (10,0)	NE [5,26; NE]	0,91 [0,06; 14,79] 0,949
Tissue	14/106 (13,2)	NE [NE; NE]	17/62 (27,4)	NE [23,89; NE]	0,41 [0,20; 0,84] 0,012
RET Fusion Result **** (p-value of the interaction term: 0,864)					
CCDC6	2/9 (22,2)	NE [0,62; NE]	2/6 (33,3)	NE [5,26; NE]	0,70 [0,10; 5,02] 0,724
KIF5B	8/50 (16,0)	NE [NE; NE]	6/36 (16,7)	NE [NE; NE]	0,86 [0,30; 2,49] 0,782
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx037_sub_msaf_a.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 142: Subgroups: Time to adverse event according to PT: Gastrointestinal disorders/Vomiting - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Baseline ECOG (p-value of the interaction term: 0,428)					
0	8/41 (19,5)	NE [22,87; NE]	7/25 (28,0)	NE [14,75; NE]	0,54 [0,19; 1,51] 0,231
1	7/74 (9,5)	NE [NE; NE]	11/47 (23,4)	NE [NE; NE]	0,35 [0,14; 0,90] 0,024
Sex (p-value of the interaction term: 0,245)					
Male	3/61 (4,9)	NE [NE; NE]	6/34 (17,6)	NE [14,75; NE]	0,22 [0,05; 0,90] 0,022
Female	12/54 (22,2)	NE [22,87; NE]	12/38 (31,6)	NE [8,31; NE]	0,59 [0,27; 1,32] 0,198
Geographic region (p-value of the interaction term: 0,680)					
East Asian	7/65 (10,8)	NE [NE; NE]	8/35 (22,9)	NE [14,75; NE]	0,38 [0,14; 1,06] 0,055
Non-EastAsian	8/50 (16,0)	NE [22,87; NE]	10/37 (27,0)	NE [NE; NE]	0,50 [0,20; 1,27] 0,138
Smoking Status (p-value of the interaction term: 0,212)					
Never	13/72 (18,1)	NE [NE; NE]	13/49 (26,5)	NE [NE; NE]	0,57 [0,26; 1,24] 0,150
Former/Current	2/43 (4,7)	NE [NE; NE]	5/23 (21,7)	NE [14,75; NE]	0,17 [0,03; 0,88] 0,017
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,475)					
Yes	2/23 (8,7)	NE [NE; NE]	4/14 (28,6)	NE [6,28; NE]	0,26 [0,05; 1,41] 0,092
No	5/44 (11,4)	NE [NE; NE]	7/23 (30,4)	NE [1,51; NE]	0,33 [0,11; 1,05] 0,049
Unknown	8/48 (16,7)	NE [NE; NE]	7/35 (20,0)	NE [NE; NE]	0,64 [0,23; 1,78] 0,387
Liver Metastasis - BICR (p-value of the interaction term: 0,985)					
Yes*	0/16 (0,0)	NE [NE; NE]	6/13 (46,2)	8,3 [1,08; NE]	0,00 [0,00; NE] 0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
No	15/98 (15,3)	NE [NE; NE]	12/59 (20,3)	NE [NE; NE]	0,66 [0,31; 1,42] 0,287
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,071)					
TPS <50%	6/48 (12,5)	NE [NE; NE]	10/27 (37,0)	14,8 [1,45; NE]	0,22 [0,08; 0,63] 0,002
TPS ≥50%	3/19 (15,8)	NE [NE; NE]	1/13 (7,7)	NE [NE; NE]	2,11 [0,22; 20,27] 0,509
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,170)					
TPS <50%	6/48 (12,5)	NE [NE; NE]	10/27 (37,0)	14,8 [1,45; NE]	0,22 [0,08; 0,63] 0,002
TPS ≥50%	3/19 (15,8)	NE [NE; NE]	1/13 (7,7)	NE [NE; NE]	2,11 [0,22; 20,27] 0,509
Unknown	6/48 (12,5)	NE [NE; NE]	7/32 (21,9)	NE [NE; NE]	0,49 [0,16; 1,46] 0,191
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,825)					
Negative*	0/26 (0,0)	NE [NE; NE]	4/12 (33,3)	NE [0,79; NE]	0,00 [0,00; NE] 0,002
Positive	10/49 (20,4)	NE [22,87; NE]	8/34 (23,5)	NE [14,75; NE]	0,76 [0,30; 1,94] 0,569
Unknown	5/40 (12,5)	NE [NE; NE]	6/26 (23,1)	NE [NE; NE]	0,48 [0,15; 1,57] 0,212
Disease Stage (p-value of the interaction term: 0,807)					
III*	0/6 (0,0)	NE [NE; NE]	0/6 (0,0)	NE [NE; NE]	NE
IVA	7/44 (15,9)	NE [NE; NE]	8/32 (25,0)	NE [NE; NE]	0,56 [0,20; 1,55] 0,259
IVB	8/65 (12,3)	NE [NE; NE]	10/34 (29,4)	NE [14,75; NE]	0,32 [0,13; 0,82] 0,012
Race (p-value of the interaction term: 0,655)					
Asian	7/66 (10,6)	NE [NE; NE]	8/35 (22,9)	NE [14,75; NE]	0,38 [0,14; 1,04] 0,051
Non-Asian	8/49 (16,3)	NE [22,87; NE]	9/33 (27,3)	NE [NE; NE]	0,50 [0,19; 1,31] 0,149

Subgroup	Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab			HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
RET Specimen Type (p-value of the interaction term: 0,316)					
Blood	3/9 (33,3)	NE [0,03; NE]	3/10 (30,0)	NE [0,13; NE]	0,95 [0,19; 4,75] 0,950
Tissue	12/106 (11,3)	NE [NE; NE]	15/62 (24,2)	NE [NE; NE]	0,38 [0,18; 0,82] 0,011
RET Fusion Result **** (p-value of the interaction term: 0,798)					
CCDC6	4/9 (44,4)	NE [0,72; NE]	2/6 (33,3)	NE [0,13; NE]	1,14 [0,21; 6,21] 0,884
KIF5B	8/50 (16,0)	NE [22,87; NE]	6/36 (16,7)	NE [NE; NE]	0,77 [0,26; 2,23] 0,626
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aeppx040_sub_msaf_a.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteae_gba
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Table 143: Subgroups: Time to adverse event according to SOC: Blood and lymphatic system disorders - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Baseline ECOG (p-value of the interaction term: 0,418)					
0	10/41 (24,4)	NE [NE; NE]	17/25 (68,0)	2,1 [1,22; 10,48]	0,23 [0,10; 0,51] <0,001
1	22/74 (29,7)	NE [22,54; NE]	30/47 (63,8)	3,5 [1,38; 6,31]	0,35 [0,20; 0,61] <0,001
Sex (p-value of the interaction term: 0,436)					
Male	18/61 (29,5)	NE [22,54; NE]	21/34 (61,8)	4,2 [1,38; NE]	0,36 [0,19; 0,68] 0,001
Female	14/54 (25,9)	NE [NE; NE]	26/38 (68,4)	2,2 [1,22; 4,17]	0,26 [0,13; 0,50] <0,001
Geographic region (p-value of the interaction term: 0,570)					
East Asian	20/65 (30,8)	NE [22,54; NE]	22/35 (62,9)	2,1 [1,22; NE]	0,36 [0,19; 0,66] <0,001
Non-EastAsian	12/50 (24,0)	NE [NE; NE]	25/37 (67,6)	4,1 [1,38; 10,48]	0,24 [0,12; 0,49] <0,001
Smoking Status (p-value of the interaction term: 0,713)					
Never	18/72 (25,0)	NE [NE; NE]	31/49 (63,3)	2,1 [1,35; 5,78]	0,30 [0,17; 0,54] <0,001
Former/Current	14/43 (32,6)	NE [11,96; NE]	16/23 (69,6)	4,1 [1,41; 10,48]	0,29 [0,14; 0,61] <0,001
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,678)					
Yes	7/23 (30,4)	NE [10,35; NE]	7/14 (50,0)	2,2 [0,49; NE]	0,39 [0,13; 1,13] 0,074
No	9/44 (20,5)	NE [NE; NE]	15/23 (65,2)	1,4 [0,92; NE]	0,25 [0,11; 0,57] <0,001
Unknown	16/48 (33,3)	NE [22,54; NE]	25/35 (71,4)	2,9 [1,41; 4,90]	0,33 [0,17; 0,62] <0,001
Liver Metastasis - BICR (p-value of the interaction term: 0,316)					
Yes	1/16 (6,3)	NE [NE; NE]	6/13 (46,2)	6,3 [4,17; NE]	0,06 [0,01; 0,56] 0,002

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
No	31/98 (31,6)	NE [22,54; NE]	41/59 (69,5)	1,9 [1,22; 3,48]	0,32 [0,20; 0,52] <0,001
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,872)					
TPS <50%	13/48 (27,1)	NE [22,54; NE]	17/27 (63,0)	4,2 [1,38; NE]	0,29 [0,14; 0,61] <0,001
TPS ≥50%	5/19 (26,3)	NE [10,38; NE]	8/13 (61,5)	2,2 [0,46; NE]	0,28 [0,09; 0,90] 0,023
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,991)					
TPS <50%	13/48 (27,1)	NE [22,54; NE]	17/27 (63,0)	4,2 [1,38; NE]	0,29 [0,14; 0,61] <0,001
TPS ≥50%	5/19 (26,3)	NE [10,38; NE]	8/13 (61,5)	2,2 [0,46; NE]	0,28 [0,09; 0,90] 0,023
Unknown	14/48 (29,2)	NE [NE; NE]	22/32 (68,8)	1,9 [1,18; 6,31]	0,32 [0,16; 0,63] <0,001
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,846)					
Negative	8/26 (30,8)	NE [11,63; NE]	7/12 (58,3)	6,5 [0,26; NE]	0,36 [0,13; 0,99] 0,039
Positive	13/49 (26,5)	NE [22,54; NE]	21/34 (61,8)	4,1 [1,41; 5,78]	0,31 [0,15; 0,63] <0,001
Unknown	11/40 (27,5)	NE [NE; NE]	19/26 (73,1)	1,6 [0,72; 6,31]	0,26 [0,12; 0,56] <0,001
Disease Stage (p-value of the interaction term: 0,501)					
III	1/6 (16,7)	NE [0,46; NE]	4/6 (66,7)	3,1 [1,22; NE]	0,22 [0,02; 1,99] 0,140
IVA	9/44 (20,5)	NE [22,54; NE]	19/32 (59,4)	1,7 [0,59; NE]	0,22 [0,10; 0,51] <0,001
IVB	22/65 (33,8)	NE [NE; NE]	24/34 (70,6)	2,9 [1,41; 5,78]	0,35 [0,19; 0,63] <0,001
Race (p-value of the interaction term: 0,686)					
Asian	20/66 (30,3)	NE [22,54; NE]	22/35 (62,9)	2,1 [1,22; NE]	0,35 [0,19; 0,65] <0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Non-Asian	12/49 (24,5)	NE [NE; NE]	22/33 (66,7)	4,2 [1,38; 11,10]	0,26 [0,13; 0,54] <0,001
RET Specimen Type (p-value of the interaction term: 0,207)					
Blood	2/9 (22,2)	NE [2,14; NE]	2/10 (20,0)	NE [2,20; NE]	1,06 [0,15; 7,57] 0,950
Tissue	30/106 (28,3)	NE [NE; NE]	45/62 (72,6)	1,9 [1,22; 4,17]	0,26 [0,17; 0,42] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,309)					
CCDC6	5/9 (55,6)	22,5 [0,76; NE]	5/6 (83,3)	2,5 [0,46; NE]	0,43 [0,12; 1,63] 0,205
KIF5B	12/50 (24,0)	NE [NE; NE]	22/36 (61,1)	2,2 [1,35; NE]	0,23 [0,11; 0,48] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteae_gba
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Table 144: Subgroups: Time to adverse event according to SOC: General disorders and administration site conditions - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,425)					
<65 years	47/76 (61,8)	5,1 [1,77; 9,69]	28/45 (62,2)	2,1 [0,26; 23,89]	0,76 [0,48; 1,21] 0,260
≥65 years	24/39 (61,5)	5,1 [0,99; 9,46]	22/27 (81,5)	1,2 [0,16; 4,83]	0,55 [0,30; 0,98] 0,041
Baseline ECOG (p-value of the interaction term: 0,666)					
0	29/41 (70,7)	4,9 [1,45; 9,46]	19/25 (76,0)	1,0 [0,16; 2,17]	0,59 [0,33; 1,06] 0,076
1	42/74 (56,8)	5,3 [1,61; NE]	31/47 (66,0)	2,9 [0,26; 6,64]	0,70 [0,44; 1,12] 0,140
Sex (p-value of the interaction term: 0,343)					
Male	38/61 (62,3)	5,5 [1,18; 11,73]	26/34 (76,5)	1,3 [0,16; 3,02]	0,56 [0,34; 0,92] 0,021
Female	33/54 (61,1)	5,1 [2,04; 9,46]	24/38 (63,2)	2,2 [0,39; 23,89]	0,81 [0,48; 1,37] 0,430
Geographic region (p-value of the interaction term: 0,476)					
East Asian	37/65 (56,9)	5,9 [1,77; NE]	21/35 (60,0)	5,1 [0,82; 23,89]	0,79 [0,46; 1,35] 0,394
Non-EastAsian	34/50 (68,0)	4,8 [1,18; 7,72]	29/37 (78,4)	0,8 [0,26; 2,89]	0,60 [0,36; 0,99] 0,048
Smoking Status (p-value of the interaction term: 0,137)					
Never	40/72 (55,6)	6,7 [2,04; NE]	29/49 (59,2)	2,3 [0,99; NE]	0,79 [0,49; 1,27] 0,328
Former/Current	31/43 (72,1)	3,9 [1,18; 6,90]	21/23 (91,3)	0,3 [0,16; 1,77]	0,40 [0,22; 0,71] 0,002
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,741)					
Yes	15/23 (65,2)	2,8 [1,08; NE]	10/14 (71,4)	1,9 [0,26; 5,13]	0,64 [0,28; 1,43] 0,294
No	26/44 (59,1)	4,8 [1,25; NE]	17/23 (73,9)	1,1 [0,10; 2,89]	0,56 [0,30; 1,03] 0,059

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	30/48 (62,5)	5,9 [1,22; 14,39]	23/35 (65,7)	2,2 [0,26; 23,89]	0,75 [0,44; 1,30] 0,309
Liver Metastasis - BICR (p-value of the interaction term: 0,139)					
Yes	6/16 (37,5)	NE [0,66; NE]	10/13 (76,9)	3,0 [0,16; 5,26]	0,30 [0,10; 0,84] 0,015
No	64/98 (65,3)	4,6 [1,51; 6,74]	40/59 (67,8)	1,2 [0,26; 5,13]	0,74 [0,50; 1,11] 0,153
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,352)					
TPS <50%	33/48 (68,8)	3,7 [1,25; 9,46]	22/27 (81,5)	0,4 [0,16; 2,10]	0,48 [0,28; 0,83] 0,008
TPS ≥50%	12/19 (63,2)	4,8 [0,53; NE]	8/13 (61,5)	0,8 [0,10; NE]	0,81 [0,33; 1,98] 0,659
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,443)					
TPS <50%	33/48 (68,8)	3,7 [1,25; 9,46]	22/27 (81,5)	0,4 [0,16; 2,10]	0,48 [0,28; 0,83] 0,008
TPS ≥50%	12/19 (63,2)	4,8 [0,53; NE]	8/13 (61,5)	0,8 [0,10; NE]	0,81 [0,33; 1,98] 0,659
Unknown	26/48 (54,2)	6,7 [1,91; NE]	20/32 (62,5)	5,1 [0,99; 23,89]	0,77 [0,43; 1,38] 0,381
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,285)					
Negative	16/26 (61,5)	7,8 [1,45; NE]	10/12 (83,3)	0,3 [0,03; 2,89]	0,39 [0,18; 0,87] 0,019
Positive	34/49 (69,4)	3,7 [1,12; 6,74]	24/34 (70,6)	1,3 [0,26; 5,13]	0,74 [0,44; 1,25] 0,267
Unknown	21/40 (52,5)	8,1 [1,77; NE]	16/26 (61,5)	5,3 [0,82; 23,89]	0,76 [0,40; 1,46] 0,424
Disease Stage (p-value of the interaction term: 0,456)					
III	1/6 (16,7)	NE [1,77; NE]	2/6 (33,3)	NE [0,10; NE]	0,41 [0,04; 4,55] 0,452
IVA	27/44 (61,4)	4,9 [1,25; 11,73]	24/32 (75,0)	0,5 [0,13; 2,17]	0,51 [0,29; 0,89] 0,018

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB	43/65 (66,2)	2,8 [1,22; 9,00]	24/34 (70,6)	2,3 [0,43; 6,64]	0,78 [0,47; 1,29] 0,331
Race (p-value of the interaction term: 0,672)					
Asian	37/66 (56,1)	5,9 [1,77; NE]	21/35 (60,0)	5,1 [0,82; 23,89]	0,77 [0,45; 1,32] 0,351
Non-Asian	34/49 (69,4)	4,8 [1,18; 7,72]	25/33 (75,8)	0,3 [0,16; 3,02]	0,65 [0,39; 1,09] 0,115
RET Fusion Result **** (p-value of the interaction term: 0,839)					
CCDC6	8/9 (88,9)	2,1 [0,03; 7,72]	5/6 (83,3)	1,6 [0,10; NE]	0,87 [0,28; 2,67] 0,822
KIF5B	33/50 (66,0)	3,4 [1,22; 9,46]	23/36 (63,9)	1,7 [0,26; 6,64]	0,79 [0,46; 1,35] 0,409
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aespx006_sub_msaf_a.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba_adtteae_gba

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Table 145: Subgroups: Time to adverse event according to SOC: Reproductive system and breast disorders - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,992)					
<65 years	9/76 (11,8)	NE [NE; NE]	1/45 (2,2)	NE [NE; NE]	4,57 [0,58; 36,12] 0,113
≥65 years*	4/39 (10,3)	NE [NE; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,104
Sex (p-value of the interaction term: 0,991)					
Male*	10/61 (16,4)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,026
Female	3/54 (5,6)	NE [NE; NE]	1/38 (2,6)	NE [NE; NE]	1,87 [0,19; 18,00] 0,584
Liver Metastasis - BICR (p-value of the interaction term: 0,993)					
Yes*	2/16 (12,5)	NE [NE; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,249
No	11/98 (11,2)	NE [NE; NE]	1/59 (1,7)	NE [NE; NE]	6,10 [0,79; 47,31] 0,048
RET Specimen Type (p-value of the interaction term: 0,994)					
Blood*	1/9 (11,1)	NE [14,29; NE]	0/10 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,527
Tissue	12/106 (11,3)	NE [NE; NE]	1/62 (1,6)	NE [NE; NE]	6,54 [0,85; 50,34] 0,038
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
 Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aespx016_sub_msaf_a.rtf
 Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 146: Subgroups: Time to adverse event according to SOC: Vascular disorders - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,328)					
<65 years	40/76 (52,6)	9,0 [2,83; NE]	8/45 (17,8)	NE [NE; NE]	3,73 [1,74; 7,97] <0,001
≥65 years	19/39 (48,7)	11,2 [2,10; NE]	2/27 (7,4)	NE [NE; NE]	8,56 [1,99; 36,78] <0,001
Baseline ECOG (p-value of the interaction term: 0,248)					
0	20/41 (48,8)	23,3 [2,10; NE]	5/25 (20,0)	NE [NE; NE]	2,82 [1,05; 7,53] 0,031
1	39/74 (52,7)	5,3 [2,99; NE]	5/47 (10,6)	NE [18,40; NE]	6,60 [2,60; 16,76] <0,001
Sex (p-value of the interaction term: 0,839)					
Male	30/61 (49,2)	9,3 [2,07; NE]	5/34 (14,7)	NE [18,40; NE]	4,33 [1,68; 11,17] <0,001
Female	29/54 (53,7)	5,8 [2,83; NE]	5/38 (13,2)	NE [NE; NE]	5,18 [2,00; 13,41] <0,001
Smoking Status (p-value of the interaction term: 0,378)					
Never	39/72 (54,2)	5,8 [2,83; NE]	6/49 (12,2)	NE [NE; NE]	5,94 [2,51; 14,06] <0,001
Former/Current	20/43 (46,5)	23,3 [2,10; NE]	4/23 (17,4)	NE [NE; NE]	3,02 [1,03; 8,87] 0,035
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,094)					
Yes	10/23 (43,5)	NE [2,14; NE]	4/14 (28,6)	NE [1,87; NE]	1,50 [0,47; 4,80] 0,496
No	19/44 (43,2)	NE [2,10; NE]	2/23 (8,7)	NE [18,40; NE]	6,83 [1,59; 29,38] 0,003
Unknown	30/48 (62,5)	5,0 [2,10; 23,29]	4/35 (11,4)	NE [NE; NE]	7,11 [2,50; 20,20] <0,001
Liver Metastasis - BICR (p-value of the interaction term: 0,138)					
Yes	7/16 (43,8)	NE [1,08; NE]	3/13 (23,1)	NE [3,65; NE]	1,73 [0,44; 6,80] 0,425

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
No	52/98 (53,1)	5,8 [2,86; NE]	7/59 (11,9)	NE [NE; NE]	6,03 [2,73; 13,29] <0,001
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,070)					
TPS <50%	22/48 (45,8)	23,3 [2,86; NE]	2/27 (7,4)	NE [NE; NE]	7,44 [1,74; 31,72] 0,001
TPS ≥50%	12/19 (63,2)	3,0 [1,45; NE]	6/13 (46,2)	7,0 [0,53; NE]	1,53 [0,57; 4,09] 0,394
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,268)					
Negative*	11/26 (42,3)	NE [2,10; NE]	0/12 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,011
Positive	26/49 (53,1)	6,9 [2,83; NE]	8/34 (23,5)	NE [NE; NE]	2,58 [1,16; 5,70] 0,015
Unknown	22/40 (55,0)	5,0 [2,14; NE]	2/26 (7,7)	NE [NE; NE]	10,45 [2,45; 44,55] <0,001
Disease Stage (p-value of the interaction term: 0,985)					
III*	4/6 (66,7)	3,0 [0,26; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,018
IVA	22/44 (50,0)	4,7 [2,07; NE]	5/32 (15,6)	NE [18,40; NE]	4,28 [1,61; 11,34] 0,001
IVB	33/65 (50,8)	11,2 [3,65; NE]	5/34 (14,7)	NE [NE; NE]	4,04 [1,58; 10,35] 0,002
Race (p-value of the interaction term: 0,069)					
Asian	40/66 (60,6)	3,6 [2,10; 9,26]	3/35 (8,6)	NE [NE; NE]	9,71 [3,00; 31,43] <0,001
Non-Asian	19/49 (38,8)	NE [4,73; NE]	6/33 (18,2)	NE [18,40; NE]	2,38 [0,94; 5,98] 0,059
RET Specimen Type (p-value of the interaction term: 0,975)					
Blood	6/9 (66,7)	1,4 [0,03; NE]	2/10 (20,0)	NE [0,53; NE]	4,48 [0,90; 22,30] 0,045
Tissue	53/106 (50,0)	9,3 [3,65; NE]	8/62 (12,9)	NE [NE; NE]	4,95 [2,35; 10,41] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,989)					

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
CCDC6*	7/9 (77,8)	2,4 [0,46; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,010
KIF5B	28/50 (56,0)	5,6 [2,10; NE]	7/36 (19,4)	NE [NE; NE]	3,16 [1,38; 7,25] 0,004
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_aespx019_sub_msaf_a.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 147: Subgroups: Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Alanine aminotransferase increased - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 1,000)					
<65 years*	18/76 (23,7)	NE [NE; NE]	0/45 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
≥65 years*	7/39 (17,9)	NE [NE; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,018
Baseline ECOG (p-value of the interaction term: 1,000)					
0*	10/41 (24,4)	NE [NE; NE]	0/25 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,010
1*	15/74 (20,3)	NE [NE; NE]	0/47 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,001
Sex (p-value of the interaction term: 1,000)					
Male*	15/61 (24,6)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,002
Female*	10/54 (18,5)	NE [NE; NE]	0/38 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,006
Geographic region (p-value of the interaction term: 1,000)					
East Asian*	18/65 (27,7)	NE [NE; NE]	0/35 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Non-EastAsian*	7/50 (14,0)	NE [NE; NE]	0/37 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,020
Smoking Status (p-value of the interaction term: 1,000)					
Never*	19/72 (26,4)	NE [NE; NE]	0/49 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Former/Current*	6/43 (14,0)	NE [NE; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,059
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 1,000)					
Yes*	4/23 (17,4)	NE [NE; NE]	0/14 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,118
No*	10/44 (22,7)	NE [NE; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,013

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown*	11/48 (22,9)	NE [NE; NE]	0/35 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
Liver Metastasis - BICR (p-value of the interaction term: 1,000)					
Yes*	3/16 (18,8)	NE [13,14; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,217
No*	22/98 (22,4)	NE [NE; NE]	0/59 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 1,000)					
TPS <50%*	13/48 (27,1)	NE [NE; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,004
TPS ≥50%*	3/19 (15,8)	NE [13,14; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,109
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 1,000)					
TPS <50%*	13/48 (27,1)	NE [NE; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,004
TPS ≥50%*	3/19 (15,8)	NE [13,14; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,109
Unknown*	9/48 (18,8)	NE [NE; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,011
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 1,000)					
Negative*	7/26 (26,9)	NE [NE; NE]	0/12 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,058
Positive*	10/49 (20,4)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,005
Unknown*	8/40 (20,0)	NE [NE; NE]	0/26 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,017
Disease Stage (p-value of the interaction term: 1,000)					
III*	3/6 (50,0)	NE [1,18; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,055
IVA*	12/44 (27,3)	NE [NE; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB*	10/65 (15,4)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,023
Race (p-value of the interaction term: 1,000)					
Asian*	19/66 (28,8)	NE [NE; NE]	0/35 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Non-Asian*	6/49 (12,2)	NE [NE; NE]	0/33 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,040
RET Specimen Type (p-value of the interaction term: 1,000)					
Blood*	1/9 (11,1)	NE [8,35; NE]	0/10 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,480
Tissue*	24/106 (22,6)	NE [NE; NE]	0/62 (0,0)	NE [NE; NE]	NE [0,00; NE] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_gr3ppx001_sub_msaf_a.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 148: Subgroups: Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Aspartate aminotransferase increased - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 1,000)					
<65 years*	10/76 (13,2)	NE [NE; NE]	0/45 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,013
≥65 years*	4/39 (10,3)	NE [NE; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,081
Geographic region (p-value of the interaction term: 1,000)					
East Asian*	12/65 (18,5)	NE [NE; NE]	0/35 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,008
Non-EastAsian*	2/50 (4,0)	NE [NE; NE]	0/37 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,265
Smoking Status (p-value of the interaction term: 1,000)					
Never*	12/72 (16,7)	NE [NE; NE]	0/49 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
Former/Current*	2/43 (4,7)	NE [NE; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,289
Liver Metastasis - BICR (p-value of the interaction term: 1,000)					
Yes*	1/16 (6,3)	NE [13,14; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,705
No*	13/98 (13,3)	NE [NE; NE]	0/59 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
Race (p-value of the interaction term: 1,000)					
Asian*	12/66 (18,2)	NE [NE; NE]	0/35 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,008
Non-Asian*	2/49 (4,1)	NE [NE; NE]	0/33 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,284
RET Specimen Type (p-value of the interaction term: 0,998)					
Blood*	0/9 (0,0)	NE [NE; NE]	0/10 (0,0)	NE [NE; NE]	NE
Tissue*	14/106 (13,2)	NE [NE; NE]	0/62 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003

Subgroup	Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.				
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine				

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_gr3ppx003_sub_msaf_a.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba

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Table 149: Subgroups: Time to adverse event with CTCAE grade ≥ 3 according to PT: Vascular disorders/Hypertension - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,989)					
<65 years	16/76 (21,1)	NE [NE; NE]	2/45 (4,4)	NE [NE; NE]	5,17 [1,19; 22,48] 0,015
≥65 years*	8/39 (20,5)	NE [NE; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,016
Baseline ECOG (p-value of the interaction term: 0,544)					
0	7/41 (17,1)	NE [NE; NE]	1/25 (4,0)	NE [NE; NE]	4,66 [0,57; 37,89] 0,113
1	17/74 (23,0)	NE [NE; NE]	1/47 (2,1)	NE [NE; NE]	11,40 [1,52; 85,68] 0,003
Sex (p-value of the interaction term: 0,987)					
Male*	14/61 (23,0)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,004
Female	10/54 (18,5)	NE [NE; NE]	2/38 (5,3)	NE [NE; NE]	3,86 [0,84; 17,61] 0,060
Geographic region (p-value of the interaction term: 0,988)					
East Asian	18/65 (27,7)	NE [NE; NE]	2/35 (5,7)	NE [NE; NE]	5,15 [1,19; 22,19] 0,014
Non-EastAsian*	6/50 (12,0)	NE [NE; NE]	0/37 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,027
Smoking Status (p-value of the interaction term: 0,990)					
Never	17/72 (23,6)	NE [NE; NE]	2/49 (4,1)	NE [NE; NE]	6,41 [1,48; 27,77] 0,004
Former/Current*	7/43 (16,3)	NE [NE; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,055
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,860)					
Yes*	5/23 (21,7)	NE [NE; NE]	0/14 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,064
No	7/44 (15,9)	NE [NE; NE]	1/23 (4,3)	NE [NE; NE]	3,96 [0,49; 32,27] 0,164

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	12/48 (25,0)	NE [NE; NE]	1/35 (2,9)	NE [NE; NE]	9,09 [1,18; 69,93] 0,010
Liver Metastasis - BICR (p-value of the interaction term: 0,989)					
Yes*	4/16 (25,0)	NE [6,93; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,086
No	20/98 (20,4)	NE [NE; NE]	2/59 (3,4)	NE [NE; NE]	6,65 [1,55; 28,45] 0,003
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,619)					
TPS <50%	9/48 (18,8)	NE [NE; NE]	1/27 (3,7)	NE [12,71; NE]	5,23 [0,66; 41,34] 0,080
TPS ≥50%	3/19 (15,8)	NE [NE; NE]	1/13 (7,7)	NE [NE; NE]	2,44 [0,25; 23,49] 0,426
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,882)					
TPS <50%	9/48 (18,8)	NE [NE; NE]	1/27 (3,7)	NE [12,71; NE]	5,23 [0,66; 41,34] 0,080
TPS ≥50%	3/19 (15,8)	NE [NE; NE]	1/13 (7,7)	NE [NE; NE]	2,44 [0,25; 23,49] 0,426
Unknown*	12/48 (25,0)	NE [NE; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 1,000)					
Negative*	4/26 (15,4)	NE [NE; NE]	0/12 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,161
Positive	8/49 (16,3)	NE [NE; NE]	2/34 (5,9)	NE [NE; NE]	2,81 [0,60; 13,24] 0,173
Unknown*	12/40 (30,0)	NE [15,41; NE]	0/26 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
Disease Stage (p-value of the interaction term: 1,000)					
III*	2/6 (33,3)	NE [0,79; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,257
IVA	7/44 (15,9)	NE [NE; NE]	2/32 (6,3)	NE [NE; NE]	2,86 [0,59; 13,79] 0,170

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB*	15/65 (23,1)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,004
Race (p-value of the interaction term: 0,989)					
Asian	18/66 (27,3)	NE [NE; NE]	2/35 (5,7)	NE [NE; NE]	5,06 [1,17; 21,81] 0,016
Non-Asian*	6/49 (12,2)	NE [NE; NE]	0/33 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,035
RET Specimen Type (p-value of the interaction term: 0,382)					
Blood	3/9 (33,3)	NE [0,26; NE]	1/10 (10,0)	NE [6,97; NE]	3,48 [0,36; 33,49] 0,251
Tissue	21/106 (19,8)	NE [NE; NE]	1/62 (1,6)	NE [NE; NE]	13,27 [1,78; 98,69] 0,001
RET Fusion Result **** (p-value of the interaction term: 0,994)					
CCDC6*	2/9 (22,2)	NE [2,40; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,281
KIF5B	10/50 (20,0)	NE [NE; NE]	2/36 (5,6)	NE [NE; NE]	3,28 [0,71; 15,09] 0,107
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc230501/t_gr3ppx005_sub_msaf_a.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 150: Subgroups: Time to adverse event with CTCAE grade ≥ 3 according to PT: Blood and lymphatic system disorders/Neutropenia - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Liver Metastasis - BICR (p-value of the interaction term: 0,998)					
Yes*	0/16 (0,0)	NE [NE; NE]	0/13 (0,0)	NE [NE; NE]	NE
No*	0/98 (0,0)	NE [NE; NE]	10/59 (16,9)	NE [NE; NE]	0,00 [0,00; NE] <0,001
RET Specimen Type (p-value of the interaction term: 0,999)					
Blood*	0/9 (0,0)	NE [NE; NE]	0/10 (0,0)	NE [NE; NE]	NE
Tissue*	0/106 (0,0)	NE [NE; NE]	10/62 (16,1)	NE [NE; NE]	0,00 [0,00; NE] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term; RET: Rearranged during transfection. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
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Table 151: Subgroups: Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Neutrophil count decreased - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Geographic region (p-value of the interaction term: 0,993)					
East Asian	2/65 (3,1)	NE [NE; NE]	8/35 (22,9)	NE [NE; NE]	0,11 [0,02; 0,51] <0,001
Non-EastAsian*	0/50 (0,0)	NE [NE; NE]	2/37 (5,4)	NE [NE; NE]	0,00 [0,00; NE] 0,100
Liver Metastasis - BICR (p-value of the interaction term: 0,993)					
Yes*	0/16 (0,0)	NE [NE; NE]	1/13 (7,7)	NE [NE; NE]	0,00 [0,00; NE] 0,243
No	2/98 (2,0)	NE [NE; NE]	9/59 (15,3)	NE [NE; NE]	0,12 [0,03; 0,56] 0,001
Race (p-value of the interaction term: 0,994)					
Asian	2/66 (3,0)	NE [NE; NE]	8/35 (22,9)	NE [NE; NE]	0,11 [0,02; 0,51] <0,001
Non-Asian*	0/49 (0,0)	NE [NE; NE]	2/33 (6,1)	NE [NE; NE]	0,00 [0,00; NE] 0,086
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine					

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Table 152: Subgroups: Time to adverse event with CTCAE grade ≥ 3 according to SOC: Blood and lymphatic system disorders - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,993)					
<65 years	1/76 (1,3)	NE [NE; NE]	7/45 (15,6)	NE [NE; NE]	0,07 [0,01; 0,60] 0,001
≥65 years*	0/39 (0,0)	NE [NE; NE]	10/27 (37,0)	NE [5,78; NE]	0,00 [0,00; NE] <0,001
Baseline ECOG (p-value of the interaction term: 0,993)					
0*	0/41 (0,0)	NE [NE; NE]	8/25 (32,0)	NE [7,23; NE]	0,00 [0,00; NE] <0,001
1	1/74 (1,4)	NE [NE; NE]	9/47 (19,1)	NE [NE; NE]	0,06 [0,01; 0,44] <0,001
Sex (p-value of the interaction term: 0,991)					
Male	1/61 (1,6)	NE [NE; NE]	9/34 (26,5)	NE [15,97; NE]	0,05 [0,01; 0,37] <0,001
Female*	0/54 (0,0)	NE [NE; NE]	8/38 (21,1)	NE [NE; NE]	0,00 [0,00; NE] <0,001
Geographic region (p-value of the interaction term: 0,993)					
East Asian	1/65 (1,5)	NE [NE; NE]	4/35 (11,4)	NE [NE; NE]	0,11 [0,01; 1,04] 0,021
Non-EastAsian*	0/50 (0,0)	NE [NE; NE]	13/37 (35,1)	NE [7,23; NE]	0,00 [0,00; NE] <0,001
Smoking Status (p-value of the interaction term: 0,993)					
Never*	0/72 (0,0)	NE [NE; NE]	12/49 (24,5)	NE [NE; NE]	0,00 [0,00; NE] <0,001
Former/Current	1/43 (2,3)	NE [NE; NE]	5/23 (21,7)	NE [15,97; NE]	0,08 [0,01; 0,72] 0,004
Liver Metastasis - BICR (p-value of the interaction term: 0,994)					
Yes*	0/16 (0,0)	NE [NE; NE]	1/13 (7,7)	NE [5,78; NE]	0,00 [0,00; NE] 0,143
No	1/98 (1,0)	NE [NE; NE]	16/59 (27,1)	NE [NE; NE]	0,03 [0,00; 0,24] <0,001

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Race (p-value of the interaction term: 0,994)					
Asian	1/66 (1,5)	NE [NE; NE]	4/35 (11,4)	NE [NE; NE]	0,11 [0,01; 1,02] 0,020
Non-Asian*	0/49 (0,0)	NE [NE; NE]	11/33 (33,3)	NE [15,97; NE]	0,00 [0,00; NE] <0,001
RET Specimen Type (p-value of the interaction term: 0,999)					
Blood*	0/9 (0,0)	NE [NE; NE]	0/10 (0,0)	NE [NE; NE]	NE
Tissue	1/106 (0,9)	NE [NE; NE]	17/62 (27,4)	NE [NE; NE]	0,03 [0,00; 0,21] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,994)					
CCDC6*	0/9 (0,0)	NE [NE; NE]	1/6 (16,7)	NE [15,97; NE]	0,00 [0,00; NE] 0,264
KIF5B	1/50 (2,0)	NE [NE; NE]	11/36 (30,6)	NE [7,23; NE]	0,05 [0,01; 0,36] <0,001
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					
* The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adtteae_gba
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Table 153: Subgroups: Time to adverse event with CTCAE grade ≥ 3 according to SOC: Investigations - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,180)					
<65 years	28/76 (36,8)	NE [14,03; NE]	7/45 (15,6)	NE [NE; NE]	2,65 [1,16; 6,07] 0,017
≥65 years	12/39 (30,8)	NE [24,90; NE]	7/27 (25,9)	NE [NE; NE]	1,06 [0,41; 2,73] 0,910
Baseline ECOG (p-value of the interaction term: 0,835)					
0	13/41 (31,7)	NE [24,90; NE]	4/25 (16,0)	NE [NE; NE]	2,00 [0,65; 6,17] 0,221
1	27/74 (36,5)	NE [14,03; NE]	10/47 (21,3)	NE [17,38; NE]	1,77 [0,86; 3,66] 0,118
Sex (p-value of the interaction term: 0,844)					
Male	21/61 (34,4)	NE [13,14; NE]	6/34 (17,6)	NE [NE; NE]	2,03 [0,82; 5,03] 0,119
Female	19/54 (35,2)	NE [14,03; NE]	8/38 (21,1)	NE [17,38; NE]	1,74 [0,76; 3,99] 0,185
Geographic region (p-value of the interaction term: 0,693)					
East Asian	29/65 (44,6)	NE [3,48; NE]	10/35 (28,6)	NE [NE; NE]	1,61 [0,78; 3,31] 0,189
Non-EastAsian	11/50 (22,0)	NE [24,90; NE]	4/37 (10,8)	NE [NE; NE]	1,87 [0,58; 5,98] 0,284
Smoking Status (p-value of the interaction term: 0,848)					
Never	28/72 (38,9)	NE [8,35; NE]	11/49 (22,4)	NE [17,38; NE]	1,87 [0,93; 3,76] 0,074
Former/Current	12/43 (27,9)	NE [24,90; NE]	3/23 (13,0)	NE [NE; NE]	2,02 [0,57; 7,19] 0,270
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,374)					
Yes	7/23 (30,4)	NE [8,35; NE]	1/14 (7,1)	NE [17,38; NE]	3,60 [0,43; 30,15] 0,206
No	19/44 (43,2)	NE [2,79; NE]	5/23 (21,7)	NE [NE; NE]	2,37 [0,89; 6,37] 0,077

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	14/48 (29,2)	NE [NE; NE]	8/35 (22,9)	NE [NE; NE]	1,20 [0,50; 2,87] 0,683
Liver Metastasis - BICR (p-value of the interaction term: 0,655)					
Yes	4/16 (25,0)	NE [13,14; NE]	1/13 (7,7)	NE [NE; NE]	2,39 [0,26; 22,29] 0,430
No	36/98 (36,7)	NE [24,90; NE]	13/59 (22,0)	NE [NE; NE]	1,77 [0,94; 3,34] 0,074
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,725)					
TPS <50%	18/48 (37,5)	24,9 [11,56; NE]	5/27 (18,5)	NE [17,38; NE]	2,03 [0,75; 5,49] 0,155
TPS ≥50%	7/19 (36,8)	14,0 [2,79; NE]	2/13 (15,4)	NE [5,45; NE]	3,11 [0,64; 15,00] 0,137
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,690)					
TPS <50%	18/48 (37,5)	24,9 [11,56; NE]	5/27 (18,5)	NE [17,38; NE]	2,03 [0,75; 5,49] 0,155
TPS ≥50%	7/19 (36,8)	14,0 [2,79; NE]	2/13 (15,4)	NE [5,45; NE]	3,11 [0,64; 15,00] 0,137
Unknown	15/48 (31,3)	NE [NE; NE]	7/32 (21,9)	NE [NE; NE]	1,46 [0,60; 3,58] 0,409
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 0,337)					
Negative	10/26 (38,5)	24,9 [8,35; NE]	3/12 (25,0)	NE [0,72; NE]	1,29 [0,35; 4,79] 0,701
Positive	17/49 (34,7)	NE [13,14; NE]	4/34 (11,8)	NE [17,38; NE]	3,35 [1,12; 9,97] 0,021
Unknown	13/40 (32,5)	NE [9,36; NE]	7/26 (26,9)	NE [NE; NE]	1,21 [0,48; 3,04] 0,687
Disease Stage (p-value of the interaction term: 0,954)					
III	3/6 (50,0)	NE [1,18; NE]	2/6 (33,3)	NE [0,26; NE]	1,28 [0,21; 7,69] 0,788
IVA	18/44 (40,9)	NE [3,48; NE]	7/32 (21,9)	NE [NE; NE]	2,10 [0,88; 5,04] 0,088

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB	19/65 (29,2)	NE [24,90; NE]	5/34 (14,7)	NE [NE; NE]	1,91 [0,71; 5,15] 0,190
Race (p-value of the interaction term: 0,621)					
Asian	30/66 (45,5)	NE [3,48; NE]	10/35 (28,6)	NE [NE; NE]	1,63 [0,80; 3,34] 0,174
Non-Asian	10/49 (20,4)	NE [24,90; NE]	3/33 (9,1)	NE [17,38; NE]	2,07 [0,56; 7,67] 0,268
RET Specimen Type (p-value of the interaction term: 0,374)					
Blood	3/9 (33,3)	NE [2,10; NE]	3/10 (30,0)	NE [2,04; NE]	0,79 [0,16; 3,97] 0,770
Tissue	37/106 (34,9)	NE [24,90; NE]	11/62 (17,7)	NE [NE; NE]	2,06 [1,05; 4,04] 0,032
RET Fusion Result **** (p-value of the interaction term: 0,565)					
CCDC6	3/9 (33,3)	NE [0,85; NE]	1/6 (16,7)	NE [0,59; NE]	1,92 [0,20; 18,46] 0,567
KIF5B	14/50 (28,0)	NE [24,90; NE]	8/36 (22,2)	NE [NE; NE]	0,97 [0,40; 2,36] 0,950
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aespt_tte_sub_dc230501.sas
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Table 154: Subgroups: Time to adverse event with CTCAE grade ≥ 3 according to SOC: Vascular disorders - study LIBRETTO-431, mSAF

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Age (p-value of the interaction term: 0,989)					
<65 years	16/76 (21,1)	NE [NE; NE]	2/45 (4,4)	NE [NE; NE]	5,17 [1,19; 22,48] 0,015
≥65 years*	10/39 (25,6)	NE [NE; NE]	0/27 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,007
Baseline ECOG (p-value of the interaction term: 0,590)					
0	8/41 (19,5)	NE [NE; NE]	1/25 (4,0)	NE [NE; NE]	5,42 [0,68; 43,33] 0,074
1	18/74 (24,3)	NE [NE; NE]	1/47 (2,1)	NE [NE; NE]	11,91 [1,59; 89,19] 0,002
Sex (p-value of the interaction term: 0,987)					
Male*	14/61 (23,0)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,004
Female	12/54 (22,2)	NE [NE; NE]	2/38 (5,3)	NE [NE; NE]	4,64 [1,04; 20,74] 0,027
Geographic region (p-value of the interaction term: 0,988)					
East Asian	19/65 (29,2)	NE [NE; NE]	2/35 (5,7)	NE [NE; NE]	5,47 [1,27; 23,50] 0,010
Non-EastAsian*	7/50 (14,0)	NE [NE; NE]	0/37 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,019
Smoking Status (p-value of the interaction term: 0,990)					
Never	19/72 (26,4)	NE [NE; NE]	2/49 (4,1)	NE [NE; NE]	7,20 [1,68; 30,93] 0,002
Former/Current*	7/43 (16,3)	NE [NE; NE]	0/23 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,055
Brain Metastases at Baseline (CRF) (p-value of the interaction term: 0,905)					
Yes*	6/23 (26,1)	NE [11,24; NE]	0/14 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,048
No	8/44 (18,2)	NE [NE; NE]	1/23 (4,3)	NE [NE; NE]	4,63 [0,58; 37,10] 0,112

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Unknown	12/48 (25,0)	NE [NE; NE]	1/35 (2,9)	NE [NE; NE]	9,09 [1,18; 69,93] 0,010
Liver Metastasis - BICR (p-value of the interaction term: 0,989)					
Yes*	5/16 (31,3)	NE [6,93; NE]	0/13 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,071
No	21/98 (21,4)	NE [NE; NE]	2/59 (3,4)	NE [NE; NE]	7,02 [1,64; 29,94] 0,002
PD-L1 Expression - SG-Analysis 1 * (p-value of the interaction term: 0,689)					
TPS <50%	10/48 (20,8)	NE [NE; NE]	1/27 (3,7)	NE [12,71; NE]	5,86 [0,75; 45,84] 0,056
TPS ≥50%	4/19 (21,1)	NE [11,24; NE]	1/13 (7,7)	NE [NE; NE]	3,07 [0,34; 27,61] 0,291
PD-L1 Expression - SG-Analysis 2 ** (p-value of the interaction term: 0,924)					
TPS <50%	10/48 (20,8)	NE [NE; NE]	1/27 (3,7)	NE [12,71; NE]	5,86 [0,75; 45,84] 0,056
TPS ≥50%	4/19 (21,1)	NE [11,24; NE]	1/13 (7,7)	NE [NE; NE]	3,07 [0,34; 27,61] 0,291
Unknown*	12/48 (25,0)	NE [NE; NE]	0/32 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
PD-L1 Expression - SG-Analysis 3 *** (p-value of the interaction term: 1,000)					
Negative*	4/26 (15,4)	NE [NE; NE]	0/12 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,161
Positive	10/49 (20,4)	NE [NE; NE]	2/34 (5,9)	NE [NE; NE]	3,49 [0,76; 15,93] 0,086
Unknown*	12/40 (30,0)	NE [15,41; NE]	0/26 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
Disease Stage (p-value of the interaction term: 1,000)					
III*	2/6 (33,3)	NE [0,79; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,257
IVA	8/44 (18,2)	NE [NE; NE]	2/32 (6,3)	NE [NE; NE]	3,32 [0,70; 15,64] 0,108

Subgroup	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
IVB*	16/65 (24,6)	NE [NE; NE]	0/34 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,003
Race (p-value of the interaction term: 0,988)					
Asian	19/66 (28,8)	NE [NE; NE]	2/35 (5,7)	NE [NE; NE]	5,38 [1,25; 23,09] 0,011
Non-Asian*	7/49 (14,3)	NE [NE; NE]	0/33 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,025
RET Specimen Type (p-value of the interaction term: 0,338)					
Blood	3/9 (33,3)	NE [0,26; NE]	1/10 (10,0)	NE [6,97; NE]	3,48 [0,36; 33,49] 0,251
Tissue	23/106 (21,7)	NE [NE; NE]	1/62 (1,6)	NE [NE; NE]	14,59 [1,97; 108,07] <0,001
RET Fusion Result **** (p-value of the interaction term: 0,994)					
CCDC6*	2/9 (22,2)	NE [2,40; NE]	0/6 (0,0)	NE [NE; NE]	NE [0,00; NE] 0,281
KIF5B	11/50 (22,0)	NE [NE; NE]	2/36 (5,6)	NE [NE; NE]	3,54 [0,78; 16,09] 0,081
Data cutoff: 01MAY2023; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: BICR: Blinded Independent Central Review; CI: Confidence Interval; CRF: Case Report Form; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; RET: Rearranged during transfection; SOC: System Organ Class. a: In months; b: from 2-sided unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: East Asian includes China, Hong Kong, Japan, Korea, Republic of, Singapore and Taiwan; Non-East Asian includes Argentina, Australia, Belgium, Brazil, Canada, Czech Republic, France, Germany, Greece, Israel, Italy, Mexico, Netherlands, Poland, Russian Federation, Spain, Turkey and Ukraine * Patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%, respectively, have not been taken into account. ** The subgroup Unknown includes patients with missing status for PD-L1 Expression and patients with TPS >1% without further specification in TPS ≥50% or <50%., respectively *** The subgroup Unknown includes patients with missing status for PD-L1 Expression. **** PCR tests yield only a positive result and do not define the specific RET fusion partner. They remain unconsidered.					

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc230501/adsl_gba, adttea_gba
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Anhang 4-G5: Angaben zum Datenschnitt vom 01.05.2024

Anhang 4-G5.1: Angaben zur Studienpopulation sowie Ergebnisse für das Gesamtüberleben

Tabelle 155: Zusammenfassung der Patientendisposition - RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
Randomisiert, aber nie behandelt	0	1 (1,4)	1 (0,5)
Grund für den Abbruch ^c			
Abbruch auf Wunsch des Patienten	0	1 (1,4)	1 (0,5)
Behandelt	115 (100,0)	72 (98,6)	187 (99,5)
In Behandlung ^a	51 (44,3)	7 (9,6)	58 (30,9)
Nicht in Behandlung ^a	64 (55,7)	65 (89,0)	129 (68,6)
Grund für den Behandlungsabbruch			
Abbruch auf Wunsch des Patienten	3 (2,6)	6 (8,2)	9 (4,8)
Entscheidung des Arztes	3 (2,6)	9 (12,3)	12 (6,4)
Krankheitsprogress	44 (38,3)	44 (60,3)	88 (46,8)
Non-Compliance With Study Drug	1 (0,9)	1 (1,4)	2 (1,1)
Tod	7 (6,1)	1 (1,4)	8 (4,3)
Unerwünschtes Ereignis	6 (5,2)	4 (5,5)	10 (5,3)
Follow-up nach Abbruch der Behandlung ^{ab}			
Nein	8 (7,0)	11 (15,1)	19 (10,1)
Ja	56 (48,7)	55 (75,3)	111 (59,0)
Follow-up nach Abbruch der Behandlung laufend ^{ab}	18 (15,7)	37 (50,7)	55 (29,3)
Follow-up - Erhebung gemäß Protokoll	6 (5,2)	31 (42,5)	37 (19,7)
Follow-up - Nur Erhebung des Überlebensstatus	12 (10,4)	6 (8,2)	18 (9,6)
Follow-up nach Abbruch der Behandlung beendet ^{ab}	38 (33,0)	18 (24,7)	56 (29,8)
Gründe für Beendigung des Follow-up nach Abbruch der Behandlung			
Abbruch auf Wunsch des Patienten	6 (5,2)	2 (2,7)	8 (4,3)
Lost To Follow-Up	3 (2,6)	1 (1,4)	4 (2,1)
Tod	29 (25,2)	15 (20,5)	44 (23,4)
Datenschnitt: 01. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; mITT: Modifizierte ITT-Pembrolizumab Population; n: Anzahl der Patienten; N: Anzahl der Patienten in der Analyse; RCT: Randomisierte kontrollierte Studie. Die Nachbeobachtung nach Behandlungsabbruch kann eine Crossover-Periode beinhalten. a: Zum Zeitpunkt des Datenschnitts am 01. Mai 2024. b: Umfasst sowohl Patienten, die die Behandlung beendet haben, als auch Patienten, die randomisiert, aber nie behandelt wurden. c: Einige randomisierte Patienten hatten zum Zeitpunkt des Datenstichtags die Behandlung noch nicht begonnen oder abgebrochen.			

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Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/t_ds_mitt.rtf

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Tabelle 156: Begleitmedikation - RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF

Wirkstoffklasse Preferred Term	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72) n (%)	Gesamt (N=187) n (%)
Patienten mit mindestens einer Medikation	114 (99,1)	72 (100,0)	186 (99,5)
FOLIC ACID AND DERIVATIVES	46 (40,4)	63 (87,5)	109 (58,6)
FOLIC ACID	45 (39,5)	61 (84,7)	106 (57,0)
GLUCOCORTICOIDS	36 (31,6)	68 (94,4)	104 (55,9)
DEXAMETHASONE	19 (16,7)	65 (90,3)	84 (45,2)
METHYLPREDNISOLONE	9 (7,9)	8 (11,1)	17 (9,1)
PREDNISONE	6 (5,3)	11 (15,3)	17 (9,1)
VITAMIN B12 (CYANOCOBALAMIN AND ANALOGUES)	27 (23,7)	70 (97,2)	97 (52,2)
VITAMIN B12 NOS	10 (8,8)	43 (59,7)	53 (28,5)
CYANOCOBALAMIN	11 (9,6)	19 (26,4)	30 (16,1)
MECOBALAMIN	4 (3,5)	6 (8,3)	10 (5,4)
PROTON PUMP INHIBITORS	41 (36,0)	47 (65,3)	88 (47,3)
OMEPRAZOLE	15 (13,2)	23 (31,9)	38 (20,4)
PANTOPRAZOLE	17 (14,9)	12 (16,7)	29 (15,6)
ESOMEPRAZOLE	7 (6,1)	11 (15,3)	18 (9,7)
LANSOPRAZOLE	4 (3,5)	11 (15,3)	15 (8,1)
SEROTONIN (5HT3) ANTAGONISTS	5 (4,4)	60 (83,3)	65 (34,9)
ONDANSETRON	2 (1,8)	26 (36,1)	28 (15,1)
PALONOSETRON	1 (0,9)	23 (31,9)	24 (12,9)
TROPISETRON	1 (0,9)	14 (19,4)	15 (8,1)
GRANISETRON	2 (1,8)	10 (13,9)	12 (6,5)
ANILIDES	39 (34,2)	22 (30,6)	61 (32,8)
PARACETAMOL	30 (26,3)	21 (29,2)	51 (27,4)
DIHYDROPYRIDINE DERIVATIVES	50 (43,9)	8 (11,1)	58 (31,2)
AMLODIPINE	32 (28,1)	6 (8,3)	38 (20,4)
NIFEDIPINE	10 (8,8)	2 (2,8)	12 (6,5)
LIVER THERAPY	44 (38,6)	11 (15,3)	55 (29,6)
GLYCYRRHIZIC ACID	25 (21,9)	3 (4,2)	28 (15,1)
POLYENE PHOSPHATIDYLCHOLINE	22 (19,3)	1 (1,4)	23 (12,4)
BICYCLOL	15 (13,2)	2 (2,8)	17 (9,1)
DL-METHIONINE;GLYCINE;GLYCYRRHIZIC ACID	9 (7,9)	1 (1,4)	10 (5,4)
SULFONAMIDES, PLAIN	31 (27,2)	14 (19,4)	45 (24,2)
FUROSEMIDE	25 (21,9)	9 (12,5)	34 (18,3)

Wirkstoffklasse Preferred Term	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72) n (%)	Gesamt (N=187) n (%)
TORASEMIDE	6 (5,3)	4 (5,6)	10 (5,4)
PROPULSIVES	11 (9,6)	31 (43,1)	42 (22,6)
METOCLOPRAMIDE	6 (5,3)	24 (33,3)	30 (16,1)
OSMOTICALLY ACTING LAXATIVES	18 (15,8)	22 (30,6)	40 (21,5)
LACTULOSE	9 (7,9)	9 (12,5)	18 (9,7)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBs), PLAIN	30 (26,3)	6 (8,3)	36 (19,4)
OTHER IMMUNOSTIMULANTS	20 (17,5)	15 (20,8)	35 (18,8)
LEUCOGEN	11 (9,6)	11 (15,3)	22 (11,8)
GLUTATHIONE	7 (6,1)	4 (5,6)	11 (5,9)
HMG COA REDUCTASE INHIBITORS	22 (19,3)	11 (15,3)	33 (17,7)
ATORVASTATIN	11 (9,6)	4 (5,6)	15 (8,1)
PROPIONIC ACID DERIVATIVES	18 (15,8)	15 (20,8)	33 (17,7)
IBUPROFEN	9 (7,9)	15 (20,8)	24 (12,9)
BETA BLOCKING AGENTS, SELECTIVE	20 (17,5)	11 (15,3)	31 (16,7)
BISOPROLOL	11 (9,6)	6 (8,3)	17 (9,1)
METOPROLOL	9 (7,9)	4 (5,6)	13 (7,0)
COVID-19 VACCINES	18 (15,8)	13 (18,1)	31 (16,7)
COVID-19 VACCINE	18 (15,8)	13 (18,1)	31 (16,7)
HEPARIN GROUP	16 (14,0)	15 (20,8)	31 (16,7)
ENOXAPARIN	8 (7,0)	6 (8,3)	14 (7,5)
BENZODIAZEPINE DERIVATIVES	19 (16,7)	11 (15,3)	30 (16,1)
OTHER ANTIEMETICS	2 (1,8)	28 (38,9)	30 (16,1)
APREPITANT	1 (0,9)	19 (26,4)	20 (10,8)
COLONY STIMULATING FACTORS	7 (6,1)	22 (30,6)	29 (15,6)
GRANULOCYTE COLONY STIMULATING FACTOR	7 (6,1)	10 (13,9)	17 (9,1)
NATURAL OPIUM ALKALOIDS	14 (12,3)	15 (20,8)	29 (15,6)
OXYCODONE	7 (6,1)	12 (16,7)	19 (10,2)
MORPHINE	8 (7,0)	5 (6,9)	13 (7,0)
ANTIPROPULSIVES	22 (19,3)	5 (6,9)	27 (14,5)
LOPERAMIDE	22 (19,3)	5 (6,9)	27 (14,5)
H2-RECEPTOR ANTAGONISTS	14 (12,3)	13 (18,1)	27 (14,5)
FAMOTIDINE	10 (8,8)	9 (12,5)	19 (10,2)
ELECTROLYTE SOLUTIONS	10 (8,8)	15 (20,8)	25 (13,4)
SODIUM CHLORIDE	4 (3,5)	9 (12,5)	13 (7,0)
DIRECT FACTOR XA INHIBITORS	17 (14,9)	7 (9,7)	24 (12,9)

Wirkstoffklasse Preferred Term	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72) n (%)	Gesamt (N=187) n (%)
RIVAROXABAN	15 (13,2)	2 (2,8)	17 (9,1)
BISPHOSPHONATES	16 (14,0)	7 (9,7)	23 (12,4)
IBANDRONIC ACID	6 (5,3)	5 (6,9)	11 (5,9)
ZOLEDRONIC ACID	9 (7,9)	2 (2,8)	11 (5,9)
COMBINATIONS AND COMPLEXES OF ALUMINIUM, CALCIUM AND MAGNESIUM COMPOUNDS	15 (13,2)	8 (11,1)	23 (12,4)
FLUOROQUINOLONES	14 (12,3)	9 (12,5)	23 (12,4)
LEVOFLOXACIN	5 (4,4)	8 (11,1)	13 (7,0)
OPIUM ALKALOIDS AND DERIVATIVES	13 (11,4)	10 (13,9)	23 (12,4)
CODEINE	4 (3,5)	6 (8,3)	10 (5,4)
THIRD-GENERATION CEPHALOSPORINS	20 (17,5)	3 (4,2)	23 (12,4)
COMBINATIONS OF PENICILLINS, INCL. BETA-LACTAMASE INHIBITORS	13 (11,4)	9 (12,5)	22 (11,8)
AMOXICILLIN;CLAVULANIC ACID	11 (9,6)	8 (11,1)	19 (10,2)
OTHER ANTIHISTAMINES FOR SYSTEMIC USE	11 (9,6)	11 (15,3)	22 (11,8)
LORATADINE	7 (6,1)	4 (5,6)	11 (5,9)
ACE INHIBITORS, PLAIN	13 (11,4)	7 (9,7)	20 (10,8)
RAMIPRIL	6 (5,3)	4 (5,6)	10 (5,4)
CORTICOSTEROIDS, POTENT (GROUP III)	12 (10,5)	8 (11,1)	20 (10,8)
MUCOLYTICS	13 (11,4)	7 (9,7)	20 (10,8)
ACETYLCYSTEINE	6 (5,3)	4 (5,6)	10 (5,4)
AMBROXOL	7 (6,1)	3 (4,2)	10 (5,4)
ANTIDOTES	16 (14,0)	3 (4,2)	19 (10,2)
GLUTATHIONE	15 (13,2)	3 (4,2)	18 (9,7)
OPIOIDS IN COMBINATION WITH NON-OPIOID ANALGESICS	12 (10,5)	7 (9,7)	19 (10,2)
THYROID HORMONES	13 (11,4)	6 (8,3)	19 (10,2)
LEVOTHYROXINE	12 (10,5)	6 (8,3)	18 (9,7)
BILE ACIDS AND DERIVATIVES	16 (14,0)	2 (2,8)	18 (9,7)
URSODEOXYCHOLIC ACID	16 (14,0)	2 (2,8)	18 (9,7)
CONTACT LAXATIVES	9 (7,9)	9 (12,5)	18 (9,7)
OTHER PLAIN VITAMIN PREPARATIONS	10 (8,8)	8 (11,1)	18 (9,7)
PYRIDOXINE	9 (7,9)	6 (8,3)	15 (8,1)
SOLUTIONS AFFECTING THE ELECTROLYTE BALANCE	10 (8,8)	8 (11,1)	18 (9,7)
ANTIDIARRHEAL MICROORGANISMS	12 (10,5)	5 (6,9)	17 (9,1)
BIGUANIDES	6 (5,3)	11 (15,3)	17 (9,1)

Wirkstoffklasse Preferred Term	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72) n (%)	Gesamt (N=187) n (%)
METFORMIN	6 (5,3)	11 (15,3)	17 (9,1)
CALCIUM, COMBINATIONS WITH VITAMIN D AND/OR OTHER DRUGS	13 (11,4)	4 (5,6)	17 (9,1)
CALCIUM CARBONATE;COLECALCIFEROL	10 (8,8)	2 (2,8)	12 (6,5)
ACETIC ACID DERIVATIVES AND RELATED SUBSTANCES	11 (9,6)	5 (6,9)	16 (8,6)
ASCORBIC ACID (VITAMIN C), PLAIN	11 (9,6)	5 (6,9)	16 (8,6)
ASCORBIC ACID	11 (9,6)	5 (6,9)	16 (8,6)
OTHER SYSTEMIC HEMOSTATICS	9 (7,9)	7 (9,7)	16 (8,6)
PIPERAZINE DERIVATIVES	11 (9,6)	5 (6,9)	16 (8,6)
VITAMIN D AND ANALOGUES	14 (12,3)	2 (2,8)	16 (8,6)
ALPHA-ADRENORECEPTOR ANTAGONISTS	11 (9,6)	4 (5,6)	15 (8,1)
SECOND-GENERATION CEPHALOSPORINS	12 (10,5)	3 (4,2)	15 (8,1)
CEFUROXIME	8 (7,0)	3 (4,2)	11 (5,9)
SOLUTIONS FOR PARENTERAL NUTRITION	7 (6,1)	8 (11,1)	15 (8,1)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBs) AND CALCIUM CHANNEL BLOCKERS	11 (9,6)	3 (4,2)	14 (7,5)
OTHER DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	8 (7,0)	6 (8,3)	14 (7,5)
DENOSUMAB	8 (7,0)	6 (8,3)	14 (7,5)
OTHER EMOLLIENTS AND PROTECTIVES	7 (6,1)	7 (9,7)	14 (7,5)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBs) AND DIURETICS	13 (11,4)	0	13 (7,0)
MAGNESIUM	4 (3,5)	9 (12,5)	13 (7,0)
OTHER DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	11 (9,6)	2 (2,8)	13 (7,0)
PLATELET AGGREGATION INHIBITORS EXCL. HEPARIN	10 (8,8)	3 (4,2)	13 (7,0)
ACETYLSALICYLIC ACID	9 (7,9)	3 (4,2)	12 (6,5)
PYRAZOLONES	9 (7,9)	4 (5,6)	13 (7,0)
METAMIZOLE	9 (7,9)	4 (5,6)	13 (7,0)
OTHER OPIOIDS	6 (5,3)	6 (8,3)	12 (6,5)
TRAMADOL	5 (4,4)	5 (6,9)	10 (5,4)
PENICILLINS WITH EXTENDED SPECTRUM	10 (8,8)	2 (2,8)	12 (6,5)
AMOXICILLIN	8 (7,0)	2 (2,8)	10 (5,4)
ALDOSTERONE ANTAGONISTS	8 (7,0)	3 (4,2)	11 (5,9)
SPIRONOLACTONE	7 (6,1)	3 (4,2)	10 (5,4)
AMINO ACIDS	7 (6,1)	4 (5,6)	11 (5,9)

Wirkstoffklasse Preferred Term	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72) n (%)	Gesamt (N=187) n (%)
AMINO ACIDS AND DERIVATIVES	8 (7,0)	3 (4,2)	11 (5,9)
ANTIINFECTIVES AND ANTISEPTICS FOR LOCAL ORAL TREATMENT	6 (5,3)	5 (6,9)	11 (5,9)
OPIUM DERIVATIVES AND EXPECTORANTS	6 (5,3)	5 (6,9)	11 (5,9)
POTASSIUM	6 (5,3)	5 (6,9)	11 (5,9)
AMIDES	7 (6,1)	3 (4,2)	10 (5,4)
BLOOD SUBSTITUTES AND PLASMA PROTEIN FRACTIONS	10 (8,8)	0	10 (5,4)
OTHER DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	8 (7,0)	2 (2,8)	10 (5,4)
NOT CODED	53 (46,5)	27 (37,5)	80 (43,0)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	14 (12,3)	4 (5,6)	18 (9,7)
Datenschnitt: 01. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; mSAF: Modifizierte Safety-Pembrolizumab Population; n: Anzahl der Patienten; N: Anzahl der Patienten in der Analyse; RCT: Randomisierte kontrollierte Studie. Nur Begleitmedikationen, die von mehr als 5% der Patienten eingenommen wurden, werden angezeigt			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_cm_concom_dc240501.sas

Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/t_cm_concom_msaf.rtf

Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240501/adsl_gba

/lillyce/prd/ly3527723/j2g_mc_jzjc/intrm2/data/analysis/restricted/adcm

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Tabelle 157: Crossover Rate - RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Patienten mit Crossover zu Selpercatinib	42 (57,5)
Datenschnitt: 01. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; mITT: Modifizierte ITT-Pembrolizumab Population; n: Anzahl der Patienten; N: Anzahl der Patienten in der Analyse; RCT: Randomisierte kontrollierte Studie.	

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_xrate_dc240501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/t_xrate_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240501/adsl_gba
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Tabelle 158: Nachfolgende Antitumor-Therapien - RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
Chirurgischer Eingriff	1 (0,9)	1 (1,4)	2 (1,1)
Strahlentherapie	7 (6,1)	8 (11,0)	15 (8,0)
Systemische Therapie			
Gesamt	37 (32,2)	22 (30,1)	59 (31,4)
CARBOPLATIN	23 (20,0)	3 (4,1)	26 (13,8)
PEMETREXED	18 (15,7)	1 (1,4)	19 (10,1)
PRALSETINIB	6 (5,2)	6 (8,2)	12 (6,4)
SELPERCATINIB	7 (6,1)	4 (5,5)	11 (5,9)
PACLITAXEL	7 (6,1)	2 (2,7)	9 (4,8)
DOCETAXEL	2 (1,7)	6 (8,2)	8 (4,3)
BEVACIZUMAB	5 (4,3)	2 (2,7)	7 (3,7)
PEMBROLIZUMAB	5 (4,3)	2 (2,7)	7 (3,7)
ATEZOLIZUMAB	4 (3,5)	2 (2,7)	6 (3,2)
CISPLATIN	1 (0,9)	3 (4,1)	4 (2,1)
INVESTIGATIONAL DRUG	2 (1,7)	1 (1,4)	3 (1,6)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	3 (2,6)	0	3 (1,6)
CABOZANTINIB	2 (1,7)	0	2 (1,1)
CATEQUENTINIB	1 (0,9)	1 (1,4)	2 (1,1)
GEMCITABINE	0	2 (2,7)	2 (1,1)
NIVOLUMAB	2 (1,7)	0	2 (1,1)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0,9)	0	1 (0,5)
CAMRELIZUMAB	1 (0,9)	0	1 (0,5)
DABRAFENIB	1 (0,9)	0	1 (0,5)
GIMERACIL;OTERACIL;TEGAFUR	0	1 (1,4)	1 (0,5)
IPILIMUMAB	1 (0,9)	0	1 (0,5)
IRINOTECAN	0	1 (1,4)	1 (0,5)
NATURAL KILLER CELLS	1 (0,9)	0	1 (0,5)
NINTEDANIB	0	1 (1,4)	1 (0,5)
RAMUCIRUMAB	1 (0,9)	0	1 (0,5)
RELATLIMAB	1 (0,9)	0	1 (0,5)
SACITUZUMAB GOVITECAN	1 (0,9)	0	1 (0,5)
TEGAFUR;URACIL	0	1 (1,4)	1 (0,5)
TEMOZOLOMIDE	0	1 (1,4)	1 (0,5)
TISLELIZUMAB	1 (0,9)	0	1 (0,5)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
TRAMETINIB	1 (0,9)	0	1 (0,5)
VINORELBINE	1 (0,9)	0	1 (0,5)
ZOLEDRONIC ACID	0	1 (1,4)	1 (0,5)
Erste nachfolgende Therapielinie	37 (32,2)	22 (30,1)	59 (31,4)
CARBOPLATIN	21 (18,3)	2 (2,7)	23 (12,2)
PEMETREXED	15 (13,0)	0	15 (8,0)
SELPERCATINIB	6 (5,2)	4 (5,5)	10 (5,3)
PRALSETINIB	4 (3,5)	5 (6,8)	9 (4,8)
PACLITAXEL	7 (6,1)	1 (1,4)	8 (4,3)
BEVACIZUMAB	5 (4,3)	2 (2,7)	7 (3,7)
PEMBROLIZUMAB	5 (4,3)	2 (2,7)	7 (3,7)
DOCETAXEL	0	6 (8,2)	6 (3,2)
ATEZOLIZUMAB	2 (1,7)	2 (2,7)	4 (2,1)
CISPLATIN	0	2 (2,7)	2 (1,1)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 (1,7)	0	2 (1,1)
CAMRELIZUMAB	1 (0,9)	0	1 (0,5)
GEMCITABINE	0	1 (1,4)	1 (0,5)
INVESTIGATIONAL DRUG	0	1 (1,4)	1 (0,5)
IPILIMUMAB	1 (0,9)	0	1 (0,5)
IRINOTECAN	0	1 (1,4)	1 (0,5)
NATURAL KILLER CELLS	1 (0,9)	0	1 (0,5)
NINTEDANIB	0	1 (1,4)	1 (0,5)
NIVOLUMAB	1 (0,9)	0	1 (0,5)
RELATLIMAB	1 (0,9)	0	1 (0,5)
TEMOZOLOMIDE	0	1 (1,4)	1 (0,5)
TISLELIZUMAB	1 (0,9)	0	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
ZOLEDRONIC ACID	0	1 (1,4)	1 (0,5)
Zweite oder spätere nachfolgende Therapielinie	13 (11,3)	4 (5,5)	17 (9,0)
CARBOPLATIN	3 (2,6)	1 (1,4)	4 (2,1)
PEMETREXED	3 (2,6)	1 (1,4)	4 (2,1)
PRALSETINIB	2 (1,7)	1 (1,4)	3 (1,6)
ATEZOLIZUMAB	2 (1,7)	0	2 (1,1)
BEVACIZUMAB	1 (0,9)	1 (1,4)	2 (1,1)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
CABOZANTINIB	2 (1,7)	0	2 (1,1)
CATEQUENTINIB	1 (0,9)	1 (1,4)	2 (1,1)
CISPLATIN	1 (0,9)	1 (1,4)	2 (1,1)
DOCETAXEL	2 (1,7)	0	2 (1,1)
INVESTIGATIONAL DRUG	2 (1,7)	0	2 (1,1)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0,9)	0	1 (0,5)
DABRAFENIB	1 (0,9)	0	1 (0,5)
GEMCITABINE	0	1 (1,4)	1 (0,5)
GIMERACIL;OTERACIL;TEGAFUR	0	1 (1,4)	1 (0,5)
NIVOLUMAB	1 (0,9)	0	1 (0,5)
PACLITAXEL	0	1 (1,4)	1 (0,5)
RAMUCIRUMAB	1 (0,9)	0	1 (0,5)
SACITUZUMAB GOVITECAN	1 (0,9)	0	1 (0,5)
SELPERCATINIB	1 (0,9)	0	1 (0,5)
TEGAFUR;URACIL	0	1 (1,4)	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
TRAMETINIB	1 (0,9)	0	1 (0,5)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1 (0,9)	0	1 (0,5)
VINORELBINE	1 (0,9)	0	1 (0,5)
Systemische Therapien: Behandlungsschema	37 (32,2)	22 (30,1)	59 (31,4)
PRALSETINIB	5 (4,3)	6 (8,2)	11 (5,9)
SELPERCATINIB	7 (6,1)	4 (5,5)	11 (5,9)
CARBOPLATIN, PEMETREXED	8 (7,0)	0	8 (4,3)
CARBOPLATIN, PACLITAXEL	3 (2,6)	2 (2,7)	5 (2,7)
DOCETAXEL	1 (0,9)	3 (4,1)	4 (2,1)
CARBOPLATIN	3 (2,6)	0	3 (1,6)
CARBOPLATIN, PEMBROLIZUMAB, PEMETREXED	3 (2,6)	0	3 (1,6)
INVESTIGATIONAL DRUG	2 (1,7)	1 (1,4)	3 (1,6)
PEMBROLIZUMAB	1 (0,9)	2 (2,7)	3 (1,6)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	3 (2,6)	0	3 (1,6)
ATEZOLIZUMAB	2 (1,7)	0	2 (1,1)
BEVACIZUMAB, CARBOPLATIN, PACLITAXEL, ATEZOLIZUMAB	2 (1,7)	0	2 (1,1)
CABOZANTINIB	2 (1,7)	0	2 (1,1)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
CATEQUENTINIB	1 (0,9)	1 (1,4)	2 (1,1)
PEMETREXED	2 (1,7)	0	2 (1,1)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0,9)	0	1 (0,5)
ATEZOLIZUMAB, BEVACIZUMAB, DOCETAXEL	0	1 (1,4)	1 (0,5)
BEVACIZUMAB	0	1 (1,4)	1 (0,5)
BEVACIZUMAB, CAMRELIZUMAB, PEMETREXED, CARBOPLATIN	1 (0,9)	0	1 (0,5)
BEVACIZUMAB, CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
BEVACIZUMAB, PEMETREXED, CARBOPLATIN	1 (0,9)	0	1 (0,5)
BEVACIZUMAB, PEMETREXED, CISPLATIN	1 (0,9)	0	1 (0,5)
CISPLATIN, DOCETAXEL	0	1 (1,4)	1 (0,5)
CISPLATIN, IRINOTECAN	0	1 (1,4)	1 (0,5)
CISPLATIN, PEMETREXED	0	1 (1,4)	1 (0,5)
DABRAFENIB, PRALSETINIB, TRAMETINIB	1 (0,9)	0	1 (0,5)
DABRAFENIB, TRAMETINIB	1 (0,9)	0	1 (0,5)
DOCETAXEL, NINTEDANIB	0	1 (1,4)	1 (0,5)
DOCETAXEL, RAMUCIRUMAB	1 (0,9)	0	1 (0,5)
GEMCITABINE	0	1 (1,4)	1 (0,5)
GIMERACIL;OTERACIL;TEGAFUR	0	1 (1,4)	1 (0,5)
IPILIMUMAB, NIVOLUMAB, RELATLIMAB	1 (0,9)	0	1 (0,5)
NATURAL KILLER CELLS	1 (0,9)	0	1 (0,5)
NIVOLUMAB	1 (0,9)	0	1 (0,5)
PACLITAXEL	1 (0,9)	0	1 (0,5)
PACLITAXEL, CARBOPLATIN	1 (0,9)	0	1 (0,5)
PEMBROLIZUMAB, CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
SACITUZUMAB GOVITECAN	1 (0,9)	0	1 (0,5)
TEGAFUR;URACIL	0	1 (1,4)	1 (0,5)
TEMOZOLOMIDE	0	1 (1,4)	1 (0,5)
TISLELIZUMAB	1 (0,9)	0	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
VINORELBINE	1 (0,9)	0	1 (0,5)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
ZOLEDRONIC ACID, ATEZOLIZUMAB, CARBOPLATIN, GEMCITABINE	0	1 (1,4)	1 (0,5)
Systemische Therapien: Erstlinien-Behandlungsschema	37 (32,2)	22 (30,1)	59 (31,4)
SELPERCATINIB	6 (5,2)	4 (5,5)	10 (5,3)
PRALSETINIB	4 (3,5)	5 (6,8)	9 (4,8)
CARBOPLATIN, PEMETREXED	7 (6,1)	0	7 (3,7)
CARBOPLATIN, PACLITAXEL	3 (2,6)	1 (1,4)	4 (2,1)
CARBOPLATIN, PEMBROLIZUMAB, PEMETREXED	3 (2,6)	0	3 (1,6)
DOCETAXEL	0	3 (4,1)	3 (1,6)
PEMBROLIZUMAB	1 (0,9)	2 (2,7)	3 (1,6)
BEVACIZUMAB, CARBOPLATIN, PACLITAXEL, ATEZOLIZUMAB	2 (1,7)	0	2 (1,1)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 (1,7)	0	2 (1,1)
ATEZOLIZUMAB, BEVACIZUMAB, DOCETAXEL	0	1 (1,4)	1 (0,5)
BEVACIZUMAB	0	1 (1,4)	1 (0,5)
BEVACIZUMAB, CAMRELIZUMAB, PEMETREXED, CARBOPLATIN	1 (0,9)	0	1 (0,5)
BEVACIZUMAB, CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
BEVACIZUMAB, PEMETREXED, CARBOPLATIN	1 (0,9)	0	1 (0,5)
CARBOPLATIN	1 (0,9)	0	1 (0,5)
CISPLATIN, DOCETAXEL	0	1 (1,4)	1 (0,5)
CISPLATIN, IRINOTECAN	0	1 (1,4)	1 (0,5)
DOCETAXEL, NINTEDANIB	0	1 (1,4)	1 (0,5)
INVESTIGATIONAL DRUG	0	1 (1,4)	1 (0,5)
IPILIMUMAB, NIVOLUMAB, RELATLIMAB	1 (0,9)	0	1 (0,5)
NATURAL KILLER CELLS	1 (0,9)	0	1 (0,5)
PACLITAXEL	1 (0,9)	0	1 (0,5)
PACLITAXEL, CARBOPLATIN	1 (0,9)	0	1 (0,5)
PEMBROLIZUMAB, CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
PEMETREXED	1 (0,9)	0	1 (0,5)
TEMOZOLOMIDE	0	1 (1,4)	1 (0,5)
TISLELIZUMAB	1 (0,9)	0	1 (0,5)

	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)	Gesamt (N=188) n (%)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
ZOLEDRONIC ACID, ATEZOLIZUMAB, CARBOPLATIN, GEMCITABINE	0	1 (1,4)	1 (0,5)
Systemische Therapien: Zweit- oder Spätlinien-Behandlungsschema	13 (11,3)	4 (5,5)	17 (9,0)
ATEZOLIZUMAB	2 (1,7)	0	2 (1,1)
CABOZANTINIB	2 (1,7)	0	2 (1,1)
CARBOPLATIN	2 (1,7)	0	2 (1,1)
CATEQUENTINIB	1 (0,9)	1 (1,4)	2 (1,1)
INVESTIGATIONAL DRUG	2 (1,7)	0	2 (1,1)
PRALSETINIB	1 (0,9)	1 (1,4)	2 (1,1)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0,9)	0	1 (0,5)
BEVACIZUMAB	0	1 (1,4)	1 (0,5)
BEVACIZUMAB, PEMETREXED, CISPLATIN	1 (0,9)	0	1 (0,5)
CARBOPLATIN, PACLITAXEL	0	1 (1,4)	1 (0,5)
CARBOPLATIN, PEMETREXED	1 (0,9)	0	1 (0,5)
CISPLATIN, PEMETREXED	0	1 (1,4)	1 (0,5)
DABRAFENIB, PRALSETINIB, TRAMETINIB	1 (0,9)	0	1 (0,5)
DABRAFENIB, TRAMETINIB	1 (0,9)	0	1 (0,5)
DOCETAXEL	1 (0,9)	0	1 (0,5)
DOCETAXEL, RAMUCIRUMAB	1 (0,9)	0	1 (0,5)
GEMCITABINE	0	1 (1,4)	1 (0,5)
GIMERACIL;OTERACIL;TEGAFUR	0	1 (1,4)	1 (0,5)
NIVOLUMAB	1 (0,9)	0	1 (0,5)
PEMETREXED	1 (0,9)	0	1 (0,5)
SACITUZUMAB GOVITECAN	1 (0,9)	0	1 (0,5)
SELPERCATINIB	1 (0,9)	0	1 (0,5)
TEGAFUR;URACIL	0	1 (1,4)	1 (0,5)
TRADITIONAL CHINESE MEDICINE (TCM) DECOCTION	1 (0,9)	0	1 (0,5)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	1 (0,9)	0	1 (0,5)
VINORELBINE	1 (0,9)	0	1 (0,5)
Datenschnitt: 01. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; mITT: Modifizierte ITT-Pembrolizumab Population; n: Anzahl der Patienten; N: Anzahl der Patienten in der Analyse; RCT: Randomisierte kontrollierte Studie.			

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_cm_pdt_dc240501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/t_cm_pdt_mitt.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240501/adsl_gba
/lillyce/prd/ly3527723/j2g_mc_jzjc/intrm2/data/analysis/restricted/adpr, adcm
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Tabelle 159: Beobachtungsdauern pro Endpunkt (Monaten) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73)
Gesamtüberleben		
Median [95% KI]	33,15 [30,42; 35,15]	33,87 [27,63; 35,52]
Q1; Q3	26,71; 36,83	24,87; 37,95
Datenschnitt: 01. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie. Die Beobachtungsdauer für Gesamtüberleben wurde mit der Kaplan-Meier-Methode und mit inverser Zensierung geschätzt.		

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_fup_dc240501.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/t_fup_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/intrm2/data/analysis/restricted/adtteos

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Tabelle 160: Ergebnisse für Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Population	Selpercatinib	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab			
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	HR [95% KI] p-Wert ^b
Gesamtüberleben					
mITT	36/115 (31,3)	NE [40,21; NE]	16/73 (21,9)	NE [43,60; NE]	1,44 [0,79; 2,60] 0,230
Datenschnitt: 01. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; IWRS: Interactive Web Response System; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; vs.: versus. a: In Monaten. b: Aus dem stratifizierten Log-rank-Test. Das HR wurde mit einem stratifizierten Cox-Modell geschätzt, mit Behandlung als Kovariable und mit geografischer Region (ostasiatisch vs. nicht ostasiatisch; laut IWRS) sowie Hirnmetastasenstatus zu Baseline (vorhanden vs. nicht vorhanden/unbekannt; laut IWRS) als Stratifizierungsvariablen.					

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_strat_dc240501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/t_ostte_mitt.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240501/adsl_gba
/lillyce/prd/ly3527723/j2g_mc_jzjc/intrm2/data/analysis/restricted/adtteos
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Tabelle 161: Ergebnisse für Gesamtüberleben (Raten) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

Endpunkt	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab	
	N unter Risiko	Überlebensrate ^{a,b} (%) [95%-KI]	N unter Risiko	Überlebensrate ^{a,b} (%) [95%-KI]
Gesamtüberleben				
≥ 6 Monate	110	95,7 [89,87; 98,17]	70	98,6 [90,55; 99,80]
≥ 12 Monate	104	93,0 [86,49; 96,44]	61	89,9 [80,02; 95,07]
≥ 18 Monate	89	83,1 [74,72; 88,84]	56	82,6 [71,31; 89,70]
≥ 24 Monate	73	75,5 [66,28; 82,49]	49	82,6 [71,31; 89,70]
≥ 30 Monate	51	69,7 [59,77; 77,61]	34	78,4 [66,04; 86,74]
≥ 36 Monate	26	66,4 [55,91; 75,02]	19	75,9 [62,72; 84,97]
≥ 42 Monate	2	50,2 [25,35; 70,75]	5	75,9 [62,72; 84,97]
Datenschnitt: 01. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; RCT: Randomisierte kontrollierte Studie. a: Die Schätzung basiert auf der Kaplan-Meier Methode. b: Das 95%-KI wurde mittels der Greenwood Formel berechnet.				

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_osr_dc240501.sas

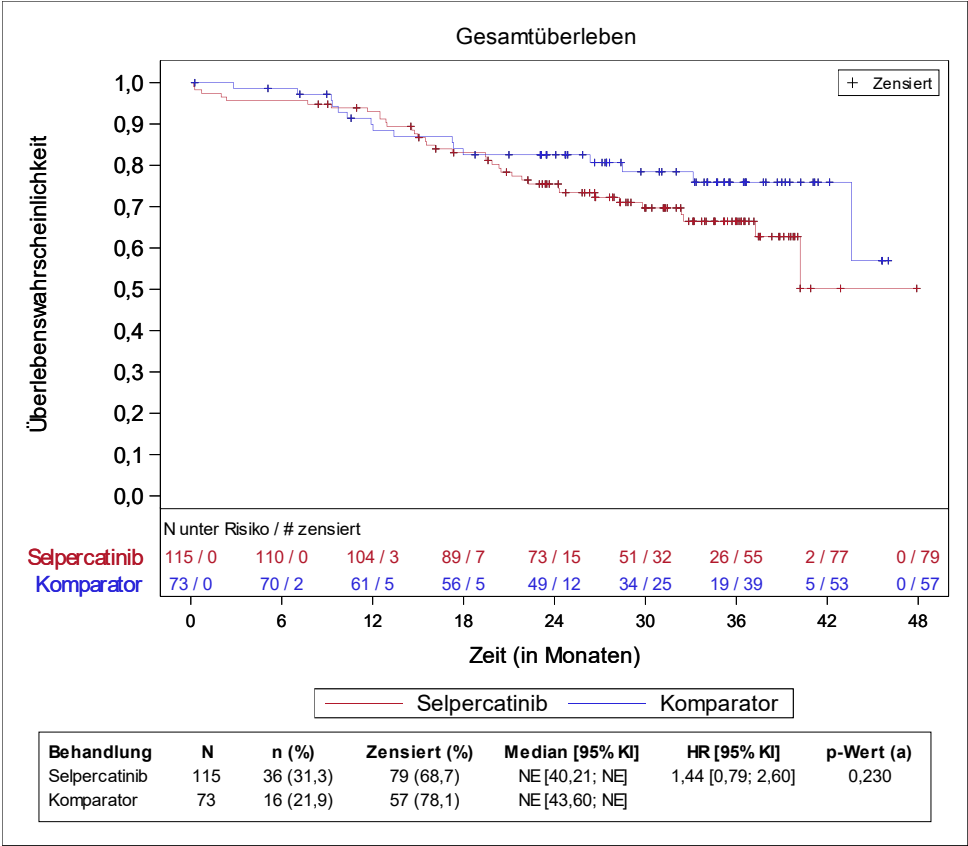
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/t_osr_mitt.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240501/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/intrm2/data/analysis/restricted/adtteos

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Abbildung 117: Kaplan-Meier Plot für Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT



Datenschnitt: 01. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg).
Abkürzungen: ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; IWRS: Interactive Web Response System; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; vs.: versus.
Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab.
a: Aus dem stratifizierten Log-rank-Test.
Das HR wurde mit einem stratifizierten Cox-Modell geschätzt, mit Behandlung als Kovariable und mit geografischer Region (ostasiatisch vs. nicht ostasiatisch; laut IWRS) sowie Hirnmetastasenstatus zu Baseline (vorhanden vs. nicht vorhanden/unbekannt; laut IWRS) als Stratifizierungsvariablen.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_tte_strat_dc240501.sas
Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/f_oskm_mitt.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240501/adsl_gba
/lilly/prd/ly3527723/j2g_mc_jzjc/intrm2/data/analysis/restricted/adtteos
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Tabelle 68: Ergebnis des Interaktionsterms der Subgruppenanalysen je Endpunkt aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431

Endpunkt	Subgruppe											
	Alter	Baseline ECOG	Geschlecht	Geografische Region	Raucherstatus	Hirnmastasen zu Baseline (CRF)	Lebermetastasen (BICR)	PD-L1 Expression - SG-Analyse 3	Krankheitsstatus	Ethnische Zugehörigkeit	RET-Probenart	RET-Fusion Resultat
Mortalität - Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg)												
Gesamtüberleben	0,677	0,277	0,584	0,583	0,818	0,892	0,268	0,750	0,819	0,641	0,959	0,990
Datenschnitt: 01. Mai 2024. Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. Die Tabelle zeigt p-Werte der Interaktionsterme von Subgruppenfaktor und Behandlungsgruppe aus dem unstratifizierten Cox-Proportional-Hazard-Modell mit Behandlung und Subgruppenfaktor als Kovariablen. Ein Interaktionstest wird nur gerechnet, wenn jede Subgruppenkategorie mindestens 10 Patienten umfasst und mindestens 10 Ereignisse in einer der Subgruppenkategorien aufgetreten sind.												

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_interact_dc240501.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240501/t_interact.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240501/adsl_gba
/lillyce/prd/ly3527723/j2g_mc_jzjc/intrm2/data/analysis/restricted/adtteos
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Tabelle 193: Subgruppen für das Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, MITT

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Alter (p-Wert des Interaktionsterms: 0,677)					
<65 Jahre	22/76 (28,9)	NE [NE; NE]	9/45 (20,0)	NE [NE; NE]	1,55 [0,71; 3,36] 0,267
≥65 Jahre	14/39 (35,9)	40,2 [28,29; NE]	7/28 (25,0)	43,6 [NE; NE]	1,47 [0,56; 3,84] 0,425
Baseline ECOG (p-Wert des Interaktionsterms: 0,277)					
0	9/41 (22,0)	NE [40,21; NE]	2/25 (8,0)	NE [NE; NE]	3,22 [0,69; 15,00] 0,115
1	27/74 (36,5)	37,3 [32,36; NE]	14/48 (29,2)	43,6 [43,60; NE]	1,29 [0,66; 2,49] 0,457
Geschlecht (p-Wert des Interaktionsterms: 0,584)					
Männlich	16/61 (26,2)	40,2 [40,21; NE]	7/34 (20,6)	43,6 [43,60; NE]	1,51 [0,59; 3,89] 0,387
Weiblich	20/54 (37,0)	NE [26,68; NE]	9/39 (23,1)	NE [NE; NE]	1,70 [0,77; 3,74] 0,181
Geografische Region (p-Wert des Interaktionsterms: 0,583)					
Ostasiatisch	18/65 (27,7)	NE [NE; NE]	8/35 (22,9)	NE [NE; NE]	1,18 [0,51; 2,72] 0,695
Nicht-Ostasiatisch	18/50 (36,0)	40,2 [32,36; NE]	8/38 (21,1)	43,6 [43,60; NE]	1,84 [0,80; 4,26] 0,146
Raucherstatus (p-Wert des Interaktionsterms: 0,818)					
Nie	24/72 (33,3)	NE [32,36; NE]	12/50 (24,0)	43,6 [43,60; NE]	1,54 [0,75; 3,14] 0,235
Ehemals/Aktuell	12/43 (27,9)	40,2 [40,21; NE]	4/23 (17,4)	NE [NE; NE]	1,75 [0,56; 5,47] 0,327
Hirnmetastasen zu Baseline (CRF) (p-Wert des Interaktionsterms: 0,892)					
Ja	11/23 (47,8)	28,3 [15,47; NE]	4/14 (28,6)	NE [9,72; NE]	1,68 [0,53; 5,29] 0,368
Nein	10/44 (22,7)	NE [NE; NE]	3/23 (13,0)	NE [NE; NE]	1,70 [0,47; 6,20] 0,413

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
Unbekannt	15/48 (31,3)	NE [37,26; NE]	9/36 (25,0)	NE [43,60; NE]	1,37 [0,59; 3,16] 0,465
Lebermetastasen (BICR) (p-Wert des Interaktionsterms: 0,268)					
Ja	9/16 (56,3)	37,3 [14,75; NE]	7/13 (53,8)	33,1 [9,26; NE]	1,03 [0,36; 2,91] 0,957
Nein	27/98 (27,6)	NE [NE; NE]	9/60 (15,0)	NE [NE; NE]	1,89 [0,89; 4,01] 0,094
PD-L1 Expression - SG-Analyse 3 *** (p-Wert des Interaktionsterms: 0,750)					
Negativ	5/26 (19,2)	NE [NE; NE]	2/12 (16,7)	NE [17,35; NE]	0,88 [0,17; 4,60] 0,878
Positiv	18/49 (36,7)	40,2 [29,80; NE]	9/35 (25,7)	NE [43,60; NE]	1,70 [0,75; 3,84] 0,198
Unbekannt	13/40 (32,5)	NE [32,53; NE]	5/26 (19,2)	NE [NE; NE]	1,74 [0,62; 4,87] 0,289
Krankheitsstatus (p-Wert des Interaktionsterms: 0,819)					
III*	3/6 (50,0)	NE [12,48; NE]	0/6 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,080
IVA	12/44 (27,3)	NE [37,26; NE]	5/33 (15,2)	NE [NE; NE]	1,71 [0,60; 4,86] 0,308
IVB	21/65 (32,3)	40,2 [32,53; NE]	11/34 (32,4)	43,6 [33,15; NE]	1,23 [0,58; 2,64] 0,586
Ethnische Zugehörigkeit (p-Wert des Interaktionsterms: 0,641)					
Asiatisch	19/66 (28,8)	NE [NE; NE]	8/35 (22,9)	NE [NE; NE]	1,24 [0,54; 2,82] 0,615
Nicht asiatisch	17/49 (34,7)	40,2 [32,36; NE]	7/34 (20,6)	43,6 [43,60; NE]	1,86 [0,77; 4,52] 0,161
RET-Probenart (p-Wert des Interaktionsterms: 0,959)					
Blut	4/9 (44,4)	40,2 [7,72; NE]	3/10 (30,0)	NE [9,26; NE]	1,55 [0,35; 6,95] 0,563
Gewebe	32/106 (30,2)	NE [37,26; NE]	13/63 (20,6)	NE [43,60; NE]	1,53 [0,80; 2,94] 0,197
RET-Fusion Resultat **** (p-Wert des Interaktionsterms: 0,990)					

Subgruppe	Selpercatinib		Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		HR [95% KI] p-Wert ^b
	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	
CCDC6*	0/9 (0,0)	NE [NE; NE]	1/6 (16,7)	NE [17,35; NE]	0,00 [0,00; NE] 0,221
KIF5B	15/50 (30,0)	NE [40,21; NE]	9/36 (25,0)	NE [33,15; NE]	1,06 [0,46; 2,42] 0,898
Datenschnitt: 01. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: BICR: Blinded Independent Central Review; CRF: Case Report Form; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mITT: Modifizierte ITT-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie; RET: Rearranged during transfection. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. Das HR wurde mit einem unstratifizierten Cox-Modell mit Behandlung als Kovariable geschätzt. * SAS Warning: The likelihood ratio test for strata homogeneity is questionable since some strata have no events. Region: Ostasiatisch beinhaltet China, Hong Kong, Japan, Singapur, Südkorea und Taiwan; nicht-Ostasiatisch beinhaltet Argentinien, Australien, Belgien, Brasilien, Deutschland, Frankreich, Griechenland, Israel, Italien, Kanada, Mexiko, Niederlande, Polen, Russland, Spanien, Tschechien, Türkei und Ukraine *** Die Subgruppe Unbekannt umfasst Patienten mit fehlendem PD-L1-Expressions-Status. **** PCR Tests ergeben nur ein positives Resultat ohne den spezifischen RET-Fusions Partner zu benennen. Sie bleiben unberücksichtigt.					

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_tte_sub_dc240501.sas

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/lilly/prd/ly3527723/j2g_mc_jzjc/intrm2/data/analysis/restricted/adtteos

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Anhang 4-G6: Angaben zum Datenschnitt vom 08.05.2024

Anhang 4-G6.1: Angaben zur Studienpopulation sowie Ergebnisse für unerwünschte Ereignisse

Tabelle 162: Crossover Rate - RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mITT

	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=73) n (%)
Patienten mit Crossover zu Selpercatinib	43 (58,9)
Datenschnitt: 08. Mai 2024; Modifizierte ITT-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; mITT: Modifizierte ITT-Pembrolizumab Population; n: Anzahl der Patienten; N: Anzahl der Patienten in der Analyse; RCT: Randomisierte kontrollierte Studie.	

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Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/t_xrate_mitt.rtf
Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba
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Tabelle 163: Behandlungsdauer - RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF

	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72)				
	Selpercatinib	Carboplatin	Cisplatin	Pembro- lizumab	Pemetrexed	Any
Dauer der Therapie (Monate)						
n	116	62	12	72	72	72
Median	24,7	2,8	2,8	11,6	7,4	12,5
Q1 - Q3	10,9 - 35,0	2,8 - 3,0	2,4 - 2,9	5,1 - 22,3	4,6 - 16,6	6,8 - 22,3
Min - Max	0,2 - 49,9	0,7 - 3,5	1,4 - 3,4	0,7 - 28,3	0,7 - 40,0	0,7 - 40,0
MW	22,9	2,7	2,7	13,2	11,7	14,5
SD	13,1	0,6	0,5	8,7	9,7	9,8
Anzahl der Therapiezyklen pro Patient^a						
n	115	62	12	72	72	72
Median	31,0	4,0	4,0	14,5	10,5	15,5
Q1 - Q3	13,0 - 46,0	4,0 - 4,0	3,0 - 4,0	7,0 - 32,0	6,5 - 22,5	9,0 - 32,0
Min - Max	1,0 - 69,0	1,0 - 4,0	2,0 - 4,0	1,0 - 36,0	1,0 - 56,0	1,0 - 56,0
MW	29,9	3,9	3,6	18,1	15,9	19,8
SD	17,8	0,5	0,7	11,9	13,2	13,6
Datenschnitt: 08. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; Max: Maximum; Min: Minimum; mSAF: Modifizierte Safety-Pembrolizumab Population; MW: Mittelwert; n: Anzahl der Patienten; N: Anzahl der Patienten in der Analyse; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung. a: Patient gilt als behandelt in einem Therapiezyklus, wenn er mindestens eine Dosis des Studienmedikaments erhalten hat.						

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_ex_dur_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/t_ex_dur_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/armay2024/data/analysis/shared/adexsum

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Tabelle 164: Beobachtungsdauern pro Endpunkt (Monaten) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF

Endpunkt Merkmal	Selpercatinib (N=115)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72)
Unerwünschte Ereignisse		
Median (Min; Max)	24,28 (0,16; 48,10)	12,70 (2,07; 39,72)
Q1; Q3	11,89; 33,87	7,59; 23,18
Datenschnitt: 08. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; Max: Maximum; Min: Minimum; mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Daten; Q1 (Q3): Quartil 1 (3); RCT: Randomisierte kontrollierte Studie. Die Beobachtungsdauer für unerwünschte Ereignisse wurde vom Tag der ersten Dosis bis zum frühesten Datum aus (letzter Behandlungstag+30, Tod, Datum des Datenschnitts) deskriptiv beschrieben.		

Program Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_fup_dc240508.sas
Output Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/t_fup_msaf.rtf
Dataset Location: /lillyce/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba
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Tabelle 165: Ergebnisse für unerwünschte Ereignisse (Gesamtraten) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF

Selpercatinib			Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab		
Population	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	n/N (%)	Mediane Ereigniszeit ^a [95% KI]	HR [95% KI] p-Wert ^b
Zeit bis zum ersten unerwünschten Ereignis (jeglicher Schweregrad)					
mSAF	115/115 (100,0)	0,3 [0,23; 0,26]	72/72 (100,0)	0,1 [0,10; 0,13]	0,84 [0,62; 1,14] 0,282
Zeit bis zum ersten schwerwiegenden unerwünschten Ereignis ^c					
mSAF	41/115 (35,7)	NE [39,23; NE]	21/72 (29,2)	NE [NE; NE]	1,04 [0,61; 1,76] 0,891
Zeit bis zum ersten unerwünschten Ereignis CTCAE Grad ≥3					
mSAF	84/115 (73,0)	4,5 [2,10; 9,36]	44/72 (61,1)	7,0 [2,92; 15,97]	1,20 [0,83; 1,73] 0,341
Zeit bis zum ersten unerwünschten Ereignis CTCAE Grad <3					
mSAF	113/115 (98,3)	0,3 [0,23; 0,30]	72/72 (100,0)	0,1 [0,10; 0,13]	0,80 [0,59; 1,09] 0,176
Zeit bis zum Behandlungsabbruch aufgrund unerwünschter Ereignisse ^c					
mSAF	11/115 (9,6)	NE [NE; NE]	5/72 (6,9)	NE [33,25; NE]	1,06 [0,36; 3,10] 0,914
Datenschnitt: 08. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie. a: In Monaten. b: Aus dem unstratifizierten Log-rank-Test. c: Es werden alle Ereignisse berücksichtigt ungeachtet dessen, ob sie als behandlungsbedingt eingestuft wurden oder nicht Das HR wurde mit einem unstratifizierten Cox-Modell geschätzt.					

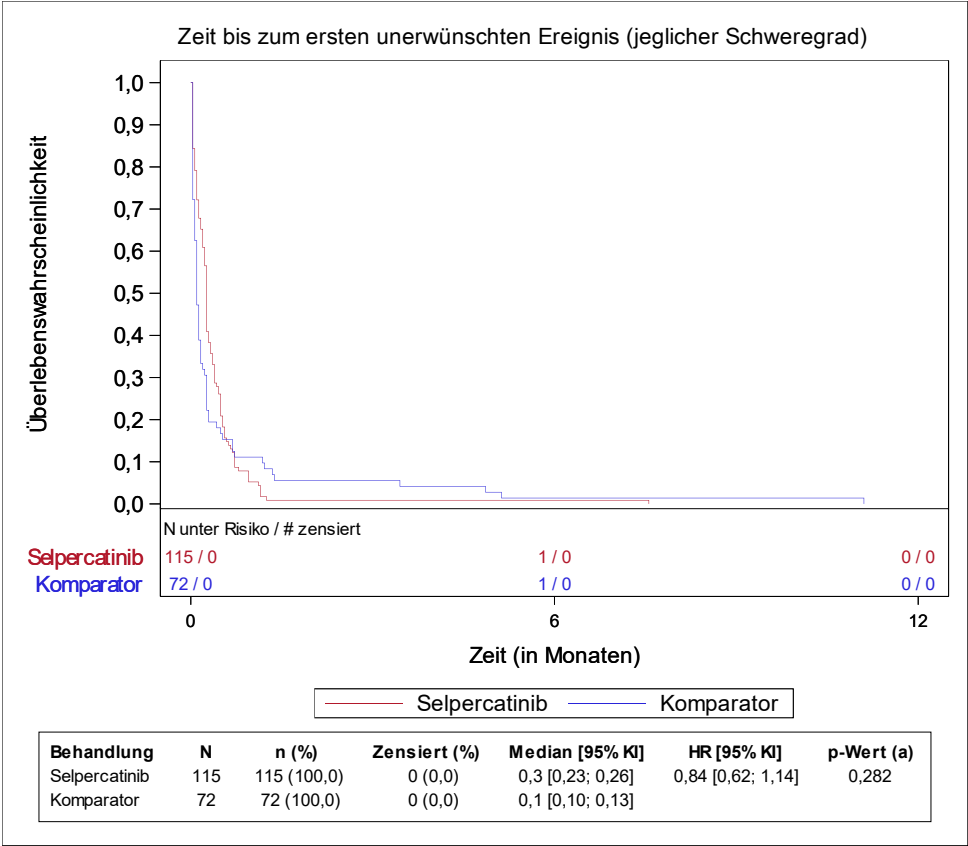
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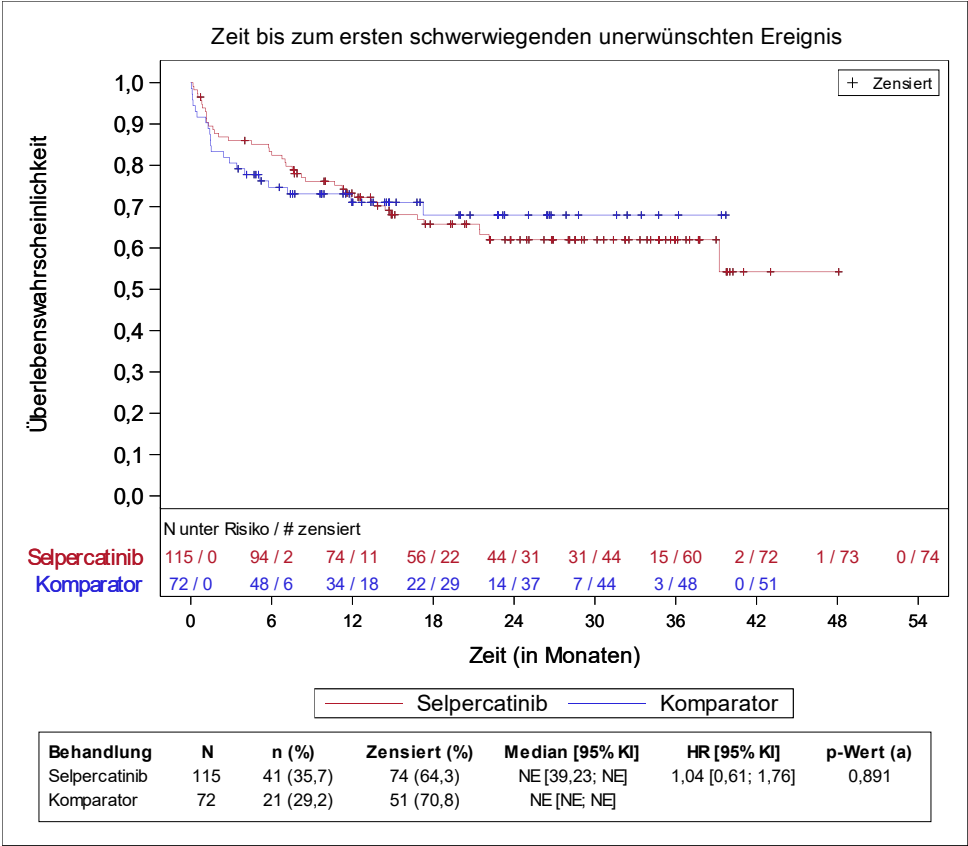
Abbildung 118: Kaplan-Meier Plot für Zeit bis zum ersten unerwünschten Ereignis (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF



Datenschnitt: 08. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg).
Abkürzungen: ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall;
mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; RCT: Randomisierte kontrollierte Studie.
Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab.
a: Aus dem unstratifizierten Log-rank-Test.
Das HR wurde mit einem unstratifizierten Cox-Modell geschätzt.

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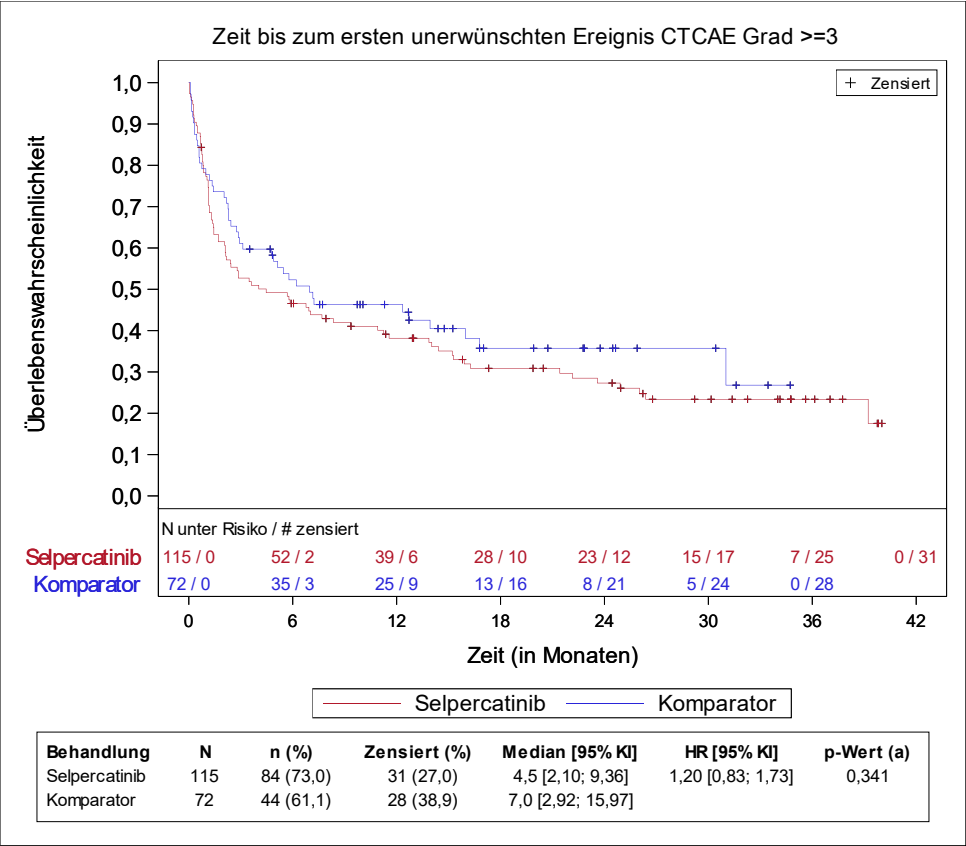
Abbildung 119: Kaplan-Meier Plot für Zeit bis zum ersten schwerwiegenden unerwünschten Ereignis aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF



Datenschnitt: 08. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg).
Abkürzungen: ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall;
mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; NE: Nicht erchenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie.
Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab.
a: Aus dem unstratifizierten Log-rank-Test.
Das HR wurde mit einem unstratifizierten Cox-Modell geschätzt.
Es werden alle Ereignisse berücksichtigt ungeachtet dessen, ob sie als behandlungsbedingt eingestuft wurden oder nicht

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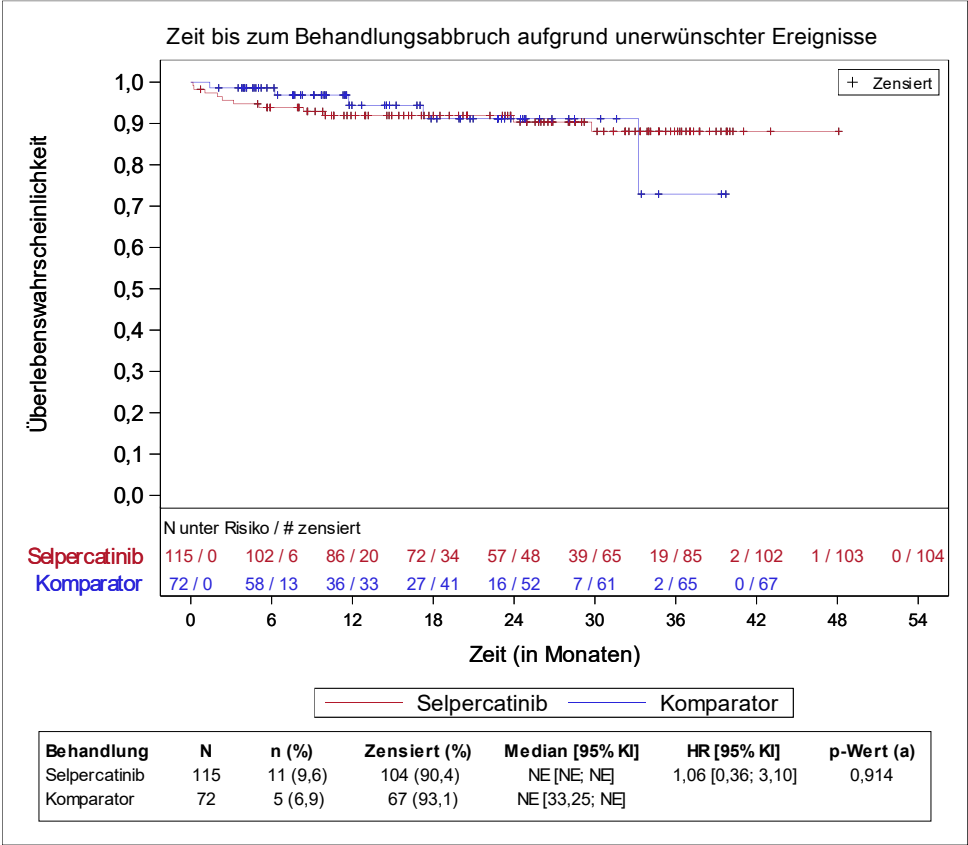
Abbildung 120: Kaplan-Meier Plot für Zeit bis zum ersten unerwünschten Ereignis CTCAE Grad ≥ 3 aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF



Datenschnitt: 08. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg).
Abkürzungen: CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group;
HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall; mSAF: Modifizierte Safety-Pembrolizumab Population; N:
Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; RCT: Randomisierte kontrollierte Studie.
Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab.
a: Aus dem unstratifizierten Log-rank-Test.
Das HR wurde mit einem unstratifizierten Cox-Modell geschätzt.

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Abbildung 121: Kaplan-Meier Plot für Zeit bis zum Behandlungsabbruch aufgrund unerwünschter Ereignisse aus RCT mit dem zu bewertenden Arzneimittel - Studie LIBRETTO-431, mSAF



Datenschnitt: 08. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥ 50 kg).
Abkürzungen: ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: Kilogramm; KI: Konfidenzintervall;
mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten
mit Ereignis; NE: Nicht errechenbar/nicht erreicht; RCT: Randomisierte kontrollierte Studie.
Komparator = Carboplatin oder Cisplatin + Pemetrexed + Pembrolizumab.
a: Aus dem unstratifizierten Log-rank-Test.
Das HR wurde mit einem unstratifizierten Cox-Modell geschätzt.
Es werden alle Ereignisse berücksichtigt ungeachtet dessen, ob sie als behandlungsbedingt eingestuft wurden oder nicht

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aeov_tte_dc240508.sas
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Table 166: Results for TEAEs occurred in $\geq 10\%$ or in ≥ 10 patients and $\geq 1\%$ in any treatment arm within analysis population - study LIBRETTO-431, mSAF

SOC Preferred term	Selpercatinib	Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab			
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	HR [95% CI] p-value ^b
TEAEs occurred in ≥10% or in ≥10 patients and ≥1% in any treatment arm within analysis population					
Investigations	98/115 (85.2)	0.7 [0.49; 1.18]	53/72 (73.6)	2.1 [1.18; 4.96]	1.40 [1.00; 1.96] 0.052
Aspartate aminotransferase increased	72/115 (62.6)	2.1 [1.48; 7.66]	30/72 (41.7)	NE [4.96; NE]	1.88 [1.23; 2.88] 0.003
Alanine aminotransferase increased	69/115 (60.0)	2.8 [1.48; 10.97]	29/72 (40.3)	NE [7.16; NE]	1.74 [1.13; 2.69] 0.011
Blood bilirubin increased*	48/115 (41.7)	NE [11.96; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] <0.001
Blood creatinine increased	30/115 (26.1)	NE [NE; NE]	14/72 (19.4)	NE [NE; NE]	1.25 [0.66; 2.37] 0.496
Neutrophil count decreased	23/115 (20.0)	NE [NE; NE]	22/72 (30.6)	30.4 [27.93; NE]	0.59 [0.33; 1.06] 0.074
Platelet count decreased	23/115 (20.0)	NE [NE; NE]	14/72 (19.4)	NE [NE; NE]	0.97 [0.50; 1.88] 0.918
White blood cell count decreased	23/115 (20.0)	NE [NE; NE]	21/72 (29.2)	31.0 [31.01; NE]	0.63 [0.35; 1.15] 0.129
Electrocardiogram QT prolonged	21/115 (18.3)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	14.23 [1.91; 105.86] <0.001
Bilirubin conjugated increased	19/115 (16.5)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	11.80 [1.58; 88.18] 0.002
Weight increased	19/115 (16.5)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	1.62 [0.68; 3.86] 0.270
Blood alkaline phosphatase increased	17/115 (14.8)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	1.92 [0.70; 5.26] 0.196
Gamma-glutamyltransfe rase increased	14/115 (12.2)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	1.52 [0.54; 4.28] 0.424
Weight decreased	10/115 (8.7)	NE [39.29; NE]	8/72 (11.1)	NE [32.56; NE]	0.49 [0.19; 1.28] 0.138

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Gastrointestinal disorders	90/115 (78.3)	1.4 [0.72; 3.45]	55/72 (76.4)	0.3 [0.13; 0.79]	0.77 [0.55; 1.08] 0.148
Diarrhoea	62/115 (53.9)	10.4 [6.44; 23.20]	20/72 (27.8)	NE [16.72; NE]	2.02 [1.22; 3.35] 0.005
Dry mouth	46/115 (40.0)	NE [14.36; NE]	4/72 (5.6)	NE [NE; NE]	8.56 [3.08; 23.79] <0.001
Constipation	25/115 (21.7)	NE [NE; NE]	29/72 (40.3)	NE [2.89; NE]	0.43 [0.25; 0.74] 0.002
Vomiting	20/115 (17.4)	NE [NE; NE]	18/72 (25.0)	NE [NE; NE]	0.53 [0.28; 1.00] 0.047
Abdominal pain	17/115 (14.8)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	2.32 [0.78; 6.90] 0.121
Nausea	17/115 (14.8)	NE [NE; NE]	30/72 (41.7)	NE [1.64; NE]	0.25 [0.14; 0.46] <0.001
Abdominal pain upper	15/115 (13.0)	NE [NE; NE]	10/72 (13.9)	NE [NE; NE]	0.85 [0.38; 1.90] 0.699
Stomatitis	10/115 (8.7)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	2.06 [0.57; 7.49] 0.263
General disorders and administration site conditions	78/115 (67.8)	5.1 [1.91; 9.00]	51/72 (70.8)	1.5 [0.39; 4.83]	0.68 [0.47; 0.97] 0.033
Oedema peripheral	30/115 (26.1)	NE [NE; NE]	13/72 (18.1)	NE [30.59; NE]	1.25 [0.65; 2.40] 0.506
Fatigue	19/115 (16.5)	NE [NE; NE]	18/72 (25.0)	NE [NE; NE]	0.53 [0.28; 1.02] 0.056
Asthenia	18/115 (15.7)	NE [NE; NE]	22/72 (30.6)	NE [31.28; NE]	0.41 [0.22; 0.76] 0.004
Pyrexia	16/115 (13.9)	NE [NE; NE]	18/72 (25.0)	NE [23.89; NE]	0.45 [0.23; 0.90] 0.021
Metabolism and nutrition disorders	64/115 (55.7)	12.6 [6.97; 21.49]	37/72 (51.4)	15.9 [2.10; NE]	0.87 [0.58; 1.30] 0.500
Hypoalbuminaemia	22/115 (19.1)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	2.17 [0.82; 5.76] 0.112

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Decreased appetite	20/115 (17.4)	NE [NE; NE]	21/72 (29.2)	NE [NE; NE]	0.49 [0.26; 0.90] 0.021
Hypokalaemia	15/115 (13.0)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	1.20 [0.49; 2.95] 0.690
Hypocalcaemia*	13/115 (11.3)	NE [NE; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] 0.006
Hyperglycaemia	5/115 (4.3)	NE [NE; NE]	9/72 (12.5)	NE [NE; NE]	0.26 [0.09; 0.80] 0.012
Infections and infestations	63/115 (54.8)	13.8 [8.25; 19.81]	39/72 (54.2)	12.1 [8.05; 17.08]	0.87 [0.58; 1.29] 0.483
COVID-19	28/115 (24.3)	NE [NE; NE]	15/72 (20.8)	31.0 [23.92; NE]	0.85 [0.45; 1.60] 0.623
Upper respiratory tract infection	10/115 (8.7)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	1.60 [0.44; 5.87] 0.470
Vascular disorders	61/115 (53.0)	9.0 [3.25; NE]	10/72 (13.9)	NE [NE; NE]	4.81 [2.46; 9.40] <0.001
Hypertension	55/115 (47.8)	27.4 [3.38; NE]	5/72 (6.9)	NE [NE; NE]	9.01 [3.60; 22.54] <0.001
Skin and subcutaneous tissue disorders	60/115 (52.2)	10.4 [5.49; NE]	38/72 (52.8)	9.2 [1.64; NE]	0.84 [0.56; 1.26] 0.398
Rash	28/115 (24.3)	NE [NE; NE]	17/72 (23.6)	NE [NE; NE]	0.90 [0.49; 1.64] 0.723
Pruritus	14/115 (12.2)	NE [NE; NE]	16/72 (22.2)	NE [NE; NE]	0.44 [0.21; 0.91] 0.023
Respiratory, thoracic and mediastinal disorders	51/115 (44.3)	31.7 [15.18; NE]	32/72 (44.4)	21.9 [6.70; NE]	0.76 [0.49; 1.19] 0.226
Cough	17/115 (14.8)	NE [NE; NE]	13/72 (18.1)	NE [NE; NE]	0.62 [0.30; 1.29] 0.198
Dyspnoea	6/115 (5.2)	NE [NE; NE]	8/72 (11.1)	NE [NE; NE]	0.37 [0.13; 1.06] 0.055
Musculoskeletal and connective tissue disorders	45/115 (39.1)	NE [16.82; NE]	25/72 (34.7)	NE [11.79; NE]	1.10 [0.67; 1.80] 0.699

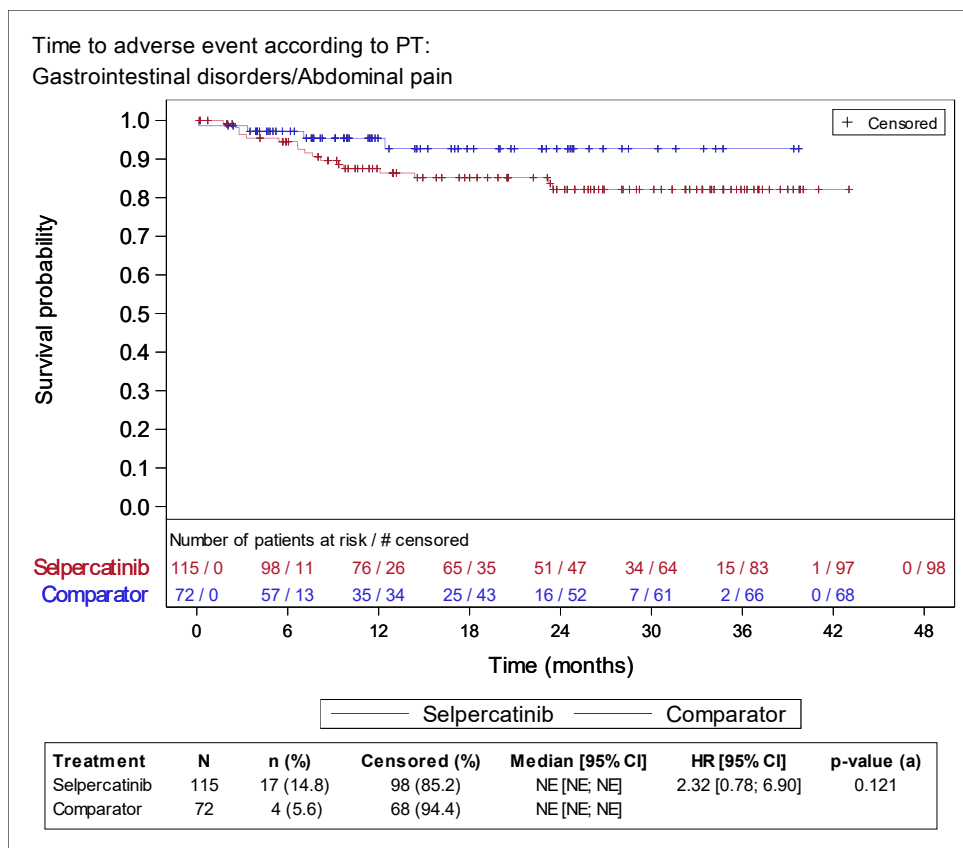
SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Arthralgia	15/115 (13.0)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	1.24 [0.50; 3.05] 0.643
Back pain	14/115 (12.2)	NE [NE; NE]	9/72 (12.5)	NE [NE; NE]	0.81 [0.35; 1.89] 0.630
Pain in extremity	12/115 (10.4)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	1.40 [0.44; 4.45] 0.562
Nervous system disorders	36/115 (31.3)	NE [NE; NE]	25/72 (34.7)	NE [21.68; NE]	0.80 [0.48; 1.33] 0.382
Headache	17/115 (14.8)	NE [NE; NE]	8/72 (11.1)	NE [NE; NE]	1.22 [0.52; 2.83] 0.645
Blood and lymphatic system disorders	35/115 (30.4)	NE [NE; NE]	47/72 (65.3)	2.2 [1.38; 5.78]	0.32 [0.20; 0.50] <0.001
Anaemia	18/115 (15.7)	NE [NE; NE]	40/72 (55.6)	4.2 [2.14; NE]	0.17 [0.09; 0.30] <0.001
Leukopenia	11/115 (9.6)	NE [NE; NE]	7/72 (9.7)	NE [NE; NE]	0.94 [0.37; 2.44] 0.904
Neutropenia	5/115 (4.3)	NE [NE; NE]	15/72 (20.8)	NE [NE; NE]	0.18 [0.07; 0.51] <0.001
Cardiac disorders	20/115 (17.4)	NE [39.23; NE]	18/72 (25.0)	NE [NE; NE]	0.58 [0.31; 1.11] 0.096
Eye disorders	20/115 (17.4)	NE [NE; NE]	17/72 (23.6)	NE [NE; NE]	0.61 [0.32; 1.18] 0.137
Lacrimation increased	2/115 (1.7)	NE [NE; NE]	9/72 (12.5)	NE [NE; NE]	0.12 [0.03; 0.57] 0.001
Psychiatric disorders	17/115 (14.8)	NE [39.46; NE]	5/72 (6.9)	NE [NE; NE]	1.87 [0.69; 5.10] 0.214
Renal and urinary disorders	16/115 (13.9)	NE [NE; NE]	10/72 (13.9)	NE [NE; NE]	0.90 [0.41; 2.00] 0.805
Injury, poisoning and procedural complications	15/115 (13.0)	NE [NE; NE]	8/72 (11.1)	NE [NE; NE]	0.89 [0.37; 2.13] 0.797
Reproductive system and breast disorders	15/115 (13.0)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	8.32 [1.10; 63.01] 0.014

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Hepatobiliary disorders	14/115 (12.2)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	2.69 [0.77; 9.38] 0.107
Endocrine disorders	13/115 (11.3)	NE [NE; NE]	11/72 (15.3)	NE [NE; NE]	0.70 [0.31; 1.56] 0.378
Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class. a: In months; b: from unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

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Figure 123: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Abdominal pain - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

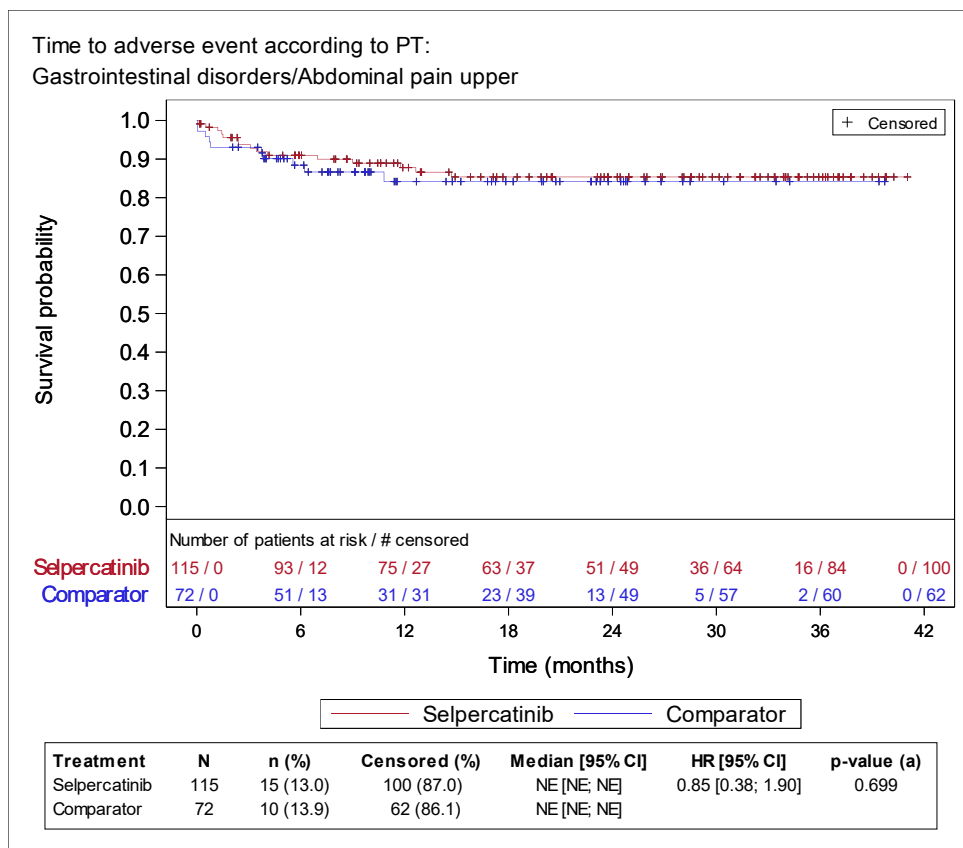
HR is based on the unstratified Cox proportional hazards model.

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Figure 124: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Abdominal pain upper - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

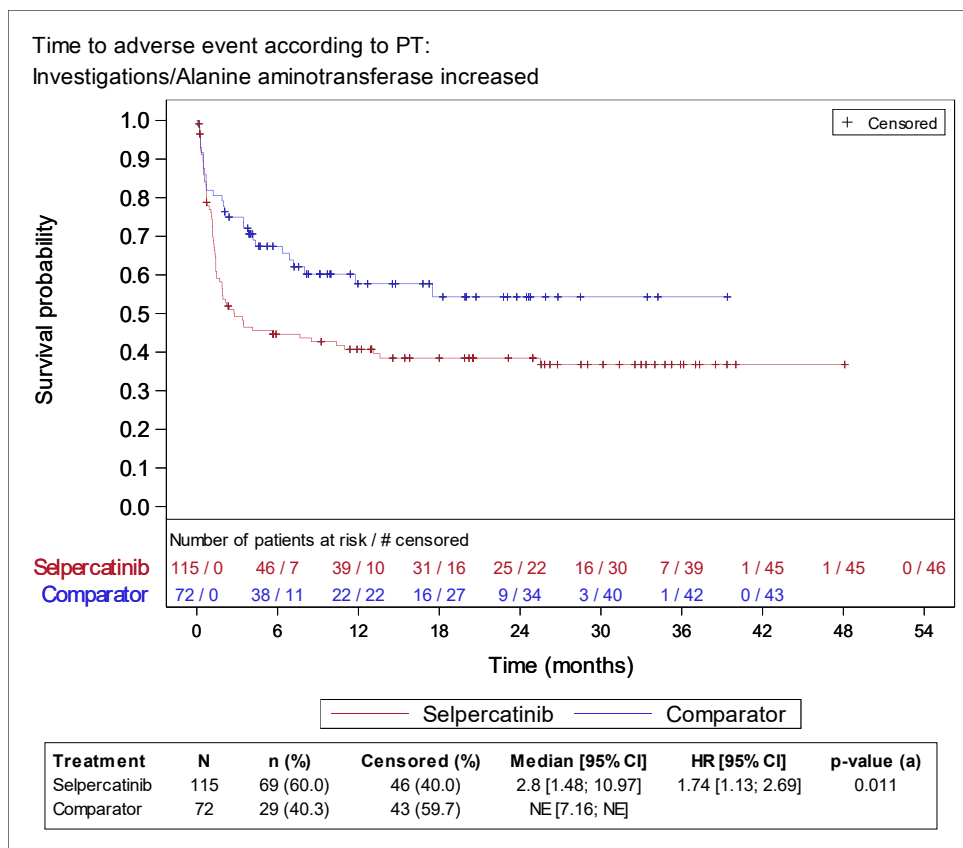
HR is based on the unstratified Cox proportional hazards model.

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 125: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Alanine aminotransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

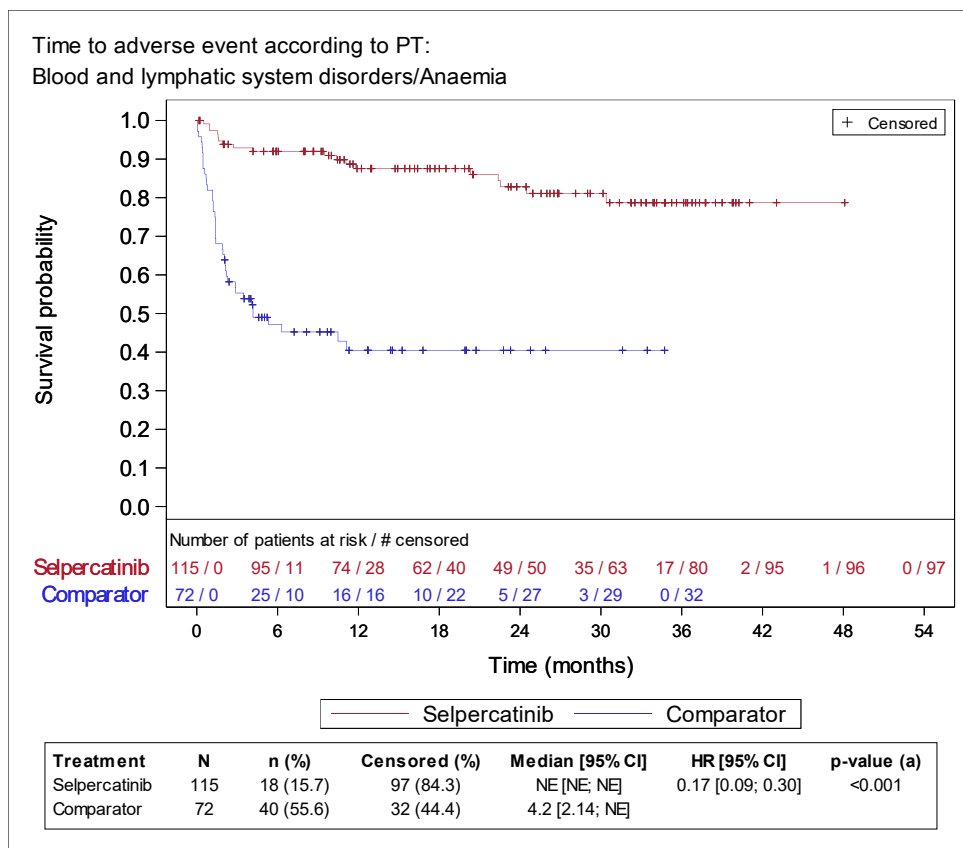
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx003_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 126: Kaplan-Meier Plot - Time to adverse event according to PT: Blood and lymphatic system disorders/Anaemia - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

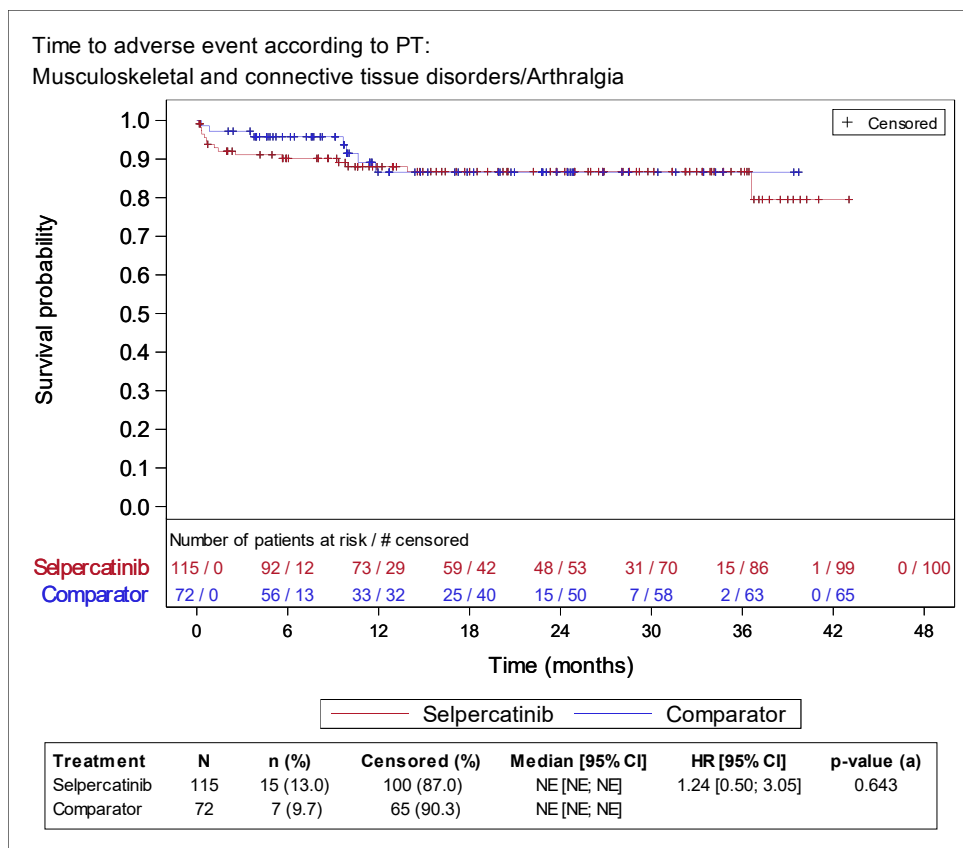
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx004_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 127: Kaplan-Meier Plot - Time to adverse event according to PT: Musculoskeletal and connective tissue disorders/Arthralgia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

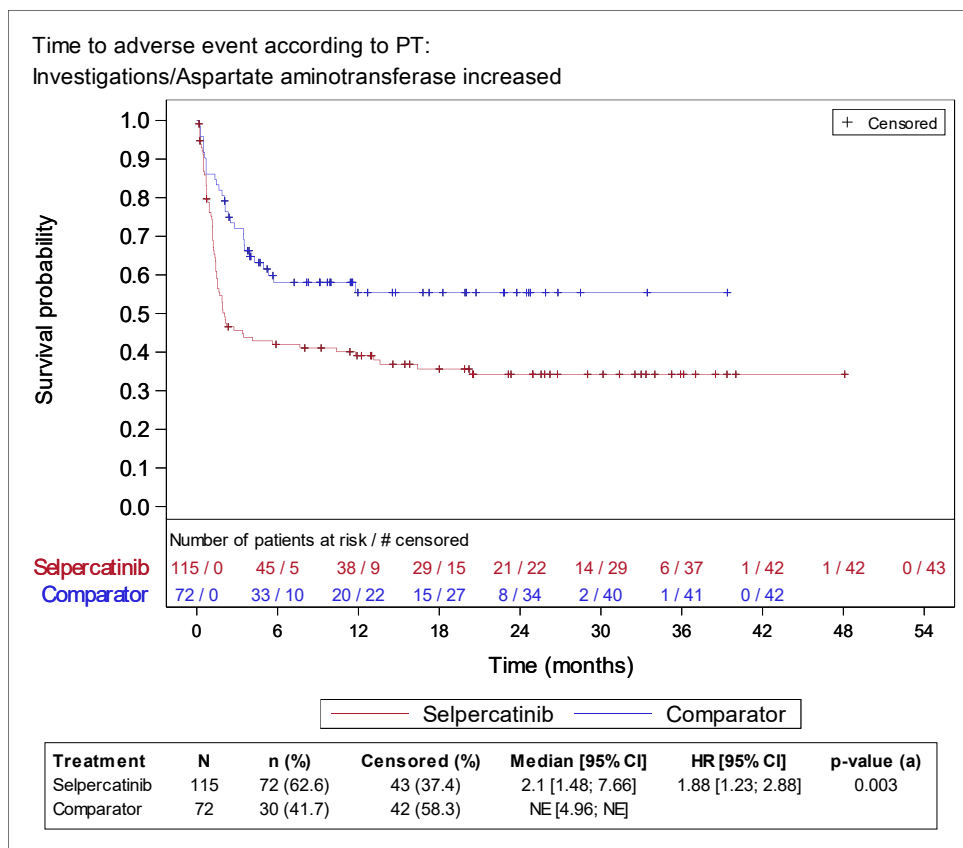
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx005_msaf.rtf

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Figure 128: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Aspartate aminotransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

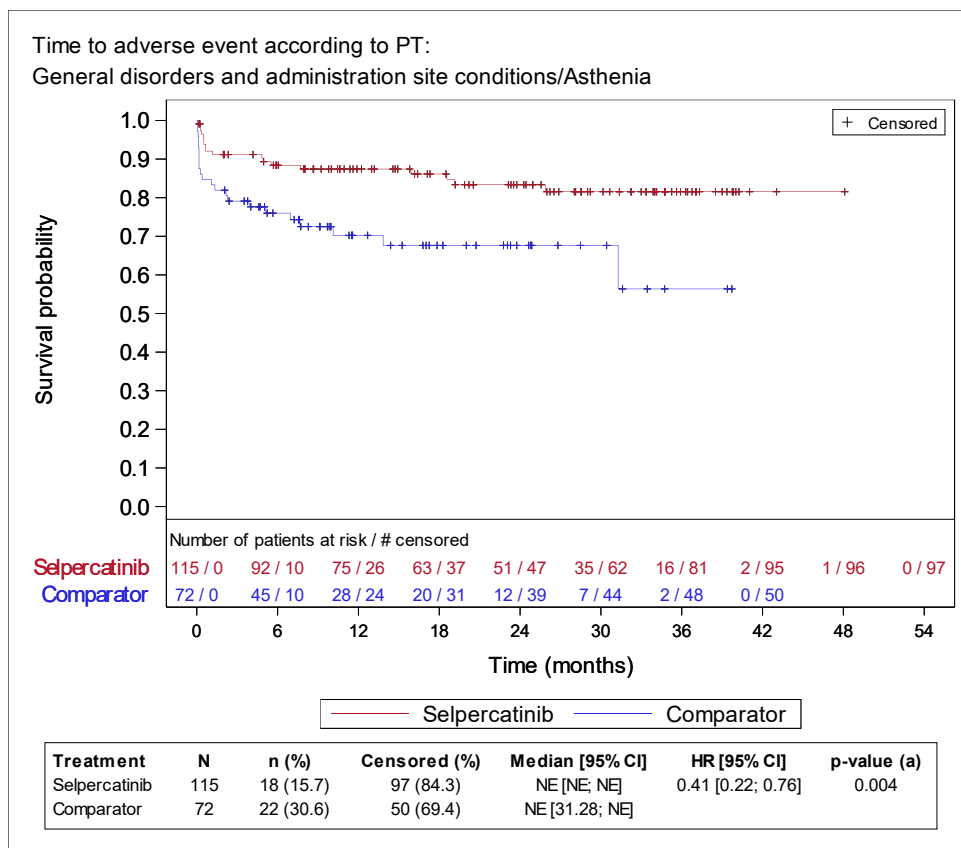
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx006_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 129: Kaplan-Meier Plot - Time to adverse event according to PT: General disorders and administration site conditions/Asthenia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

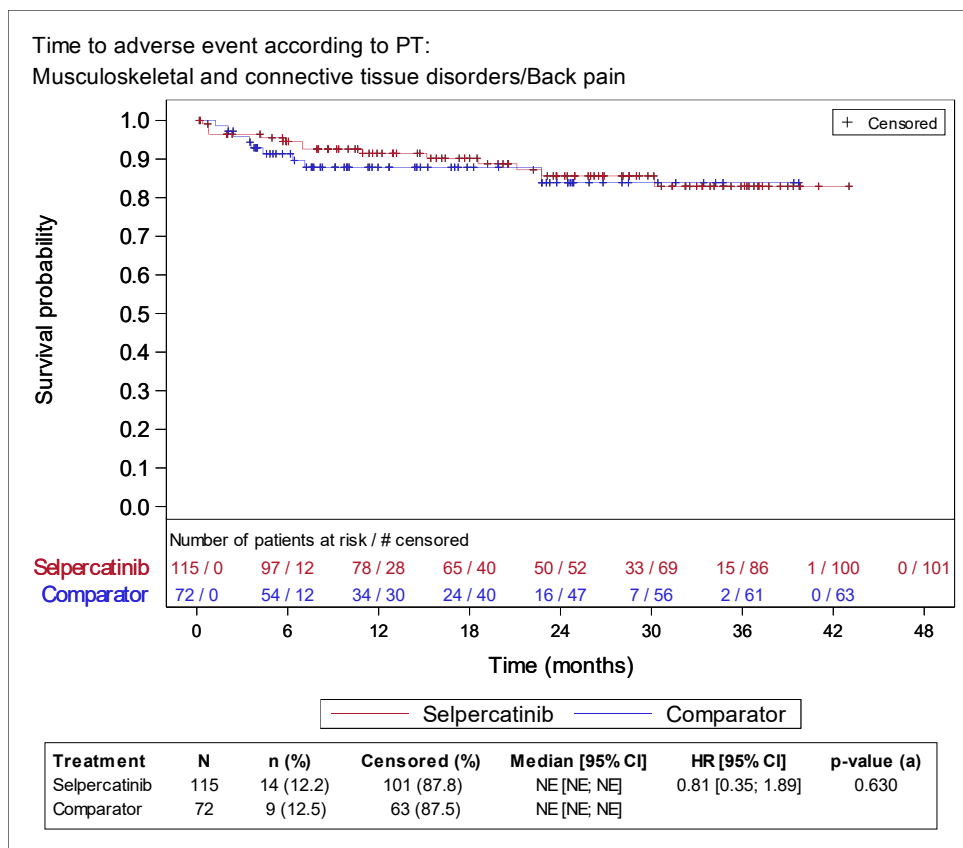
HR is based on the unstratified Cox proportional hazards model.

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Figure 130: Kaplan-Meier Plot - Time to adverse event according to PT: Musculoskeletal and connective tissue disorders/Back pain - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

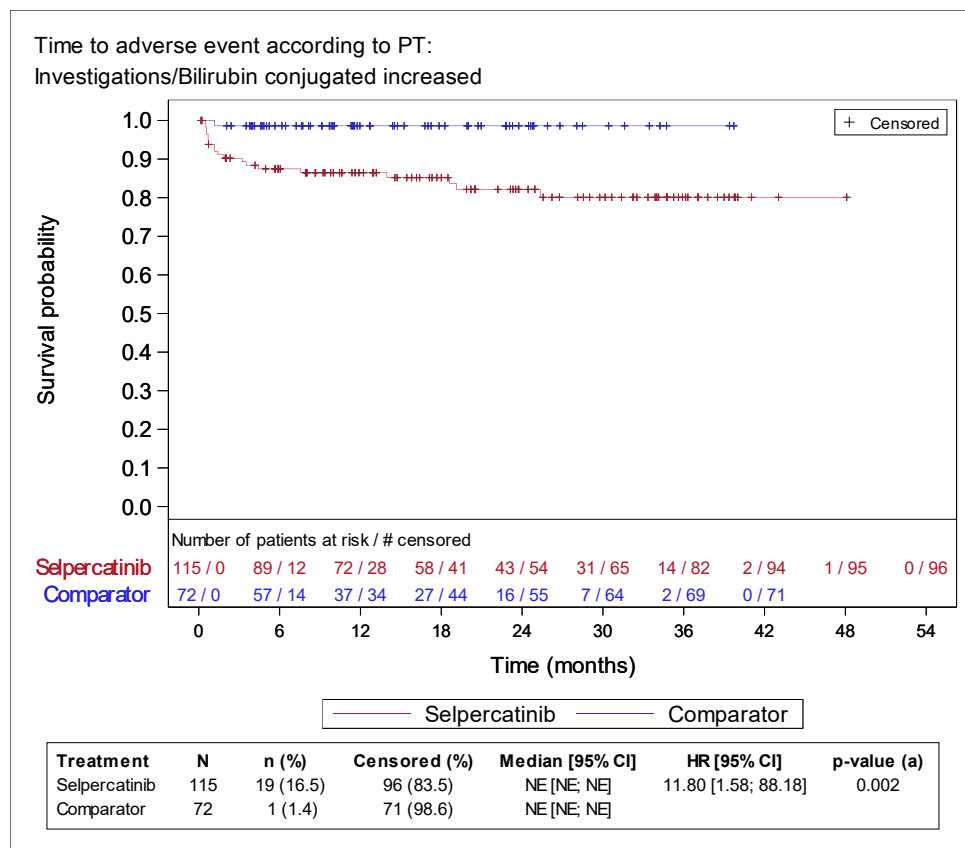
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 131: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Bilirubin conjugated increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

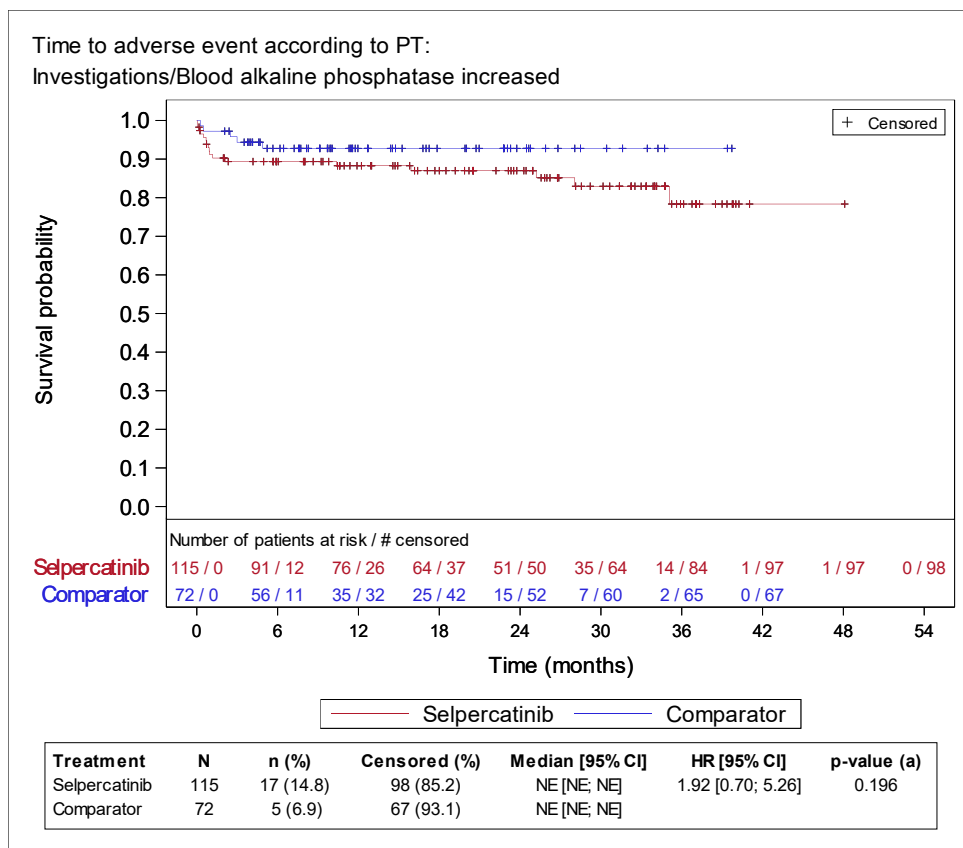
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 132: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Blood alkaline phosphatase increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

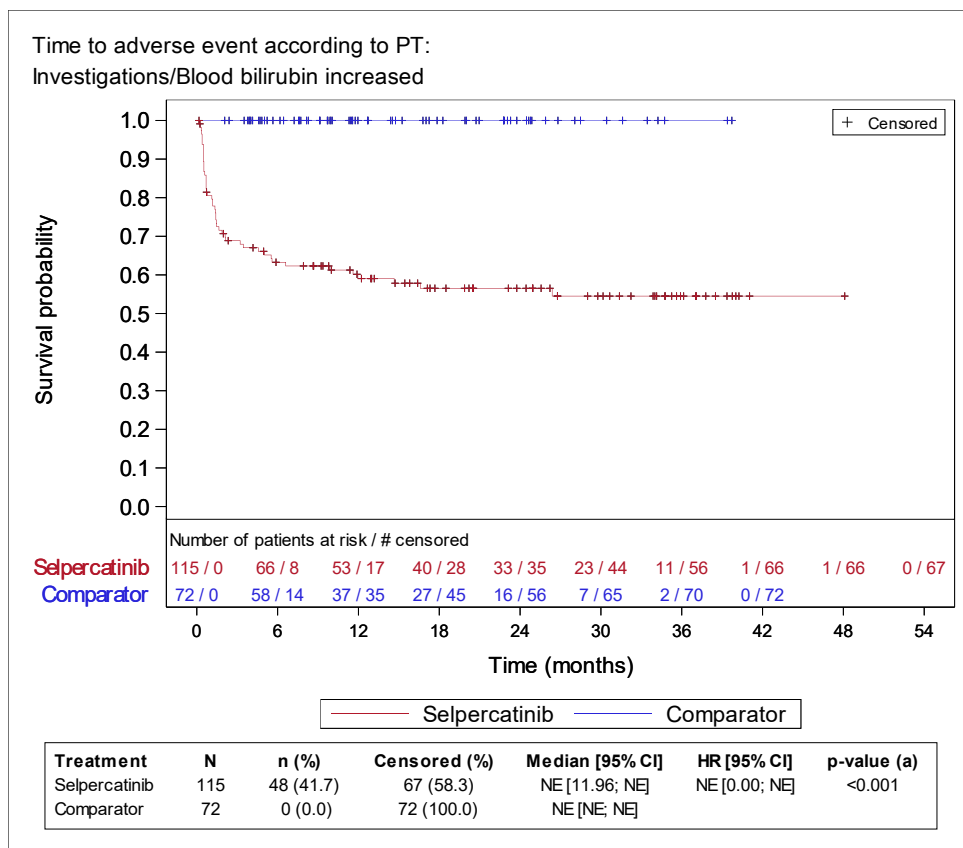
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 133: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Blood bilirubin increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

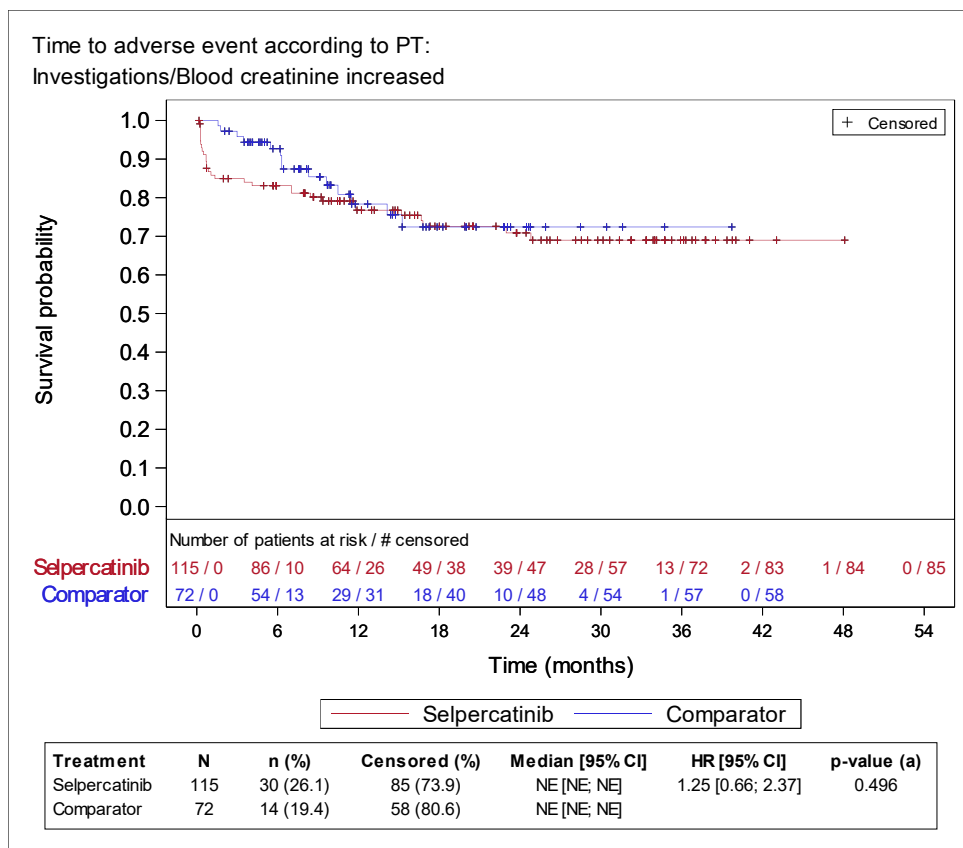
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx011_msaf.rtf

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Figure 134: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Blood creatinine increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

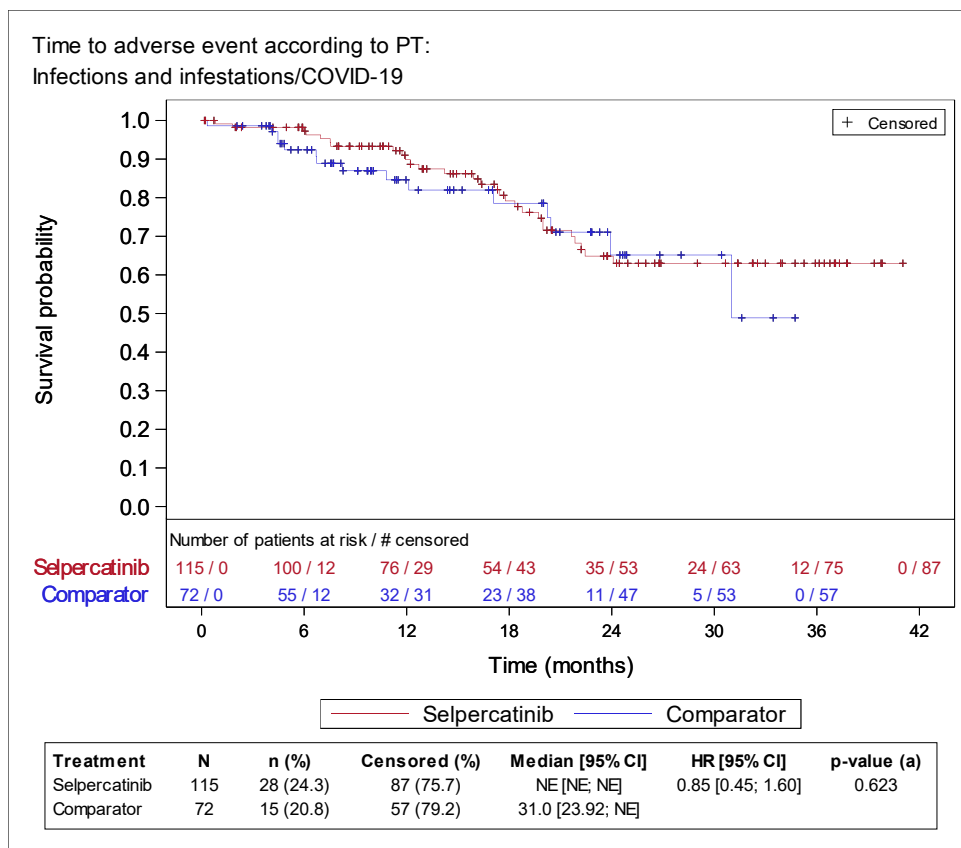
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx012_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 135: Kaplan-Meier Plot - Time to adverse event according to PT: Infections and infestations/COVID-19 - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

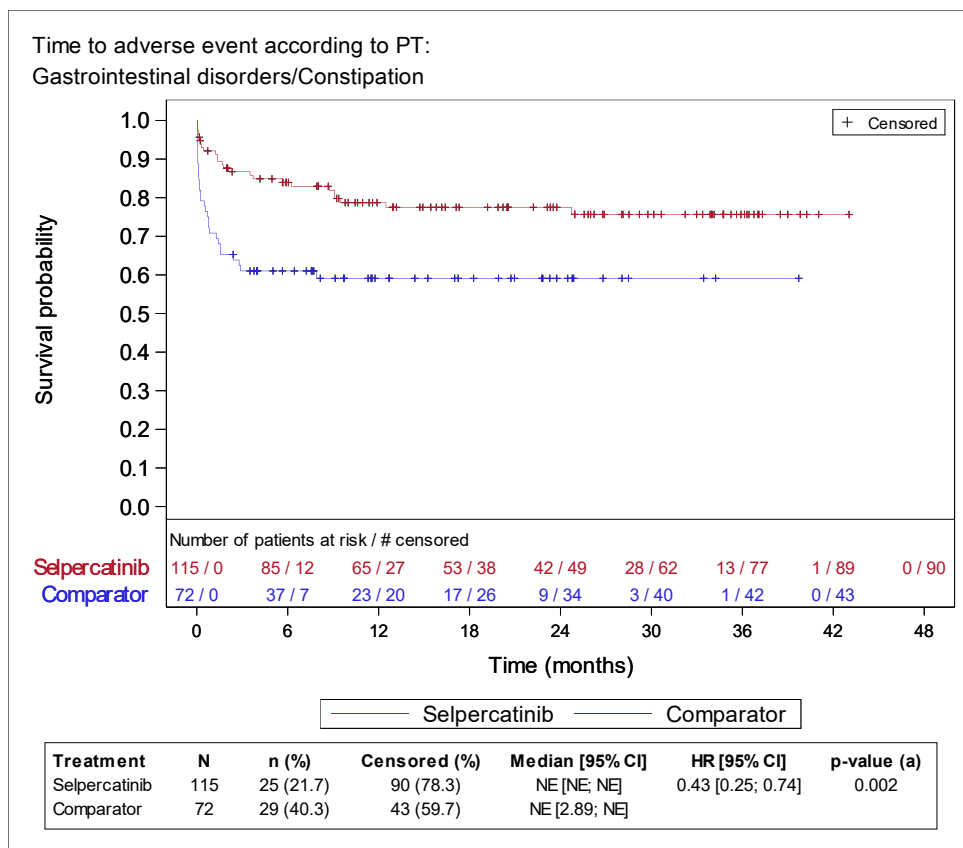
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 136: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Constipation - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

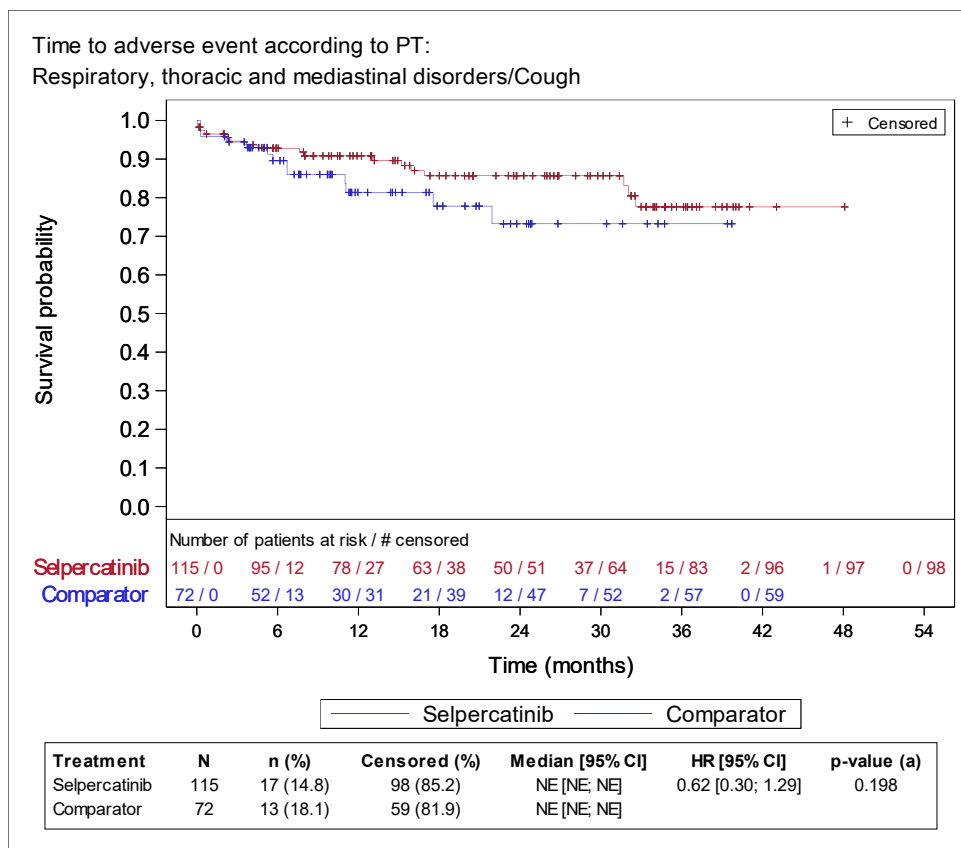
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx014_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 137: Kaplan-Meier Plot - Time to adverse event according to PT: Respiratory, thoracic and mediastinal disorders/Cough - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

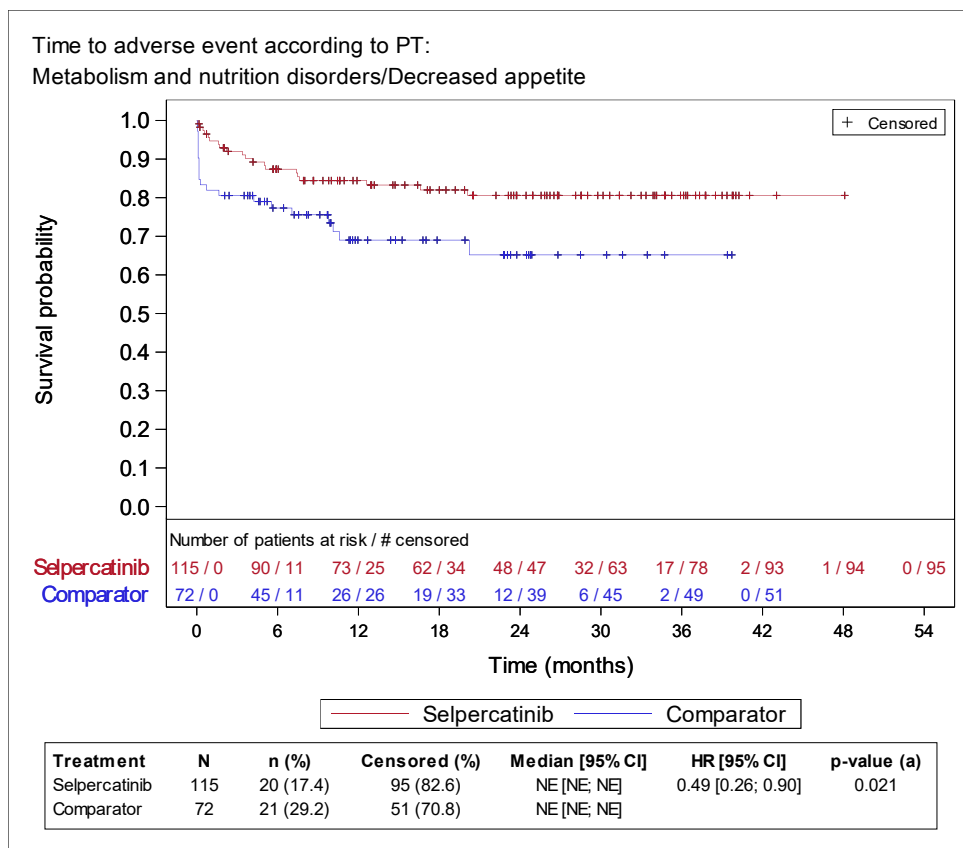
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba_adtteae_gba
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Figure 138: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Decreased appetite - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

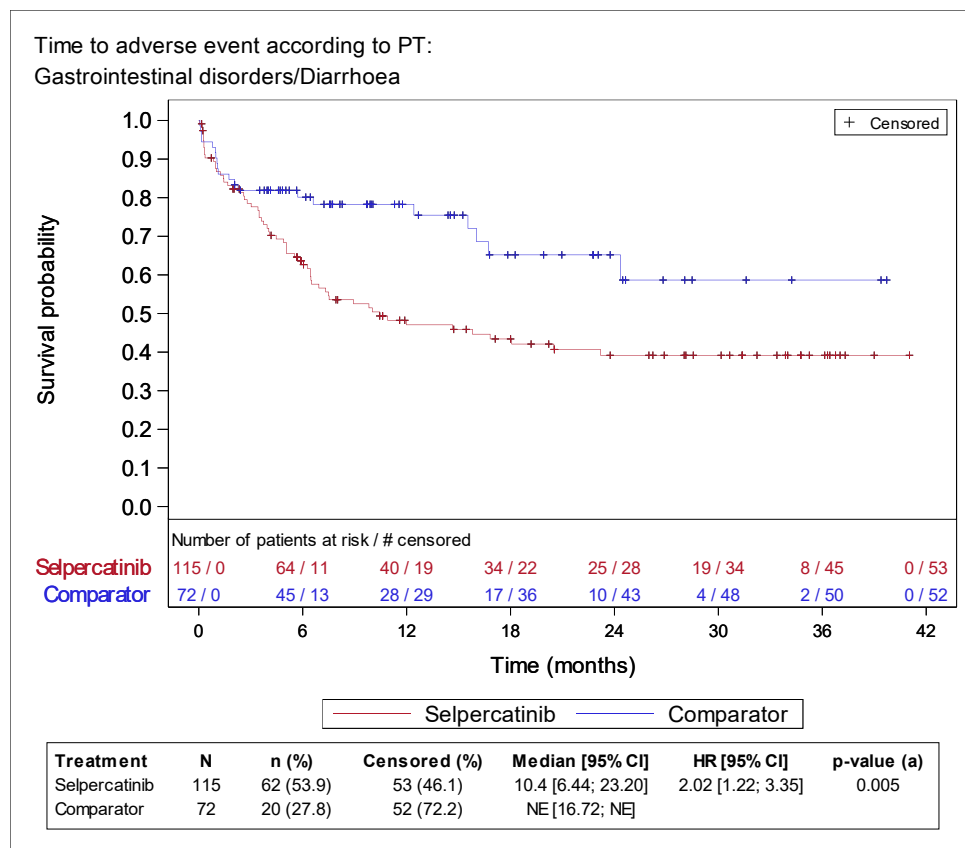
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 139: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Diarrhoea - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

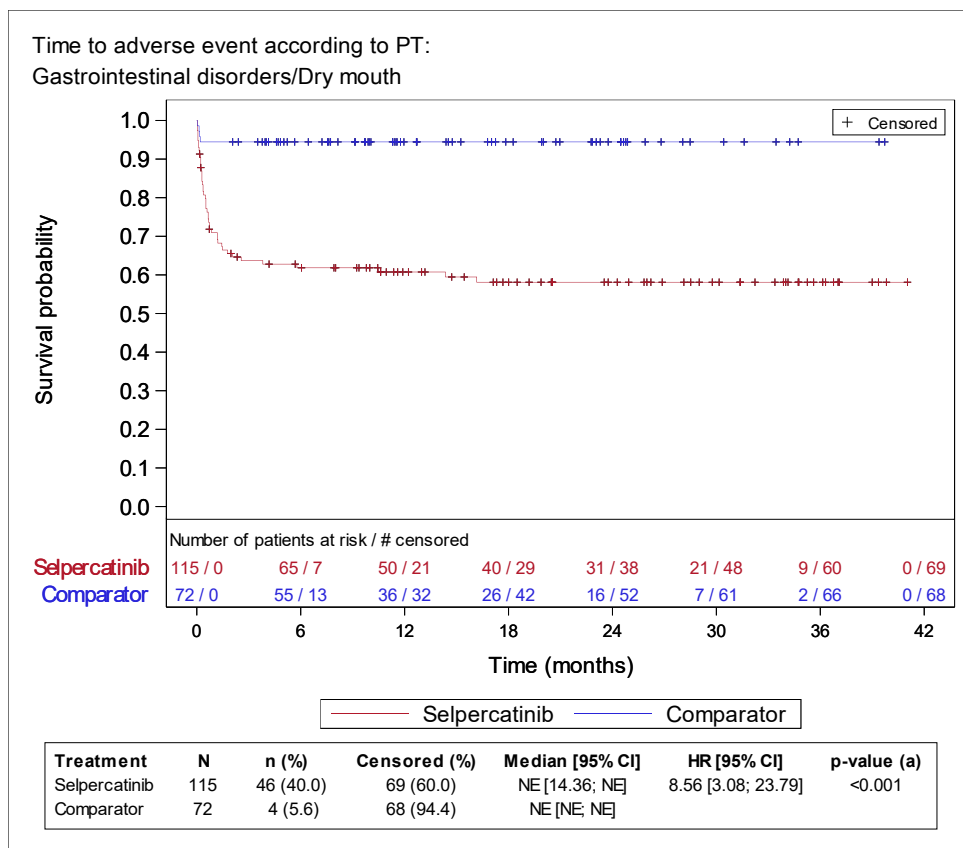
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 140: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Dry mouth - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

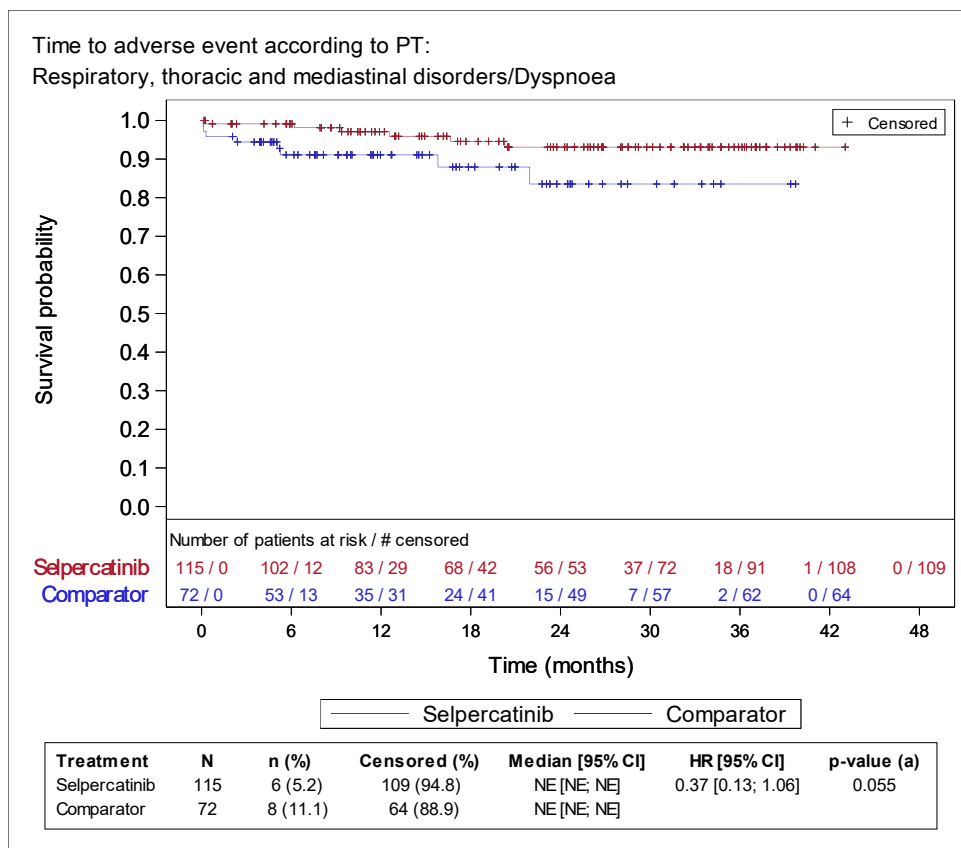
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 141: Kaplan-Meier Plot - Time to adverse event according to PT: Respiratory, thoracic and mediastinal disorders/Dyspnoea - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

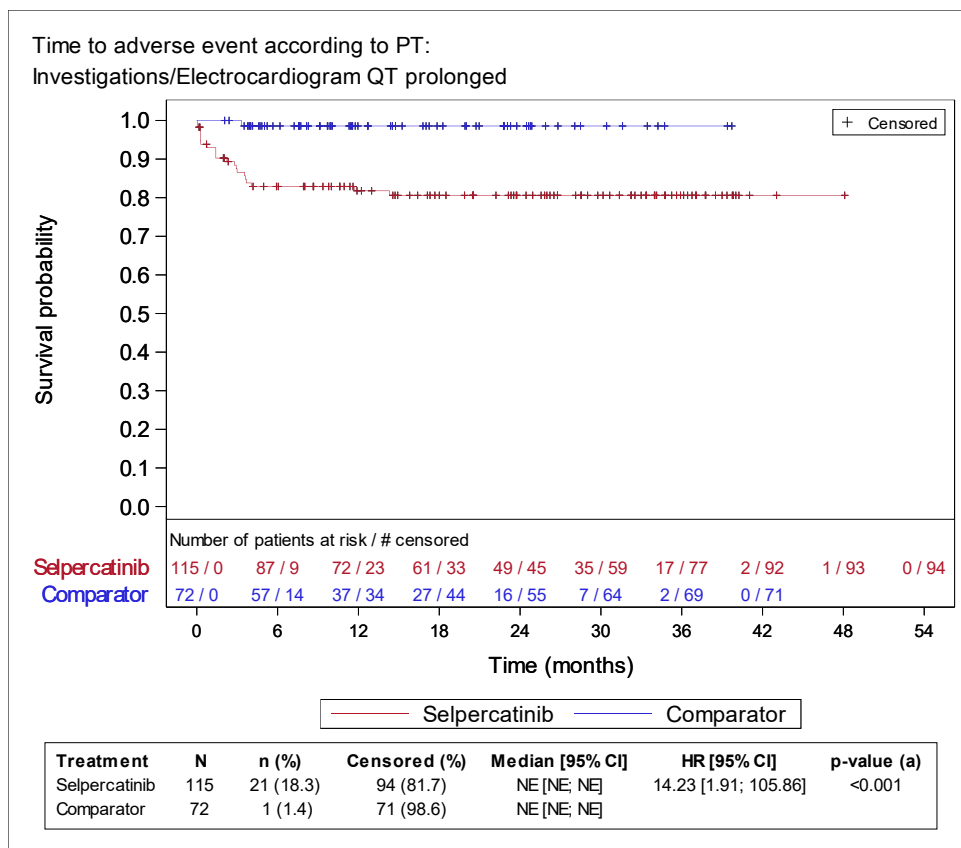
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 142: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Electrocardiogram QT prolonged - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

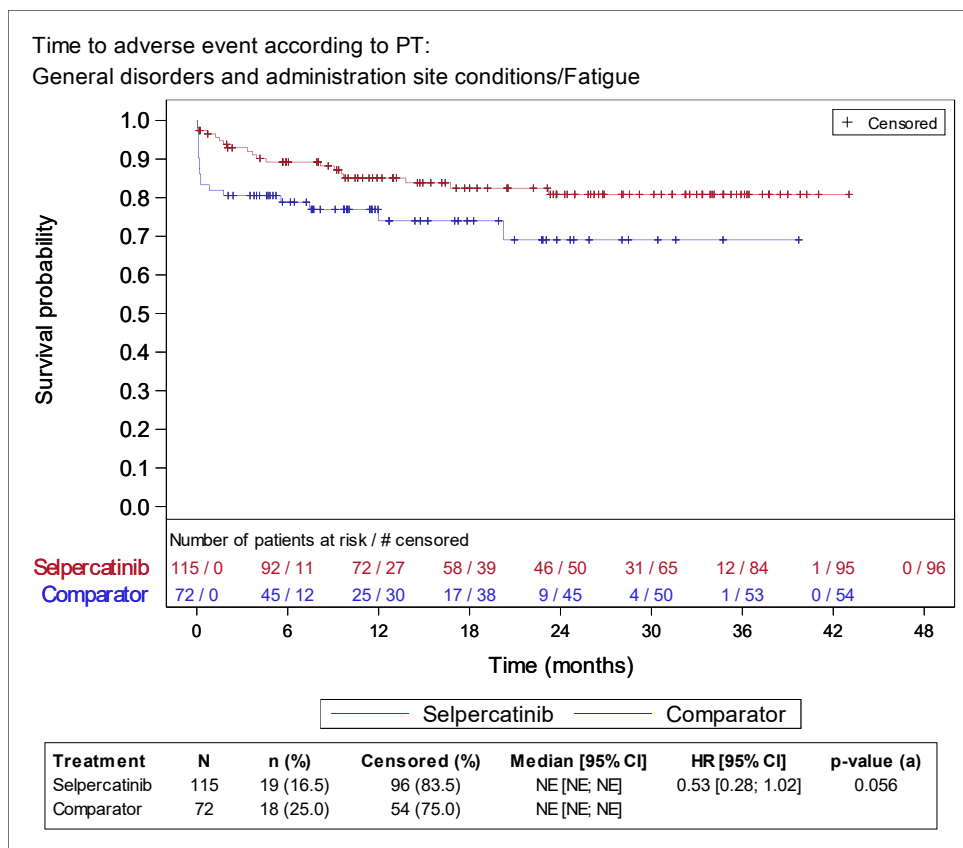
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx020_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 143: Kaplan-Meier Plot - Time to adverse event according to PT: General disorders and administration site conditions/Fatigue - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

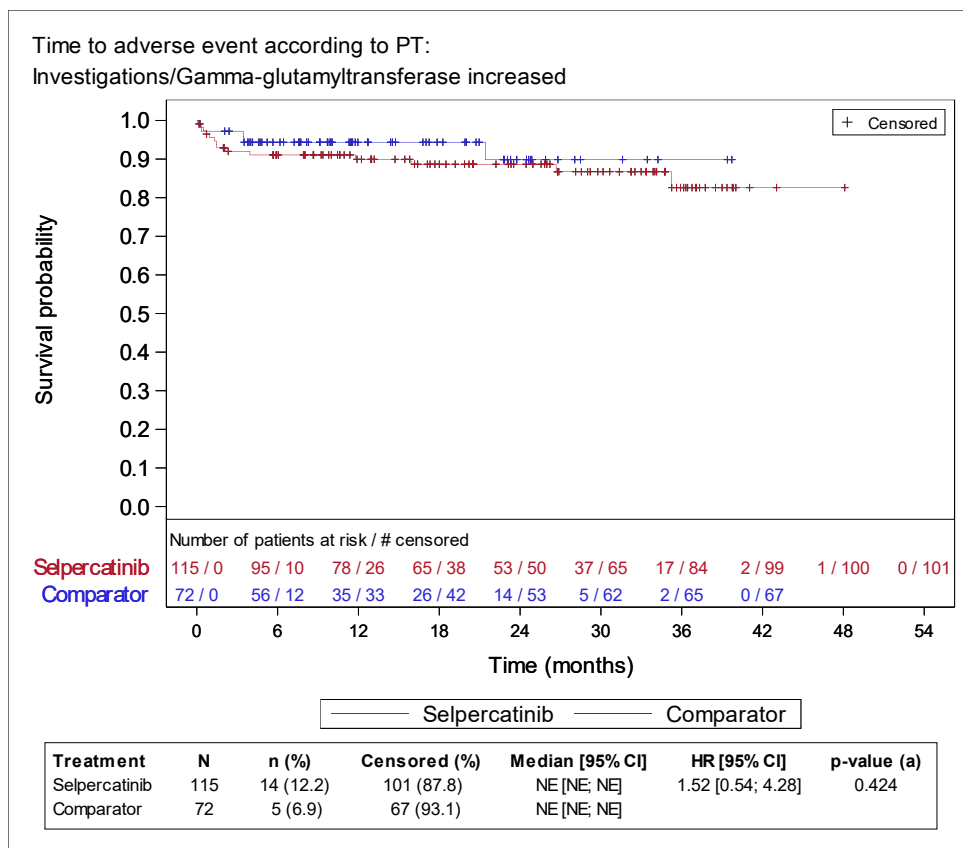
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx021_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 144: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Gamma-glutamyltransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

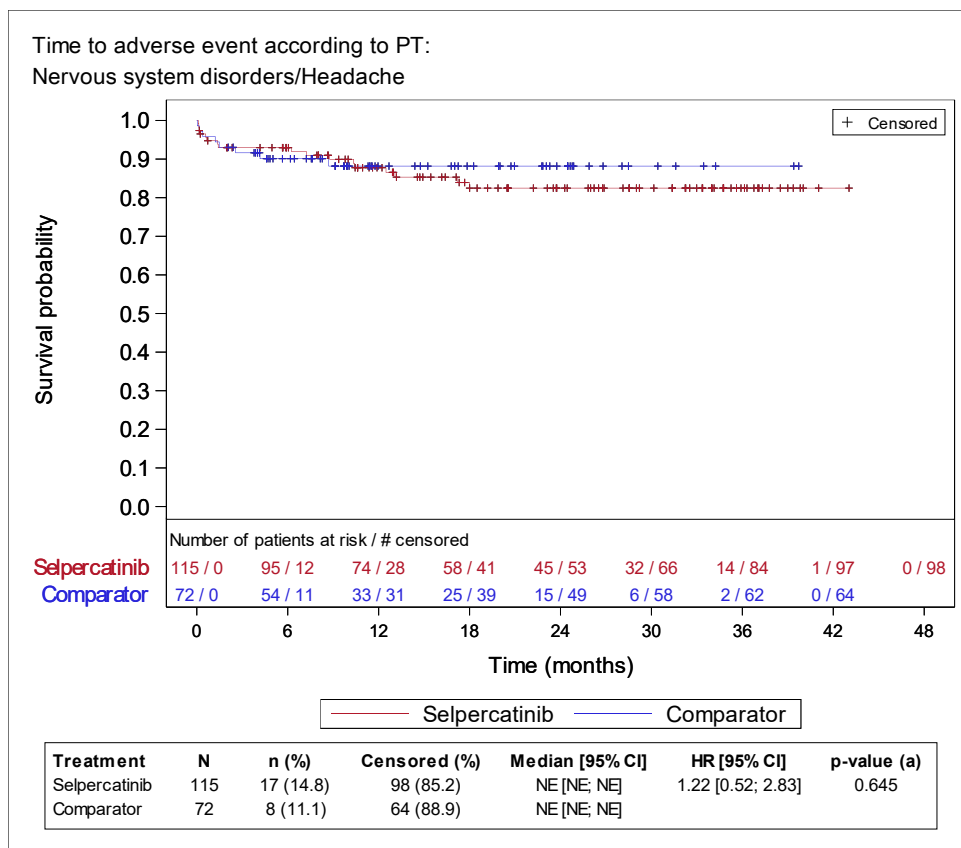
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx022_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 145: Kaplan-Meier Plot - Time to adverse event according to PT: Nervous system disorders/Headache - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

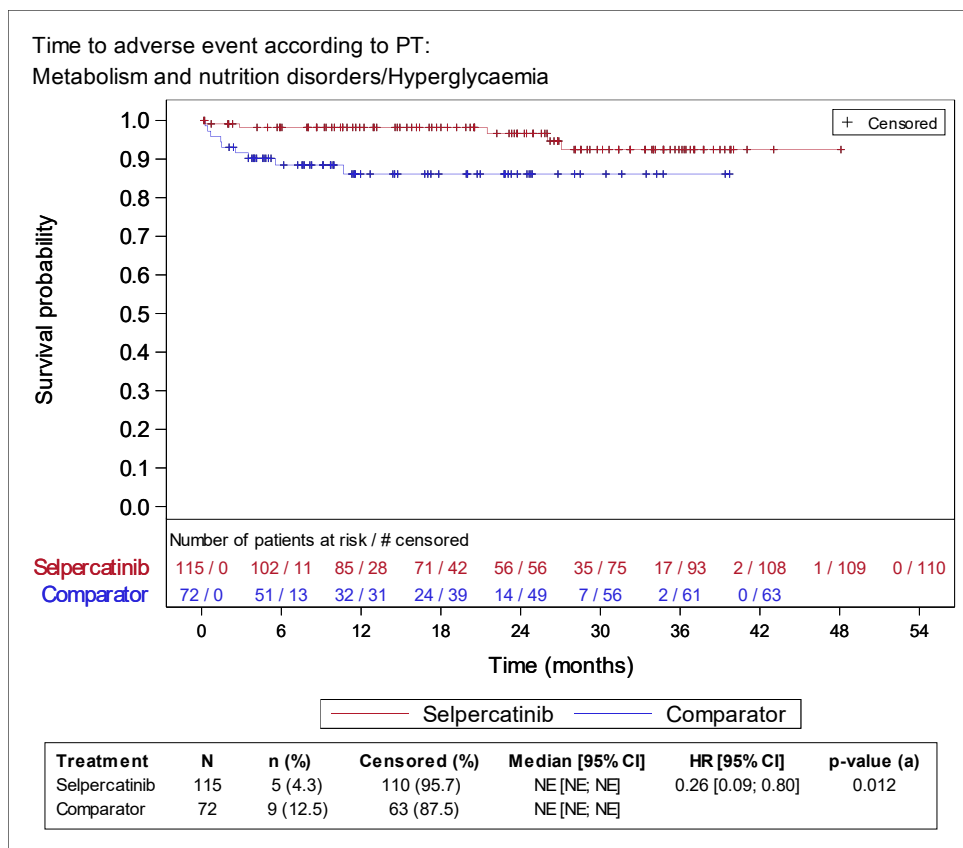
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx023_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
23OCT2025 / 06:22

Figure 146: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Hyperglycaemia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

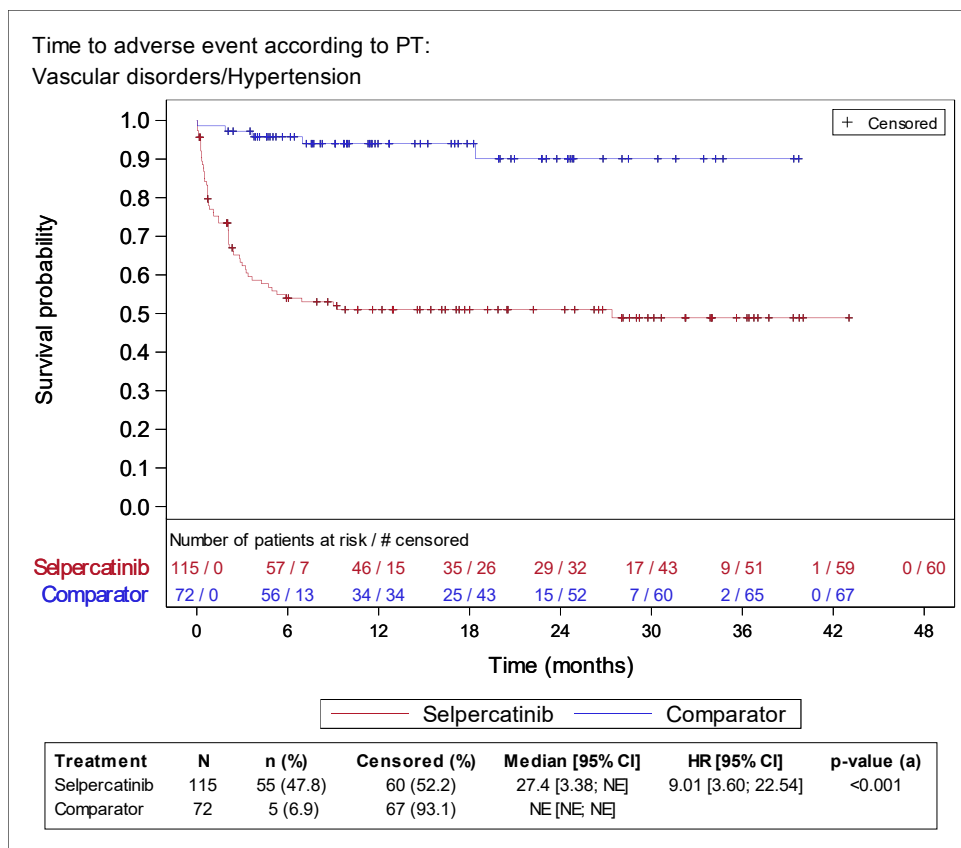
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx024_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 147: Kaplan-Meier Plot - Time to adverse event according to PT: Vascular disorders/Hypertension - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

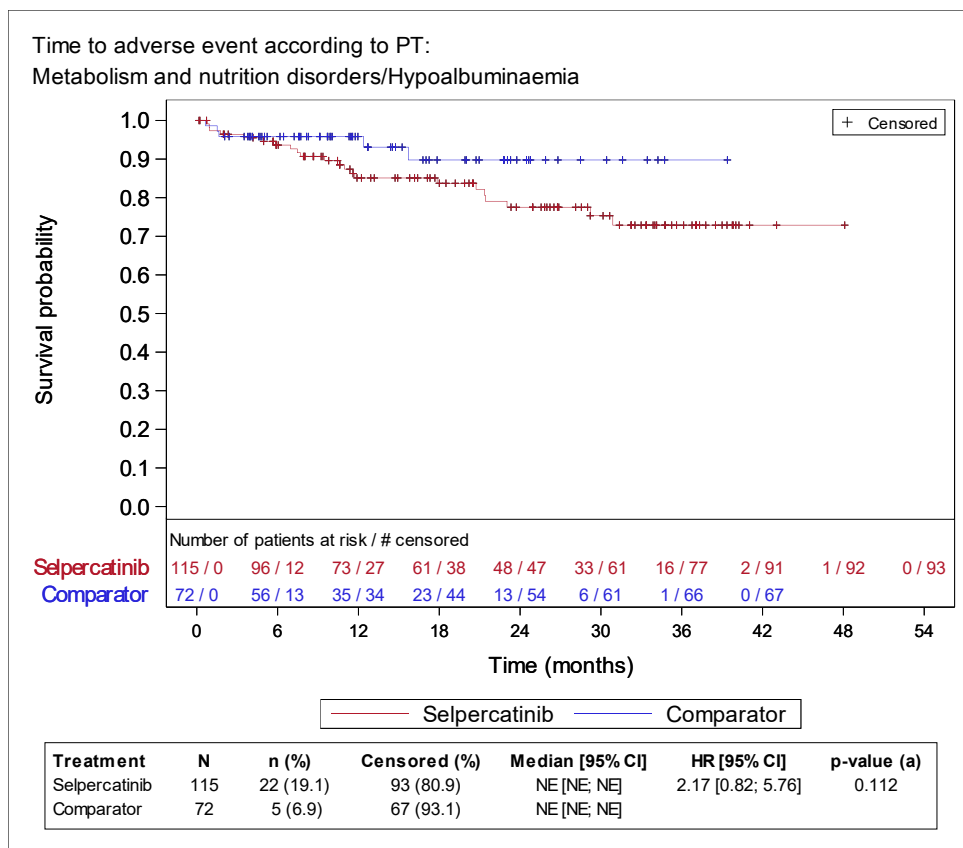
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx025_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 148: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Hypoalbuminaemia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

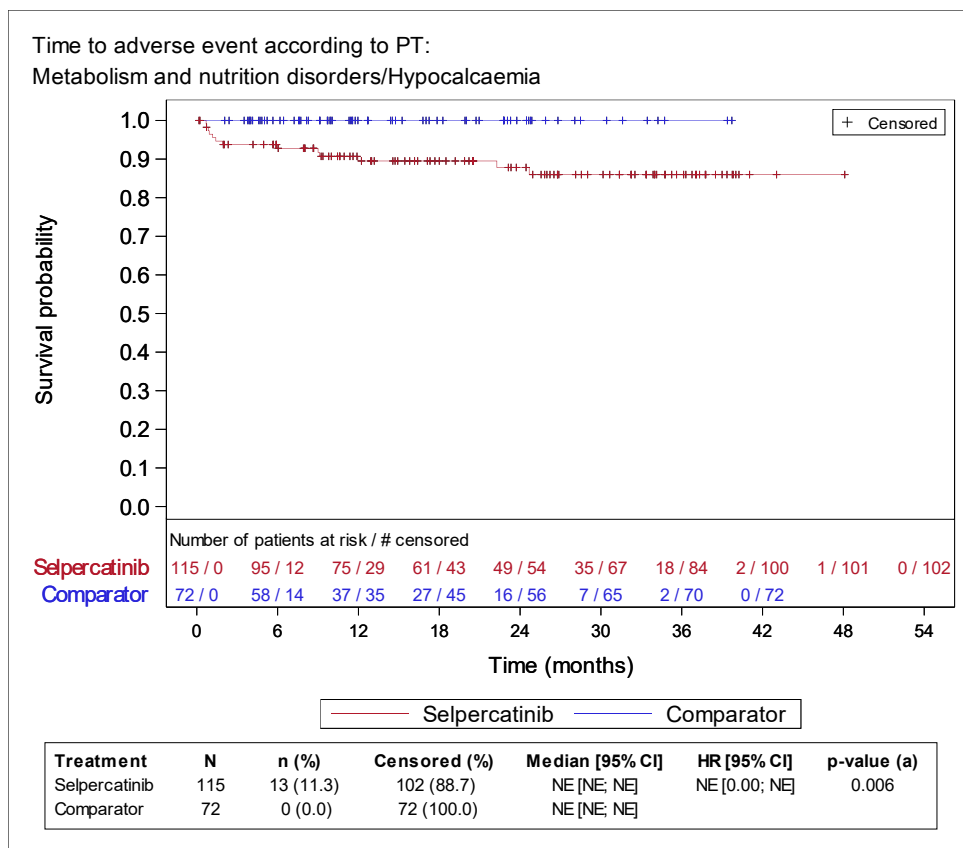
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx026_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 149: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Hypocalcaemia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

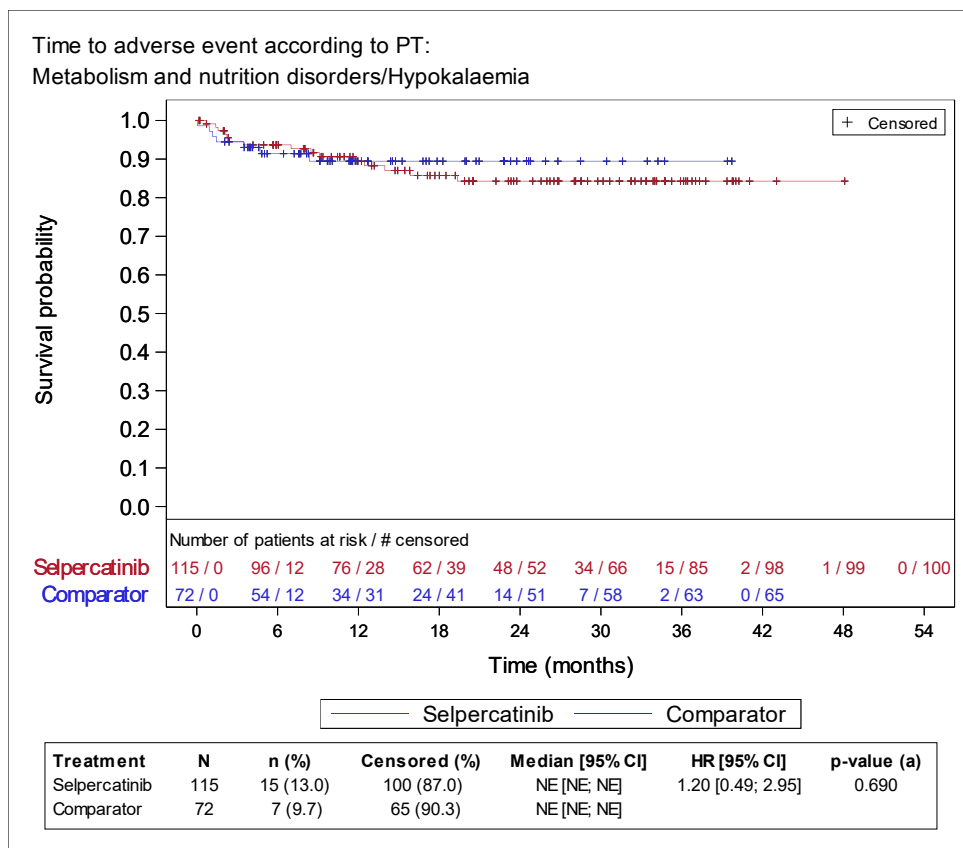
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx027_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 150: Kaplan-Meier Plot - Time to adverse event according to PT: Metabolism and nutrition disorders/Hypokalaemia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

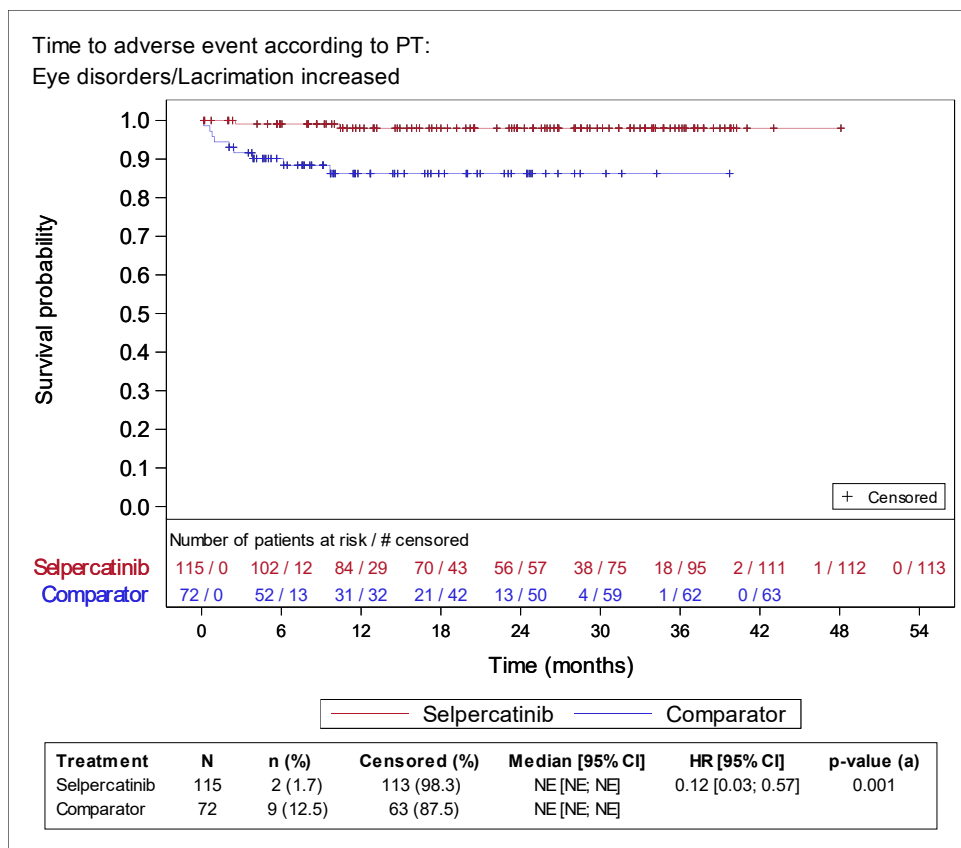
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx028_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 151: Kaplan-Meier Plot - Time to adverse event according to PT: Eye disorders/Lacrimation increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

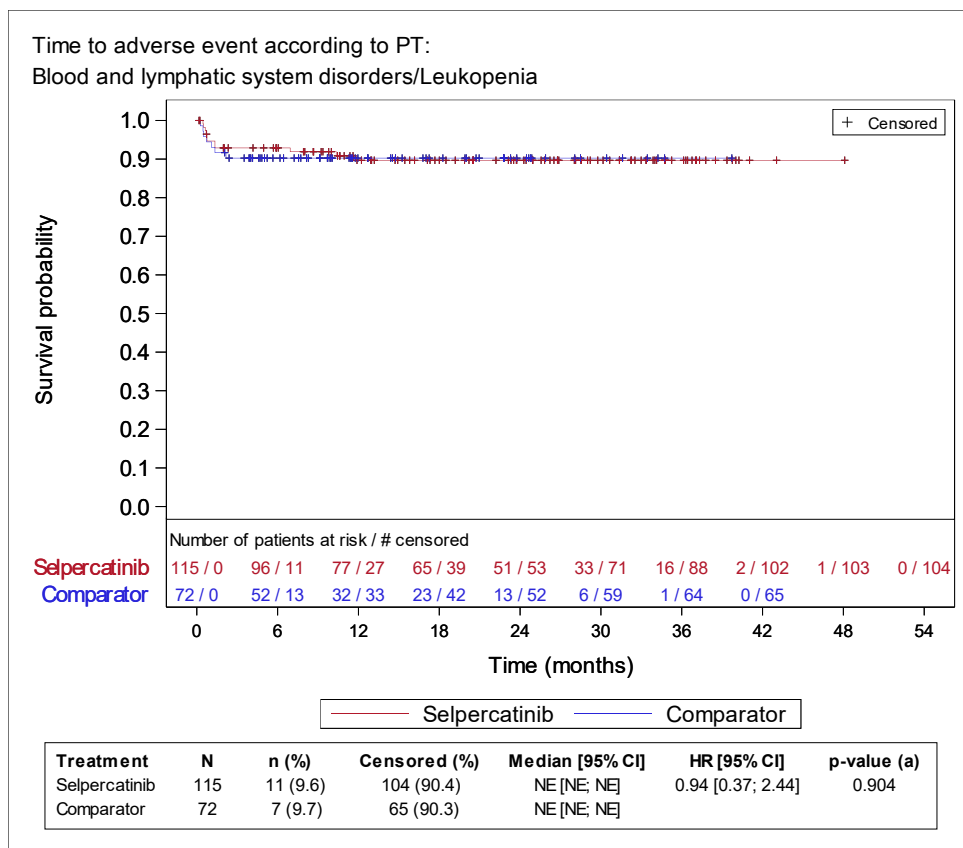
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx029_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 152: Kaplan-Meier Plot - Time to adverse event according to PT: Blood and lymphatic system disorders/Leukopenia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

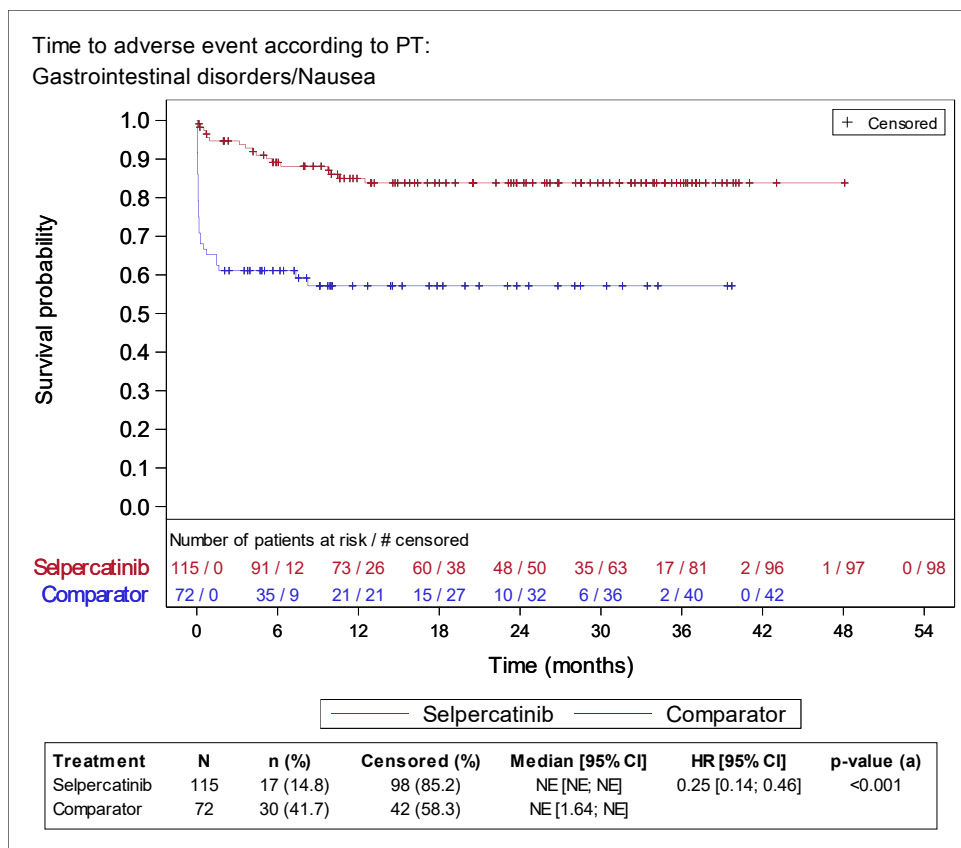
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx030_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
23OCT2025 / 06:22

Figure 153: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Nausea - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

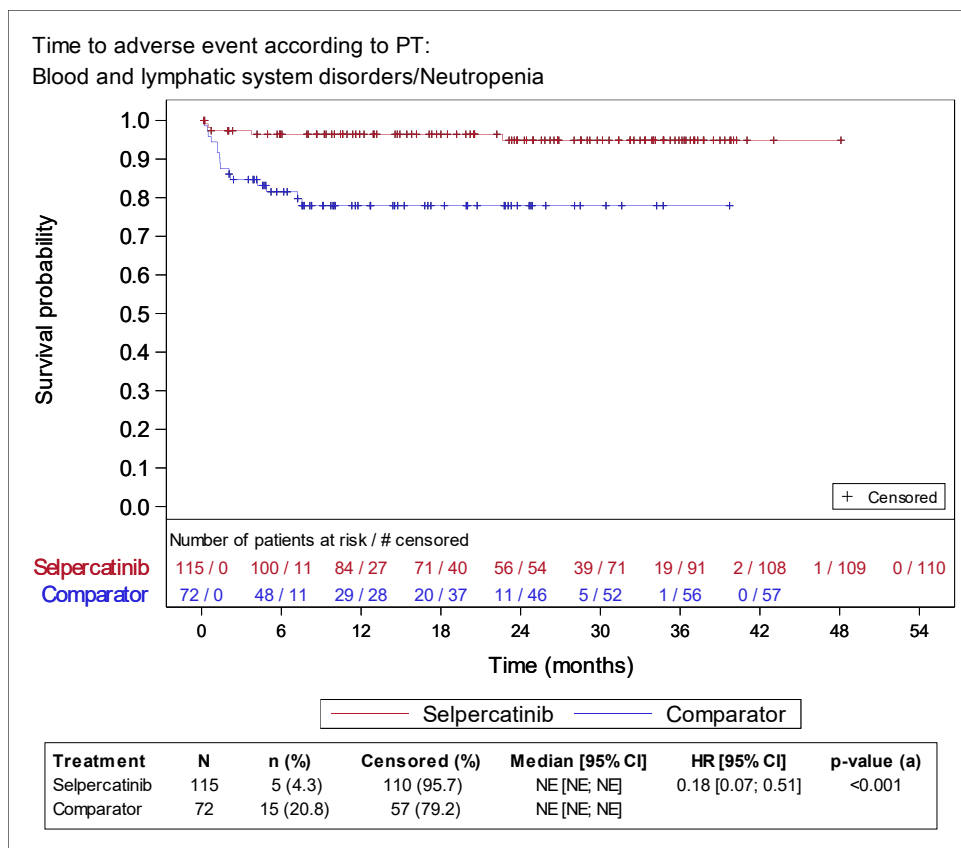
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx031_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
23OCT2025 / 06:22

Figure 154: Kaplan-Meier Plot - Time to adverse event according to PT: Blood and lymphatic system disorders/Neutropenia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

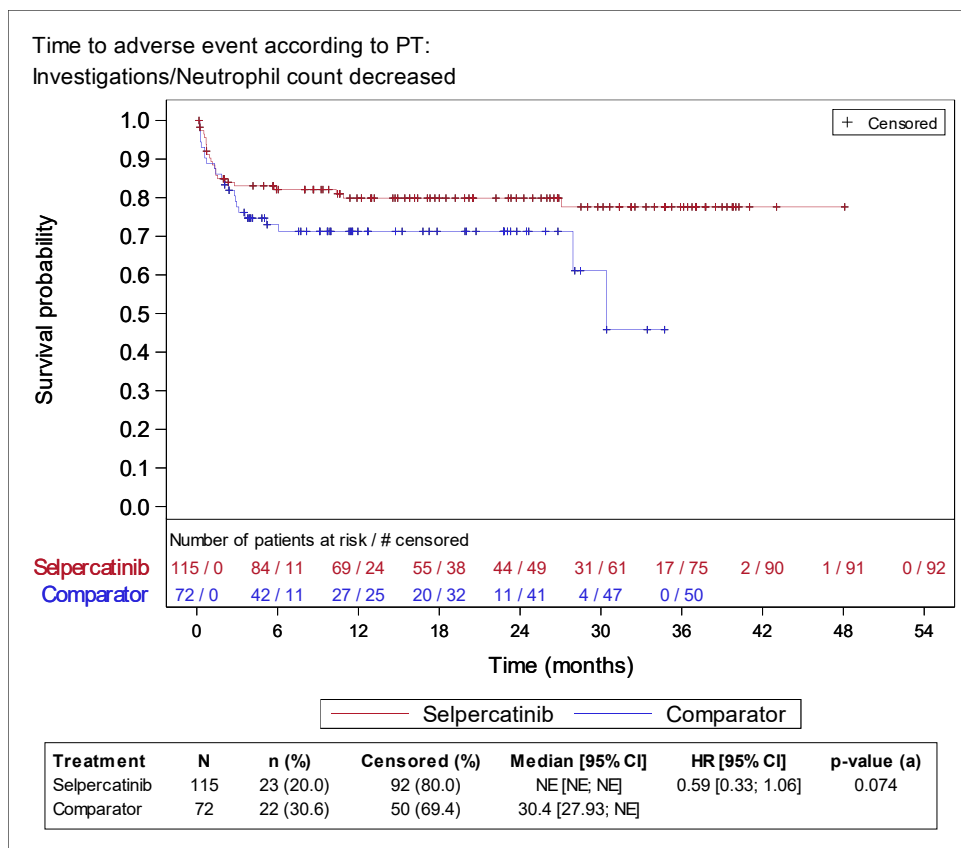
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx032_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 155: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Neutrophil count decreased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

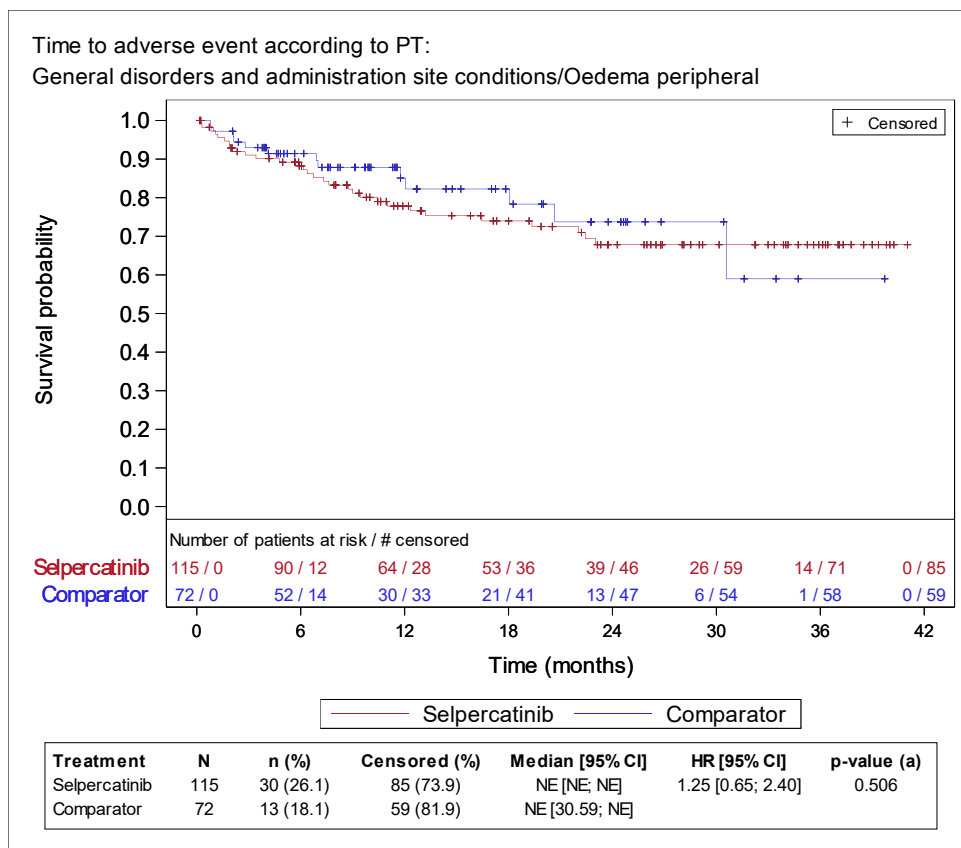
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx033_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
23OCT2025 / 06:22

Figure 156: Kaplan-Meier Plot - Time to adverse event according to PT: General disorders and administration site conditions/Oedema peripheral - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

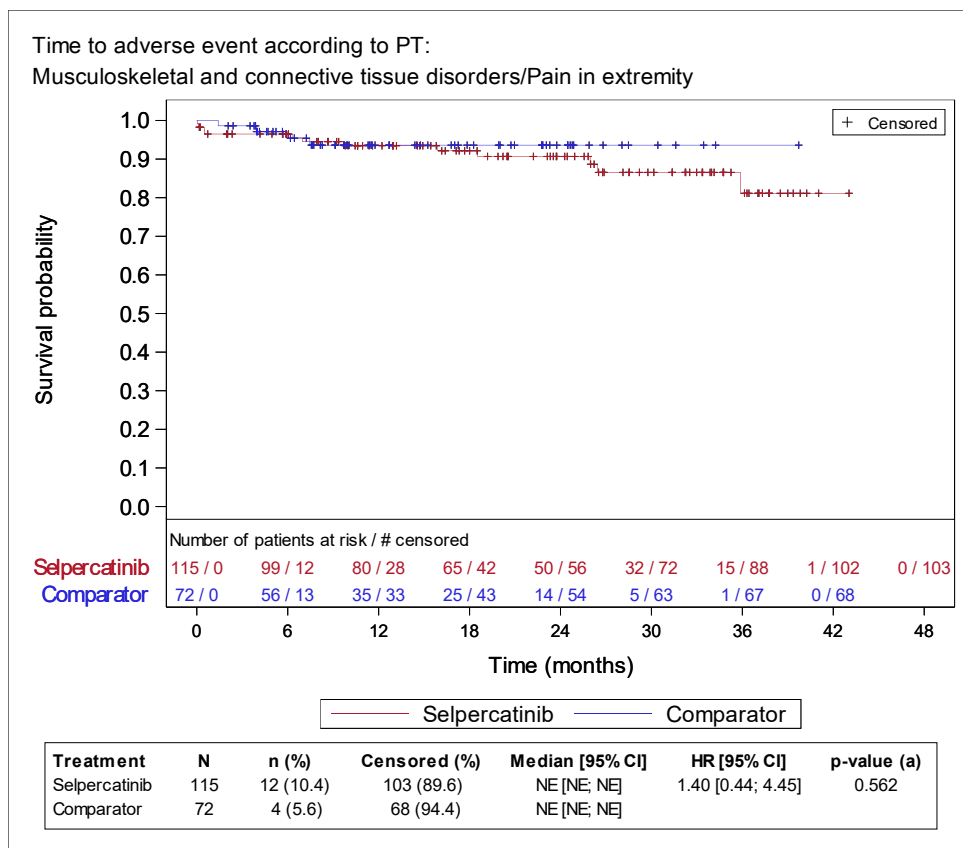
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx034_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
23OCT2025 / 06:22

Figure 157: Kaplan-Meier Plot - Time to adverse event according to PT: Musculoskeletal and connective tissue disorders/Pain in extremity - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

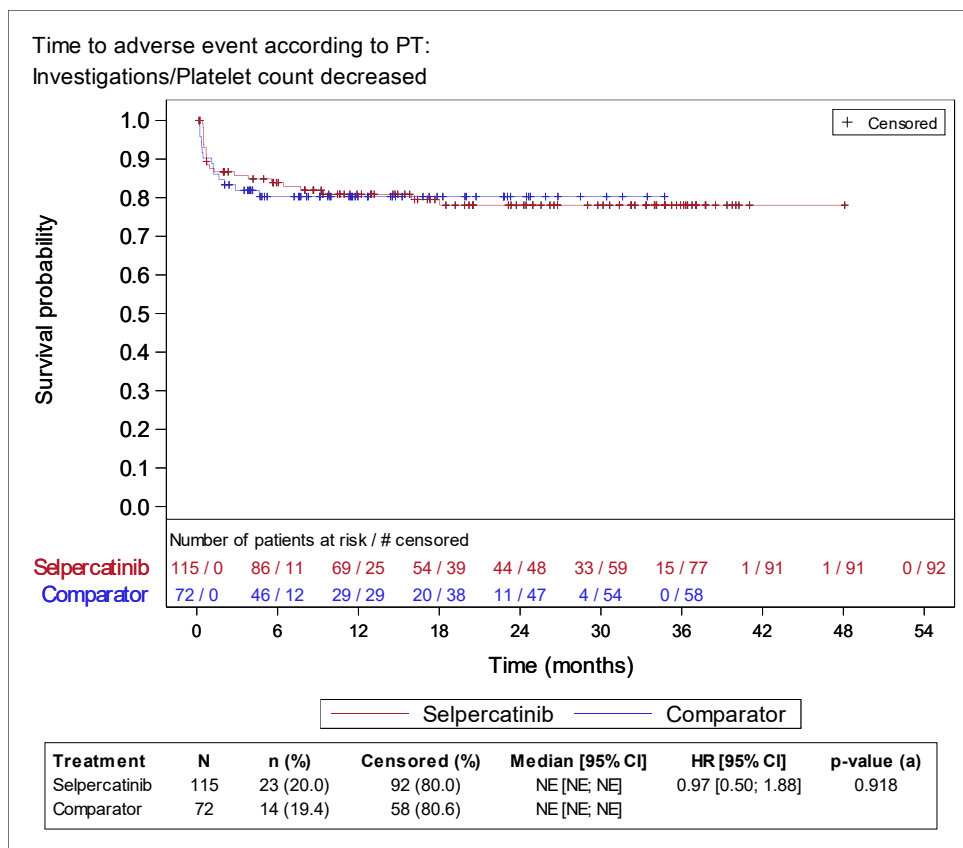
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx035_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 158: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Platelet count decreased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

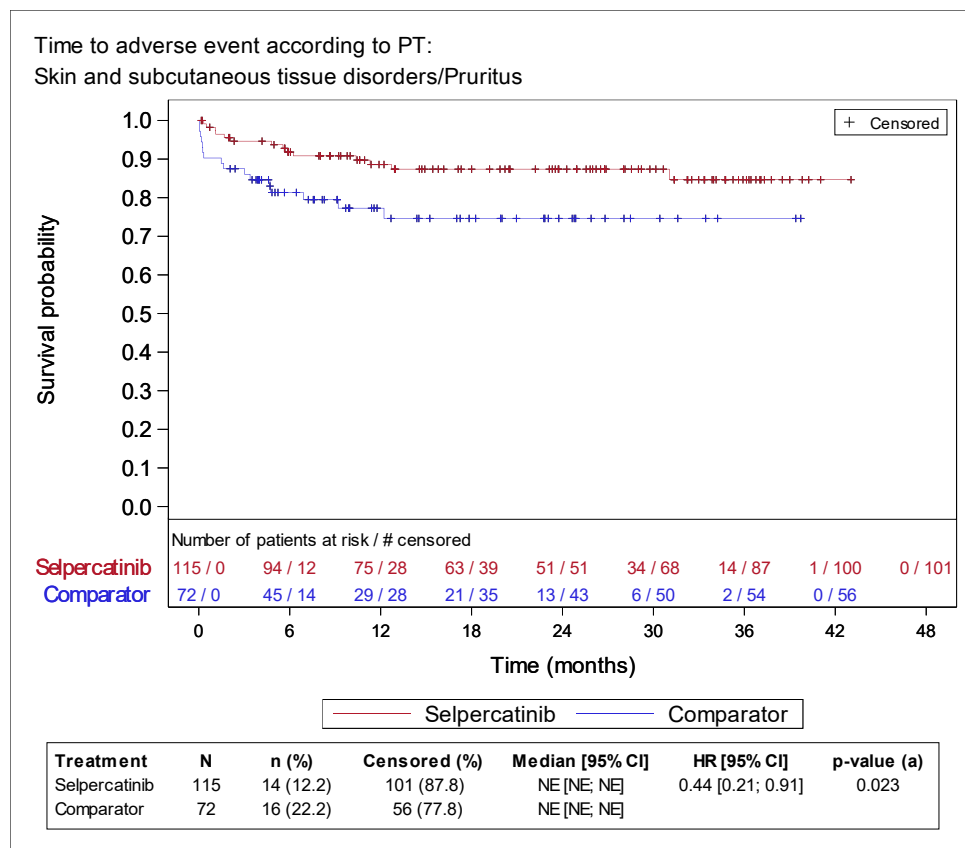
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 159: Kaplan-Meier Plot - Time to adverse event according to PT: Skin and subcutaneous tissue disorders/Pruritus - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

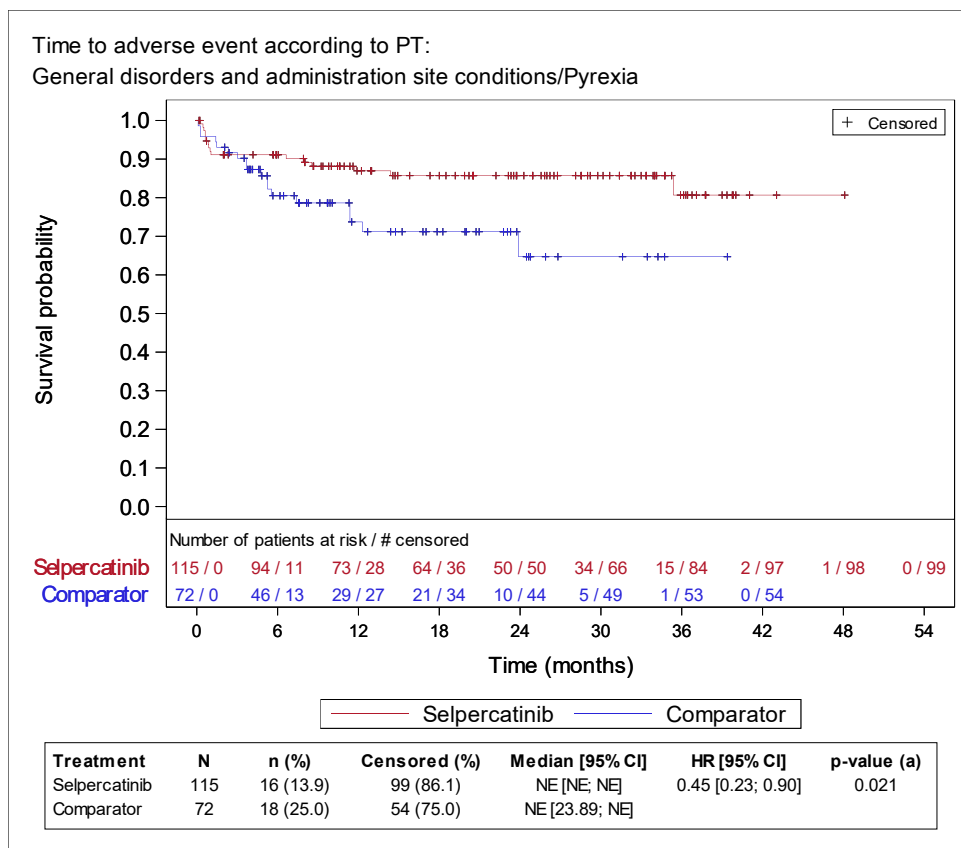
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx037_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
23OCT2025 / 06:22

Figure 160: Kaplan-Meier Plot - Time to adverse event according to PT: General disorders and administration site conditions/Pyrexia - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

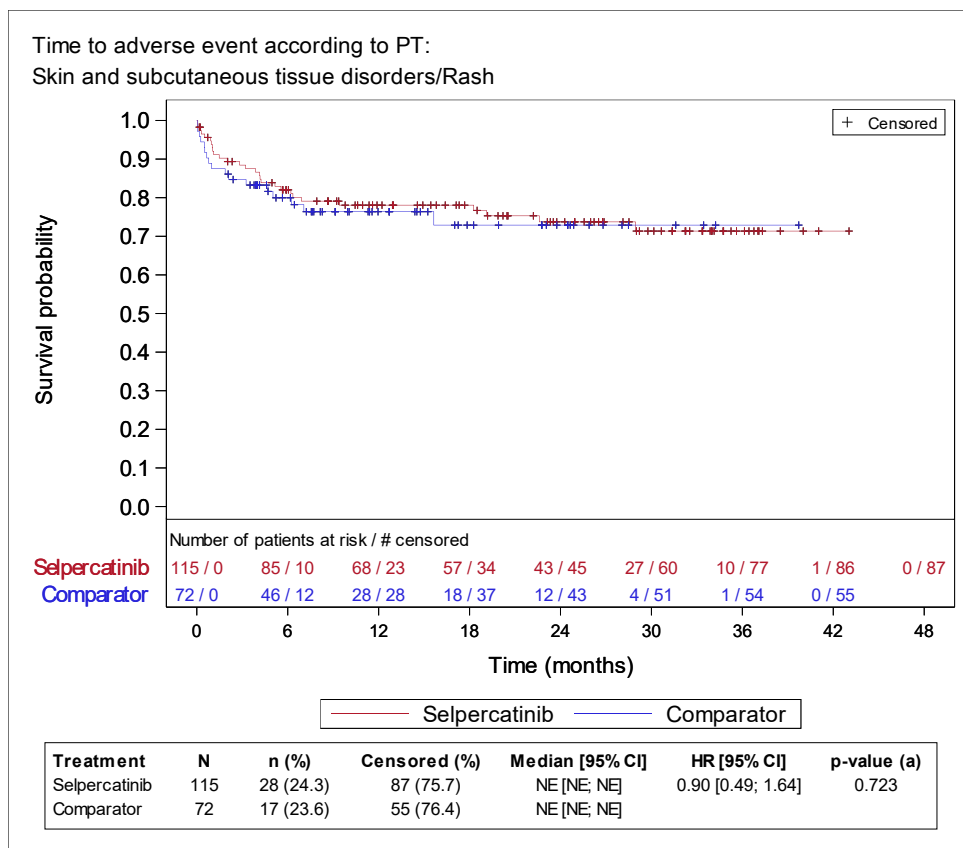
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx038_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 161: Kaplan-Meier Plot - Time to adverse event according to PT: Skin and subcutaneous tissue disorders/Rash - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

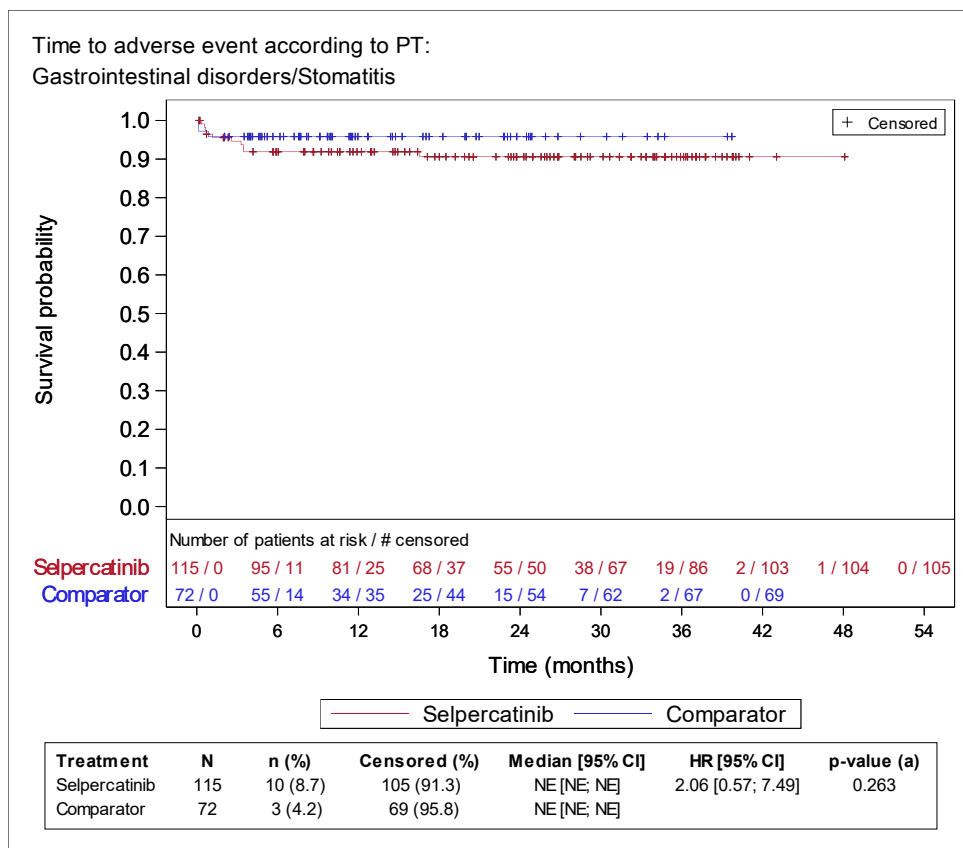
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 162: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Stomatitis - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

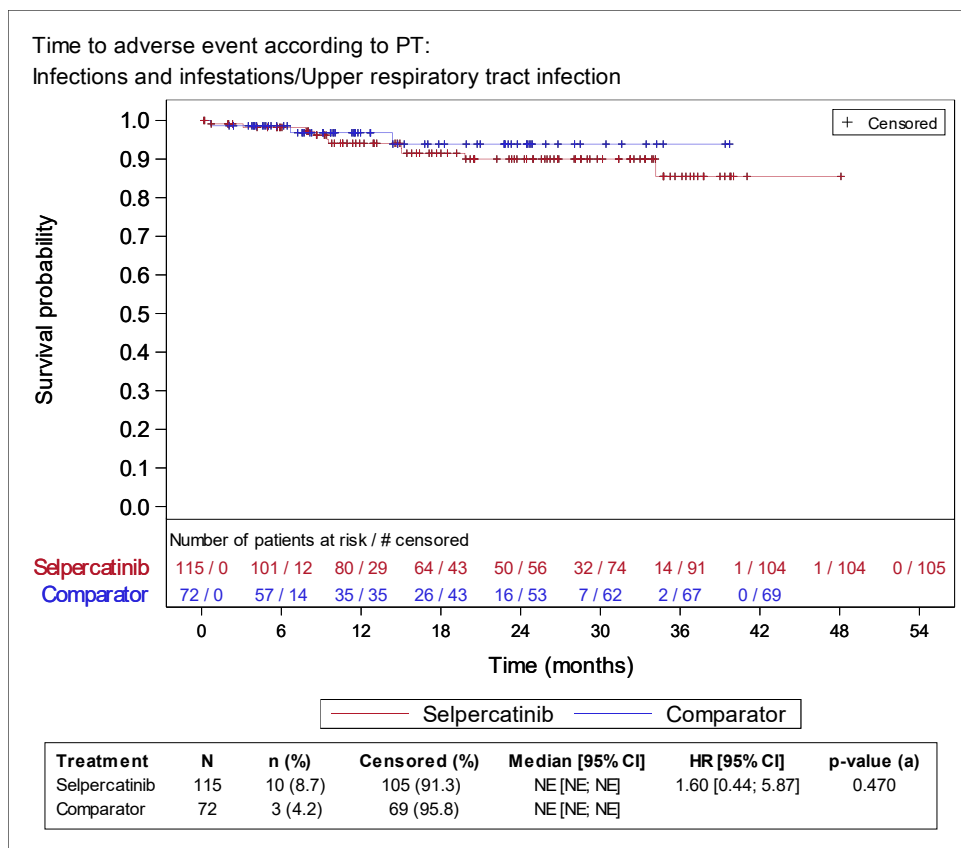
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx040_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 163: Kaplan-Meier Plot - Time to adverse event according to PT: Infections and infestations/Upper respiratory tract infection - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

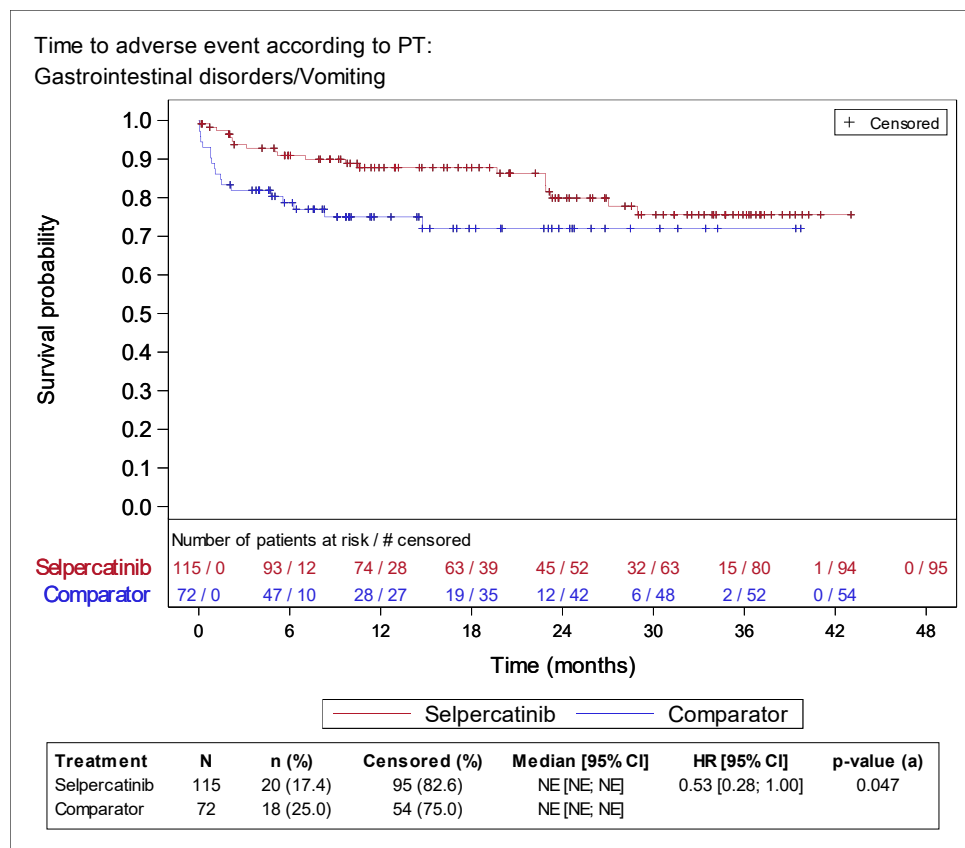
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 164: Kaplan-Meier Plot - Time to adverse event according to PT: Gastrointestinal disorders/Vomiting - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

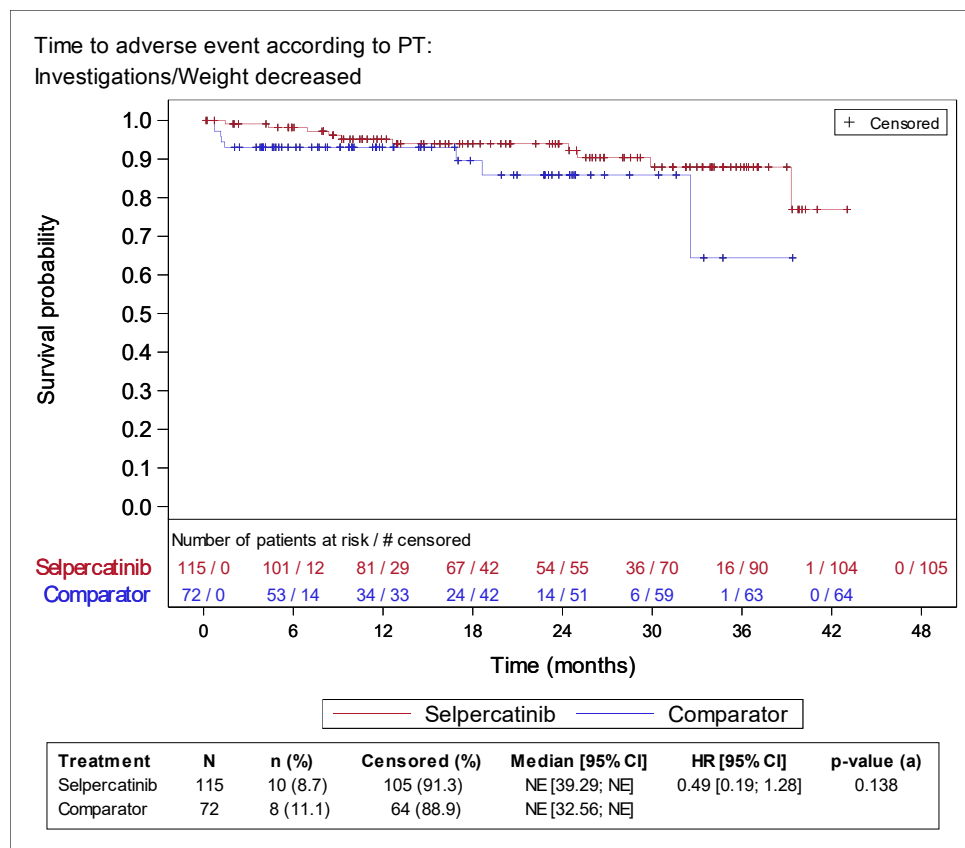
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 165: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Weight decreased - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

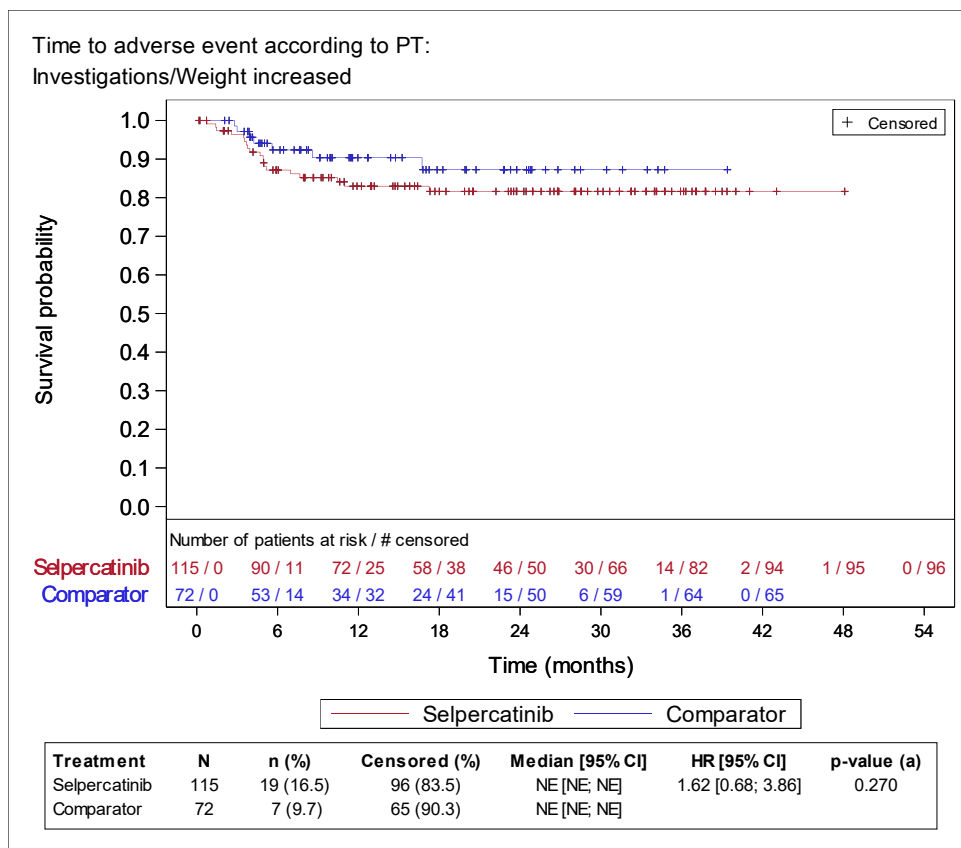
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aeppx043_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 166: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/Weight increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

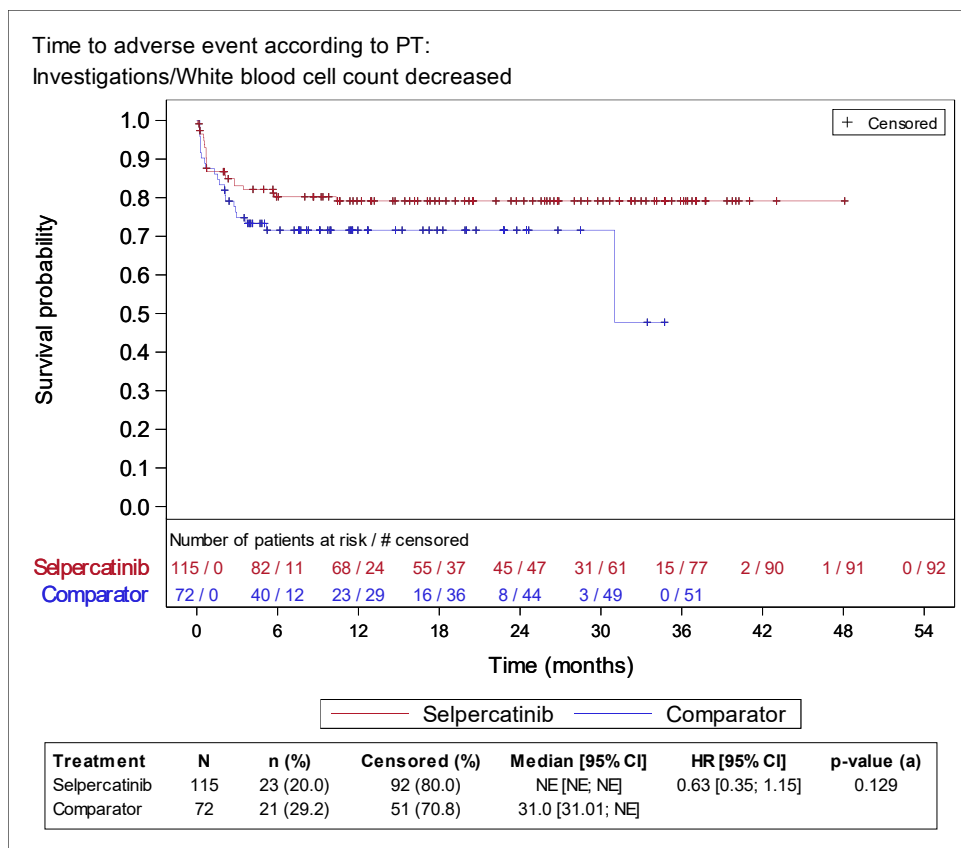
HR is based on the unstratified Cox proportional hazards model.

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 167: Kaplan-Meier Plot - Time to adverse event according to PT: Investigations/White blood cell count decreased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

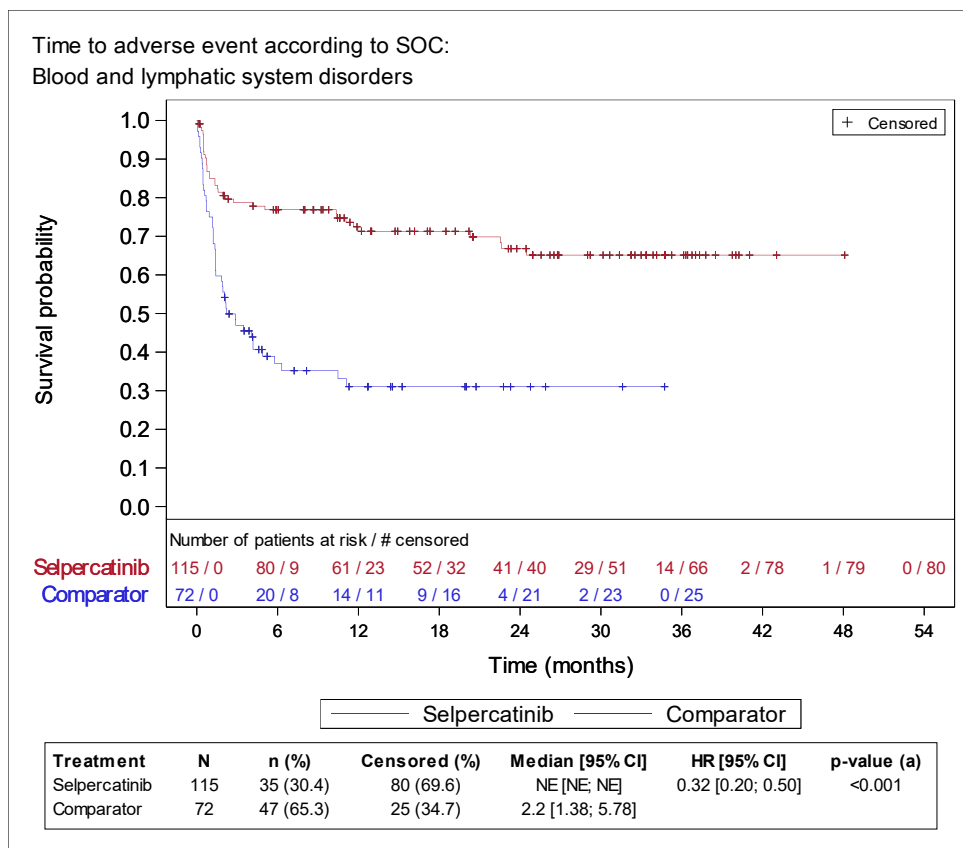
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
23OCT2025 / 06:22

Figure 168: Kaplan-Meier Plot - Time to adverse event according to SOC: Blood and lymphatic system disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

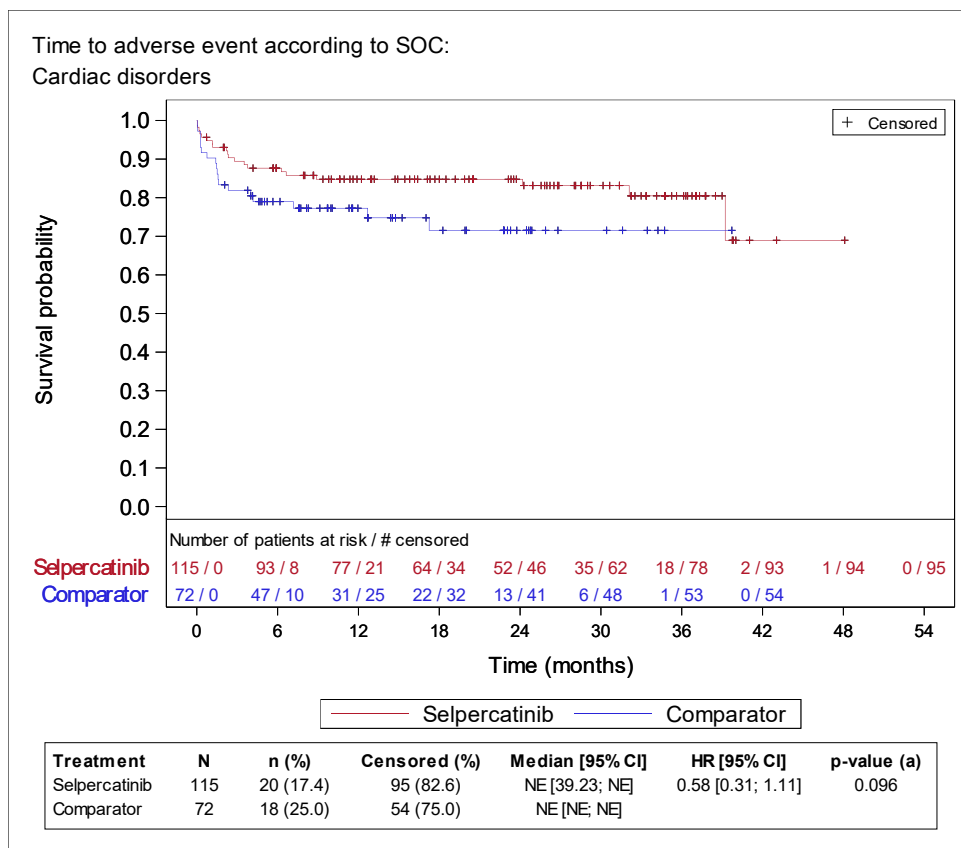
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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23OCT2025 / 06:22

Figure 169: Kaplan-Meier Plot - Time to adverse event according to SOC: Cardiac disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

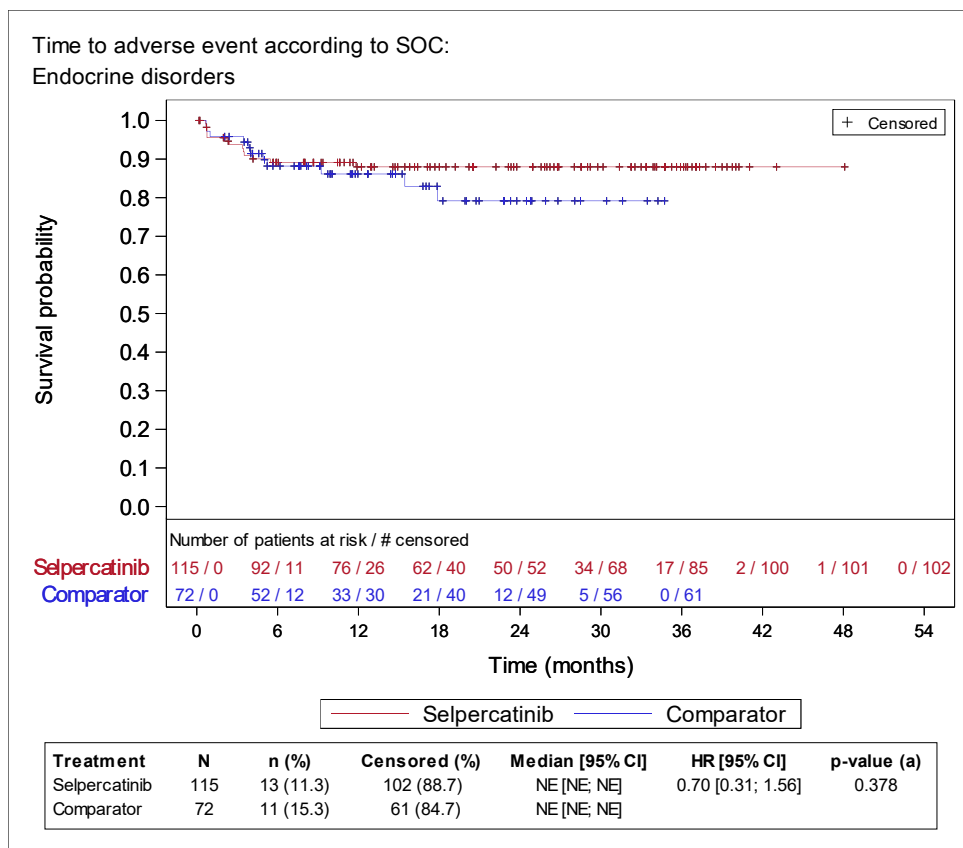
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 170: Kaplan-Meier Plot - Time to adverse event according to SOC: Endocrine disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

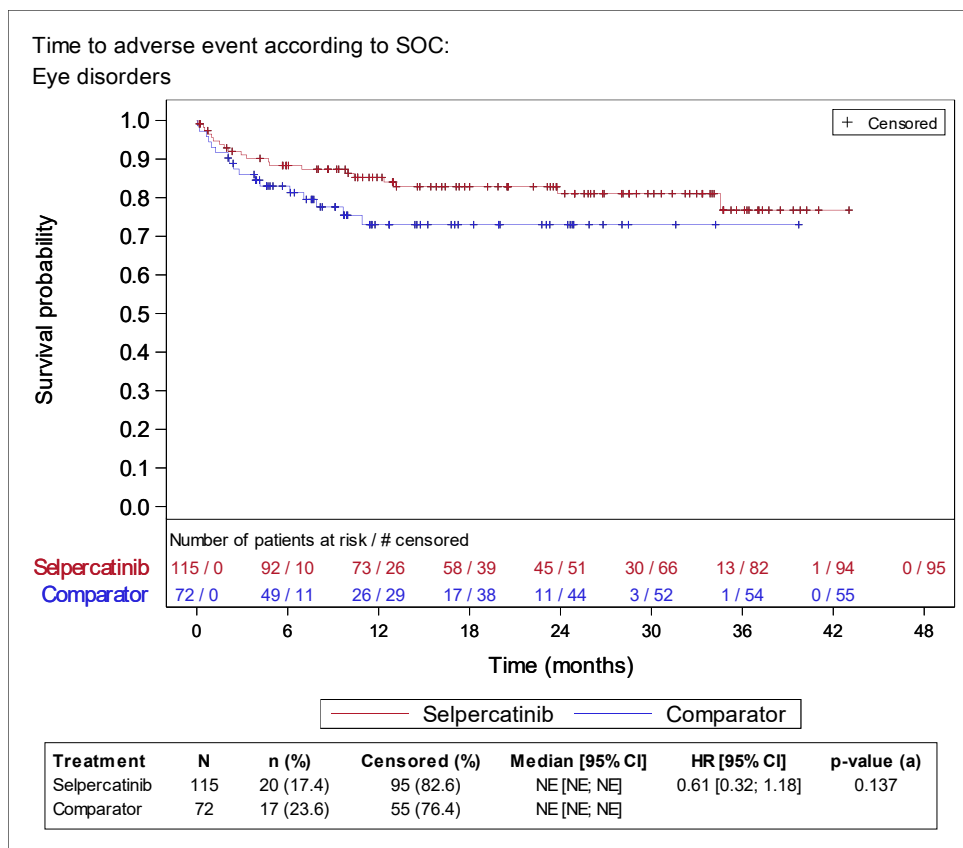
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_aespx003_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
23OCT2025 / 06:22

Figure 171: Kaplan-Meier Plot - Time to adverse event according to SOC: Eye disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

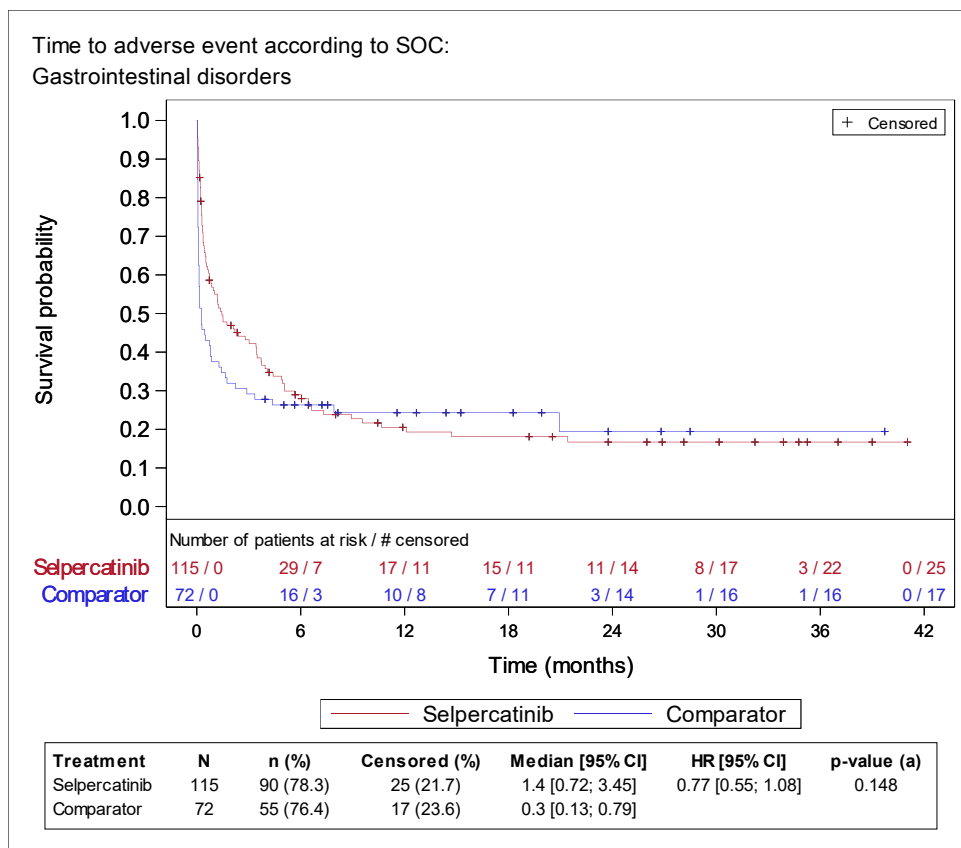
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 172: Kaplan-Meier Plot - Time to adverse event according to SOC: Gastrointestinal disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

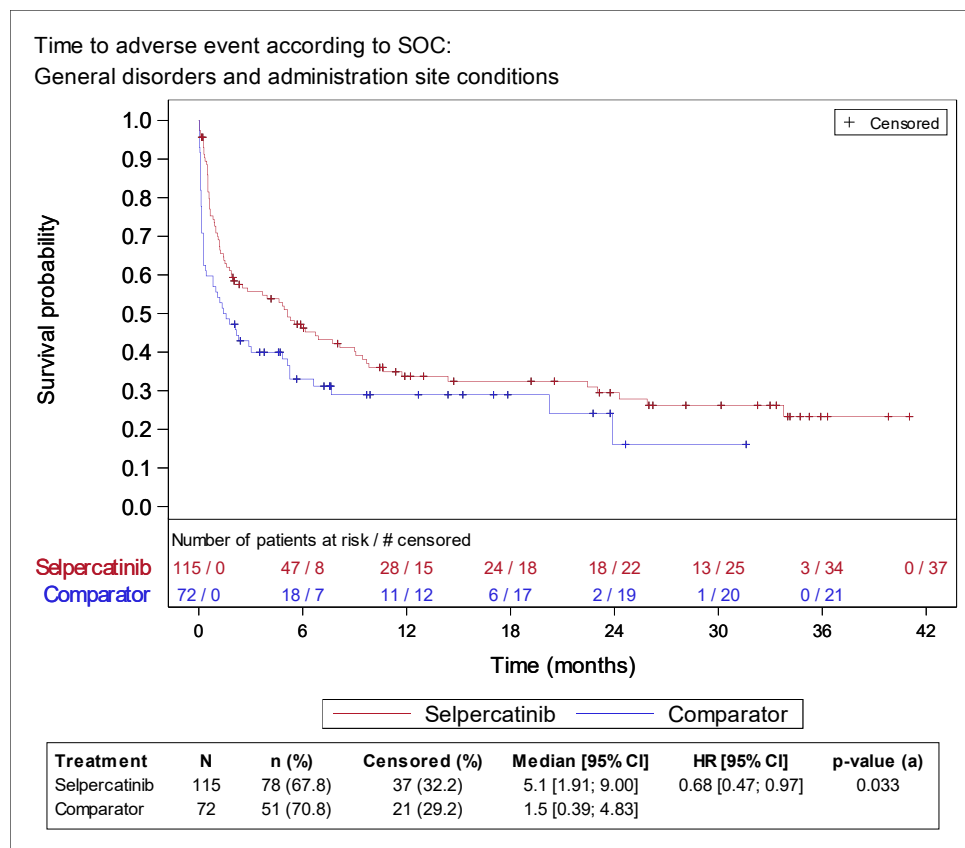
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 173: Kaplan-Meier Plot - Time to adverse event according to SOC: General disorders and administration site conditions - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

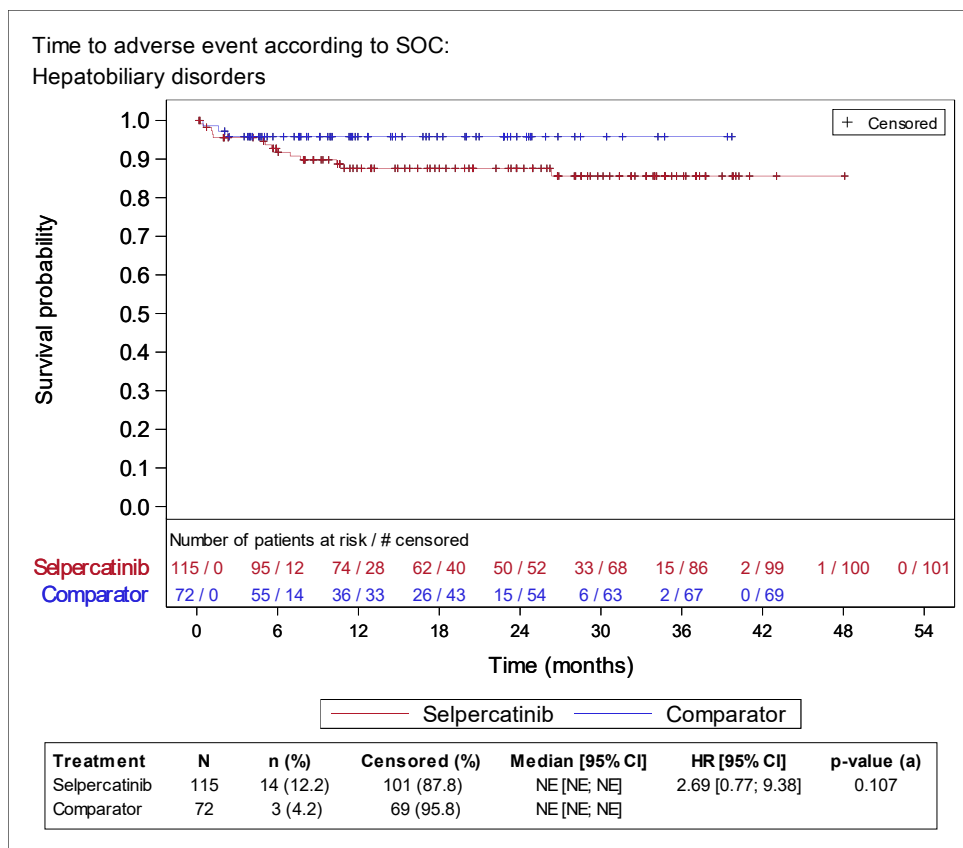
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 174: Kaplan-Meier Plot - Time to adverse event according to SOC: Hepatobiliary disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

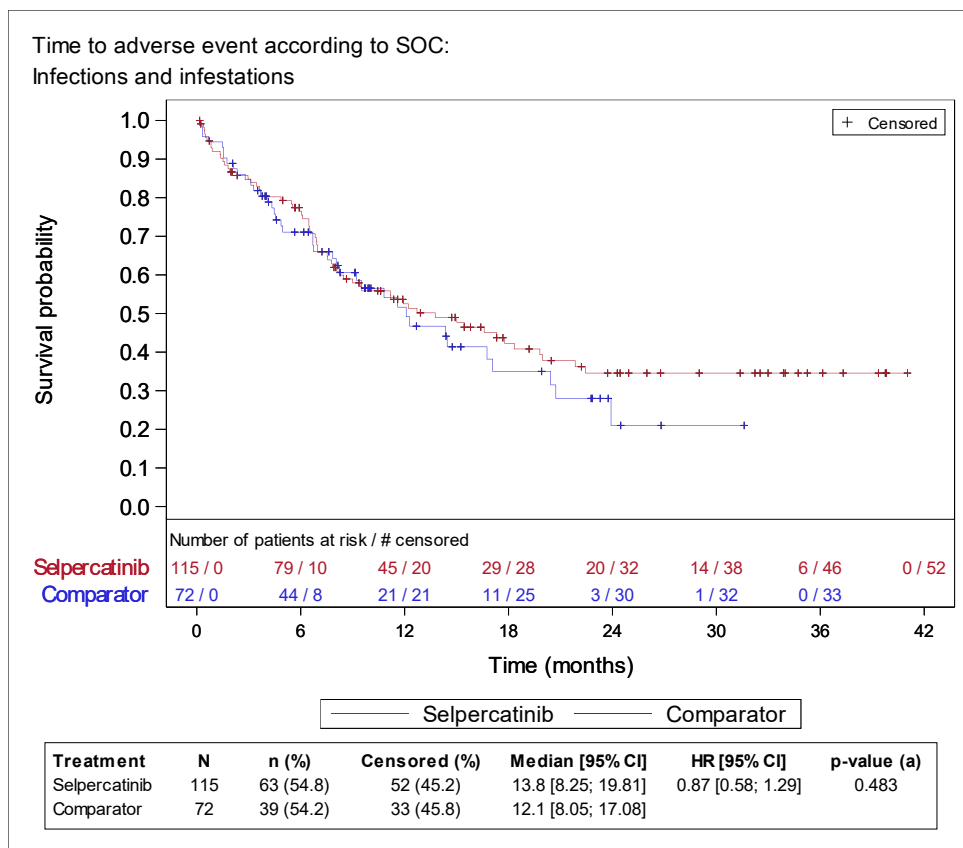
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 175: Kaplan-Meier Plot - Time to adverse event according to SOC: Infections and infestations - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

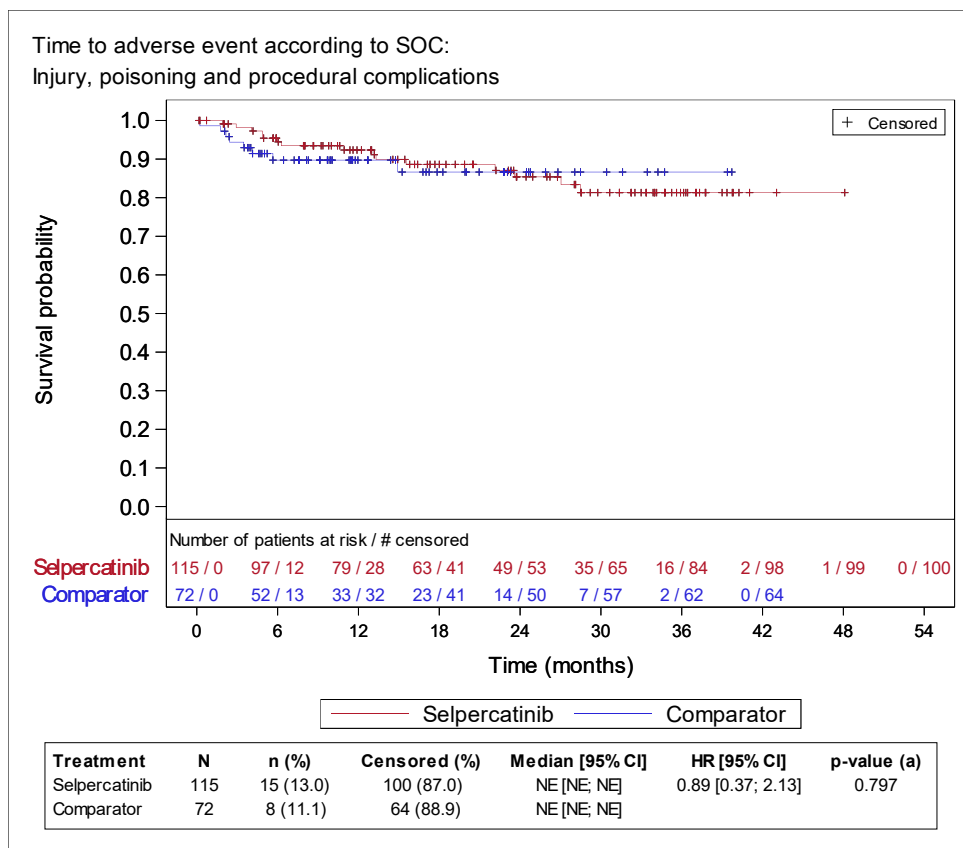
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 176: Kaplan-Meier Plot - Time to adverse event according to SOC: Injury, poisoning and procedural complications - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

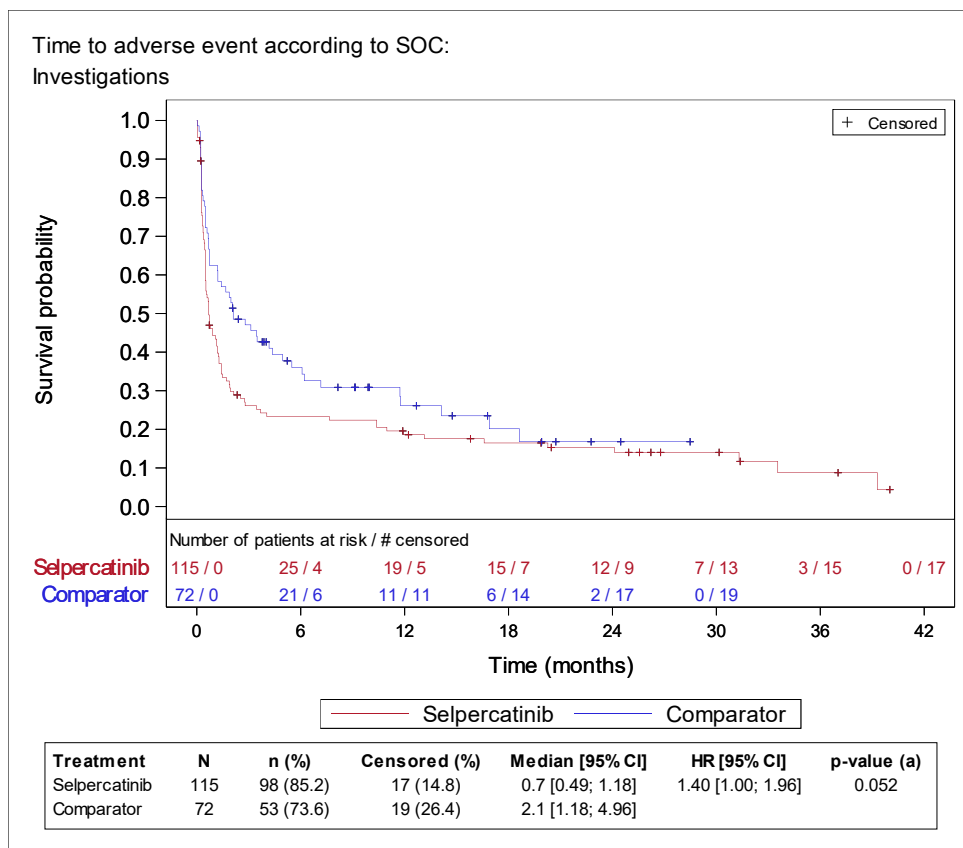
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 177: Kaplan-Meier Plot - Time to adverse event according to SOC: Investigations - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

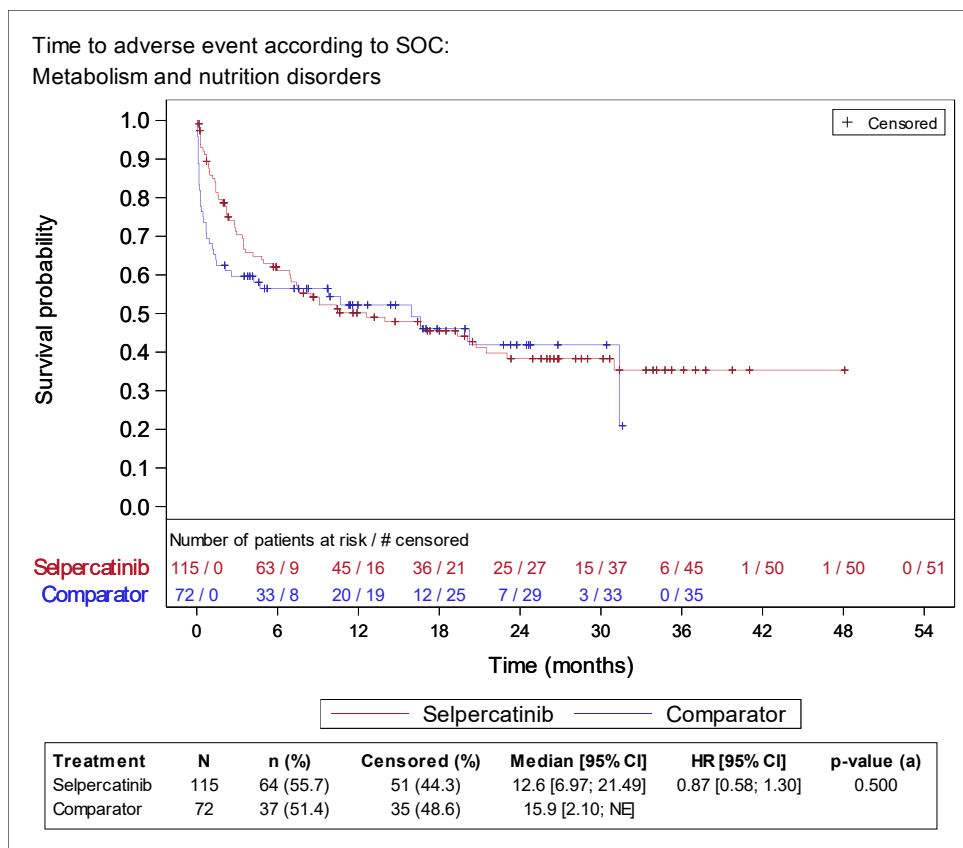
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 178: Kaplan-Meier Plot - Time to adverse event according to SOC: Metabolism and nutrition disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

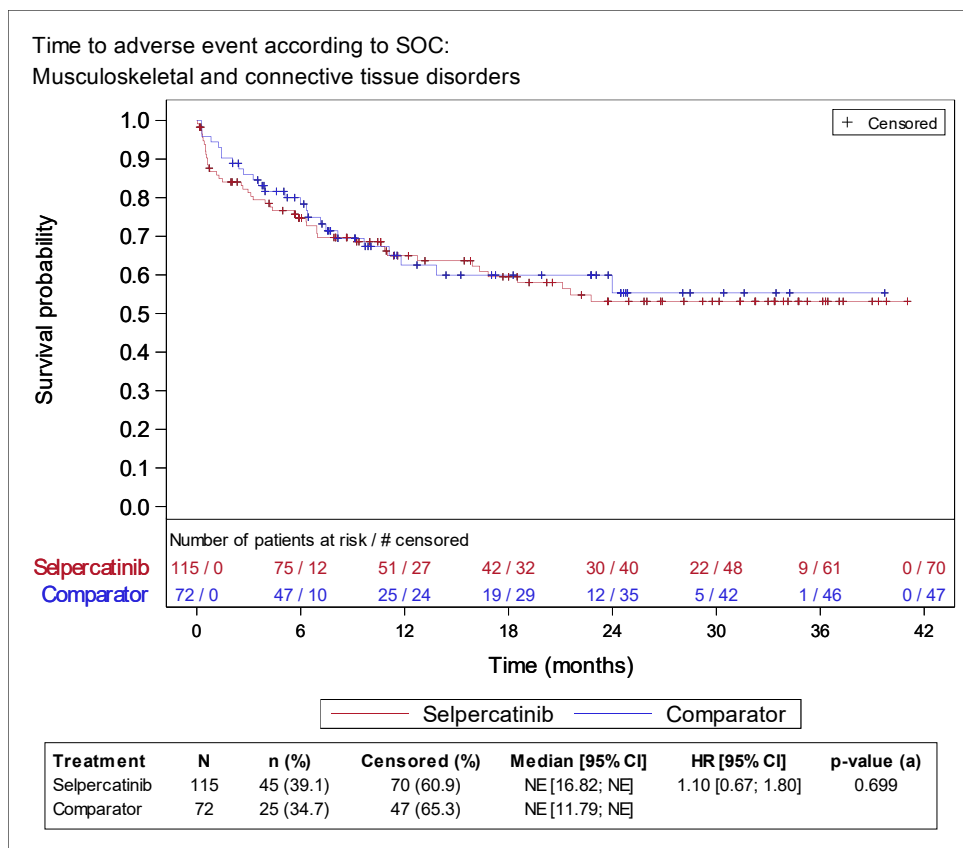
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 179: Kaplan-Meier Plot - Time to adverse event according to SOC: Musculoskeletal and connective tissue disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

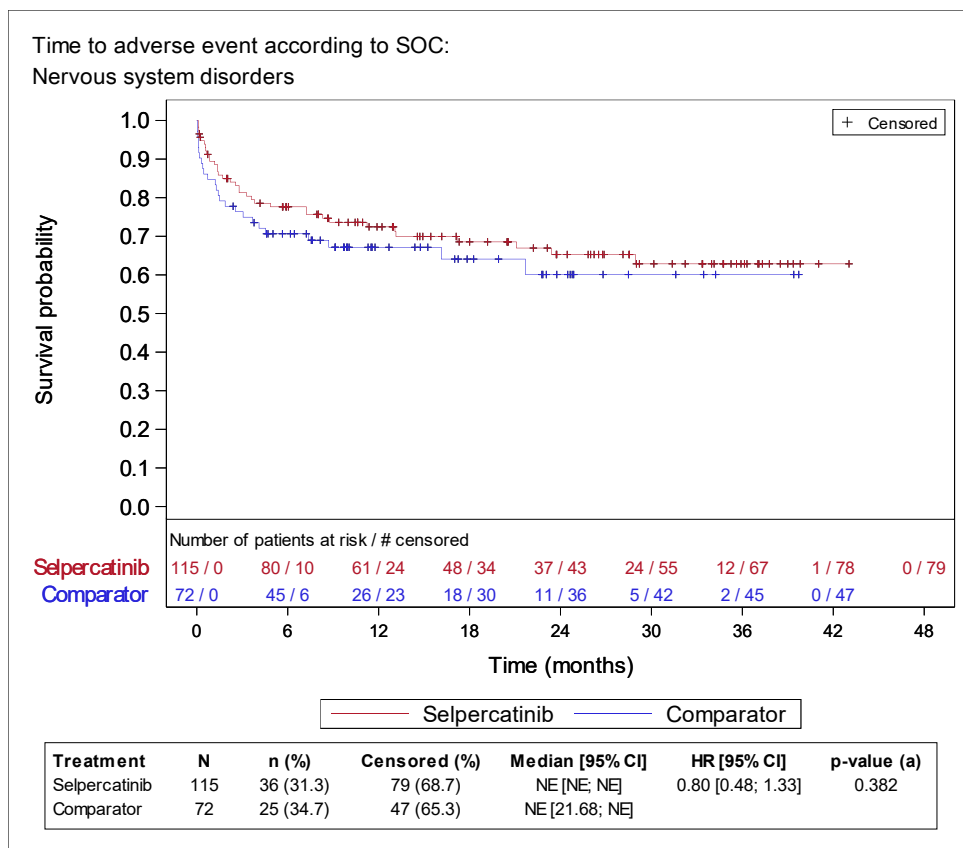
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Figure 180: Kaplan-Meier Plot - Time to adverse event according to SOC: Nervous system disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

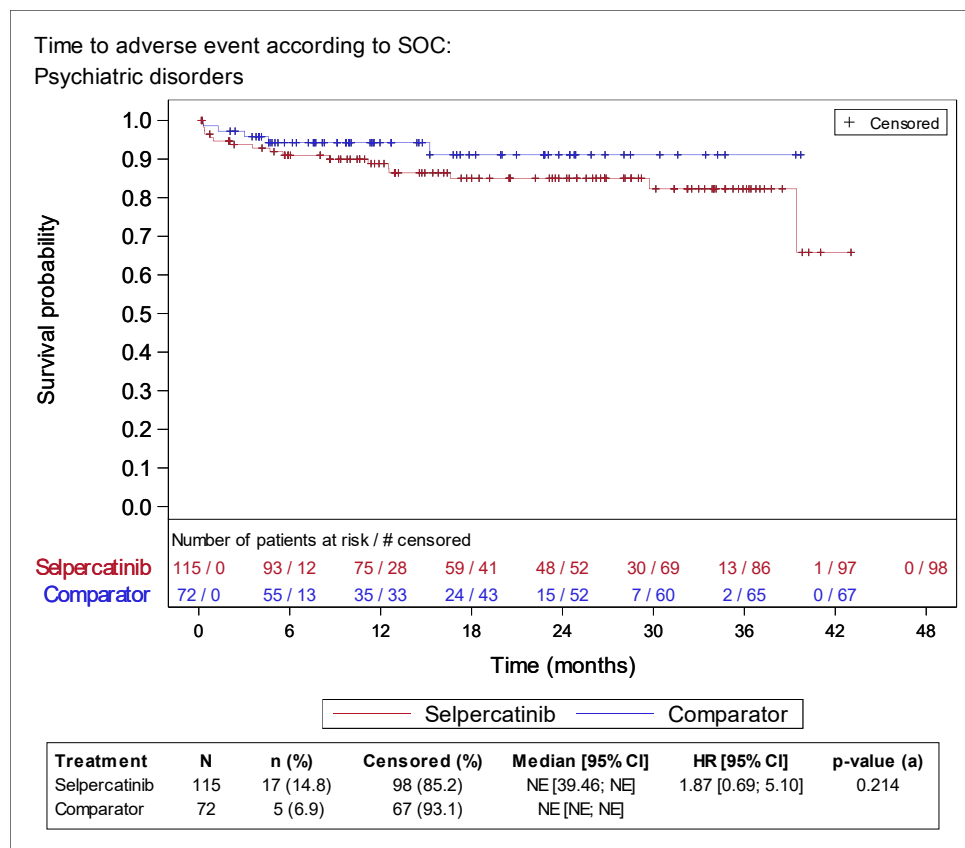
HR is based on the unstratified Cox proportional hazards model.

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Figure 181: Kaplan-Meier Plot - Time to adverse event according to SOC: Psychiatric disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

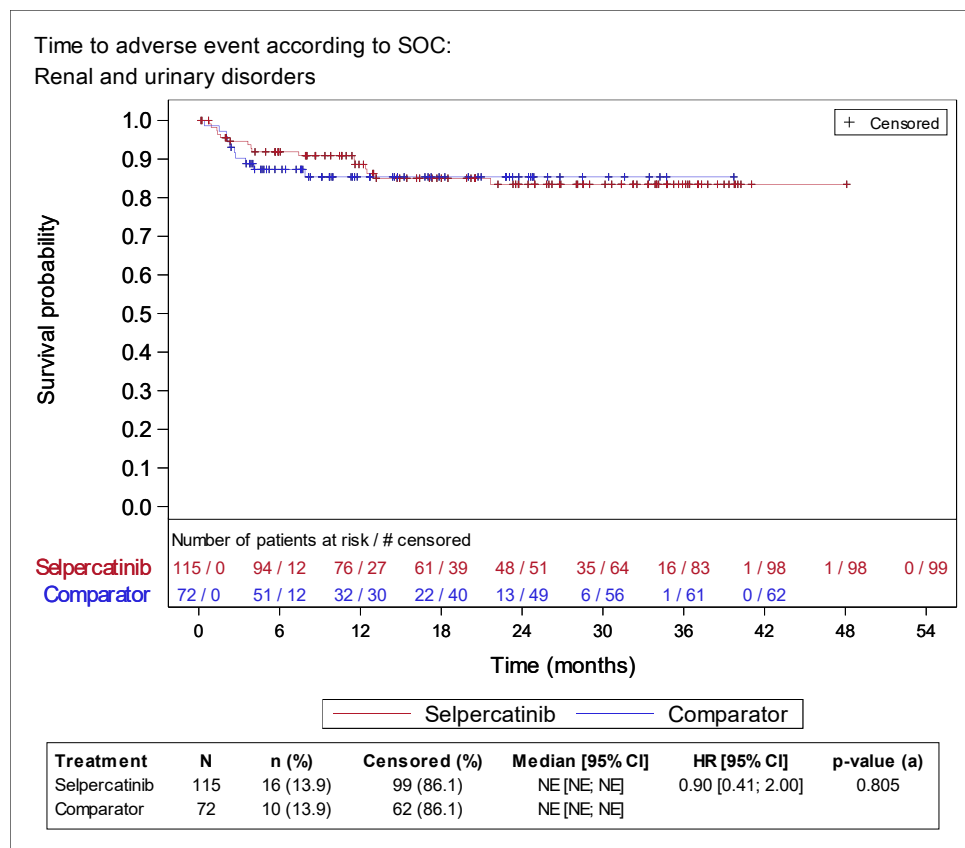
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 182: Kaplan-Meier Plot - Time to adverse event according to SOC: Renal and urinary disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

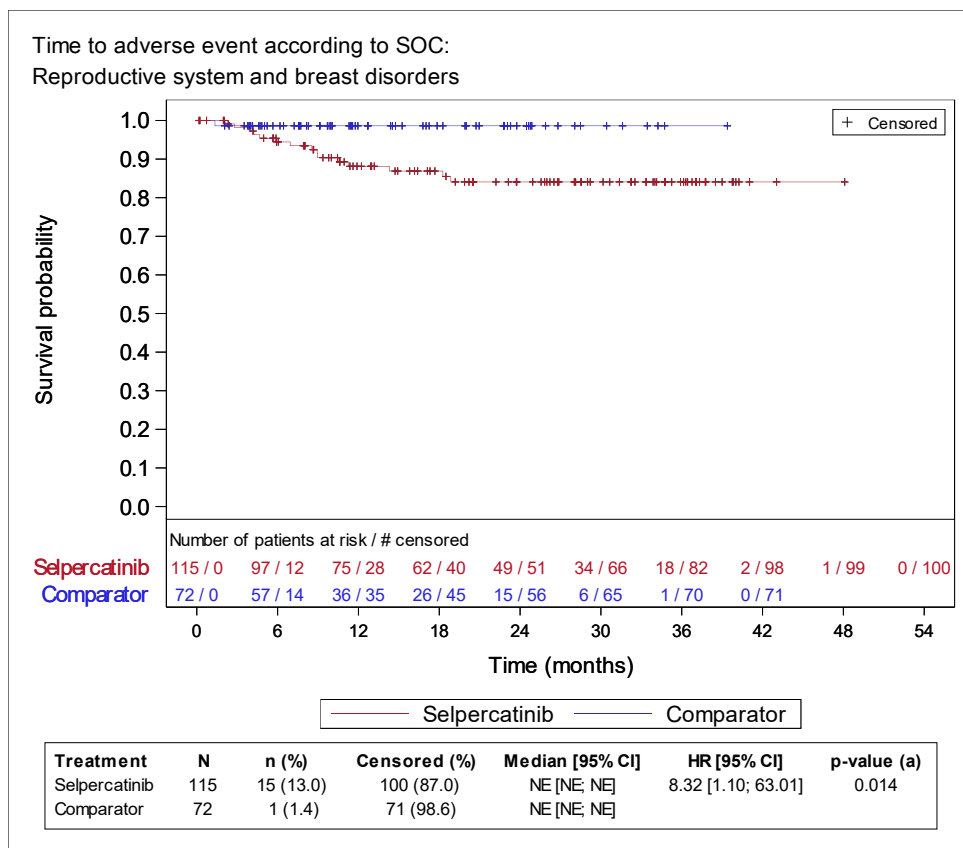
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 183: Kaplan-Meier Plot - Time to adverse event according to SOC: Reproductive system and breast disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

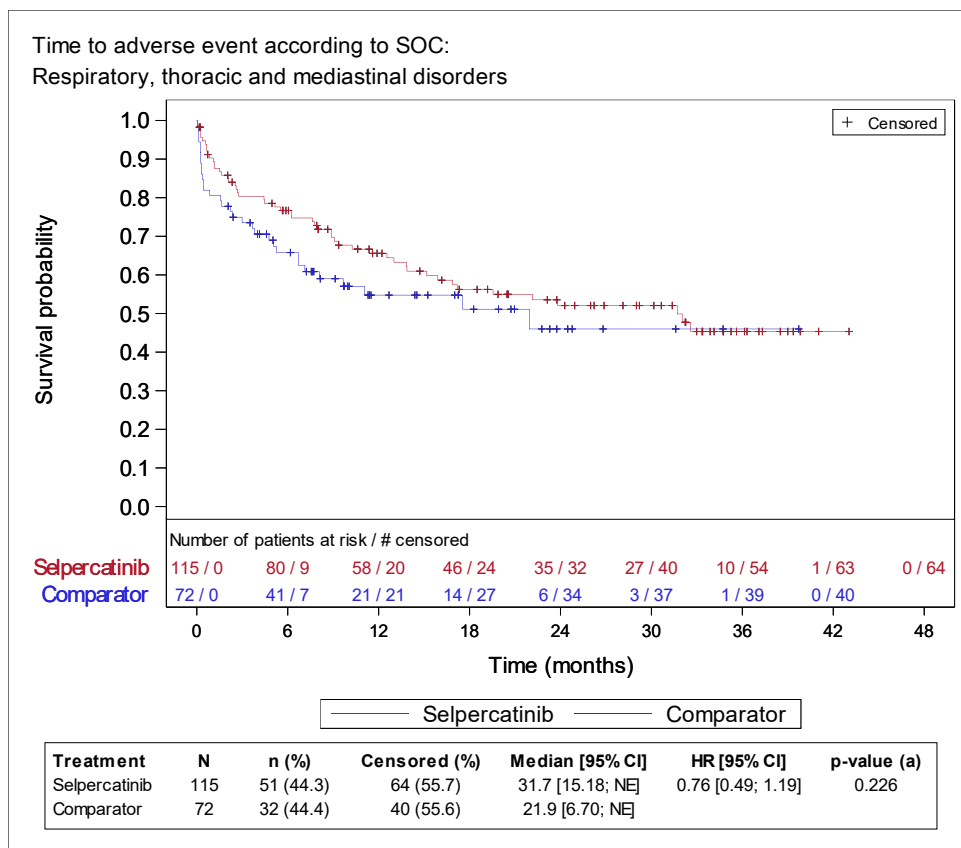
HR is based on the unstratified Cox proportional hazards model.

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Figure 184: Kaplan-Meier Plot - Time to adverse event according to SOC: Respiratory, thoracic and mediastinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

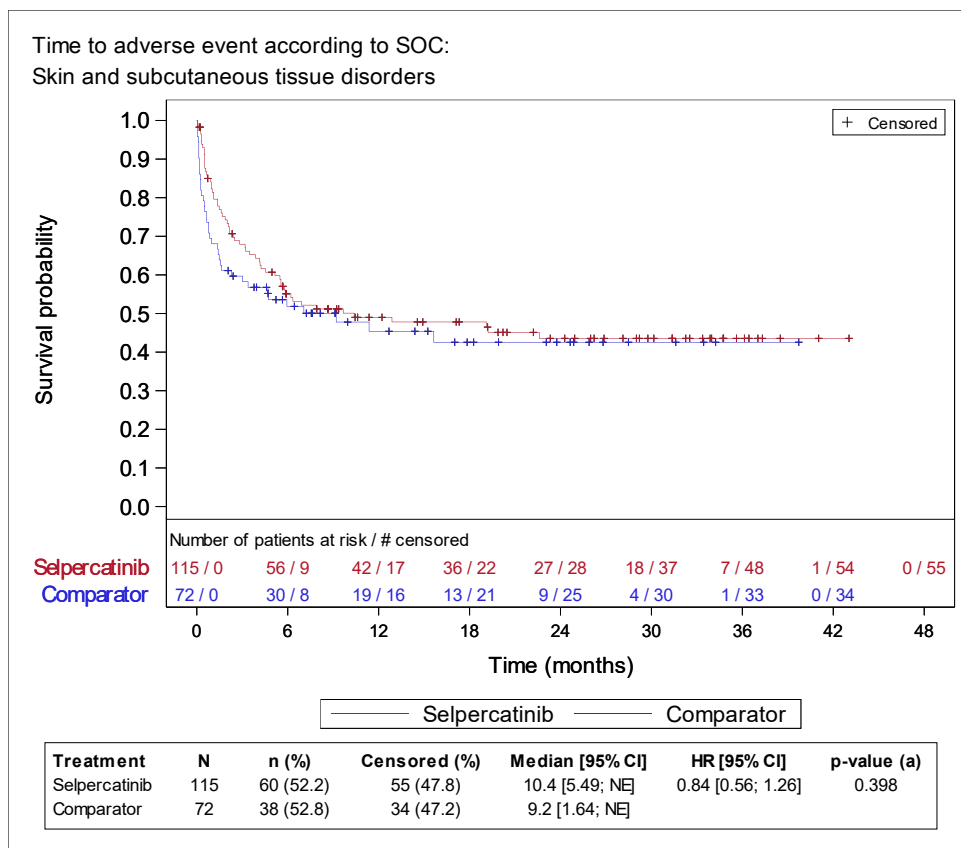
HR is based on the unstratified Cox proportional hazards model.

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23OCT2025 / 06:22

Figure 185: Kaplan-Meier Plot - Time to adverse event according to SOC: Skin and subcutaneous tissue disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

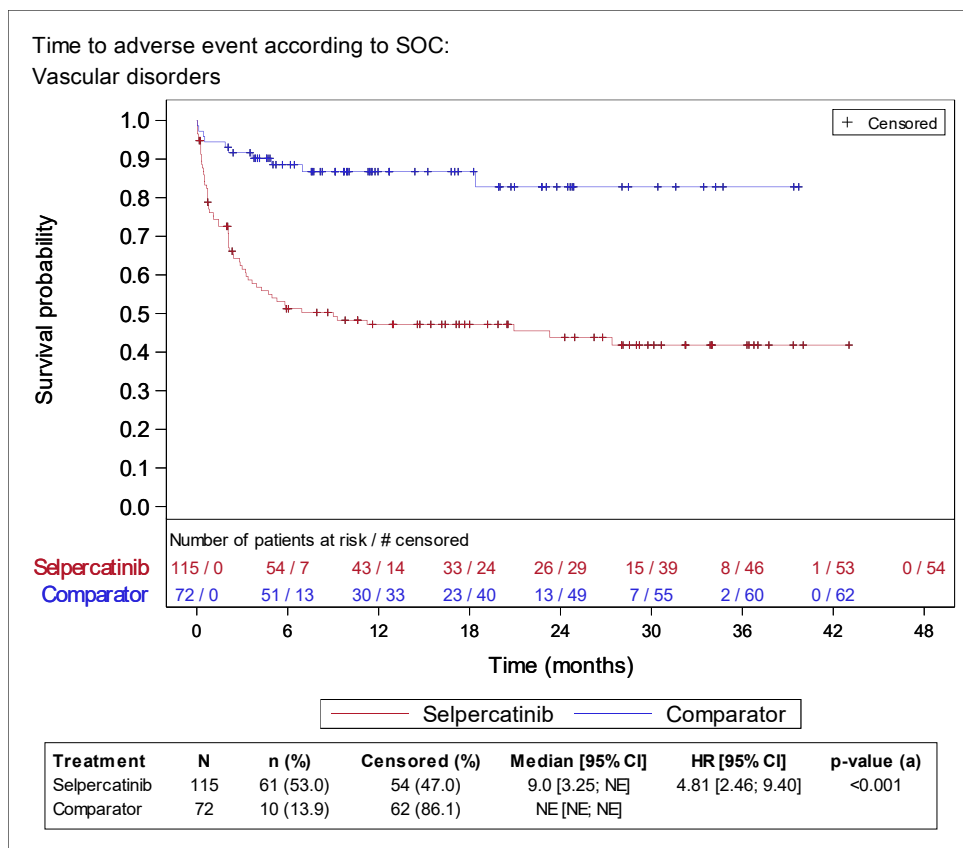
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 186: Kaplan-Meier Plot - Time to adverse event according to SOC: Vascular disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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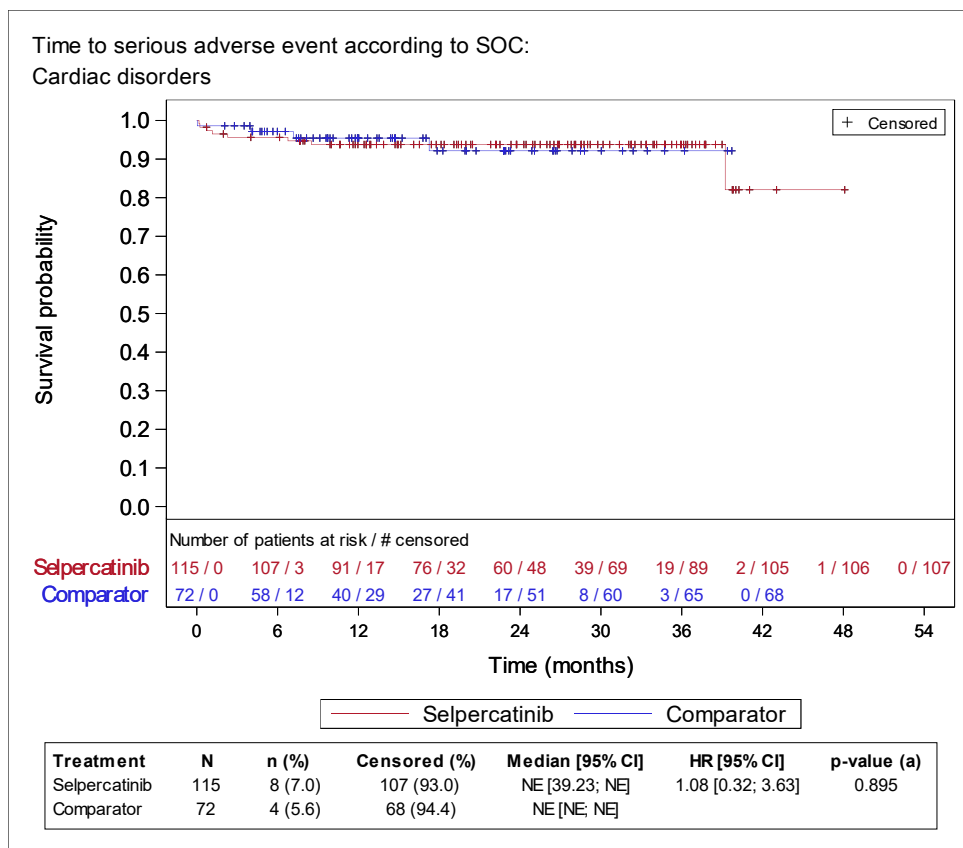
Table 167: Results for Serious TEAEs occurred in $\geq 5\%$ or in ≥ 10 patients and $\geq 1\%$ in any treatment arm within analysis population - study LIBRETTO-431, mSAF

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	HR [95% CI] p-value ^b
Serious TEAEs occurred in ≥5% or in ≥10 patients and ≥1% in any treatment arm within analysis population					
Respiratory, thoracic and mediastinal disorders	13/115 (11.3)	NE [NE; NE]	2/72 (2.8)	NE [NE; NE]	3.27 [0.73; 14.54] 0.100
Infections and infestations	10/115 (8.7)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	1.63 [0.45; 5.97] 0.452
Gastrointestinal disorders	9/115 (7.8)	NE [NE; NE]	3/72 (4.2)	NE [NE; NE]	1.49 [0.40; 5.54] 0.549
Cardiac disorders	8/115 (7.0)	NE [39.23; NE]	4/72 (5.6)	NE [NE; NE]	1.08 [0.32; 3.63] 0.895
Investigations	1/115 (0.9)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	0.15 [0.02; 1.33] 0.048
Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class. a: In months; b: from unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model.					

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Figure 187: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Cardiac disorders - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

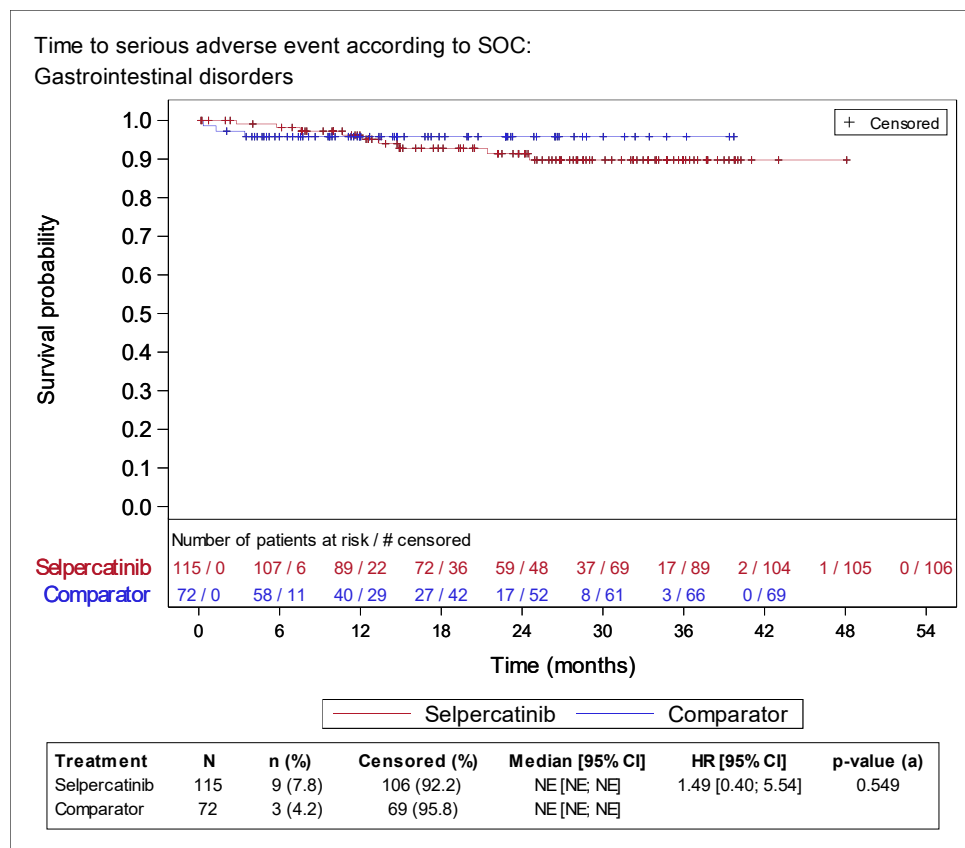
HR is based on the unstratified Cox proportional hazards model.

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Figure 188: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Gastrointestinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

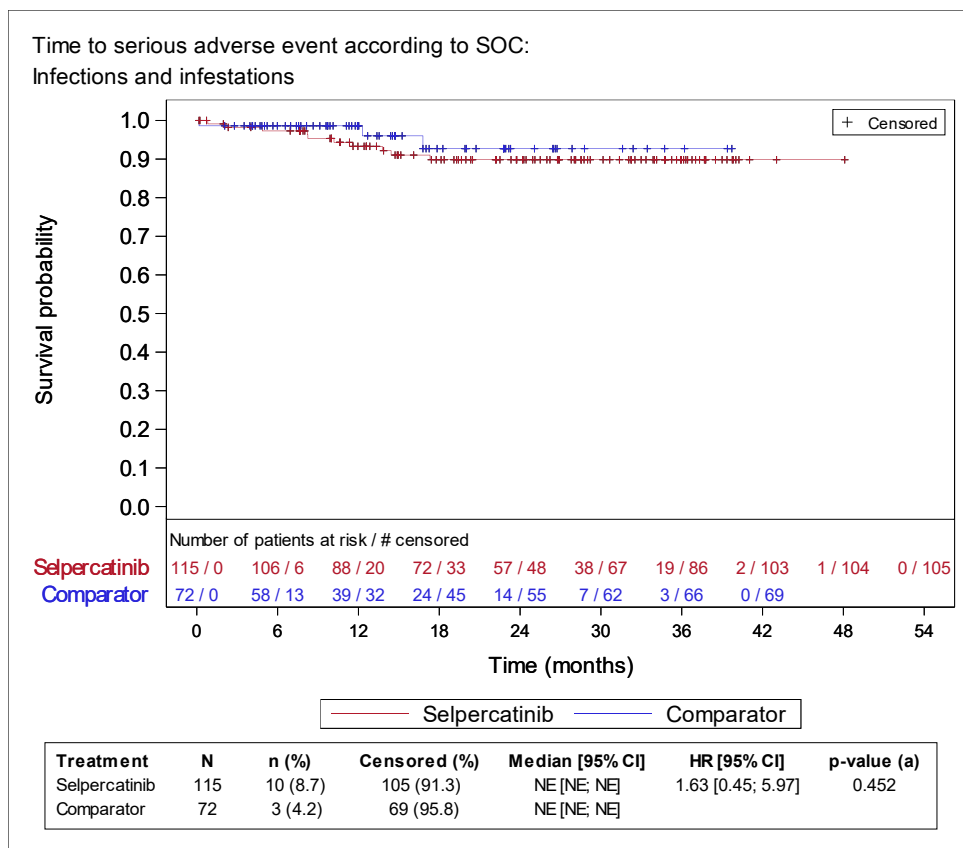
a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

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Figure 189: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Infections and infestations - study LIBRETTO-431, mSAF

Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

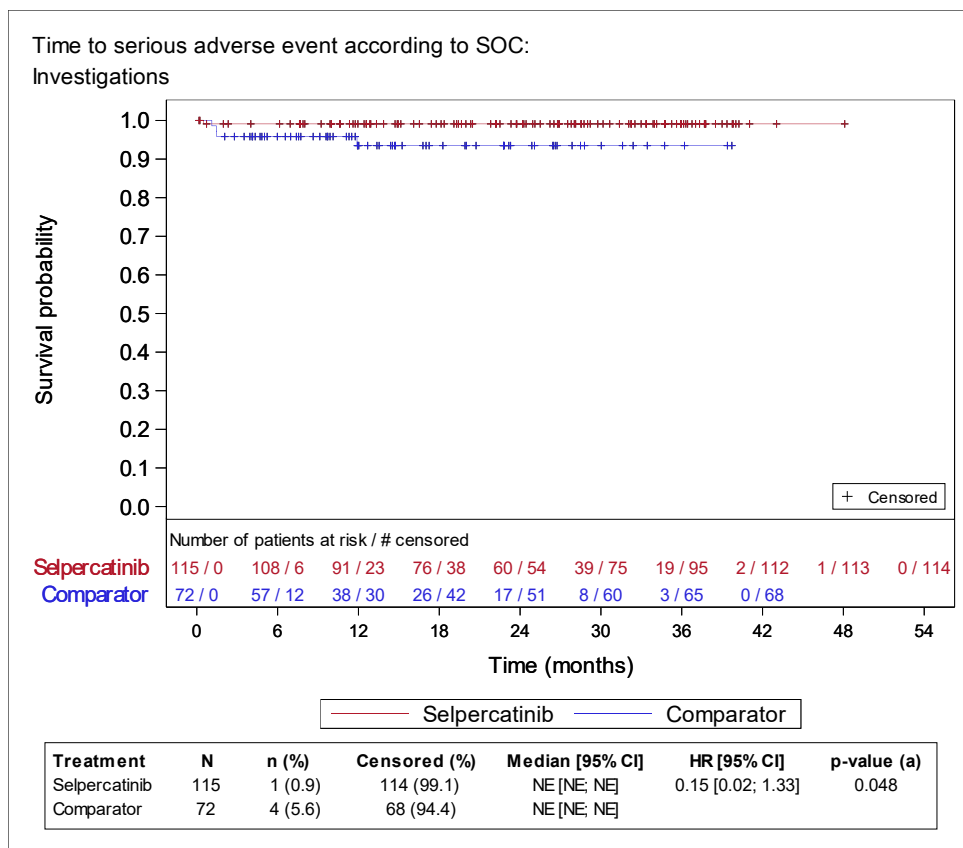
HR is based on the unstratified Cox proportional hazards model.

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Figure 190: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Investigations - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

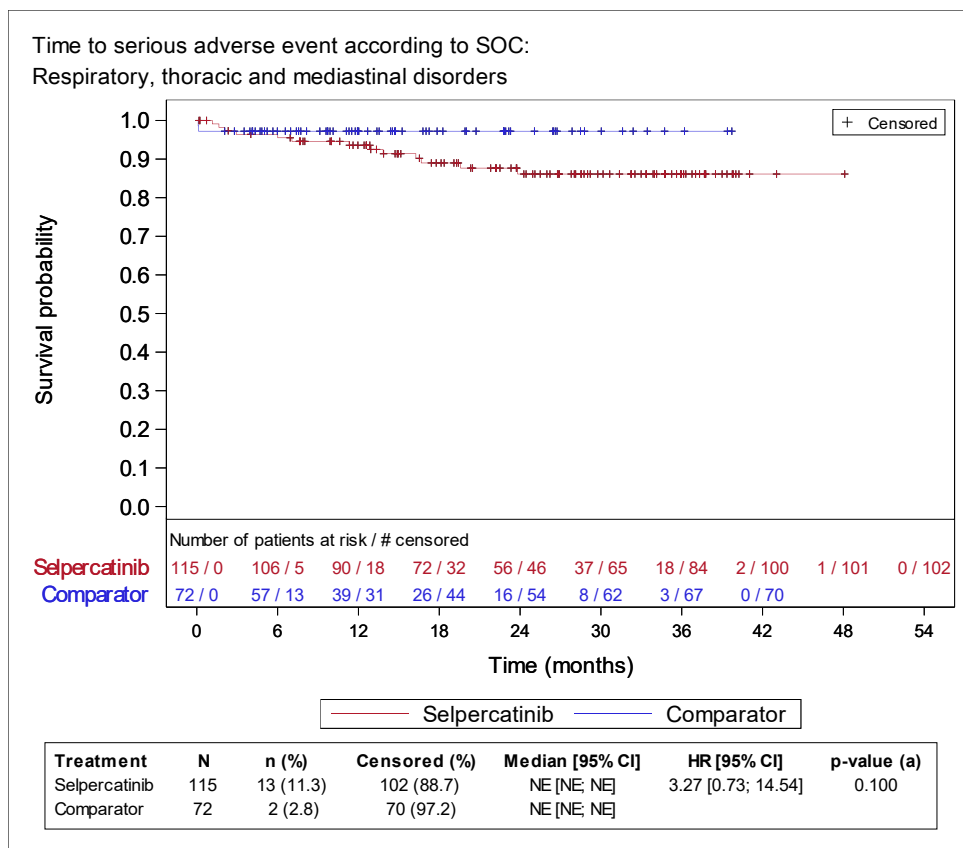
HR is based on the unstratified Cox proportional hazards model.

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Figure 191: Kaplan-Meier Plot - Time to serious adverse event according to SOC: Respiratory, thoracic and mediastinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Table 168: Results for TEAEs with CTCAE grade ≥ 3 occurred in $\geq 5\%$ or in ≥ 10 patients and $\geq 1\%$ in any treatment arm within analysis population - study LIBRETTO-431, mSAF

SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
TEAEs with CTCAE grade ≥3 occurred in ≥5% or in ≥10 patients and ≥1% in any treatment arm within analysis population					
Investigations	43/115 (37.4)	NE [24.90; NE]	14/72 (19.4)	NE [31.01; NE]	1.93 [1.06; 3.54] 0.030
Alanine aminotransferase increased*	26/115 (22.6)	NE [NE; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] <0.001
Aspartate aminotransferase increased*	15/115 (13.0)	NE [NE; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] 0.002
Electrocardiogram QT prolonged*	9/115 (7.8)	NE [NE; NE]	0/72 (0.0)	NE [NE; NE]	NE [0.00; NE] 0.015
Platelet count decreased	3/115 (2.6)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	0.32 [0.07; 1.38] 0.108
Neutrophil count decreased	2/115 (1.7)	NE [NE; NE]	11/72 (15.3)	NE [31.01; NE]	0.09 [0.02; 0.40] <0.001
White blood cell count decreased	2/115 (1.7)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	0.28 [0.05; 1.52] 0.114
Vascular disorders	27/115 (23.5)	NE [NE; NE]	2/72 (2.8)	NE [NE; NE]	8.89 [2.11; 37.42] <0.001
Hypertension	26/115 (22.6)	NE [NE; NE]	2/72 (2.8)	NE [NE; NE]	8.58 [2.04; 36.20] <0.001
Gastrointestinal disorders	9/115 (7.8)	NE [NE; NE]	4/72 (5.6)	NE [NE; NE]	1.18 [0.36; 3.86] 0.779
Infections and infestations	9/115 (7.8)	NE [NE; NE]	1/72 (1.4)	NE [NE; NE]	4.55 [0.57; 36.07] 0.115
Metabolism and nutrition disorders	8/115 (7.0)	NE [NE; NE]	6/72 (8.3)	NE [NE; NE]	0.64 [0.22; 1.90] 0.421
Cardiac disorders	7/115 (6.1)	NE [39.23; NE]	4/72 (5.6)	NE [NE; NE]	0.97 [0.28; 3.33] 0.958
General disorders and administration site conditions	7/115 (6.1)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	0.61 [0.19; 1.93] 0.393

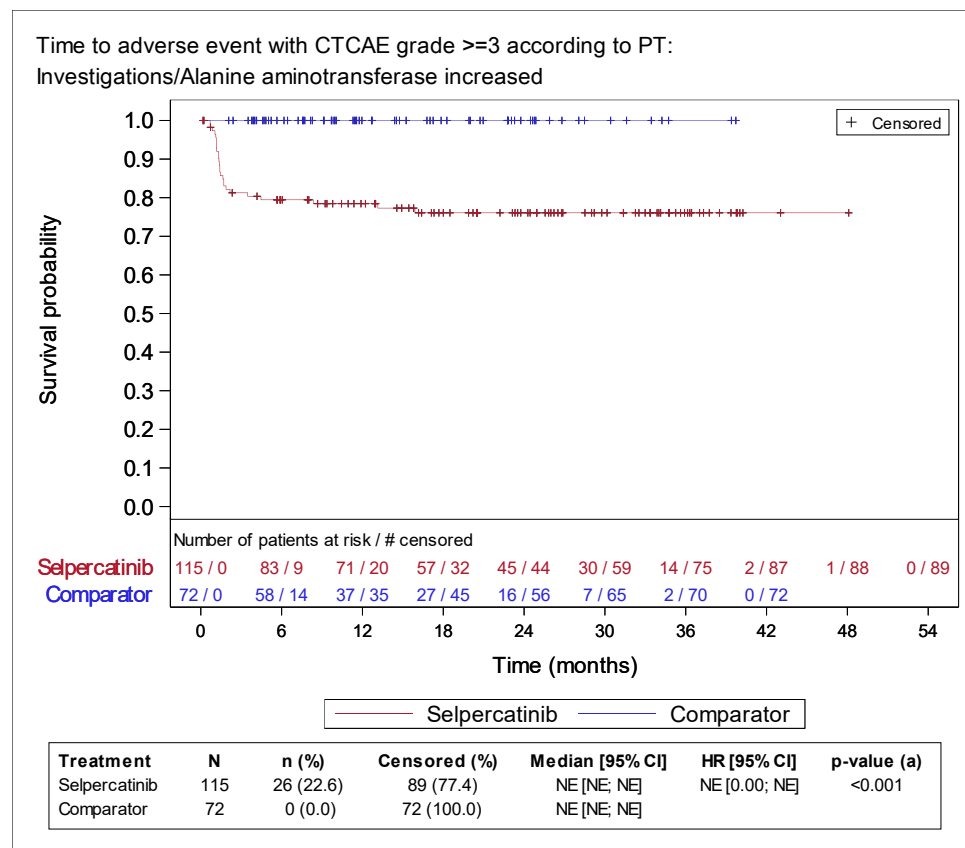
SOC Preferred term	Selpercatinib		Carboplatin or Cisplatin +Pemetrexed +Pembrolizumab		HR [95% CI] p-value ^b
	n/N (%)	Median time to event ^a [95% CI]	n/N (%)	Median time to event ^a [95% CI]	
Respiratory, thoracic and mediastinal disorders	7/115 (6.1)	NE [NE; NE]	5/72 (6.9)	NE [NE; NE]	0.75 [0.24; 2.38] 0.622
Blood and lymphatic system disorders	2/115 (1.7)	NE [NE; NE]	18/72 (25.0)	NE [NE; NE]	0.05 [0.01; 0.23] <0.001
Anaemia	1/115 (0.9)	NE [NE; NE]	8/72 (11.1)	NE [NE; NE]	0.06 [0.01; 0.52] <0.001
Neutropenia*	0/115 (0.0)	NE [NE; NE]	10/72 (13.9)	NE [NE; NE]	0.00 [0.00; NE] <0.001
Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥50 kg). Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class. a: In months; b: from unstratified Log-rank-Test. HR is based on the unstratified Cox proportional hazards model. * The likelihood ratio test for strata homogeneity is questionable since some strata have no events.					

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Figure 192: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Alanine aminotransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

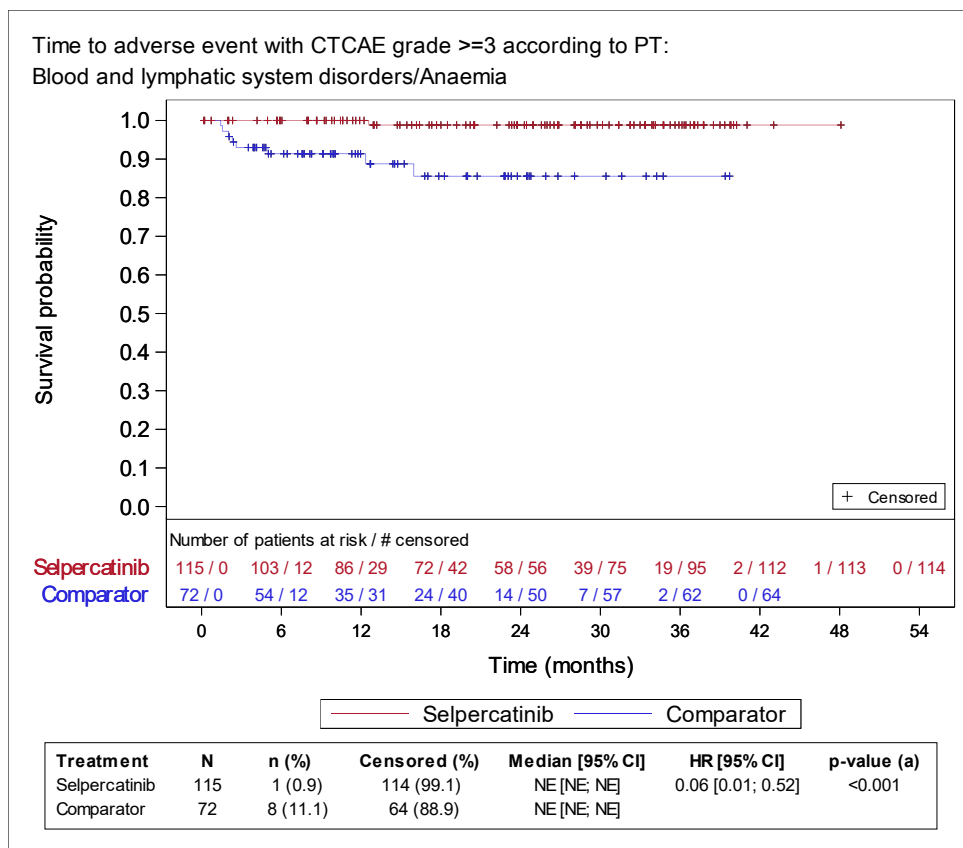
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

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Figure 193: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Blood and lymphatic system disorders/Anaemia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

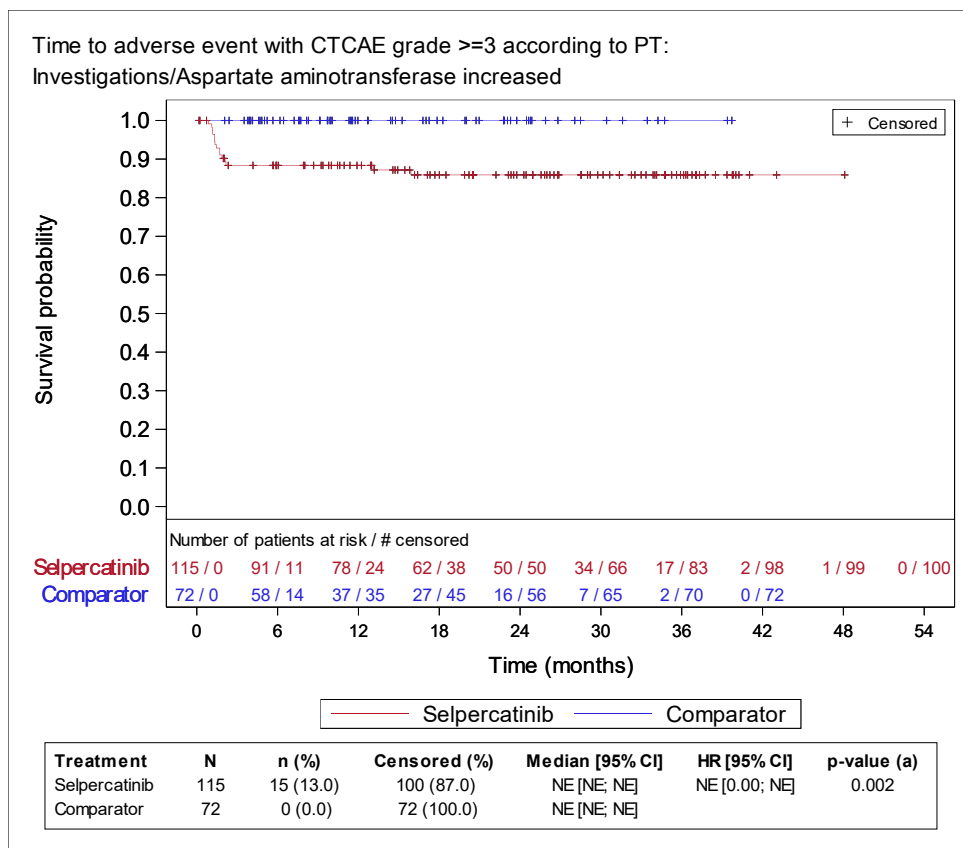
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 194: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Aspartate aminotransferase increased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

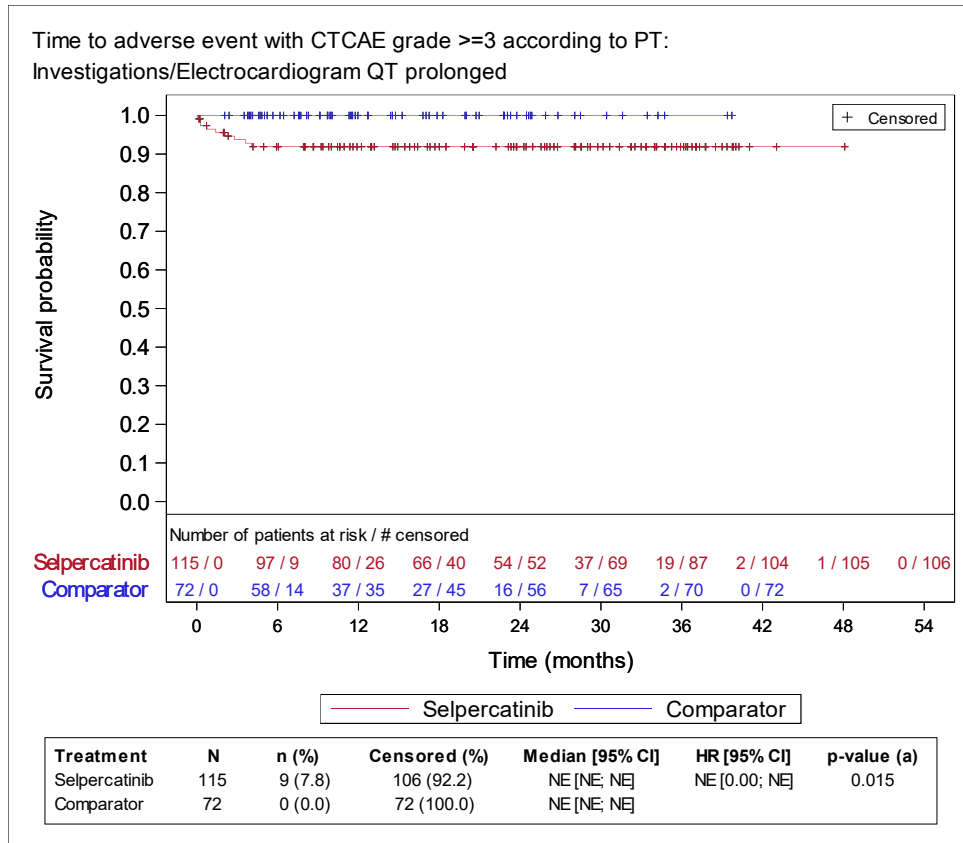
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 195: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Electrocardiogram QT prolonged - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

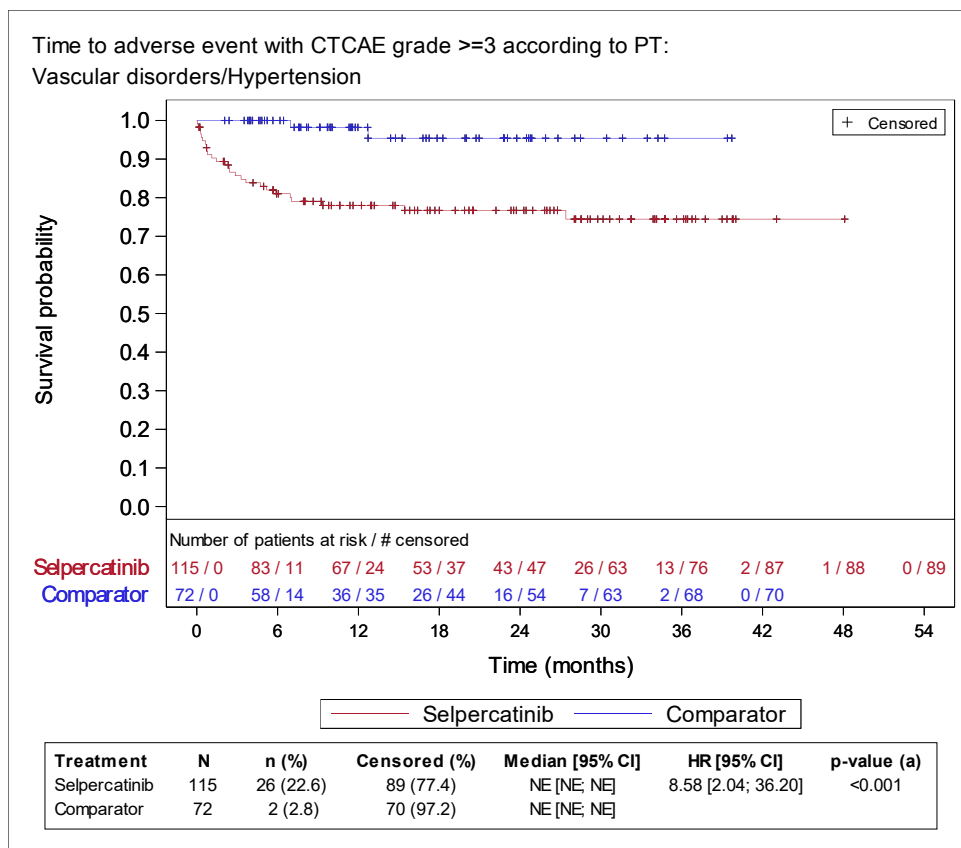
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

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Figure 196: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Vascular disorders/Hypertension - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

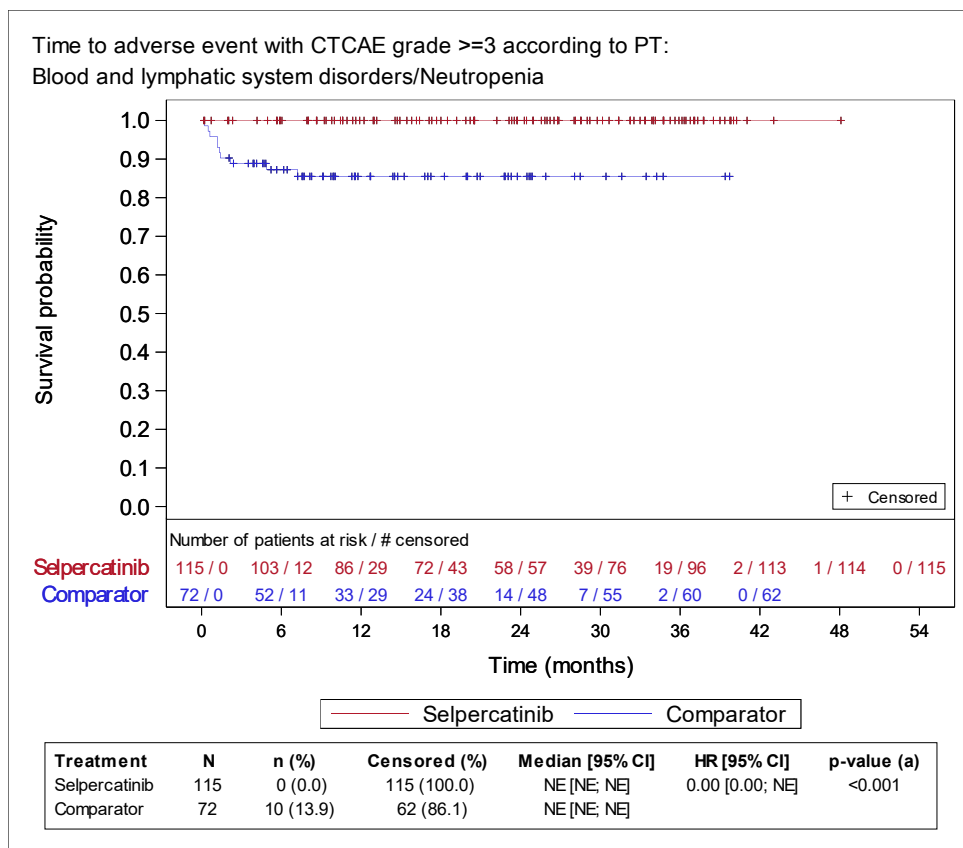
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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23OCT2025 / 06:22

Figure 197: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Blood and lymphatic system disorders/Neutropenia - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

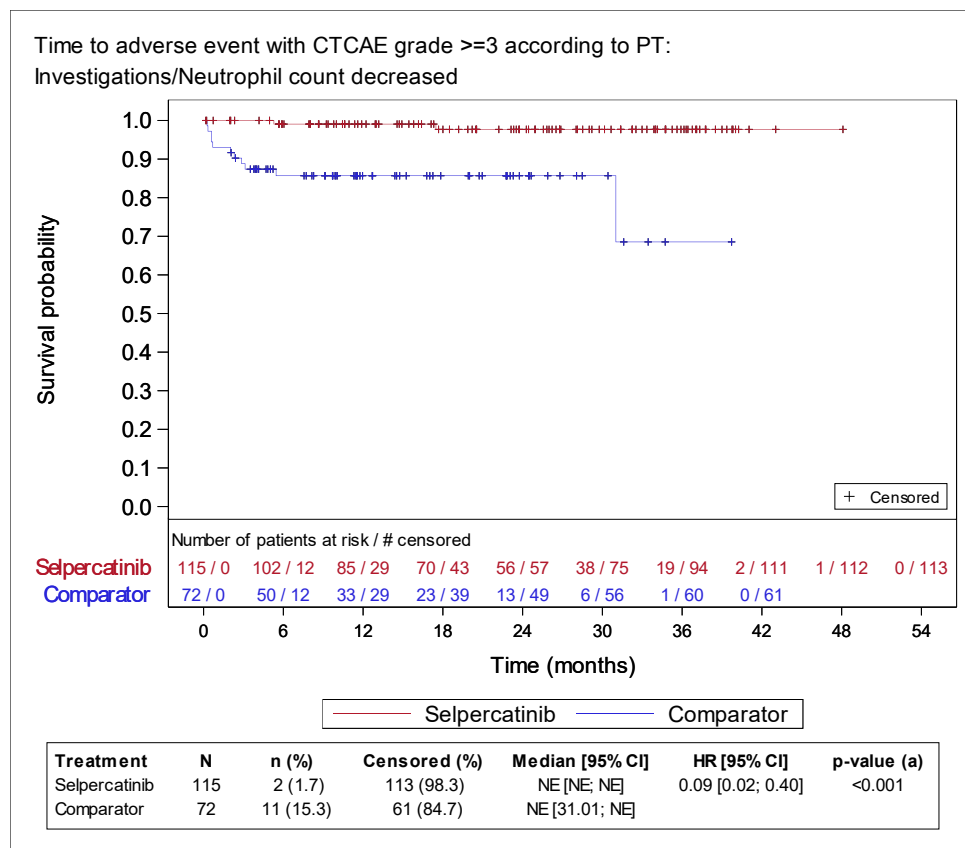
The likelihood ratio test for strata homogeneity is questionable since some strata have no events.

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Figure 198: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Neutrophil count decreased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

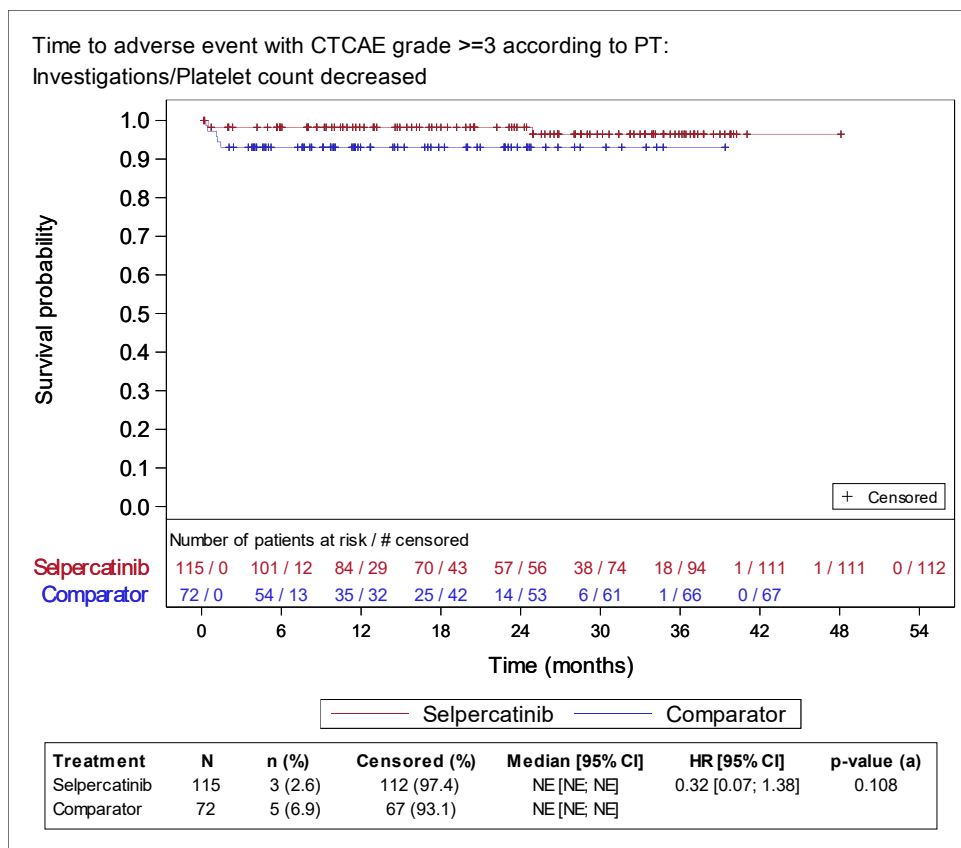
HR is based on the unstratified Cox proportional hazards model.

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Figure 199: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/Platelet count decreased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

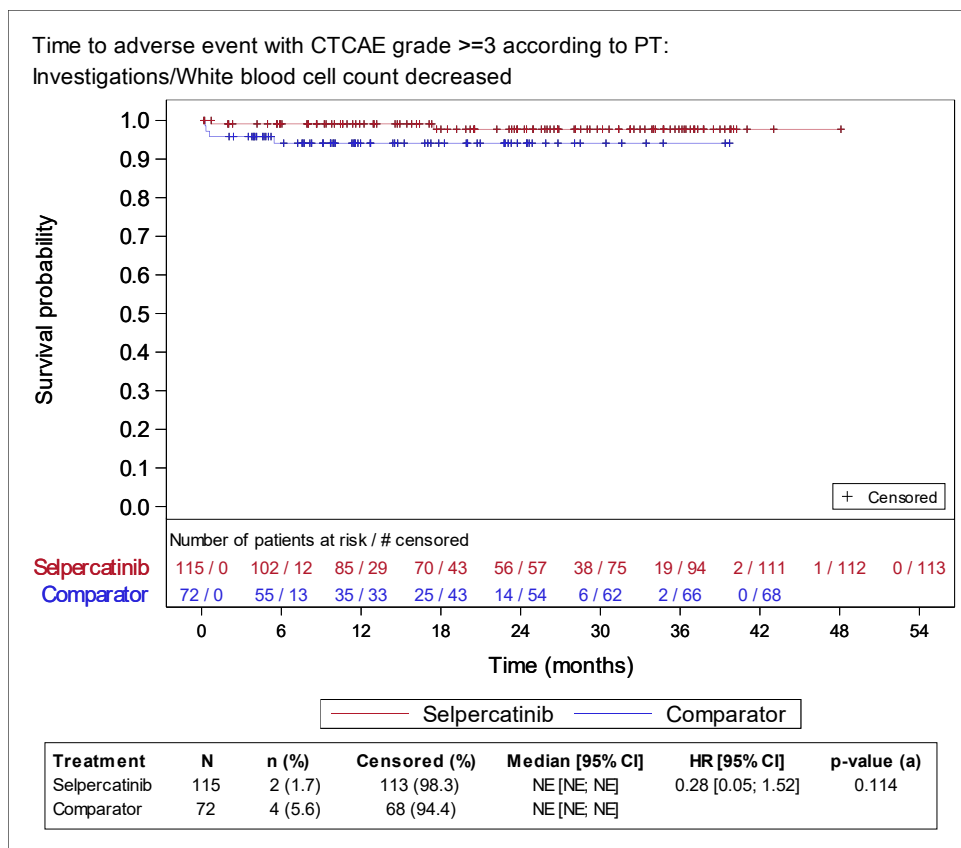
HR is based on the unstratified Cox proportional hazards model.

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Figure 200: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to PT: Investigations/White blood cell count decreased - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; PT: Preferred Term.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

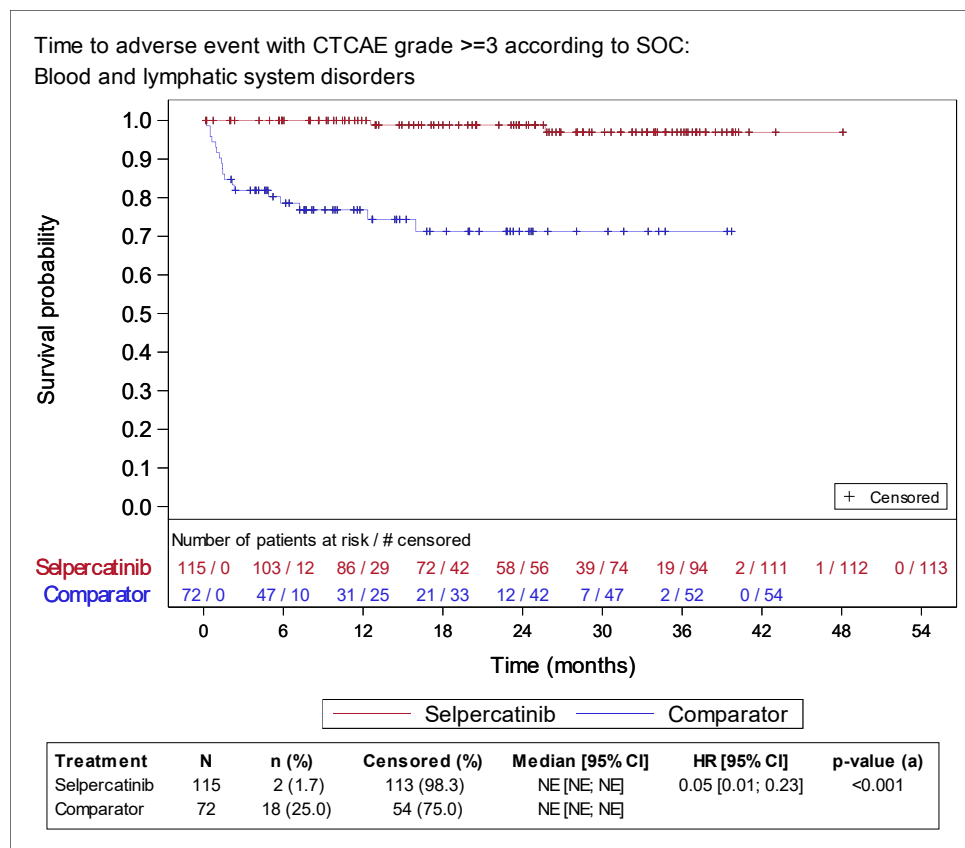
HR is based on the unstratified Cox proportional hazards model.

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Figure 201: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Blood and lymphatic system disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

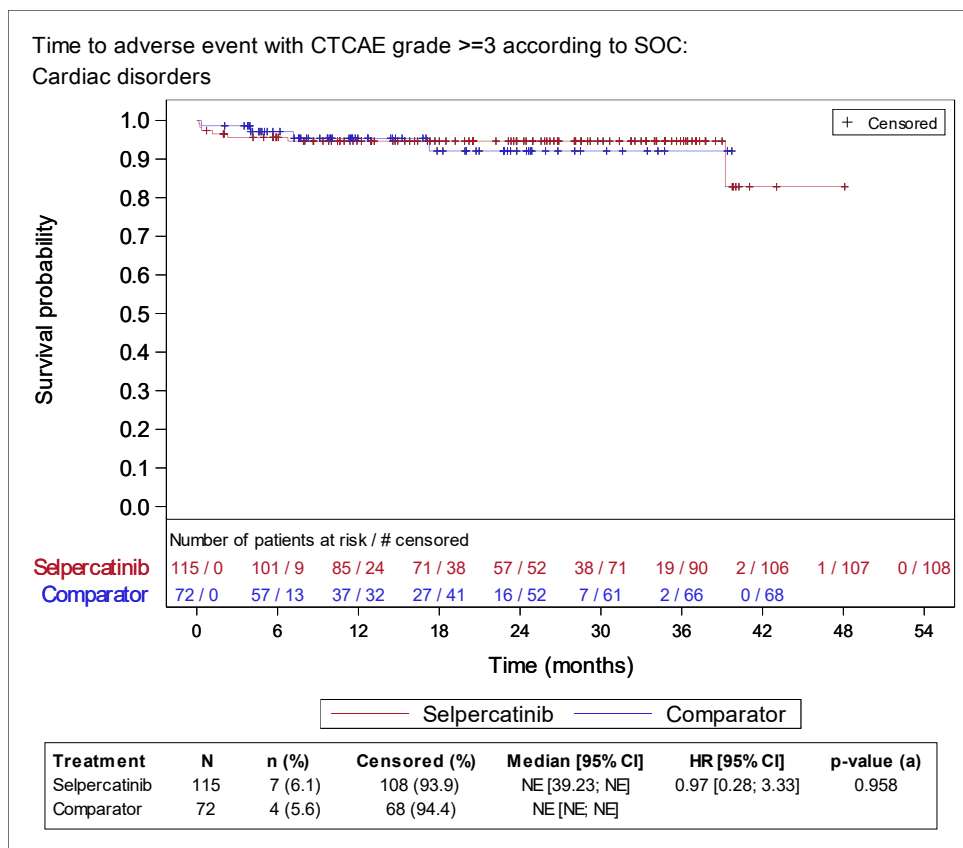
HR is based on the unstratified Cox proportional hazards model.

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Figure 202: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Cardiac disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

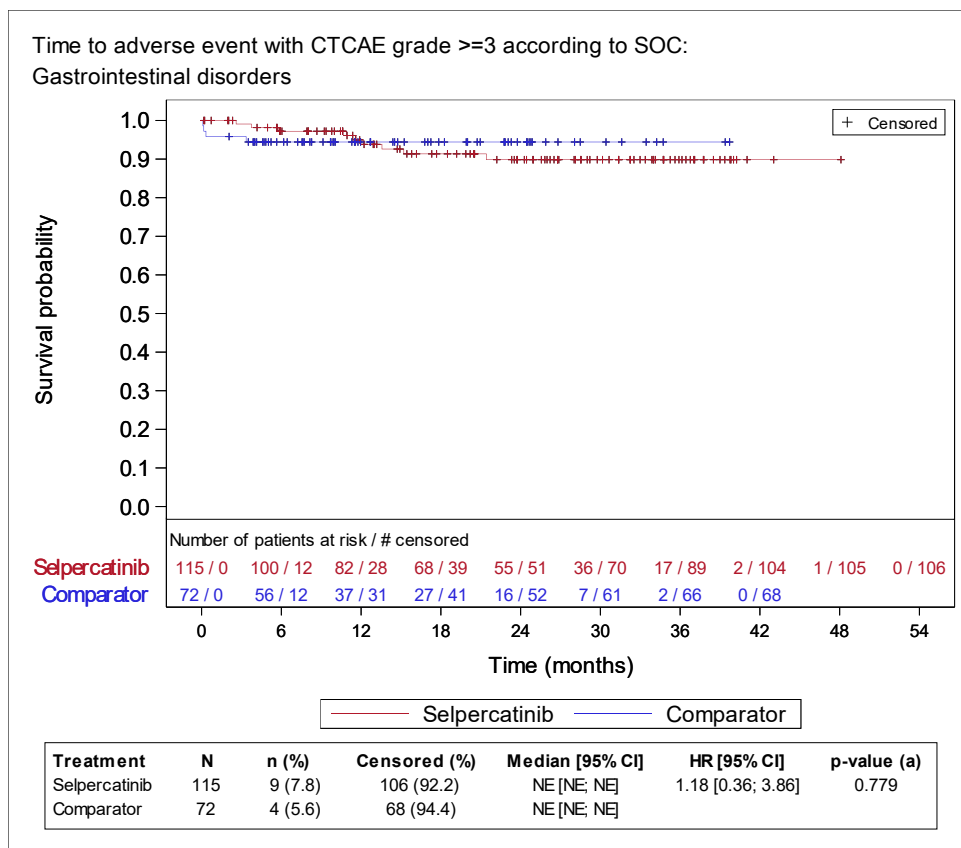
HR is based on the unstratified Cox proportional hazards model.

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Figure 203: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Gastrointestinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

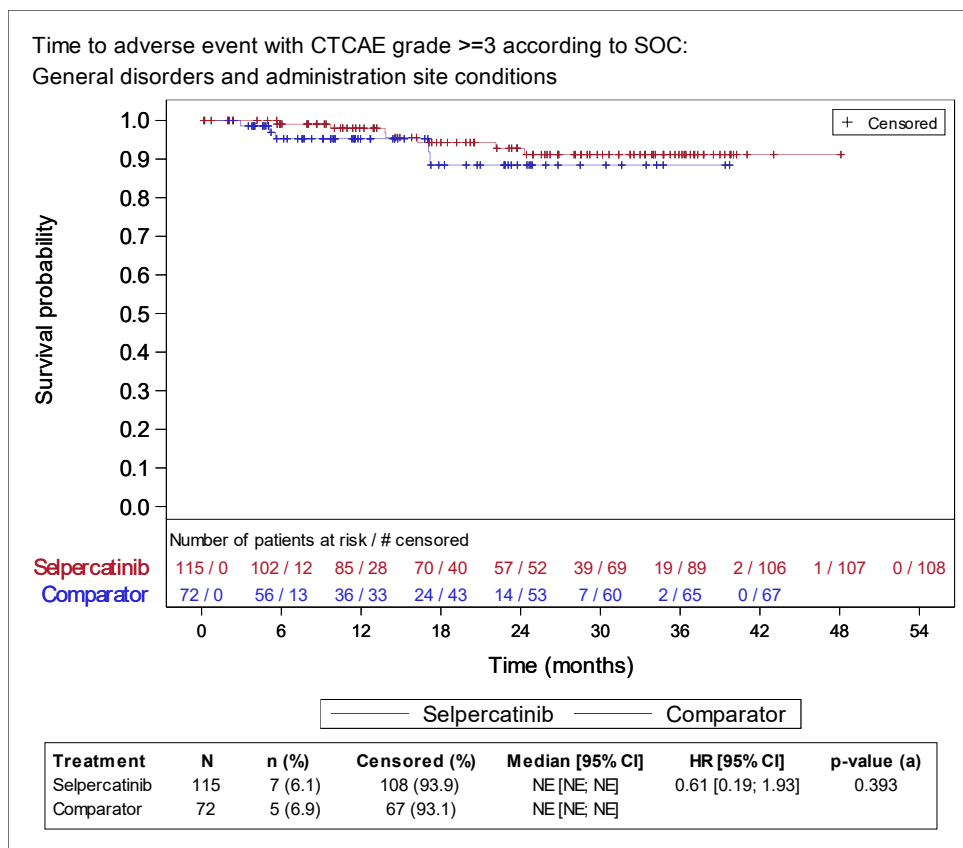
HR is based on the unstratified Cox proportional hazards model.

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Figure 204: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: General disorders and administration site conditions - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

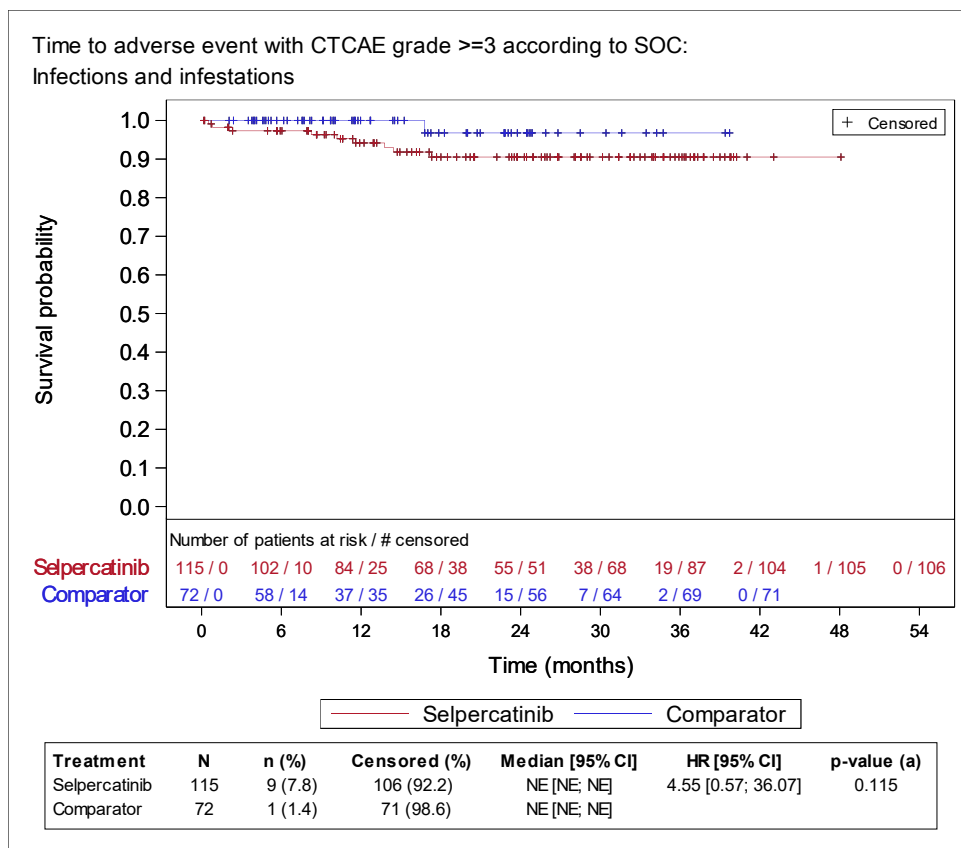
HR is based on the unstratified Cox proportional hazards model.

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Figure 205: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Infections and infestations - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

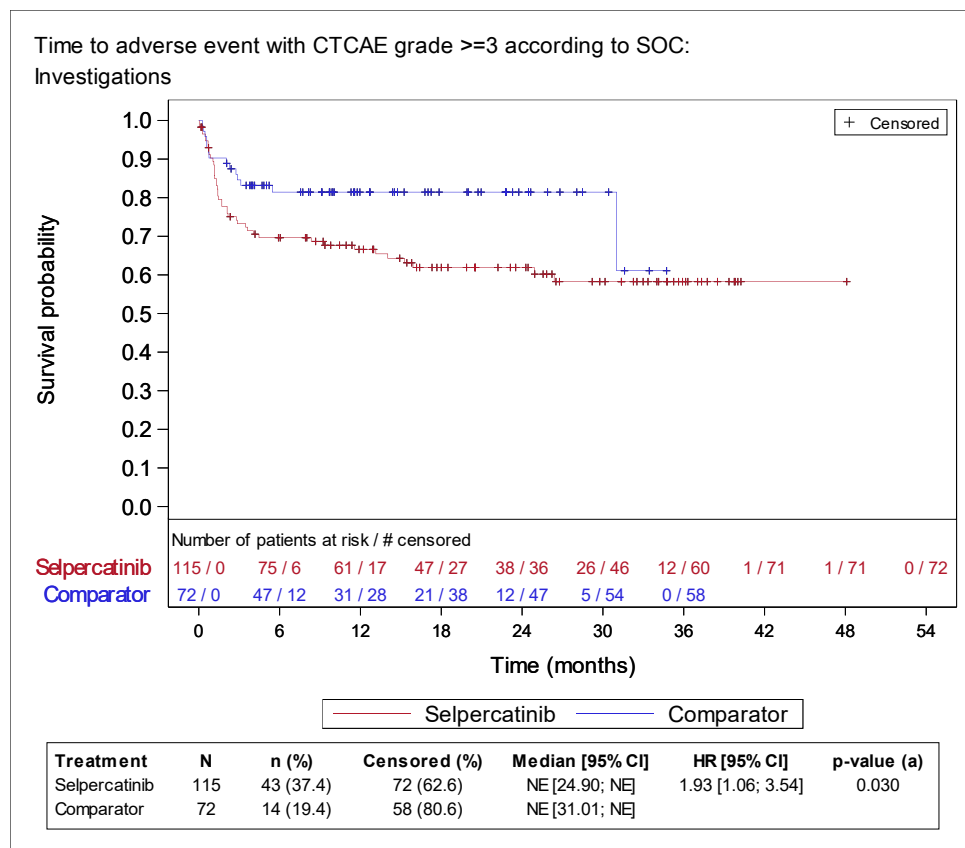
HR is based on the unstratified Cox proportional hazards model.

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Figure 206: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Investigations - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

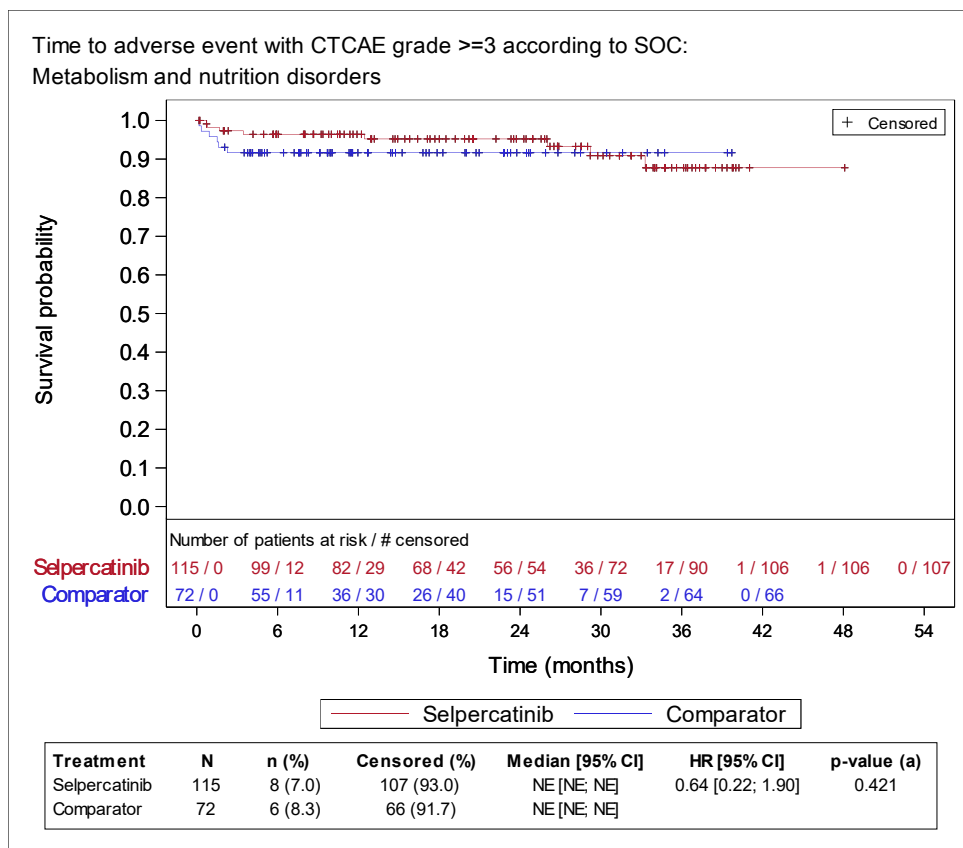
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

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Figure 207: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Metabolism and nutrition disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

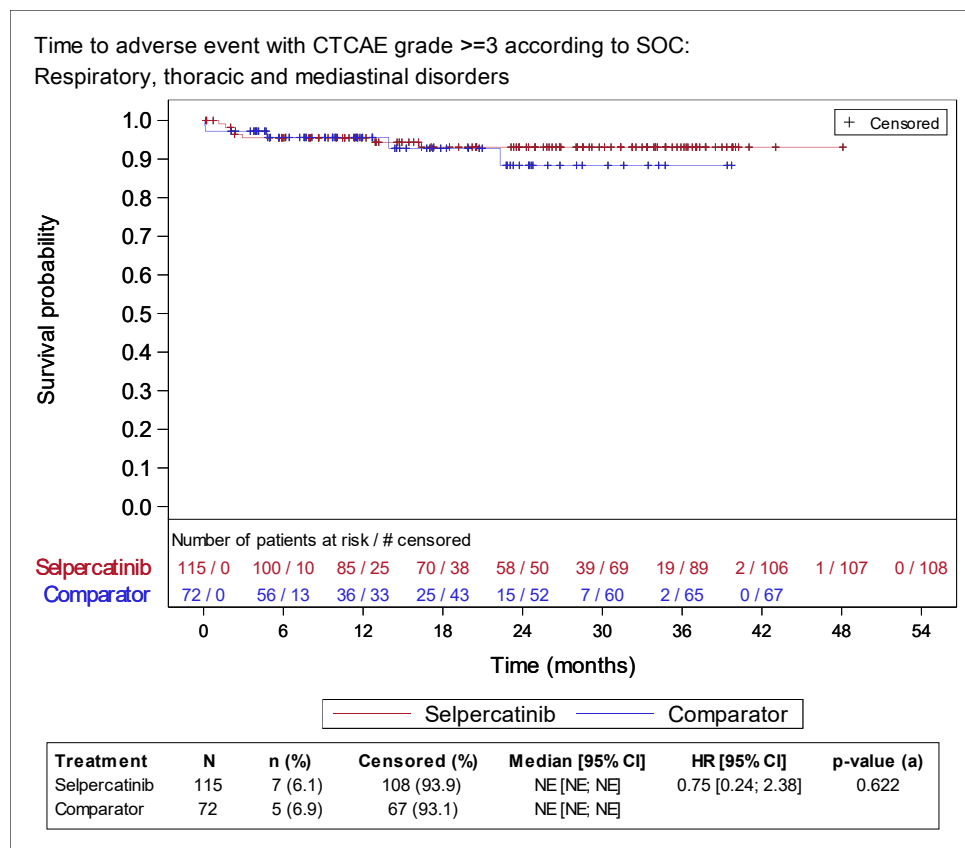
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_gr3spx007_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 208: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Respiratory, thoracic and mediastinal disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

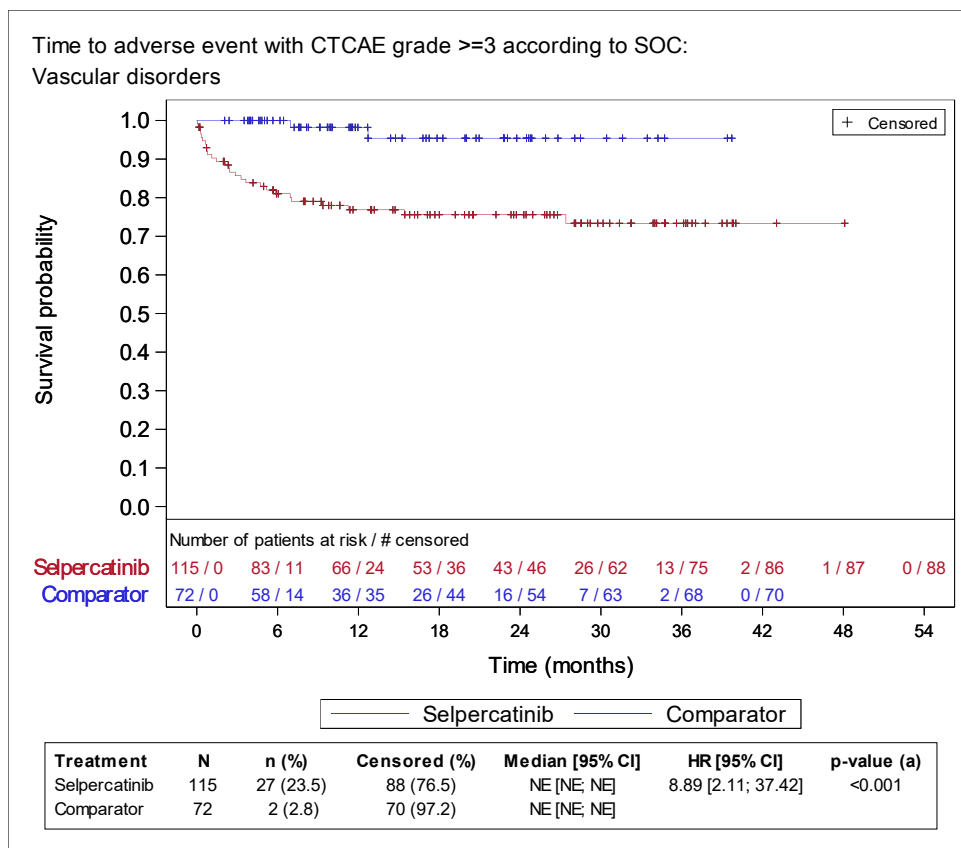
HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_gr3spx008_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Figure 209: Kaplan-Meier Plot - Time to adverse event with CTCAE grade ≥ 3 according to SOC: Vascular disorders - study LIBRETTO-431, mSAF



Data cutoff: 08MAY2024; Modified Safety-Pembrolizumab Population (ECOG 0-1, Weight ≥ 50 kg).

Abbreviations: CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; kg: kilogram; mSAF: Modified Safety-Pembrolizumab Population; n: Number of patients with event; N: Total number of patients in the analysis; NE: Not evaluable/not calculated; SOC: System Organ Class.

Comparator = Carboplatin or Cisplatin + Pemetrexed + Pembrolizumab.

a: from unstratified Log-rank-Test.

HR is based on the unstratified Cox proportional hazards model.

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/f_aespt_tte_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/f_gr3spx009_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba, adtteae_gba
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Tabelle 169: Behandlungsbedingte unerwünschte Ereignisse, die zum Behandlungsabbruch führen - Studie LIBRETTO-431, mSAF

SOC Preferred term	Selpercatinib (N=115) n (%)	Carboplatin oder Cisplatin +Pemetrexed +Pembrolizumab (N=72) n (%)	Gesamt (N=187) n (%)
Behandlungsbedingte unerwünschte Ereignisse, die zum Behandlungsabbruch führen	11 (9,6)	5 (6,9)	16 (8,6)
Cardiac disorders	3 (2,6)	1 (1,4)	4 (2,1)
Myocardial infarction	2 (1,7)	0 (0,0)	2 (1,1)
Cardiac arrest	1 (0,9)	1 (1,4)	2 (1,1)
Respiratory, thoracic and mediastinal disorders	2 (1,7)	0 (0,0)	2 (1,1)
Acute respiratory failure	1 (0,9)	0 (0,0)	1 (0,5)
Interstitial lung disease	1 (0,9)	0 (0,0)	1 (0,5)
General disorders and administration site conditions	1 (0,9)	0 (0,0)	1 (0,5)
Asthenia	1 (0,9)	0 (0,0)	1 (0,5)
Infections and infestations	1 (0,9)	0 (0,0)	1 (0,5)
Soft tissue infection	1 (0,9)	0 (0,0)	1 (0,5)
Injury, poisoning and procedural complications	1 (0,9)	0 (0,0)	1 (0,5)
Femur fracture	1 (0,9)	0 (0,0)	1 (0,5)
Investigations	1 (0,9)	3 (4,2)	4 (2,1)
Alanine aminotransferase increased	1 (0,9)	0 (0,0)	1 (0,5)
Blood creatinine increased	0 (0,0)	2 (2,8)	2 (1,1)
Neutrophil count decreased	0 (0,0)	1 (1,4)	1 (0,5)
Psychiatric disorders	1 (0,9)	0 (0,0)	1 (0,5)
Completed suicide	1 (0,9)	0 (0,0)	1 (0,5)
Skin and subcutaneous tissue disorders	1 (0,9)	0 (0,0)	1 (0,5)
Drug eruption	1 (0,9)	0 (0,0)	1 (0,5)
Gastrointestinal disorders	0 (0,0)	1 (1,4)	1 (0,5)
Intestinal obstruction	0 (0,0)	1 (1,4)	1 (0,5)
Datenschnitt: 08. Mai 2024; Modifizierte Safety-Pembrolizumab Population (ECOG 0-1, Gewicht ≥50 kg). Abkürzungen: ECOG: Eastern Cooperative Oncology Group; kg: Kilogramm; mSAF: Modifizierte Safety-Pembrolizumab Population; N: Anzahl der Patienten in der Analyse; n: Anzahl der Patienten mit Ereignis; SOC: System Organ Class.			

Program Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/programs/primary/tfl/gba/t_aeldst_sm_dc240508.sas

Output Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/output/shared/gba/dc240508/t_aeldstsm_msaf.rtf

Dataset Location: /lilly/prd/ly3527723/j2g_mc_jzjc/misc2/data/analysis/shared/gba/dc240508/adsl_gba

/lilly/prd/ly3527723/j2g_mc_jzjc/armay2024/data/analysis/shared/adae

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