

12º SIMPÓSIO  
INTERNACIONAL DE

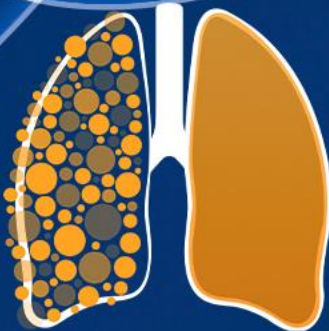
# CÂNCER DE PULMÃO

2ª JORNADA ONCONNECTION MULTICARE

2024

GERENCIAMENTO E PRODUÇÃO

**RV+**  
EVENTOS MÉDICOS



12º SIMPÓSIO  
INTERNACIONAL DE

CÂNCER DE  
PULMÃO

2ª JORNADA ONCONNECTION MULTICARE

2024

# Personalizando a imunoterapia de primeira linha no câncer de pulmão - Caso Clínico: Eu faço EMPOWER-Lung 3

**Marcelo Corassa**

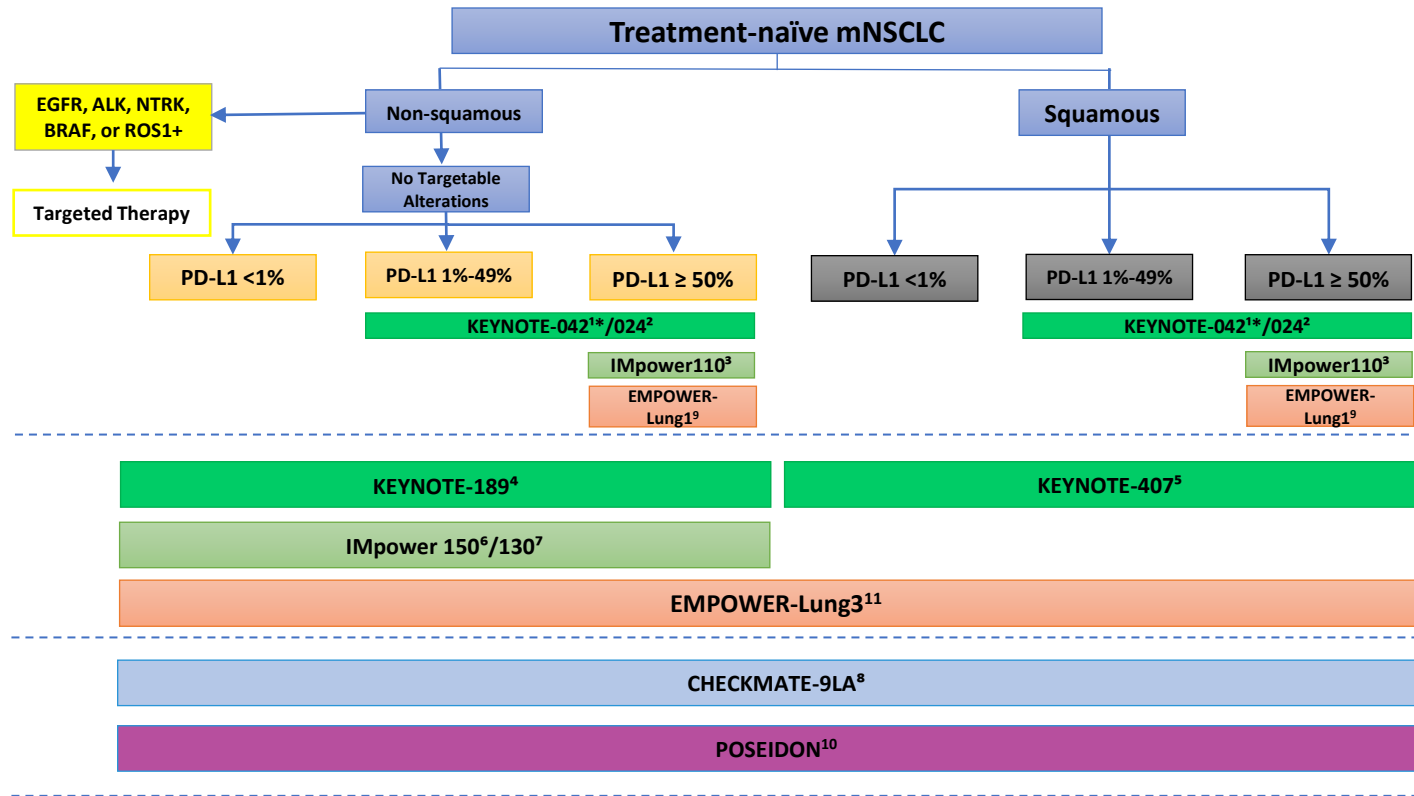
BP – A Beneficência Portuguesa de São Paulo

GERENCIAMENTO E PRODUÇÃO



# Conflitos de Interesse

- Honoraria: MSD, Roche, Pfizer, Astra Zeneca, Takeda, Lilly, Janssen, Amgen, Novartis, BMS, Sanofi, Daiichi-Sankyo.
- Travel Grants: MSD, Roche, Astra Zeneca.
- Participation in Advisory Boards: Roche, MSD, Takeda, AstraZeneca, Sanofi, Janssen.
- Participation in Clinical Trials: MSD, BMS, Roche, AstraZeneca, Boehringer, Pfizer, Abbvie, Janssen, Daiichi, Libbs, Servier.

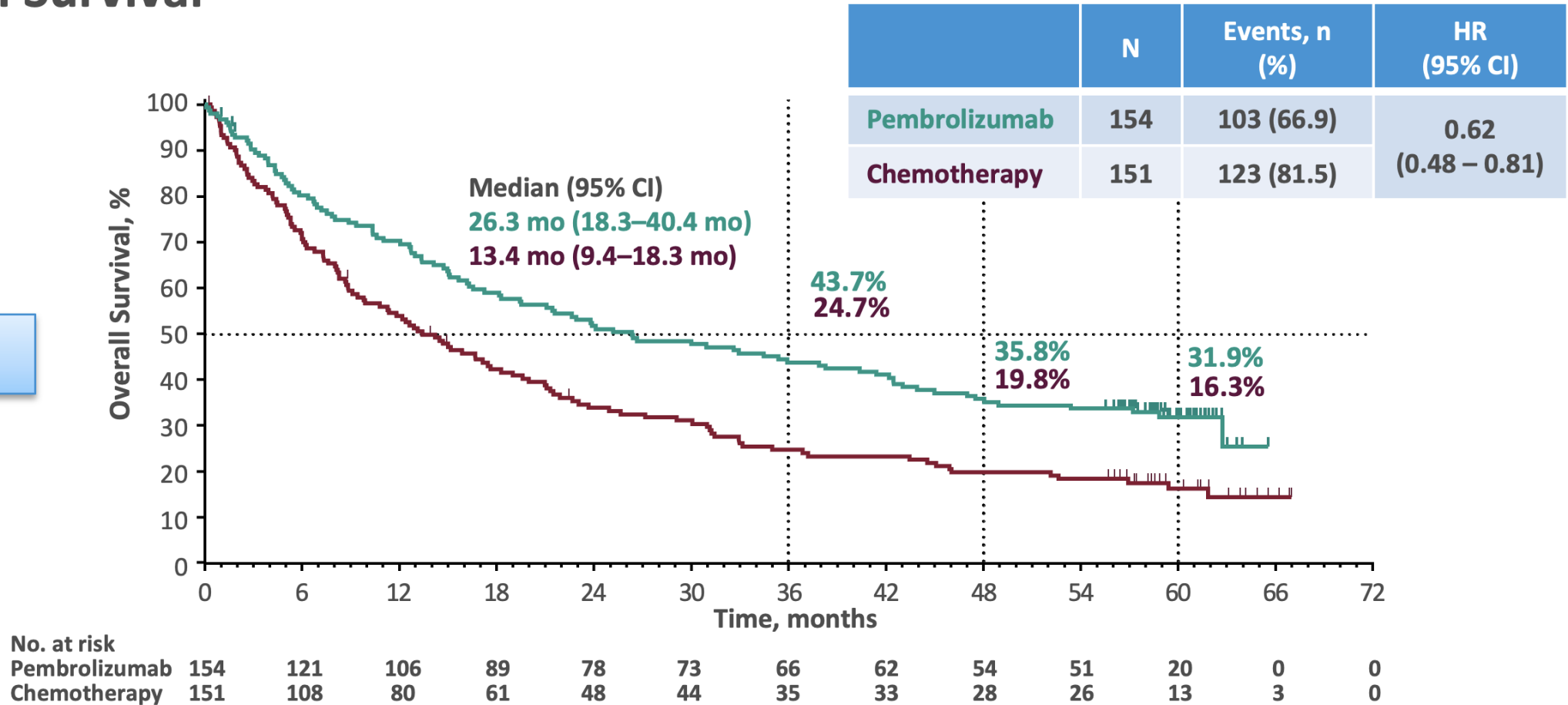


1L= First Line; NSCLC = non-small cell lung cancer; OS: overall survival I-O: Immunotherapy. \*In patients with EGFR-mutant or ALK-positive NSCLC, atezolizumab, in combination with bevacizumab, paclitaxel, and carboplatin, is indicated in the EU after failure of appropriate targeted therapies.

1. Mok TSK, et al. Oral presentation at ELCC 2019: abstract 2020; 2. Brahmer J, et al. Oral presentation at ESMO 2020: abstract LBA51; 3. Spigel D, et al. Oral presentation at ESMO 2019: abstract LBA78; 4. Rodriguez-Abreu D, et al. Poster presentation at ASCO 2020: abstract 9582; 5. Paz-Ares L, et al. J Thorac Oncol 15(10):1657-1669, 2020; 6. Socinski MA, et al. Oral presentation at AACR 2020: abstract CT216; 7. West H, et al. Lancet Oncol 20(7):924-937, 2019; 8. Paz-Ares L, et al. Lancet Oncol 22(2):198-21, 2021; 9. Sezer, A et al. Lancet 397:592-604, 2021. 10. Johnson ML et al. J Clin Oncol 41:1213,-1227, 2022. 11. Gogishivili M et al. Nat Med 28:2374-2380, 2022.

## Overall Survival<sup>a</sup>

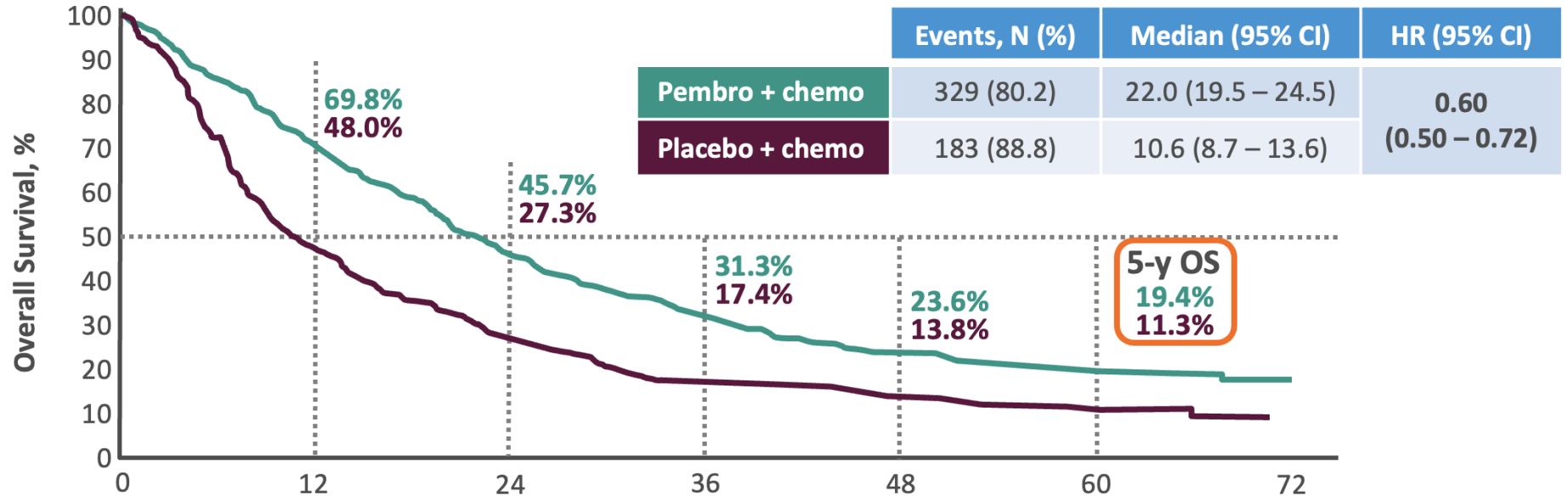
KN024



<sup>a</sup>ITT population. <sup>b</sup>Effective crossover rate from chemotherapy to anti-PD-(L)1 therapy, 66.0% (99 patients in total crossed over to anti-PD-[L]1 therapy: 83 patients crossed over to pembrolizumab during the study, and 16 patients received subsequent anti-PD-[L]1 therapy outside of crossover; patients may have received >1 subsequent anti-PD-[L]1 therapy). Data cutoff: June 1, 2020.

**OS: ITT Population**

KN189

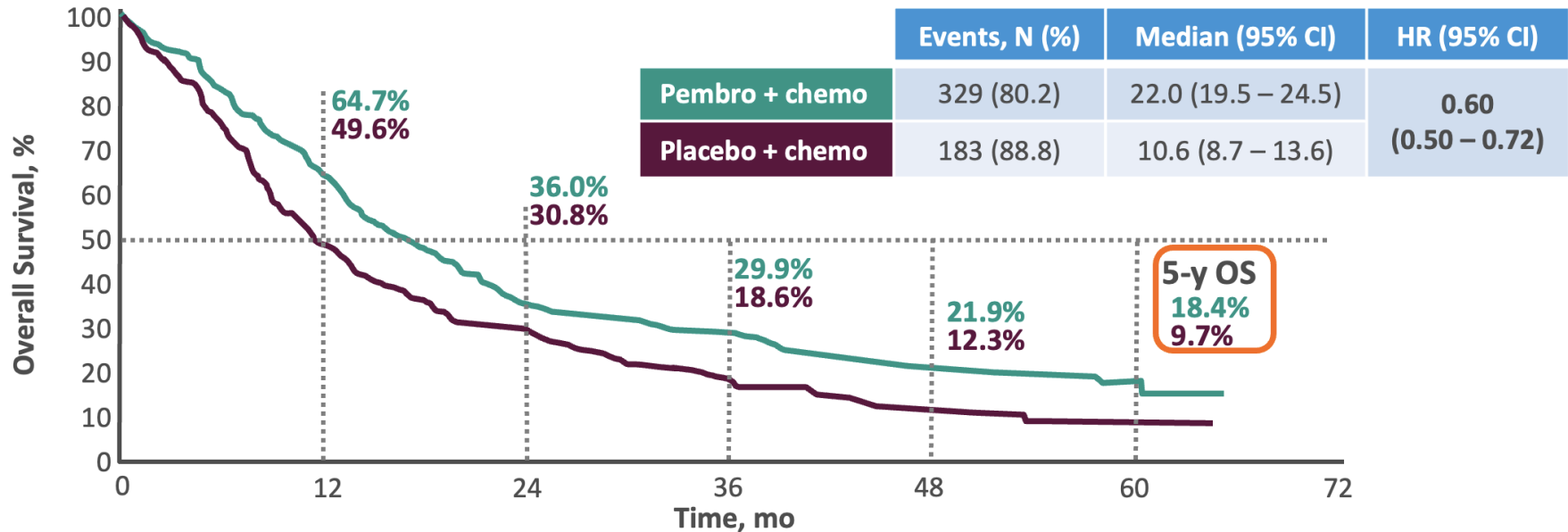


	PD-L1 TPS ≥ 50%		PD-L1 TPS 1% - 49%		PD-L1 TPS < 1%	
	Pembro + chemo (n = 132)	Placebo + chemo (n = 70)	Pembro + chemo (n = 128)	Placebo + chemo (n = 58)	Pembro + chemo (n = 127)	Placebo + chemo (n = 63)
OS HR (95% CI)	0.68 (0.49 – 0.96)		0.65 (0.46 – 0.90)		0.55 (0.39 – 0.76)	
5-y OS rate, <sup>a</sup> %	29.6	21.4	19.8	7.7	9.6	5.3

<sup>a</sup>Kaplan-Meier estimate. Data cutoff date: March 8, 2022.

### OS: ITT Population

KN407



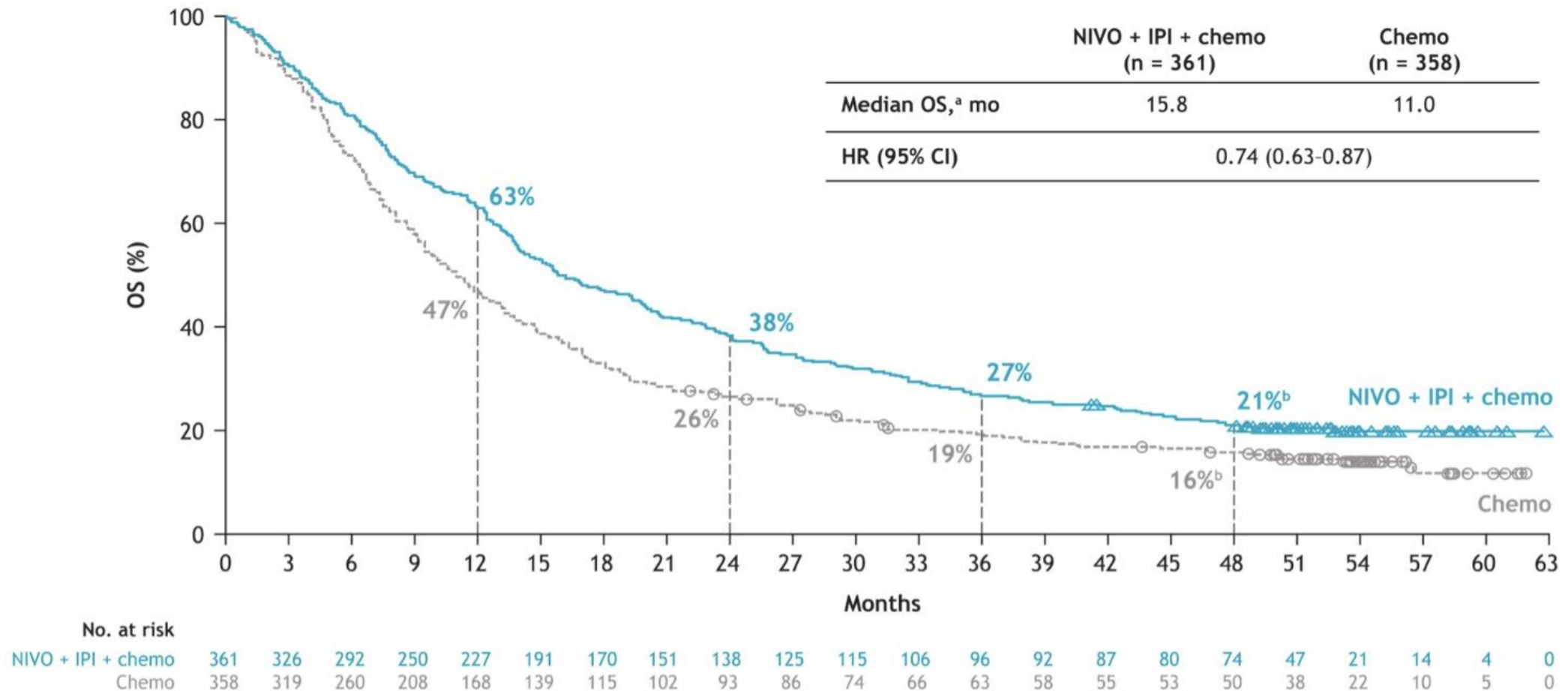
No. at risk  
Pembrolizumab  
Chemotherapy

	0	12	24	36	48	60	72
Pembrolizumab	278	180	100	83	60	10	0
Chemotherapy	281	137	84	50	33	7	0

	PD-L1 TPS ≥ 50%		PD-L1 TPS 1% - 49%		PD-L1 TPS < 1%	
	Pembro + chemo (n = 73)	Placebo + chemo (n = 73)	Pembro + chemo (n = 103)	Placebo + chemo (n = 104)	Pembro + chemo (n = 95)	Placebo + chemo (n = 99)
OS HR (95% CI)	0.68 (0.47–0.97)		0.61 (0.45–0.83)		0.83 (0.61–1.13)	
5-y OS rate, <sup>a</sup> %	23.3	8.3	20.6	7.6	10.7	13.1

<sup>a</sup>Kaplan-Meier estimate. Data cutoff date: February 23, 2022.

## 4-year update: OS in all randomized patients



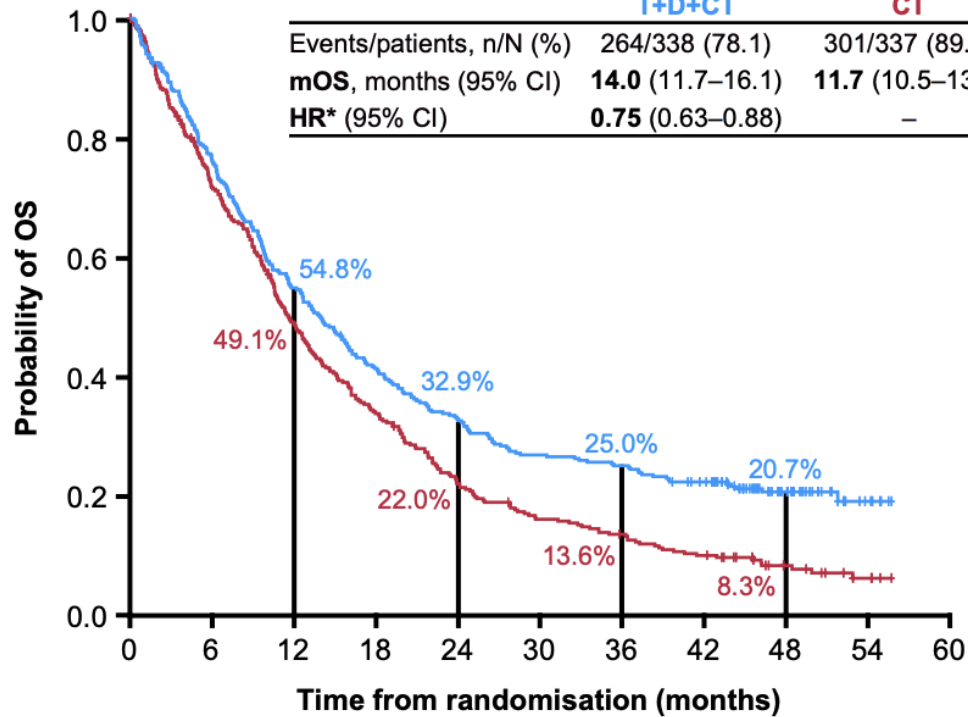


## OS Update

Durable long-term OS benefit for T+D+CT vs CT with HR 0.75 and estimated 25.0% alive at 3 yrs vs 13.6%

### T+D+CT vs CT

	T+D+CT	CT
Events/patients, n/N (%)	264/338 (78.1)	301/337 (89.3)
mOS, months (95% CI)	<b>14.0</b> (11.7–16.1)	11.7 (10.5–13.1)
HR* (95% CI)	<b>0.75</b> (0.63–0.88)	–

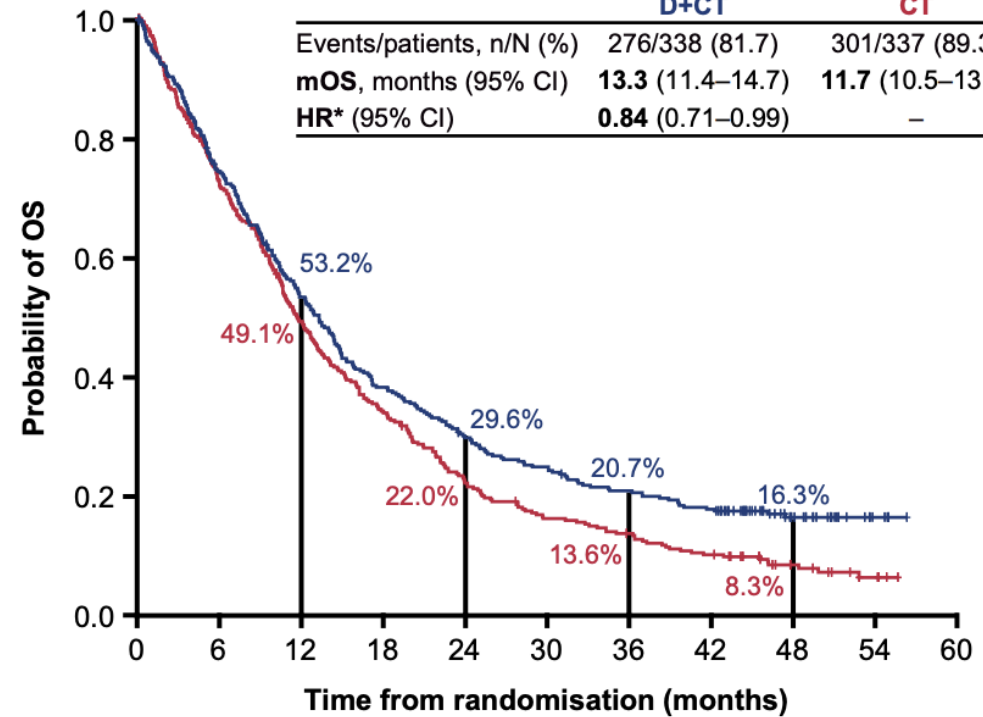


No. at risk

	0	6	12	18	24	30	36	42	48	54	60
T+D+CT	338	256	183	137	109	89	83	70	32	6	0
CT	337	236	160	111	71	51	42	31	14	5	0

### D+CT vs CT

	D+CT	CT
Events/patients, n/N (%)	276/338 (81.7)	301/337 (89.3)
mOS, months (95% CI)	<b>13.3</b> (11.4–14.7)	11.7 (10.5–13.1)
HR* (95% CI)	<b>0.84</b> (0.71–0.99)	–



No. at risk

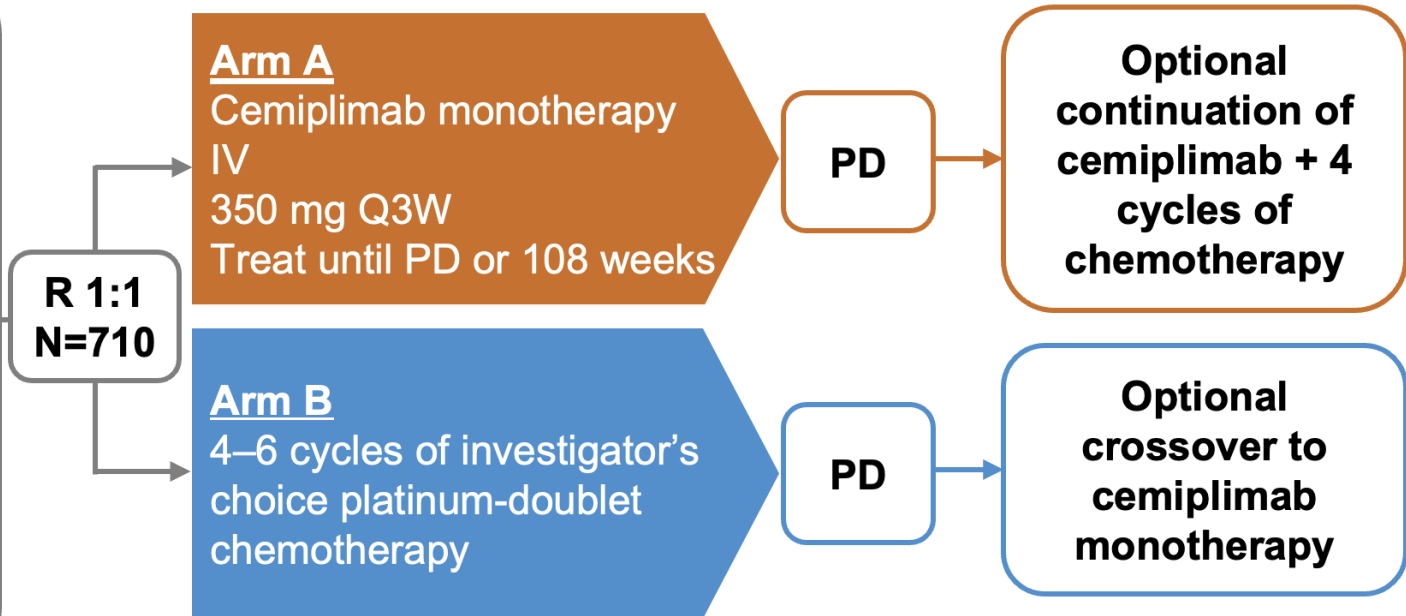
	0	6	12	18	24	30	36	42	48	54	60
D+CT	338	247	176	126	97	81	67	57	26	5	0
CT	337	236	160	111	71	51	42	31	14	5	0

### Key Eligibility Criteria

- Treatment-naïve advanced NSCLC
- PD-L1  $\geq 50\%$
- No *EGFR*, *ALK* or *ROS1* mutations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases and controlled hepatitis B or C or HIV were allowed

### Stratification Factors:

- Histology (squamous vs nonsquamous)
- Region (Europe, Asia or ROW)



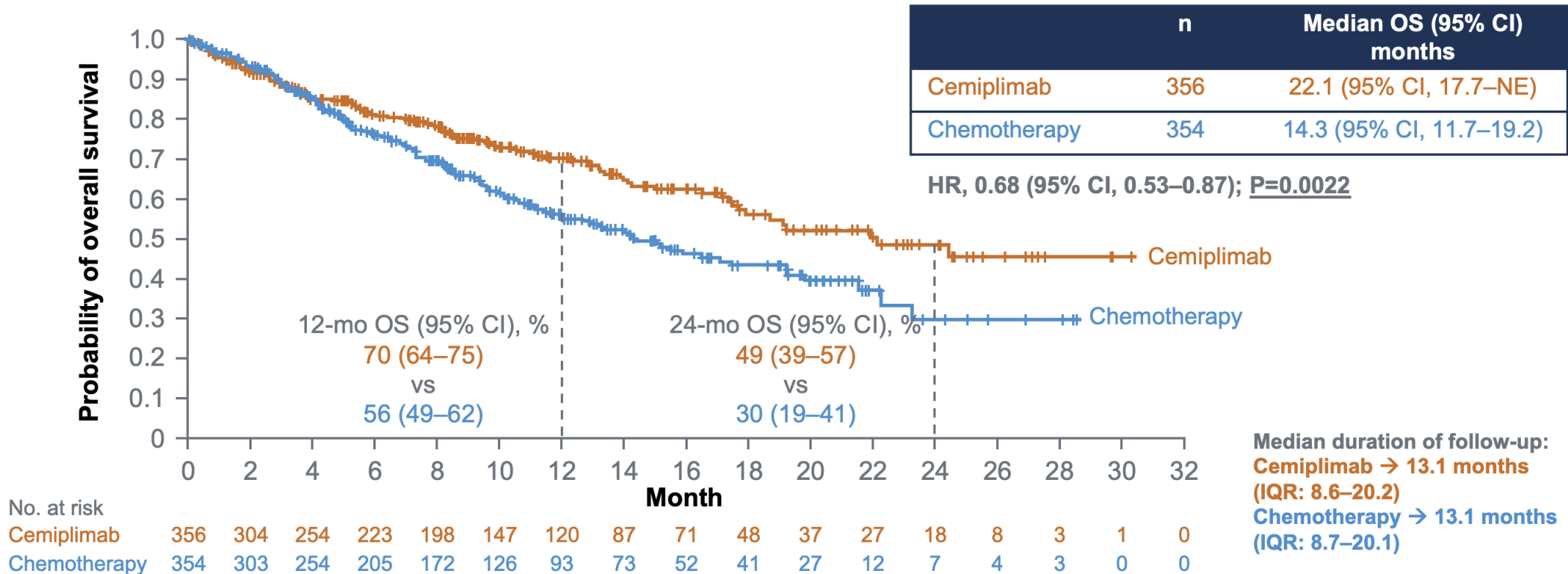
### Endpoints:

- Primary: OS and PFS
- Secondary: ORR (key), DOR, HRQoL and safety

Five interim analyses were prespecified per protocol. Second interim analysis (1 March 2020) presented here.

ALK, anaplastic lymphoma kinase; CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HIV, human immunodeficiency virus; HRQoL, health-related quality of life; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed death-ligand-1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomized; ROS1, c-ros oncogene 1; ROW, rest of the world. 1. Sezer A et al. *Lancet*. 2021;397:592–604. 2. Regeneron Pharmaceuticals Inc. LIBTAYO prescribing information (United States). February 2021. 3. Kilickap S et al. IASLC-WCLC Virtual Congress 2021.

## Overall Survival by IRC: ITT (N=710)<sup>1,2</sup>



CI, confidence interval; HR, hazard ratio; IQR, interquartile range; IRC, independent review committee; ITT, intention-to-treat; mo, month; NE, not evaluable; OS, overall survival. Data cut-off date: 1 March 2020 (interim analysis #2). 1. Sezer A et al. *Lancet*. 2021;397:592–604 (including supplementary materials). 2. Regeneron Pharmaceuticals Inc. LIBTAYO prescribing information (United States). February 2021. Reproduced from *The Lancet*, Vol. 397, Sezer A, et al. Cemiplimab monotherapy for first-line treatment of advanced NSCLC with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial, 592–604, Copyright (2021), with permission from Elsevier

### Demographics and Baseline Characteristics

	ITT <b>Cemiplimab (n=357)</b>	Beyond Progression <b>Cemiplimab (N=64)</b>
n (%), unless stated otherwise		
Age		
Median (Q1 : Q3)	63.0 (58.0 : 69.0)	62.5 (57.5 : 69.0)
≥65, n (%)	157 (44.0)	28 (43.8)
Sex		
Male	313 (87.7)	55 (85.9)
Female	44 (12.3)	9 (14.1)
Region of enrolment		
Europe	276 (77.3)	51 (79.7)
Asia	39 (10.9)	7 (10.9)
Rest of the world	42 (11.8)	6 (9.4)
ECOG performance status score		
0	96 (26.9)	20 (31.3)
1	261 (73.1)	44 (68.8)
Histology/Cytology, n (%)		
Squamous	160 (44.8)	37 (57.8)
Non-squamous	197 (55.2)	27 (42.2)
Cancer stage at screening n (%)		
Stage III	63 (17.6)	12 (18.7)
Stage IV	294 (82.4)	52 (81.3)

ECOG, Eastern Cooperative Oncology Group; ITT, intention-to-treat; Data cutoff date: Left column – March 4, 2022; Right column – March 1, 2020

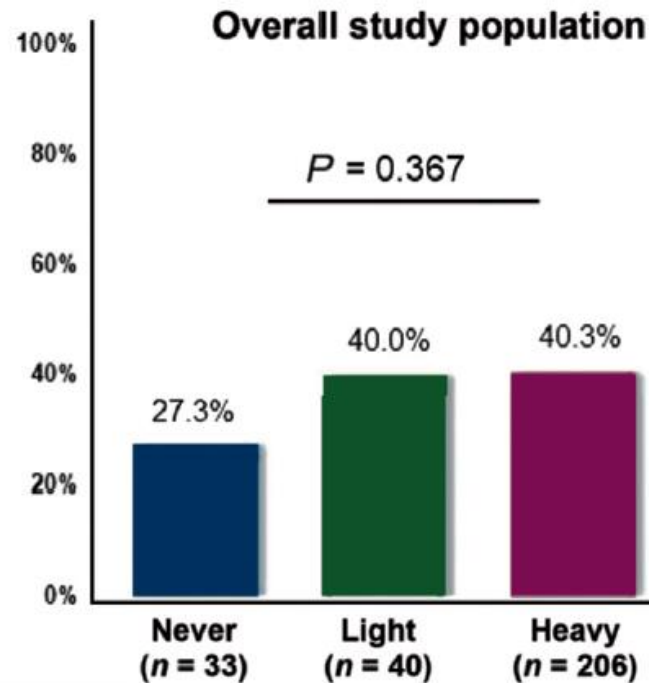
### Induction of Tumor Response by Addition of Chemotherapy to Continued Cemiplimab Beyond Progression

Cemiplimab Beyond Progression N=64		
	Period 1	Period 2
<b>Objective Response Rate (ORR: CR+PR), n (%)</b>	<b>19 (29.7)</b>	<b>20 (31.3)</b>
95% CI for ORR (range %)	(18.9, 42.4)	(20.2, 44.1)
Best Overall Tumor Response, n (%)		
Complete Response (CR)	0	3 (4.7)
Partial Response (PR)	19 (29.7)	17 (26.6)
Stable Disease (SD)	28 (43.8)	35 (54.7)
Non-CR/Non-PD	0	0
Progressive Disease (PD)	13 (20.3)	9 (14.1)
Not Evaluable (NE)	4 (6.3)	0

CI, confidence interval

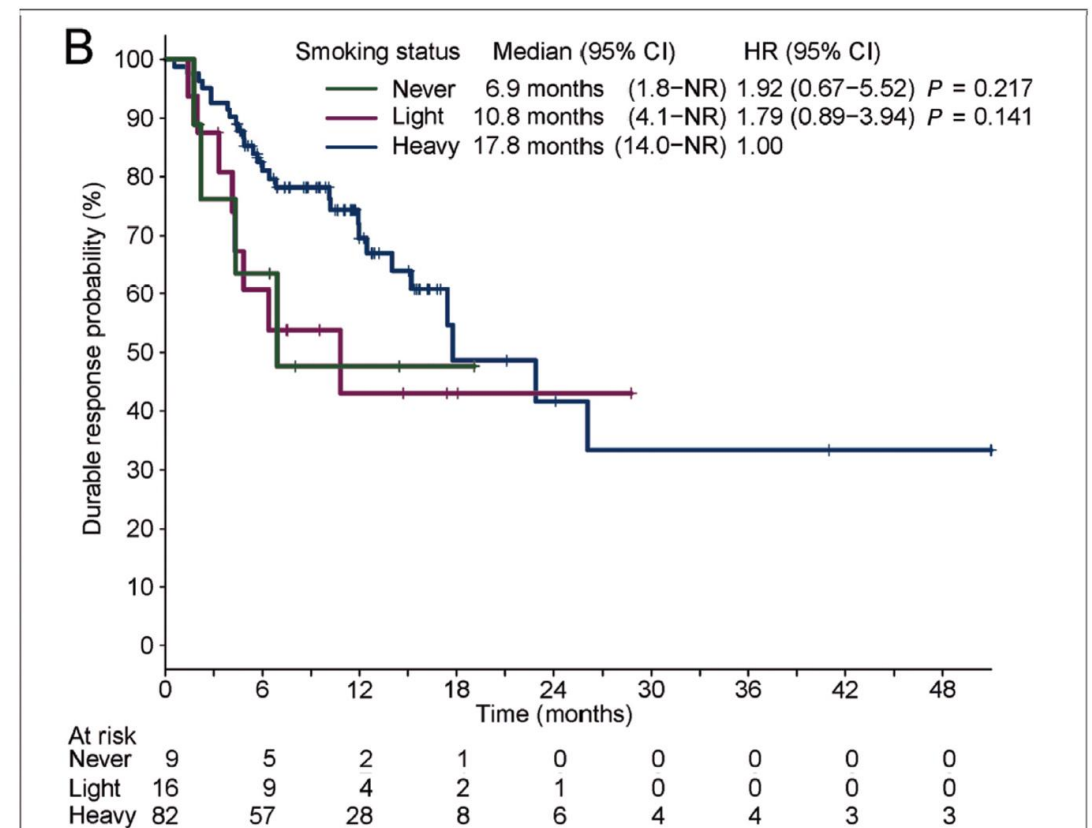
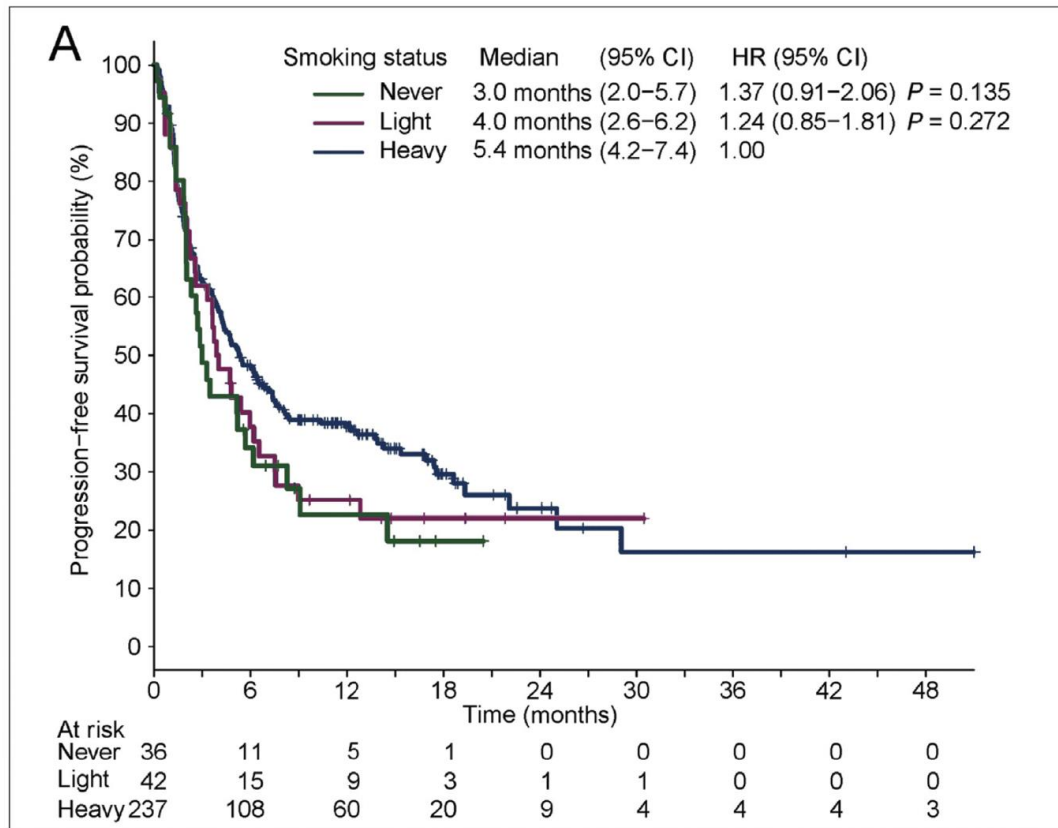
Data cutoff date: March 1, 2020 – Left Column; Oct 1, 2021 – Right column

Clinical activity of programmed cell death 1 (PD-1) blockade in never, light, and heavy smokers with non-small-cell lung cancer and PD-L1 expression  $\geq 50\%$



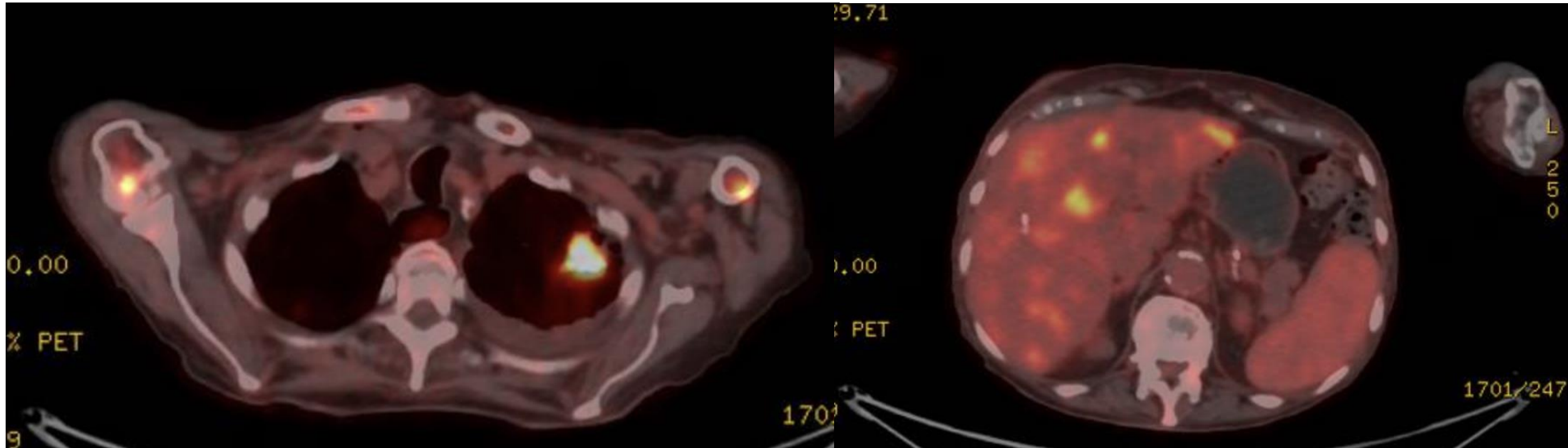
Best overall response	Never smokers (n = 33)		Light smokers (n = 40)		Heavy smokers (n = 206)	
	No.	%	No.	%	No.	%
Complete response	0	0	0	0	5	2.4
Partial response	9	27.2	16	40.0	78 <sup>1</sup>	37.9
Stable disease	9	27.2	10	25.0	60	29.1
Progressive disease	15	45.4	14	35.0	63	30.6
<b>Objective response rate</b>	27.3%		40.0%		40.3%	

Clinical activity of programmed cell death 1 (PD-1) blockade in never, light, and heavy smokers with non-small-cell lung cancer and PD-L1 expression  $\geq 50\%$



- **Male, 67 years-old.**
- **Current smoker: 60 pack-years.**
- **ECOG 0.**
- **No brain mets.**
- **Dyspnea at exertion.**
- **Lung biopsy: squamous cell carcinoma.**

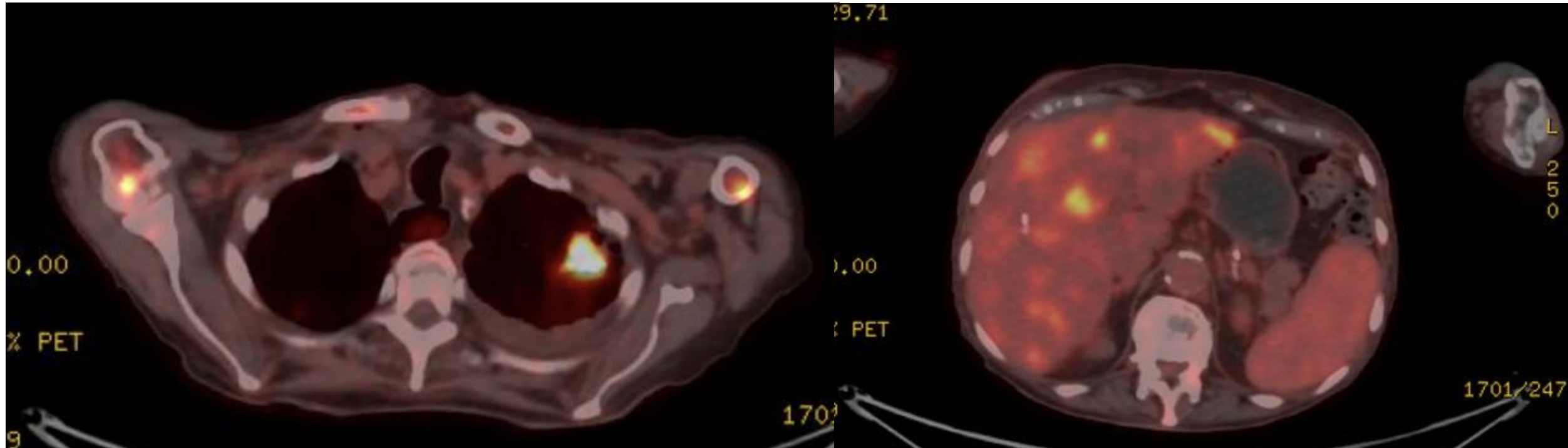




**PD-L1 IMMUNOHISTOCHEMISTRY (IHC) ANALYSIS – VENTANA PD-L1 (SP263) Assay**

Tumor Cell (TC) Score (%) 10





**PD-L1 IMMUNOHISTOCHEMISTRY (IHC) ANALYSIS (Dako 22C3 pharmDx™)**

**Tumor Proportion Score (TPS) (%) 50**

## EMPOWER-Lung 3 (Part 2) Study Design (NCT03409614)

### Key eligibility criteria

- Treatment-naïve advanced NSCLC (non-squamous and squamous histology; Stage IIIb/c<sup>†</sup> IV)
- Any PD-L1 expression
- No EGFR, ALK or ROS1 aberrations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases were allowed

### Stratification factors

- PD-L1 expression: < 1% vs 1 – 49% vs ≥ 50%
- Histology: non-squamous vs squamous

### Endpoints

- Primary: OS
- Key secondary: PFS and ORR
- Additional secondary: DOR, BOR, safety and PROs
- Prespecified interim OS analyses planned When ~146 deaths (50% of total OS events) and ~204 deaths (70% of total OS events) were observed
- Final OS analysis was prespecified When ~291 deaths were observed

R 2:1

### Arm A

Cemiplimab 350 mg Q3W + investigator's choice of platinum-doublet chemotherapy Q3W for 4 cycles

Progressive disease or 108 weeks

### Arm B

Placebo Q3W + investigator's choice of platinum-doublet chemotherapy Q3W for 4 cycles

Progressive disease or 108 weeks

Follow-up

N = 466

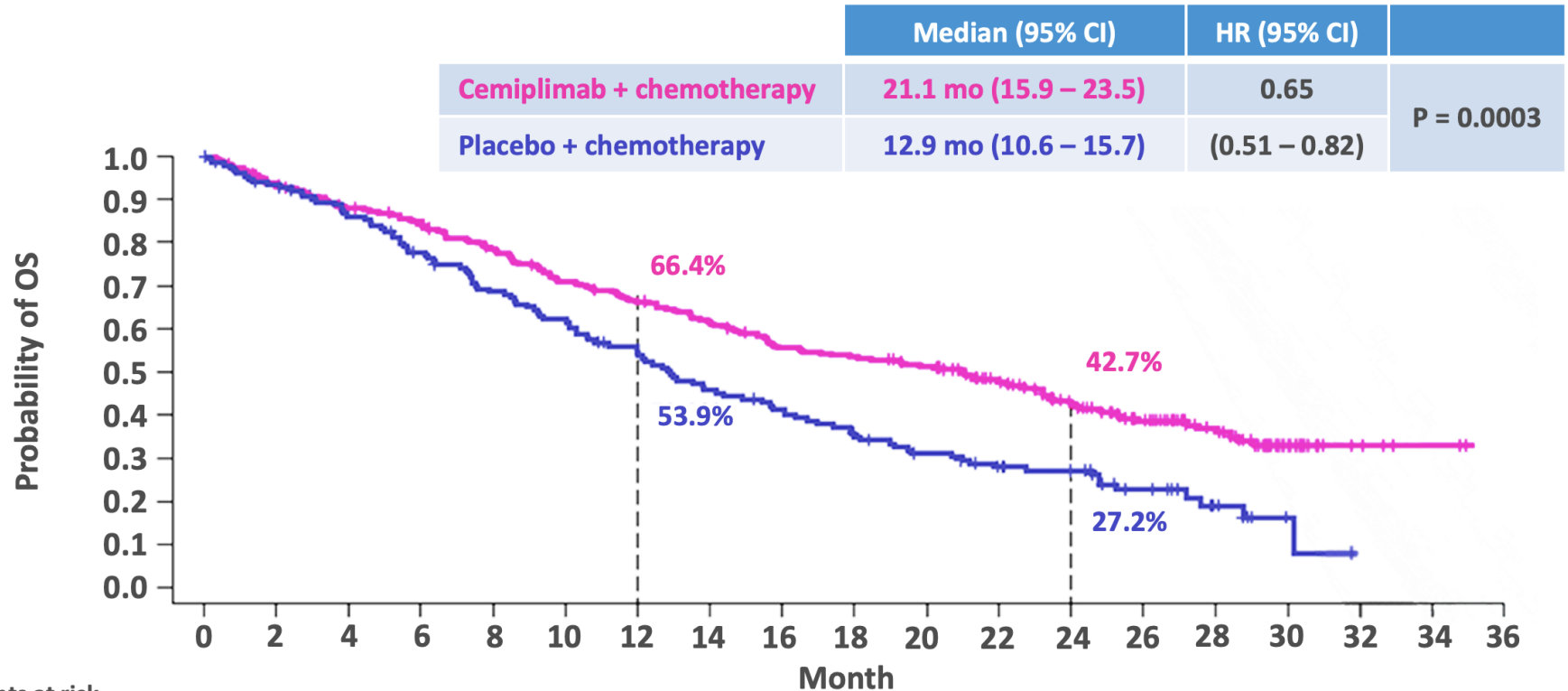
Here we report data per cutoff of 14 June 2022  
Median (range) duration of follow-up<sup>†</sup>: 28.4 months (20.5 – 35.9)

<sup>†</sup>From randomisation to data cut-off date. BOR, best overall response; CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, Every 3 weeks.

## Disposition and Baseline Characteristics - Selected

n (%), unless otherwise stated		Cemiplimab + chemo (n=312)	Placebo + chemo (n=154)	Total (n=466)
<b>Age</b>	Median (range), years	63.0 (25–82)	63.0 (34–84)	63.0 (25–84)
	≥65 year	128 (41.0)	60 (39.0)	188 (40.3)
<b>Male</b>		268 (85.9)	123 (79.9)	391 (83.9)
<b>Histology</b>	Non-squamous	179 (57.4)	87 (56.5)	266 (57.1)
	Squamous	133 (42.6)	67 (43.5)	200 (42.9)
<b>PD-L1 expression</b>	<1%	95 (30.4)	44 (28.6)	139 (29.8)
	1–49%	114 (36.5)	61 (39.6)	175 (37.6)
	≥50%	103 (33.0)	49 (31.8)	152 (32.6)
<b>ECOG PS</b>	0	51 (16.3)	18 (11.7)	69 (14.8)
	1	259 (83.0)	134 (87.0)	393 (84.3)
<b>Brain metastases</b>		24 (7.7)	7 (4.5)	31 (6.7)
<b>Cancer stage at screening</b>	Metastatic	267 (85.6)	130 (84.4)	397 (85.2)
	Locally advanced	45 (14.4)	24 (15.6)	69 (14.8)
<b>Smoking history</b>	Current smoker	173 (55.4)	75 (48.7)	248 (53.2)
	Past smoker	96 (30.8)	55 (35.7)	151 (32.4)
	Never smoked	43 (13.8)	24 (15.6)	67 (14.4)

### Overall Survival

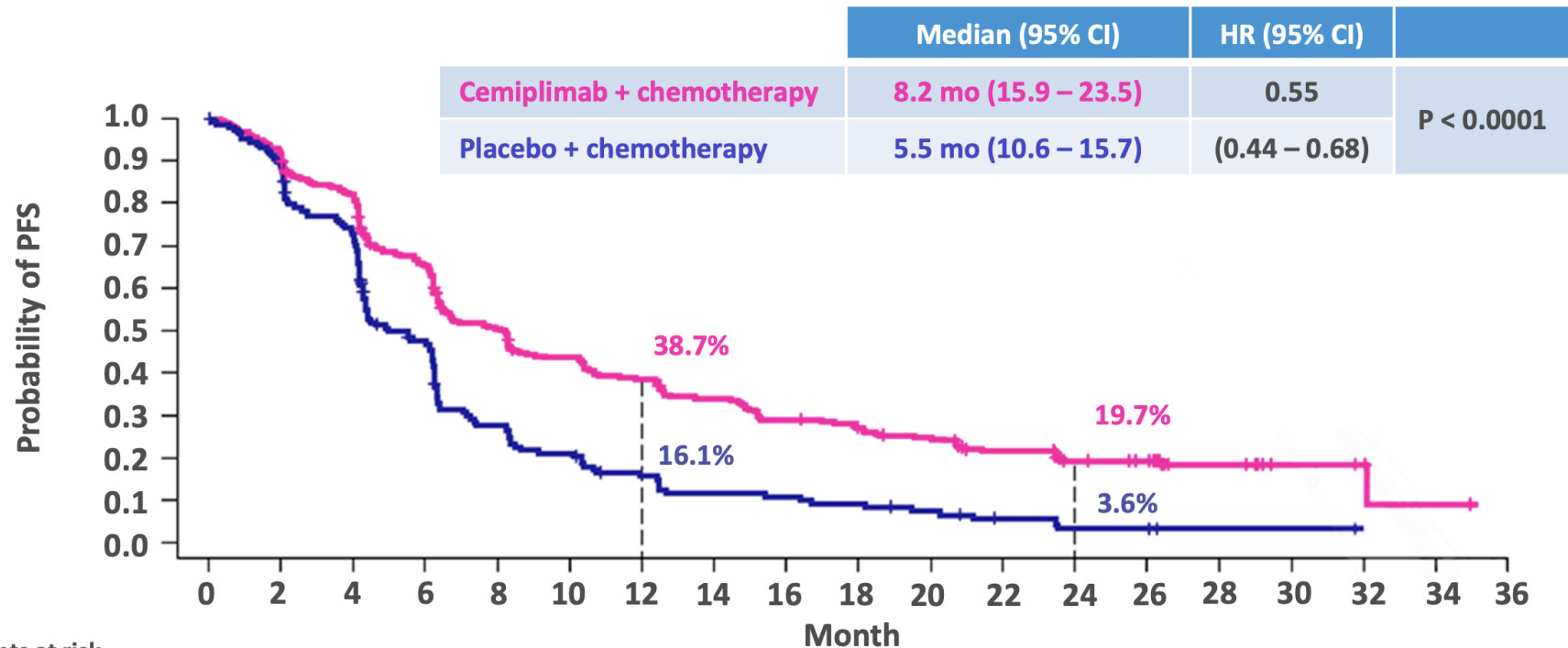


Number of patients at risk

Cemiplimab + chemotherapy	312	289	269	256	233	210	195	180	160	154	145	121	94	71	40	16	5	2	0
Placebo + chemotherapy	154	141	126	112	98	89	75	64	57	48	40	34	31	19	18	2	0	0	0

Data cutoff date: 14 June 2022. Median (range) duration of follow-up†: 28.4 (20.5 – 35.9) months. †From randomisation to data cut-off date.  
CI, confidence interval; hazard ratio; mo, months; OS, overall survival.

## Progression-Free Survival

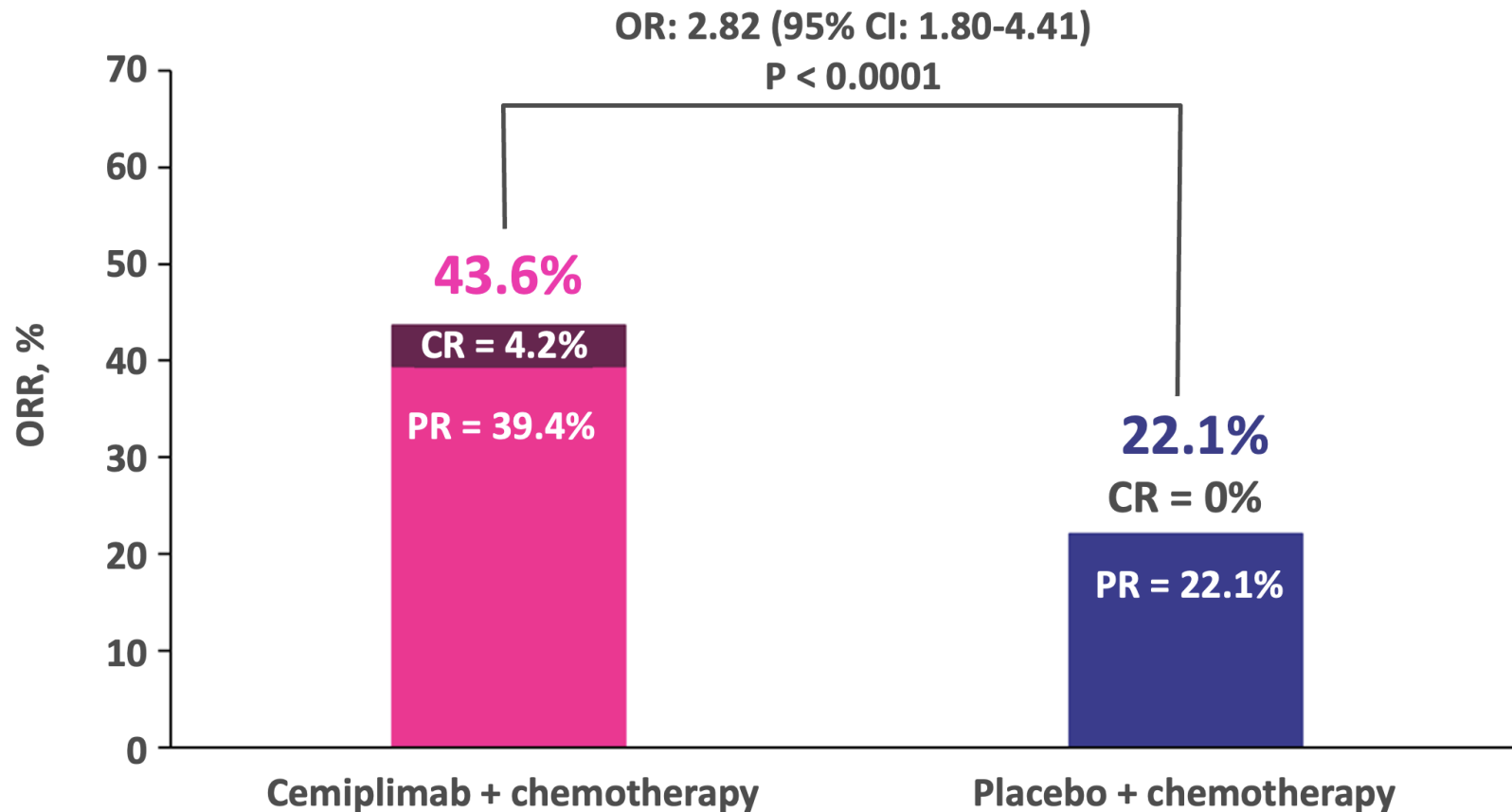


**Number of patients at risk**

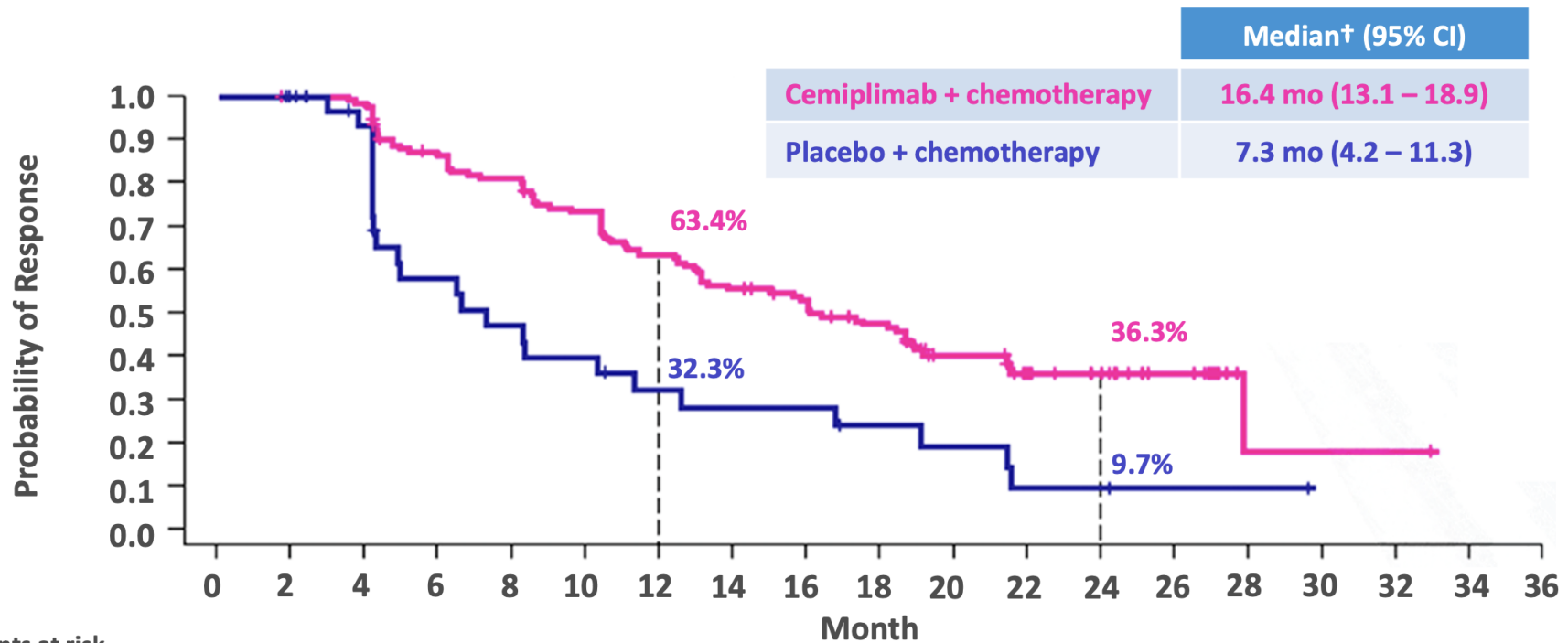
<b>Cemiplimab + chemotherapy</b>	312	280	247	194	146	125	110	96	82	75	68	51	37	34	15	4	3	1	0
<b>Placebo + chemotherapy</b>	154	134	107	66	38	29	20	15	14	12	9	5	3	3	1	1	0	0	0

Data cutoff date: 14 June 2022. Median (range) duration of follow-up†: 28.4 (20.5 – 35.9) months. †From randomisation to data cut-off date.  
CI, confidence interval; hazard ratio; mo, months; PFS, progression-free survival.

## Tumour Response and DOR



## Tumour Response and DOR



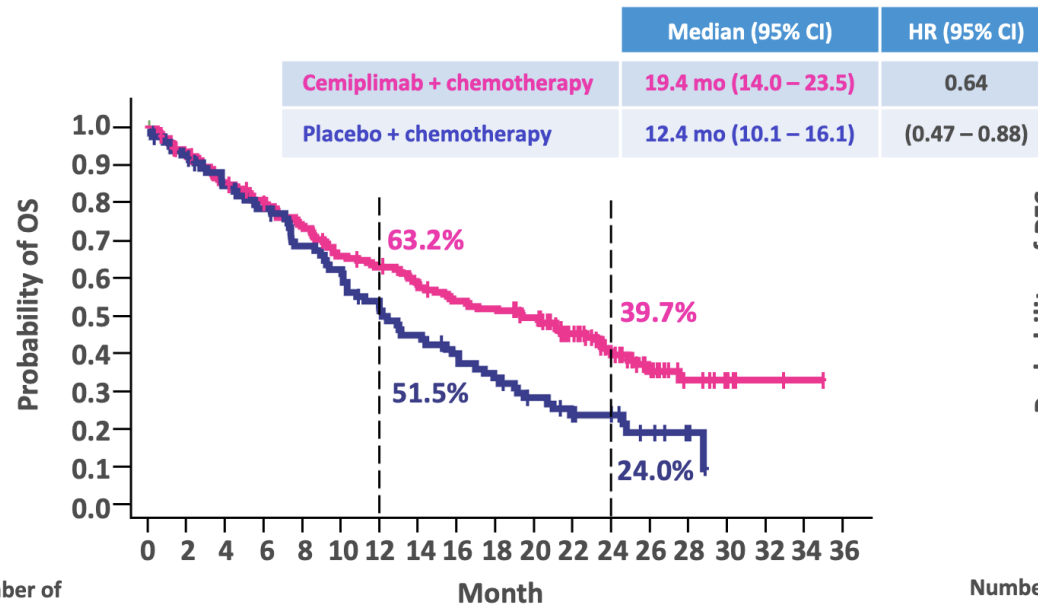
**Number of patients at risk**

<b>Cemiplimab + chemotherapy</b>	136	135	133	113	106	95	82	72	66	57	40	30	25	13	1	1	1	0	0
<b>Placebo + chemotherapy</b>	34	32	27	16	13	11	8	7	7	5	4	2	2	1	1	0	0	0	0

Data cutoff date: 14 June 2022. †Based on patients with confirmed CR or PR.  
CI, confidence interval; CR, complete response; mo, months; PR, partial response.

## OS and PFS in Patients with Non-Squamous Histology

### Overall survival



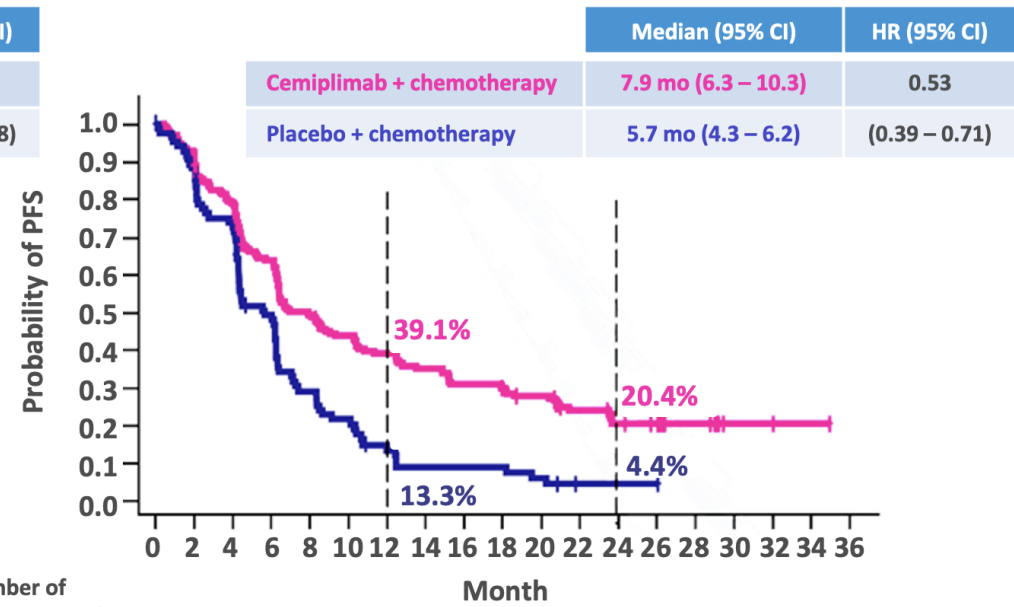
Number of patients at risk

Month	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36
Cemiplimab + chemotherapy	179	164	149	138	125	111	105	96	87	84	77	57	37	24	12	6	2	1	0
Placebo + chemotherapy	87	80	70	65	56	51	41	36	31	26	20	15	13	7	3	0	0	0	0

Data cutoff date: 14 June 2022.

CI, confidence interval; HR, hazard ratio; mo, Months; OS, overall survival; PFS, progression-free survival

### Progression-free survival



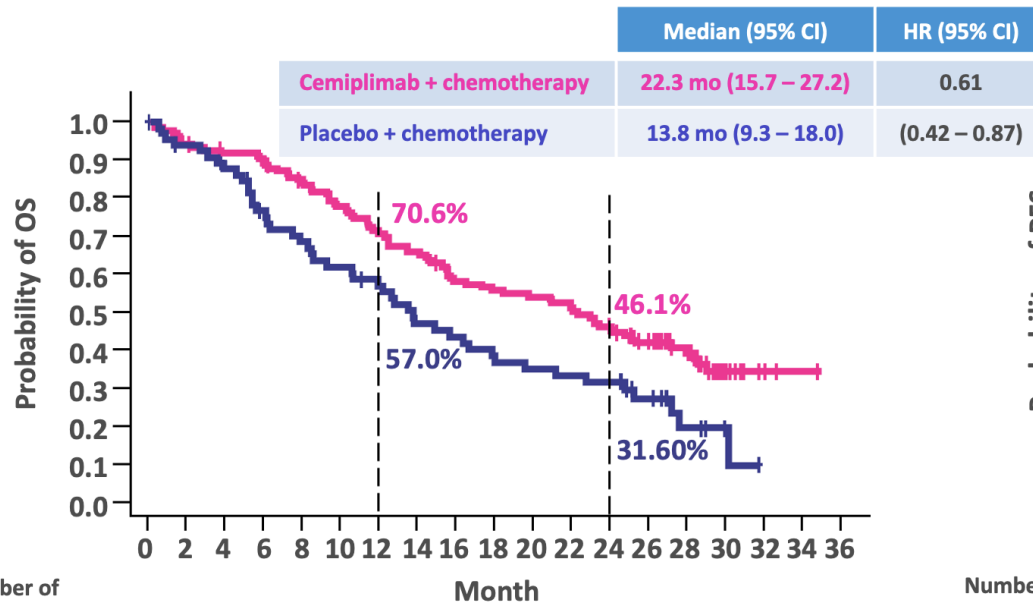
Number of patients at risk

Month	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36
Cemiplimab + chemotherapy	179	158	133	104	78	67	60	53	47	44	40	26	16	14	8	2	2	1	0
Placebo + chemotherapy	87	75	60	39	23	17	9	6	6	6	4	1	1	1	0	0	0	0	0



## OS and PFS in Patients with Squamous Histology

### Overall survival



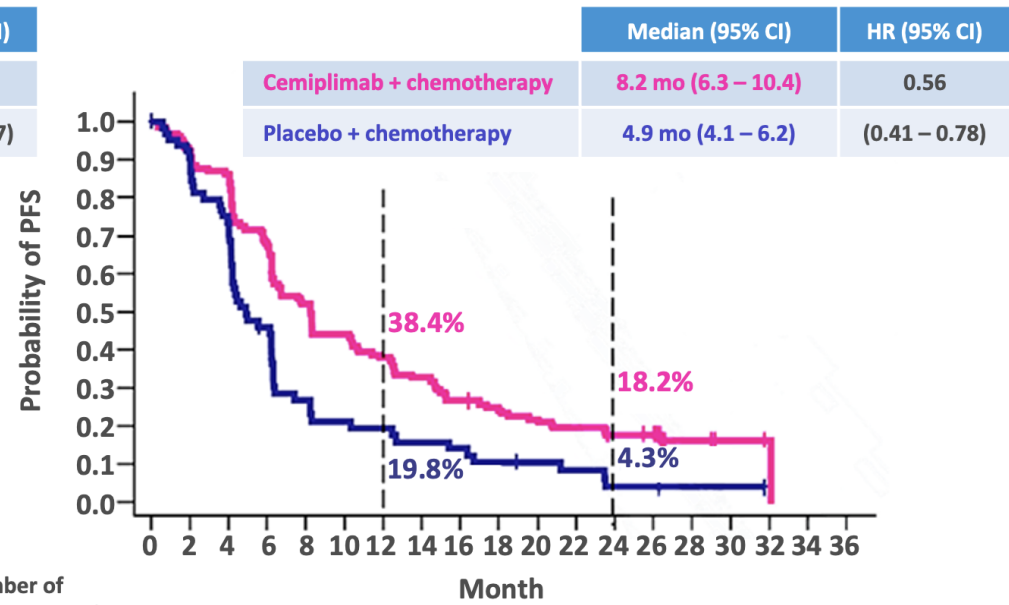
Number of patients at risk

Cemiplimab + chemotherapy	133	125	120	118	108	99	90	84	73	70	68	64	57	47	28	10	3	1	0
Placebo + chemotherapy	67	61	56	47	42	38	34	28	26	22	20	19	18	12	5	2	0	0	0

Data cutoff date: 14 June 2022.

CI, confidence interval; HR, hazard ratio; mo. Months; OS, overall survival; PFS, progression-free survival

### Progression-free survival



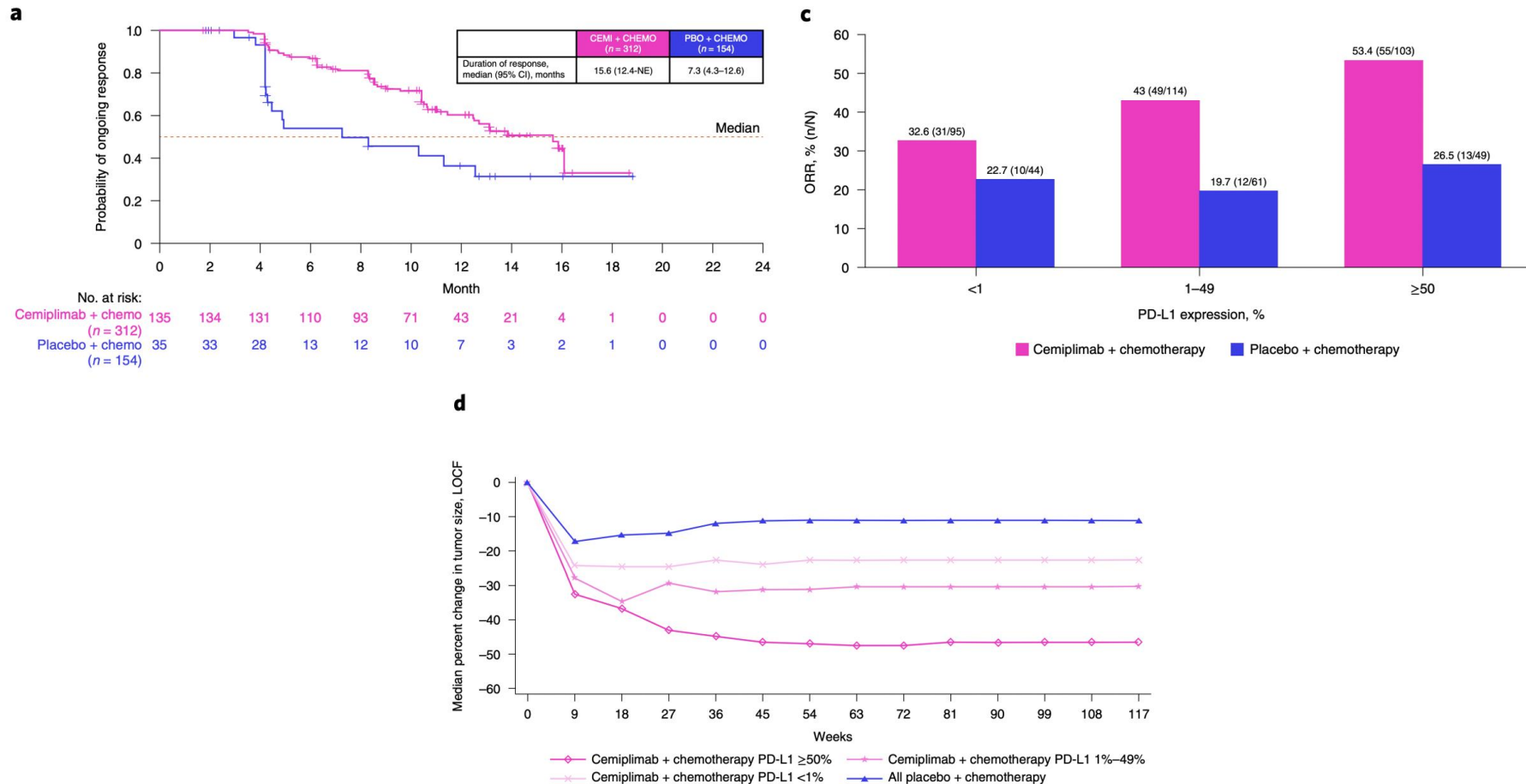
Number of patients at risk

Cemiplimab + chemotherapy	133	122	114	90	68	58	50	43	35	31	28	25	21	20	7	2	1	0	0
Placebo + chemotherapy	67	59	47	27	15	12	11	9	8	6	5	4	2	2	1	1	0	0	0

### Efficacy According to PD-L1 Levels

PD-L1 expression	OS Median (95% CI), months			PFS (Median (95% CI), months)			ORR Median (95% CI), months		
	Cemiplimab + chemotherapy (n = 312)	Placebo + chemotherapy (n = 154)	HR (95% CI)	Cemiplimab + chemotherapy (n = 312)	Placebo + chemotherapy (n = 154)	HR (95% CI)	Cemiplimab + chemotherapy (n = 312)	Placebo + chemotherapy (n = 154)	HR (95% CI)
≥ 50%	<b>23.5</b> (17.9 – NE)	14.4 (9.3 – 19.5)	0.56 (0.36 – 0.86)	<b>10.8</b> (6.7 – 15.2)	5.5 (4.3 – 6.3)	0.48 (0.32 – 0.72)	<b>53.4</b> (43.3 – 63.3)	26.5 (14.9 – 41.1)	3.17 (1.51 – 6.67)
1 – 49%	<b>23.2</b> (18.1 – 27.2)	12.0 (8.3 – 15.7)	0.50 (0.34 – 0.74)	<b>8.2</b> (6.3 – 10.4)	6.1 (4.7 – 7.0)	0.48 (0.34 – 0.68)	<b>43.0</b> (33.7 – 52.6)	19.7 (10.6 – 31.8)	3.08 (1.48 – 6.40)
< 1%	<b>12.8</b> (9.6 – 15.6)	14.2 (9.1 – 18.0)	0.94 (0.62 – 1.42)	<b>6.2</b> (4.4 – 8.3)	4.4 (4.2 – 6.2)	0.73 (0.50 – 1.08)	<b>33.7</b> (24.3 – 44.1)	20.5 (9.8 – 35.3)	1.98 (0.85 – 4.61)

### Responders x Long Time Responders



## Safety Summary

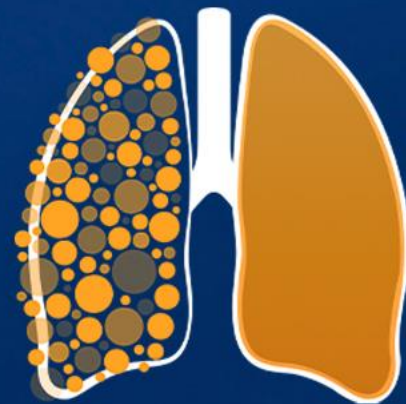
n (%), unless stated	Cemiplimab + chemo (n=312)		Placebo + chemo (n=153)	
Duration of exposure, median (range), weeks	38.5 (1.4–102.6)		21.3 (0.6–95.0)	
Treatment-emergent AEs, regardless of attribution	Any grade	Grade 3–5	Any grade	Grade 3–5
Overall	299 (96)	136 (44)	144 (94)	48 (31)
Led to discontinuation	16 (5)	13 (4)	4 (3)	4 (3)
Led to death	19 (6)	19 (6)	12 (8)	12 (8)
Treatment-related AEs				
Overall	275 (88)	90 (29)	129 (84)	28 (18)
Led to discontinuation	10 (3)	7 (2)	1 (1)	1 (1)
Led to death	4 (1)	4 (1)	1 (1)	1 (1)
Immune-related AEs <sup>†</sup>				
Overall	59 (19)	9 (3)	–	–
Led to discontinuation	3 (1)	3 (1)	–	–
Led to death	1 (0.3)	1 (0.3)	–	–

## PRO Summary

- **Delay** in the time to definitive clinically meaningful deterioration in GHS/QoL [HR, 0.78 (95% CI, 0.51–1.19);  $P=0.248$ ] and pain symptoms [HR, 0.39 (95% CI, 0.26–0.60);  $P<0.0001$ ].
- **Improvement** in overall change from baseline in GHS/QoL [0.61 (95% CI, -2.23, 3.45)  $P=0.673$ ] and pain symptoms [-4.98 (95% CI, -8.36, -1.60);  $P=0.004$ ].

Treatment-emergent AEs in ≥10% of patients in either arm, n (%)	Cemiplimab + chemo (n=312)		Placebo + chemo (n=153)	
	Any grade	Grade 3–5	Any grade	Grade 3–5
Overall	299 (96)	136 (44)	144 (94)	48 (31)
Anaemia	136 (44)	31 (10)	61 (40)	10 (7)
Decreased appetite	53 (17)	3 (1)	18 (12)	0
Fatigue	38 (12)	7 (2)	11 (7)	1 (1)
Constipation	43 (14)	1 (0)	17 (11)	0
Nausea	78 (25)	0	25 (16)	0
Vomiting	38 (12)	0	15 (10)	0
Thrombocytopenia	41 (13)	8 (3)	19 (12)	2 (1)
Neutropenia	48 (15)	18 (6)	19 (12)	9 (6)
Alopecia	115 (37)	0	66 (43)	0
Hyperglycaemia	55 (18)	6 (2)	18 (12)	0
Alanine aminotransferase increased	51 (16)	7 (2)	22 (14)	3 (2)
Arthralgia	48 (15)	2 (1)	20 (13)	0
Aspartate aminotransferase increased	46 (15)	1 (0)	18 (12)	3 (2)
Dyspnoea	39 (13)	7 (2)	10 (7)	1 (1)
Asthenia	38 (12)	6 (2)	18 (12)	2 (1)
Decreased weight	35 (11)	4 (1)	13 (8)	0
Insomnia	34 (11)	0	11 (7)	0
Diarrhoea	33 (11)	4 (1)	10 (7)	0
Hypoalbuminaemia	32 (10)	2 (1)	9 (6)	0





12º SIMPÓSIO  
INTERNACIONAL DE

CÂNCER DE  
PULMÃO

2ª JORNADA ONCONNECTION MULTICARE

2024

## Marcelo Corassa

BP – A Beneficência Portuguesa de São Paulo

[marcelo.corassa@bp.org.br](mailto:marcelo.corassa@bp.org.br)

GERENCIAMENTO E PRODUÇÃO

