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Immunotherapy in Metastatic NSCLC: How to Choose Initial Therapy and What's New?

Tina Cascone, MD, PhD

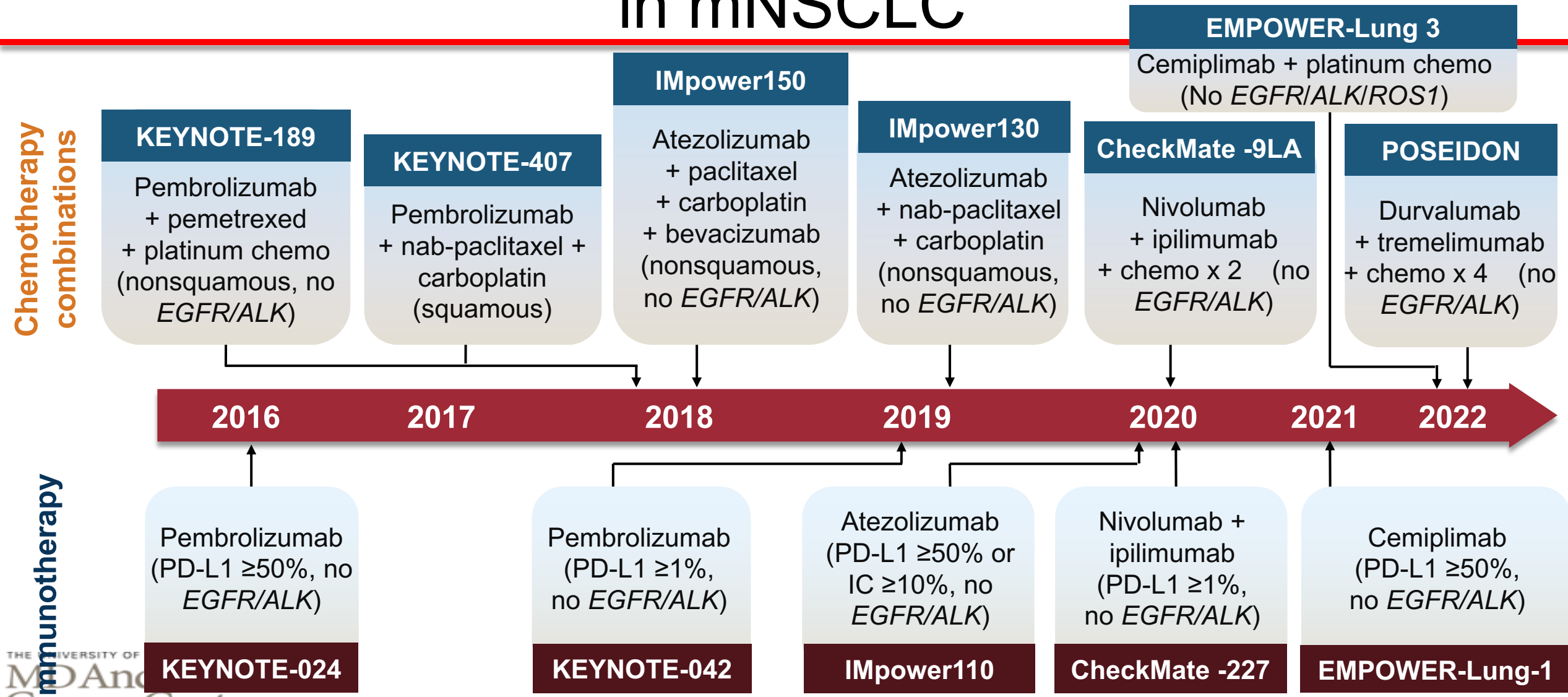
Associate Professor

Thoracic/Head and Neck Medical Oncology

MD Anderson Cancer Center

March 3, 2024

Approvals for first-line immunotherapy in mNSCLC



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From PeerView
Cascone, Heymach, Patel, TTLC24 Meeting

Treatment landscape for mNSCLC has evolved with several treatment options

For tumors without a molecular driver:

PD-L1 ≥50%	PD-L1 <50%
• Checkpoint inhibitor alone • Chemotherapy plus checkpoint inhibitor • I-O/I-O combination (?)	• Checkpoint inhibitor alone (?) • Chemotherapy plus checkpoint inhibitor • I-O/I-O combination

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Adapted from Dr. Borghaei

mNSCLC with PD-L1 > 50%

Phase 3 RCT KEYNOTE-024

Key eligibility criteria
- Untreated stage IV NSCLC
- PD-L1 TPS ≥ 50%
- ECOG PS 0 or 1
- No activating *EGFR* mutation or *ALK* translocation
- No untreated brain metastases
- No active autoimmune disease requiring systemic therapy

R (1:1)
N = 305

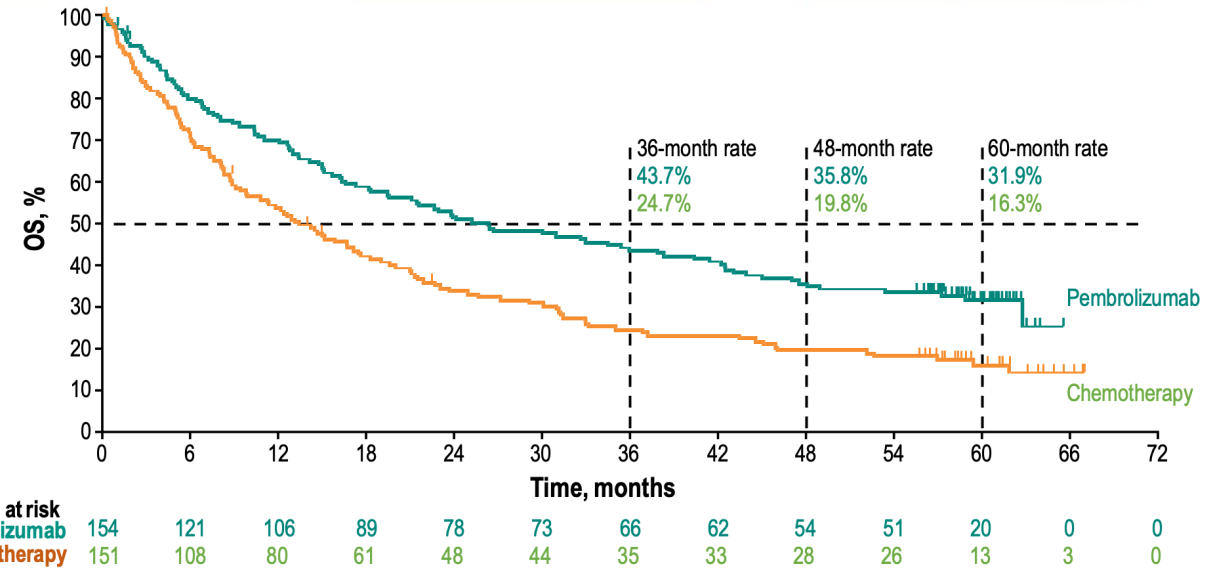
Pembrolizumab
200 mg IV Q3W
(2 years)

Platinum-Doublet Chemotherapy
(4 to 6 cycles)

PD[a]

Pembrolizumab
200 mg Q3W
for 2 years

Key endpoints
- Primary: PFS (RECIST v1.1 per blinded, independent central review)
- Secondary: OS, ORR, safety
- Exploratory: DoR



No. at risk												
Pembrolizumab	154	121	106	89	78	73	66	62	54	51	20	0	0
Chemotherapy	151	108	80	61	48	44	35	33	28	26	13	3	0

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Reck M et al. J Clin Oncol. 2021

Pembrolizumab is not the only option in this disease space

Trial	Drug	PD-L1	N pts	mOS, months (HR)	3-years OS, %	5-years OS, %	mPFS, months (HR)	ORR, %
KEYNOTE-024 [1,2]	Pembrolizumab	TPS ≥50%	154	26,3 (HR 0.62)	43,7	31,9	7,7 (HR 0.50)	46,1
IMpower-110 [3,4]	Atezolizumab	TC3 or IC3	107	20,2 (HR 0.76)	38		8,2 (HR .59)	40,2
Empower-Lung 01 [5,6]	Cemiplimab	TPS ≥50%	284	26,1 (HR 0.57)	40		8,1 (HR 0.51)	46.5

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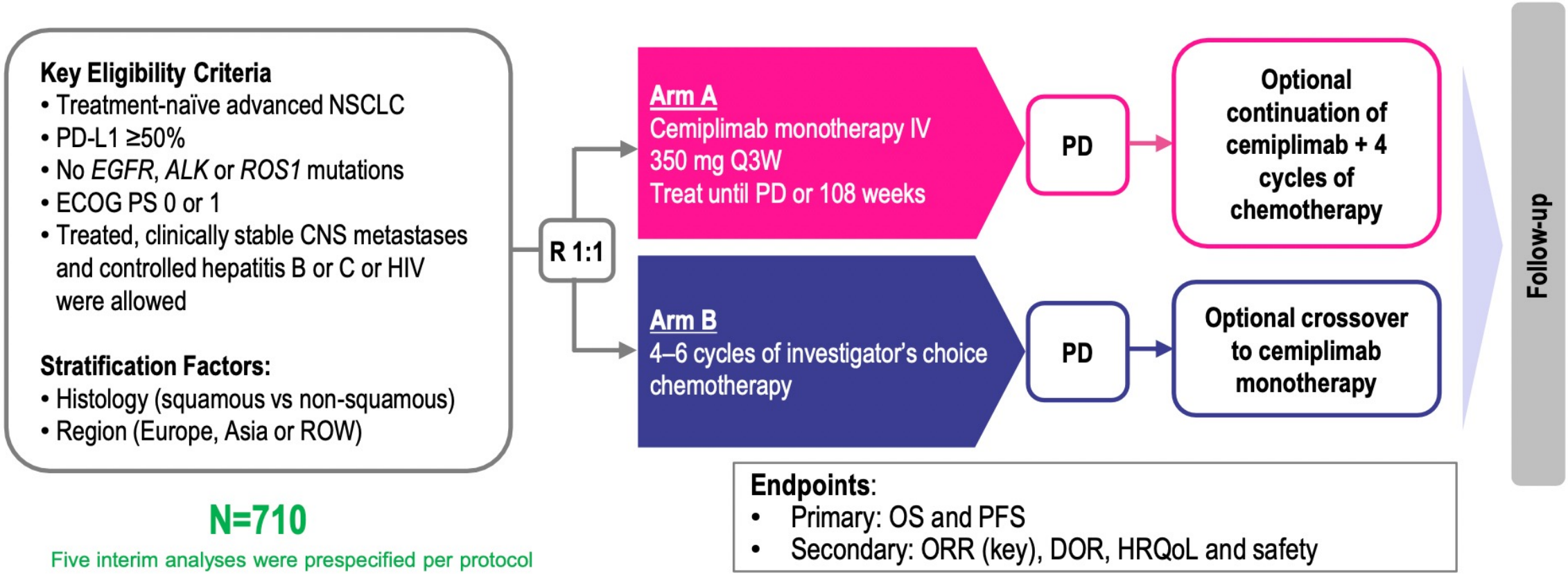
Reck M et al, NEJM 2016; Reck M et al. J Clin Oncol. 2021
Herbst RS et al NEJM 2020; Jassem J et al. JTO 2021
Ahmet S et al. Lancet 2021; Ozguroglu M, et al ESMO22

EMPOWER-Lung 1: Cemiplimab



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Sezer, *ESMO 2020*

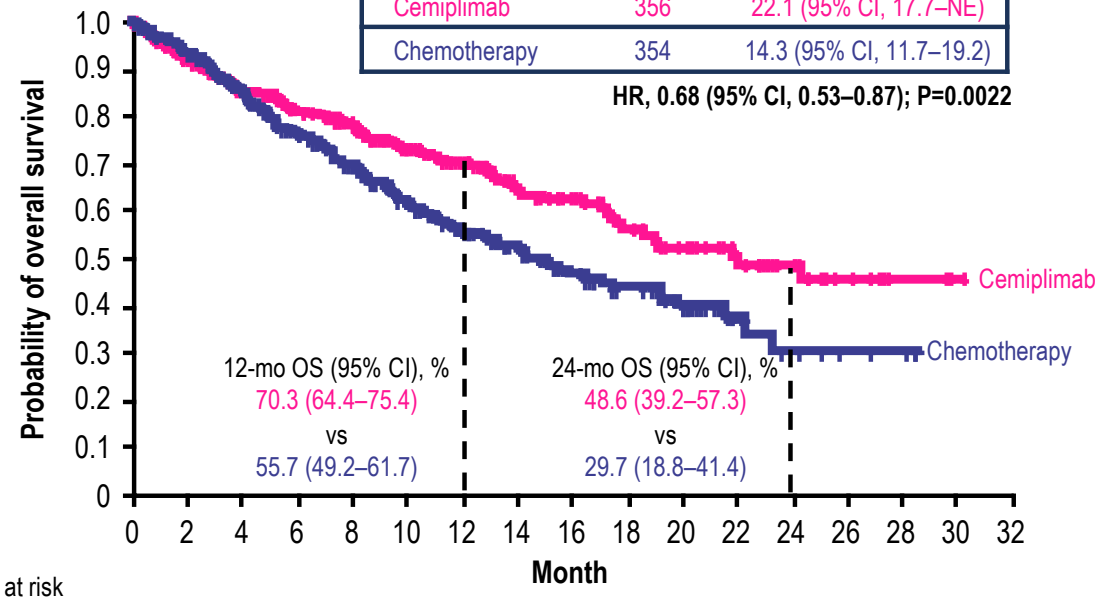
Cemiplimab: EMPOWER-Lung 1 Trial

Crossover: 74%

ITT

	No. of Patients	Median OS (95% CI) *mo*
Cemiplimab	356	22.1 (95% CI, 17.7–NE)
Chemotherapy	354	14.3 (95% CI, 11.7–19.2)

HR, 0.68 (95% CI, 0.53–0.87); P=0.0022



No. at risk

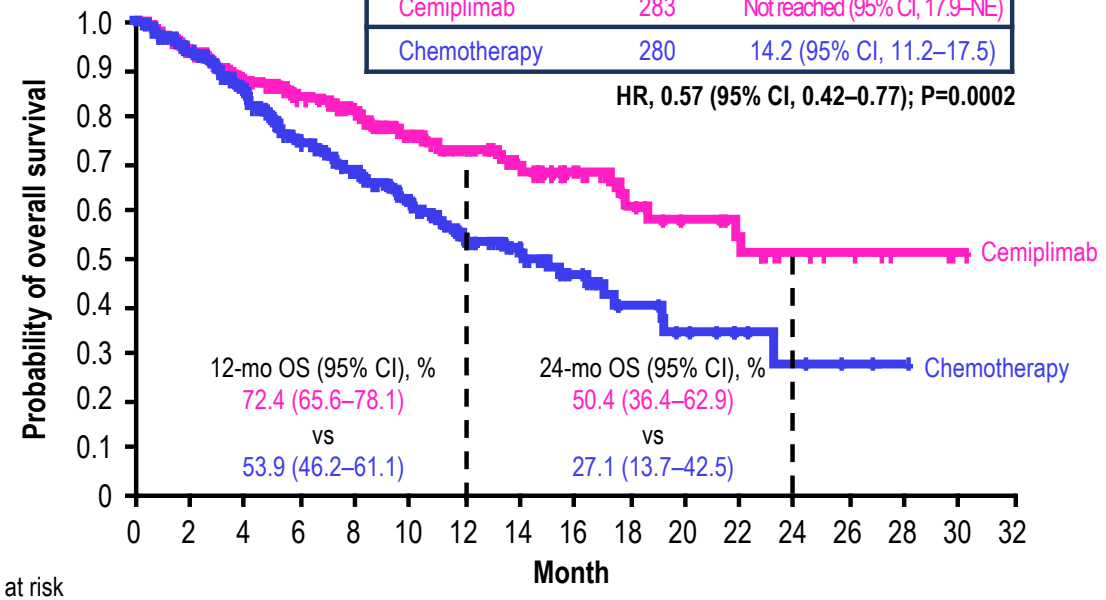
Cemiplimab	356	304	254	223	198	147	120	87	71	48	37	27	18	8	3	1	0
Chemotherapy	354	303	254	205	172	126	93	73	52	41	27	12	7	4	3	0	0

Median duration of follow-up:
Cemiplimab → 13.1 months (range: 0.1–31.9)
Chemotherapy → 13.1 months (range: 0.2–32.4)

PD-L1 ≥50% ITT

	No. of Patients	Median OS (95% CI) *mo*
Cemiplimab	283	Not reached (95% CI, 17.9–NE)
Chemotherapy	280	14.2 (95% CI, 11.2–17.5)

HR, 0.57 (95% CI, 0.42–0.77); P=0.0002



No. at risk

Cemiplimab	283	244	203	177	154	108	83	55	42	24	18	15	10	6	3	1	0
Chemotherapy	280	239	198	153	125	87	57	41	25	15	11	6	4	2	1	0	0

Median duration of follow-up:
Cemiplimab → 10.8 months (range: 0.1–31.9)
Chemotherapy → 10.2 months (range: 0.2–29.5)

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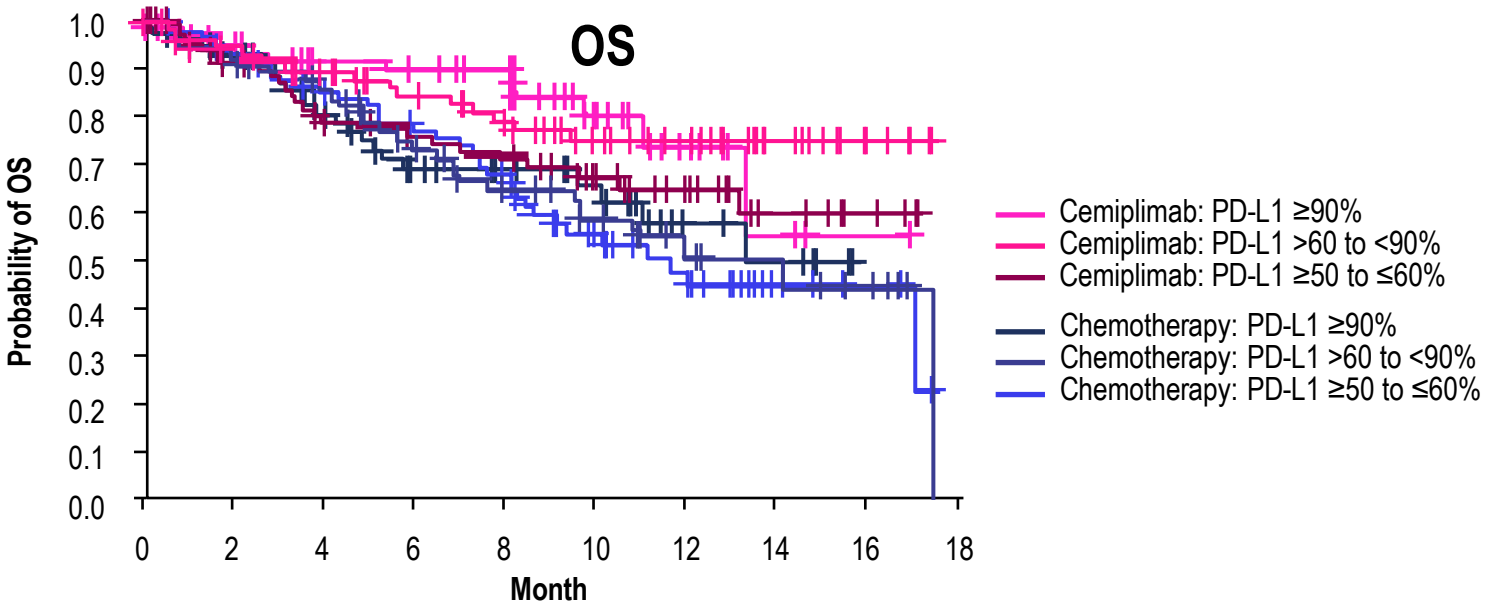
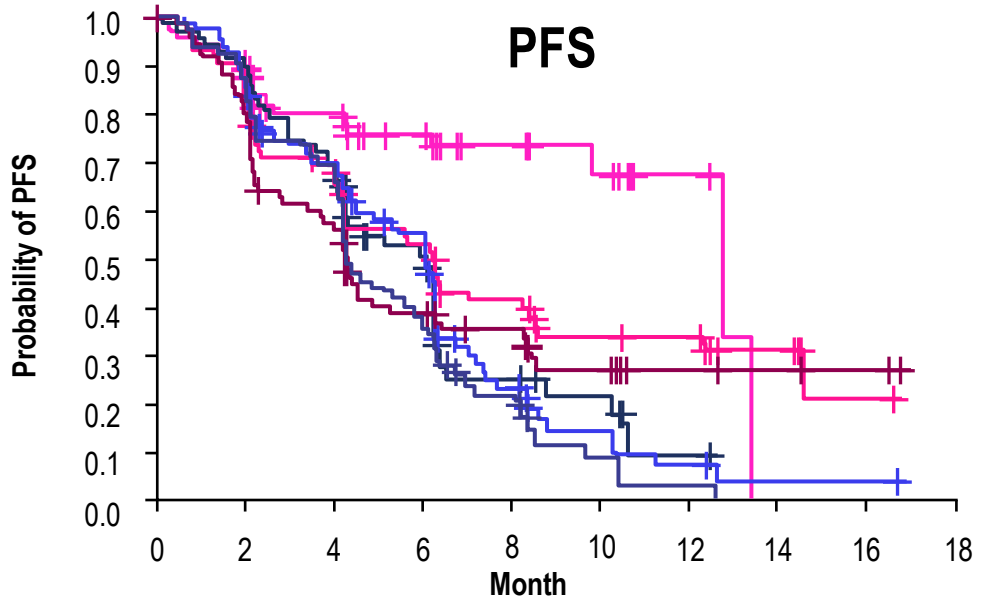
Sezer A, et al. *Ann Oncol*. 2020;31(suppl): abstract LBA52.

EMPOWER-Lung 1 by PD-L1 Expression

PD-L1 Expression Levels Correlate With OS and PFS (N=475)





	Median, months (95% CI)			HR (95% CI)
	Cemiplimab (N=238)		Chemotherapy (N=237)	
≥90%	NR (13.4–NE)	vs	13.3 (10.2–NE)	0.54 (0.27–1.10)
>60 to <90%	NR (NE–NE)	vs	14.2 (9.6–17.5)	0.49 (0.26–0.92)
≥50 to ≤60%	NR (13.2–NE)	vs	11.7 (8.3–NE)	0.74 (0.44–1.24)

	Median, months (95% CI)			HR (95% CI)
	Cemiplimab (N=238)		Chemotherapy (N=237)	
≥90%	12.7 (9.8–13.4)	vs	6.1 (4.2–6.2)	0.33 (0.19–0.58)
>60 to <90%	6.2 (4.2–8.4)	vs	4.3 (4.1–5.9)	0.57 (0.38–0.85)
≥50 to ≤60%	4.3 (2.8–5.2)	vs	6.0 (4.4–6.2)	0.89 (0.61–1.29)

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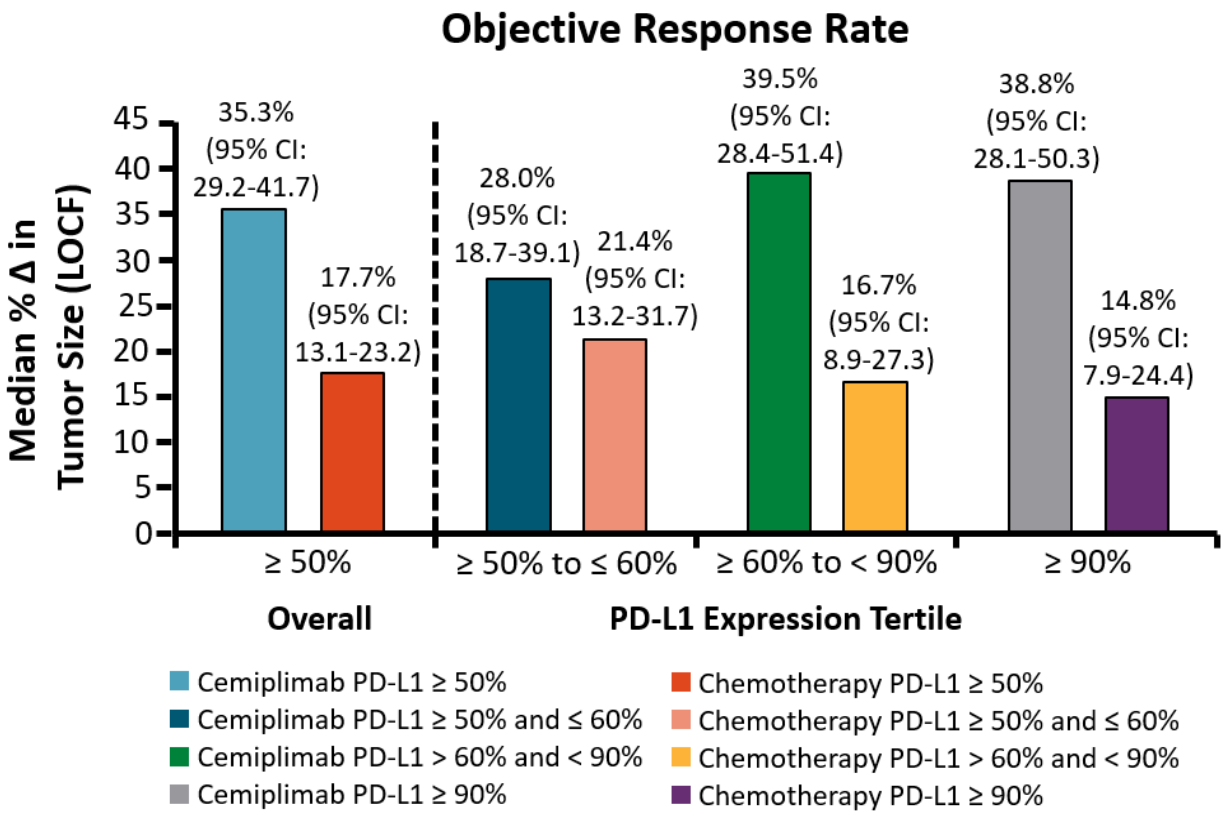
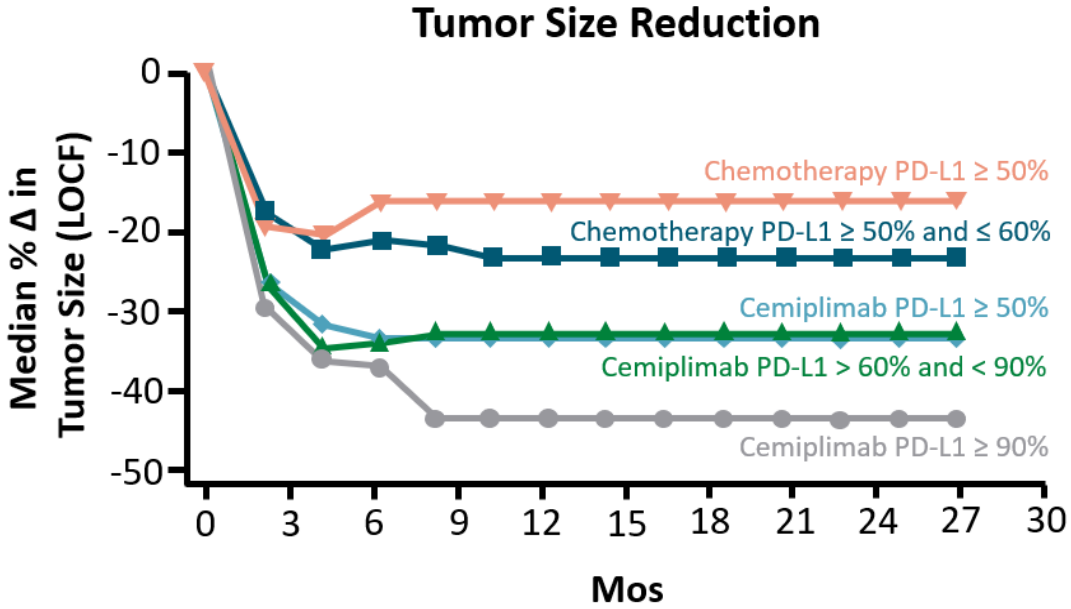
HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival.

Kilickap S, et al. WCLC 2020. Abstract OA01.03.

EMPOWER Lung 1: Responses by PD-L1 expression level

PD-L1 expression levels correlate with tumor responses





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Sezer A et al. Lancet 2021

Adding chemotherapy after cemiplimab monotherapy progression in PD-L1>50% mNSCLC may confer benefit

First-line cemiplimab monotherapy and continued cemiplimab beyond progression plus chemotherapy for advanced non-small-cell lung cancer with PD-L1 50% or more (EMPOWER-Lung 1): 35-month follow-up from a mutlicentre, open-label, randomised, phase 3 trial

Table 2. Tumour response in patients receiving continued cemiplimab beyond progression (n=64), before and after initial progression

	Initial cemiplimab monotherapy	After added chemotherapy
Best overall tumour response		
Complete response	0	3 (5%)
Partial response	19 (30%)	17 (27%)
Stable disease	28 (44%)	35 (55%)
Non-complete response or non-progressive disease	0	0
Progressive disease	13 (20%)	9 (14%)
Not evaluable	4 (6%)	0
Objective response rate (95% CI)	19 (30%; 19–42)	20 (31%; 20–44)

Data are n (%), unless otherwise indicated.

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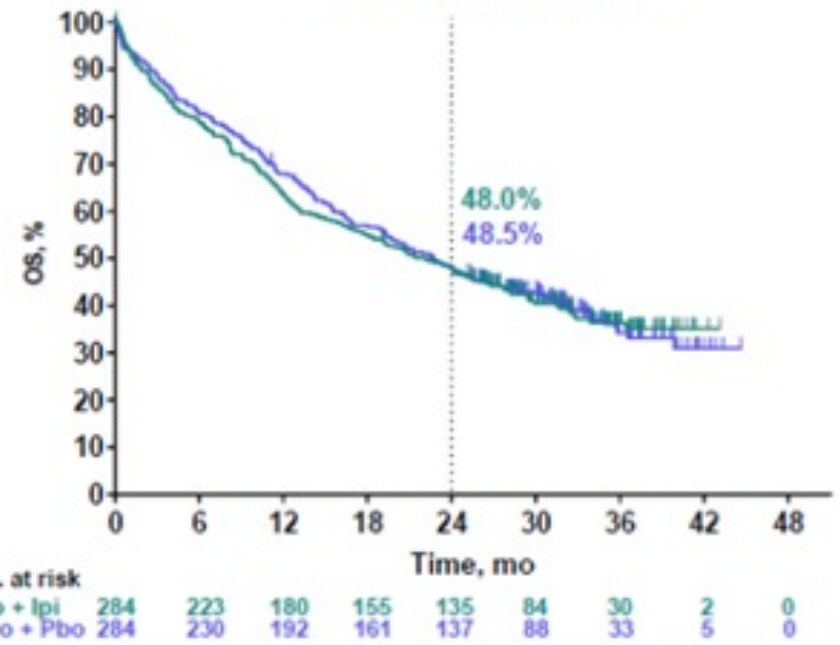
Özgüroğlu et al. *Lancet Onc* 2023

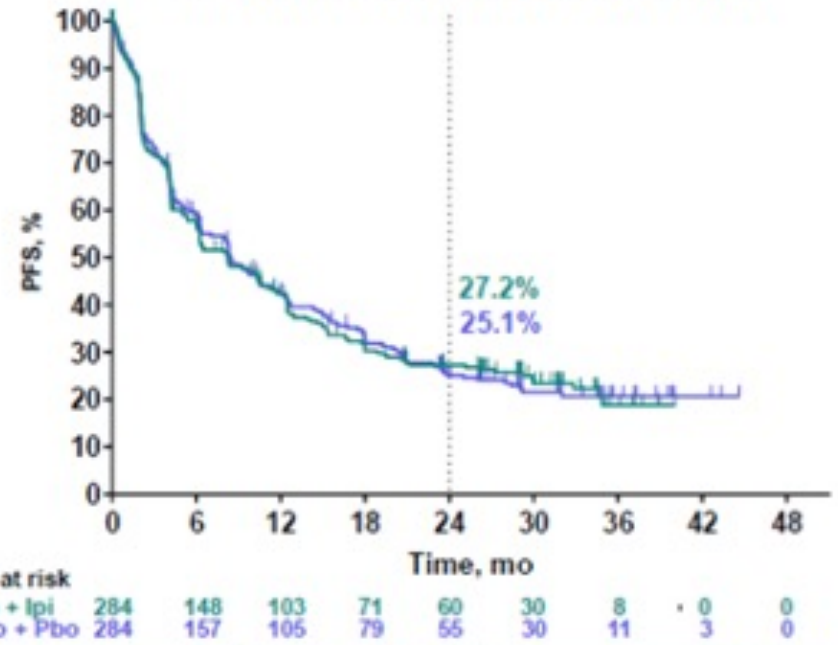
Impact of anti-CTLA-4 in PD-L1 > 50% mNSCLC: The KEYNOTE-598 P3 trial

Overall Survival



	Events, n (%)	Median (95% CI)	OS HR (95% CI)
Pembro + Ipi	173 (60.9)	22.1 (17.1–27.4)	1.05 (0.85–1.29)
Pembro + Pbo	176 (62.0)	22.7 (19.0–26.8)	

Progression-Free Survival[b]



	Events, n (%)	Median (95% CI)	PFS HR (95% CI)
Pembro + Ipi	198 (69.7)	8.2 (6.1–10.6)	0.99 (0.81–1.21)
Pembro + Pbo	203 (71.5)	8.4 (6.3–10.5)	

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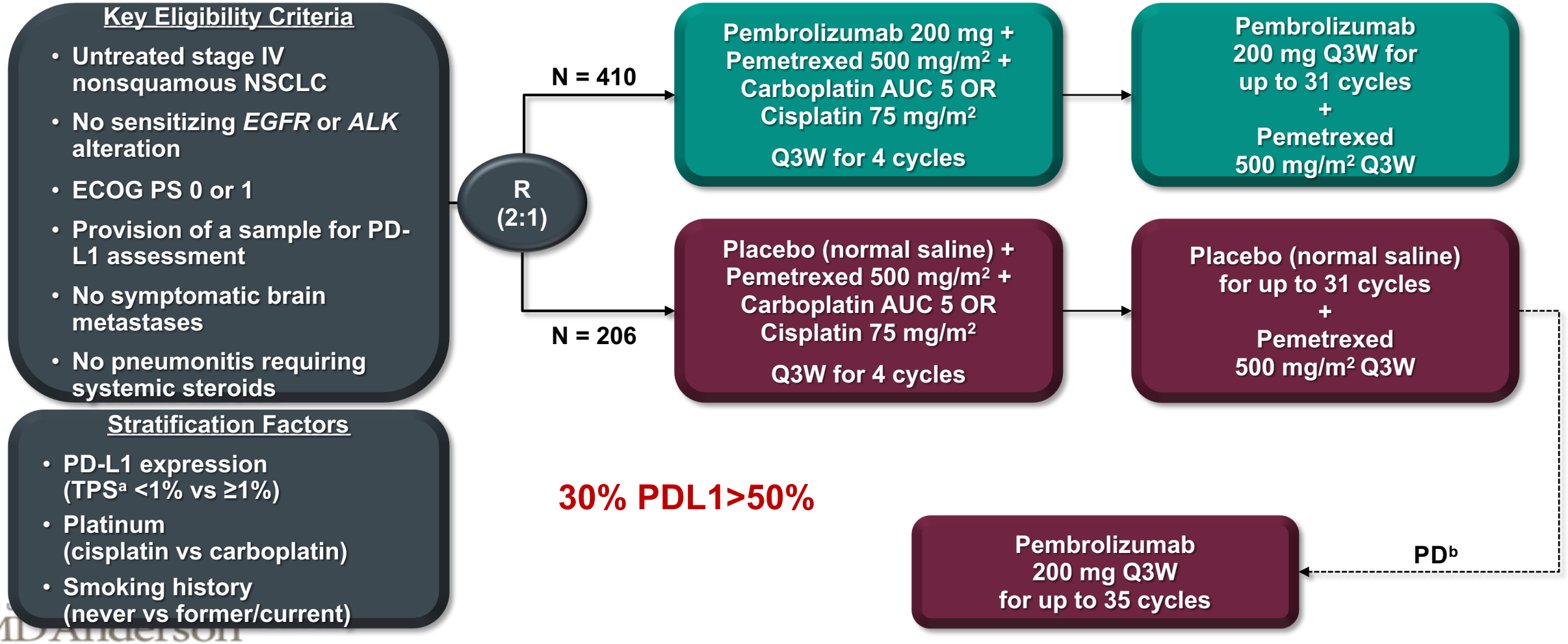
Boyer, JCO,2021; Rodriguez-Abreau, ELCC 2022

PD-L1 all comers and <50%

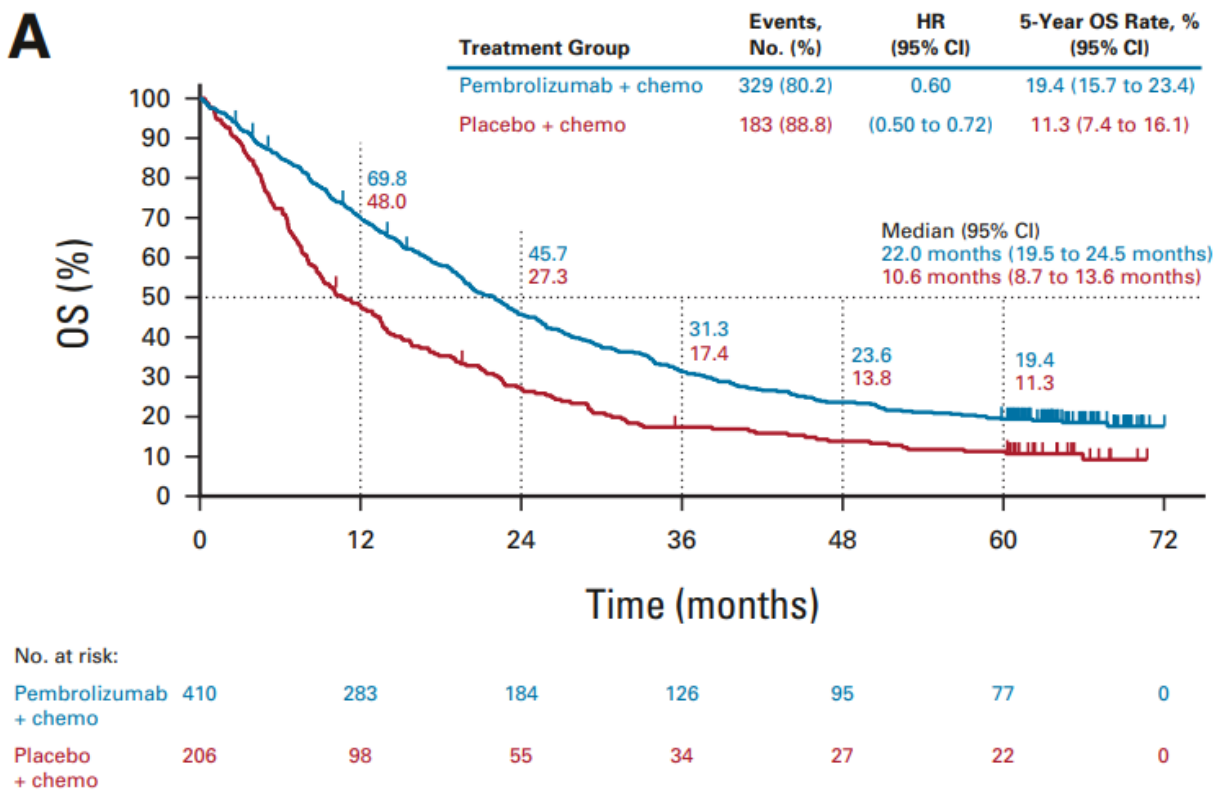
KEYNOTE-189 Study Design (NCT02578680)



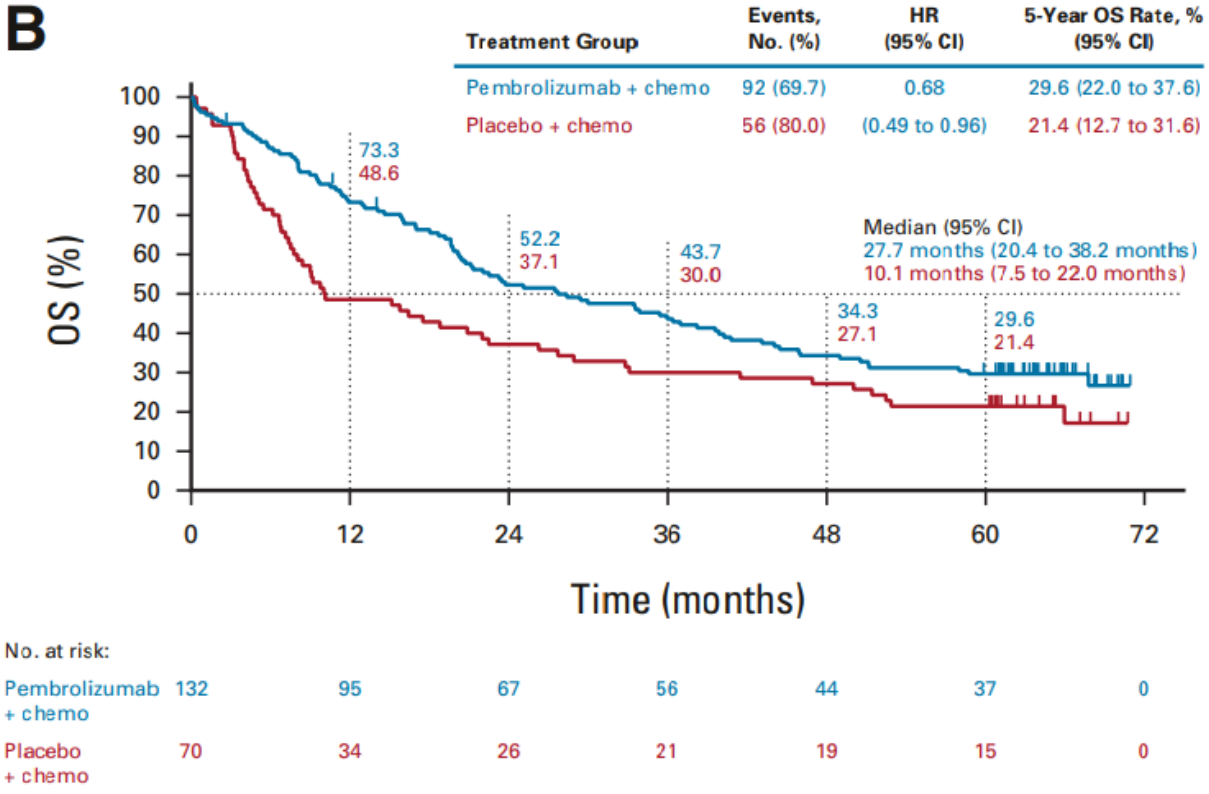
[a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay. [b]Patients could crossover during the induction or maintenance phases. To be eligible for crossover, PD must have been verified by blinded, independent central radiologic review and all safety criteria had to be met.

KEYNOTE-189 in ITT and PD-L1 >50% mNSCLC

ITT Population



PD-L1>50%



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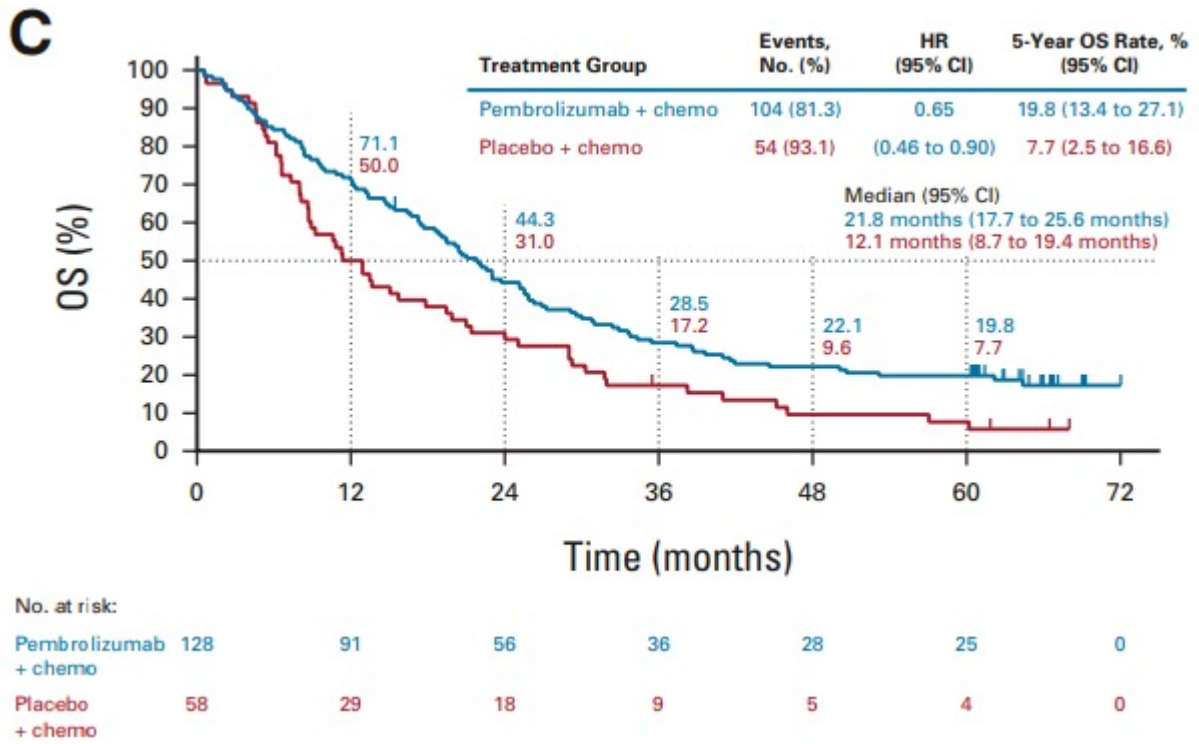
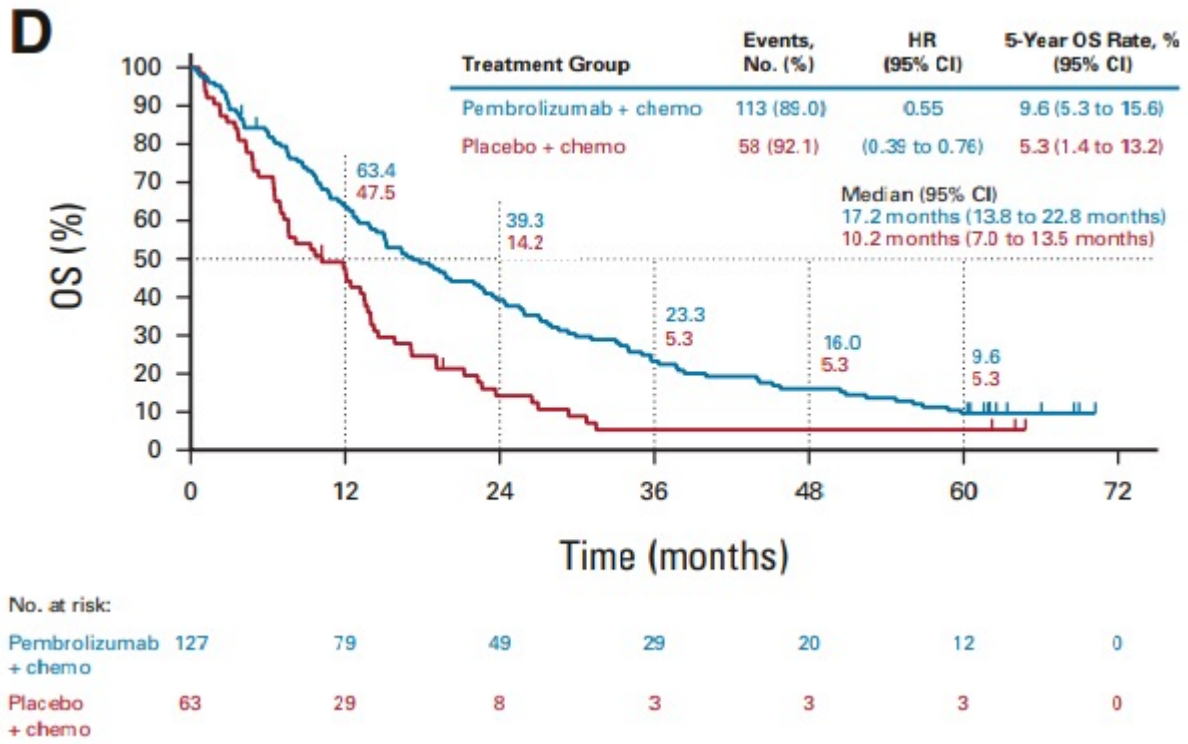
Garassino MC et al JCO 2023

KEYNOTE-189 in low and negative PD-L1 mNSCLC

PD-L1 1-49%



PD-L1 < 1%



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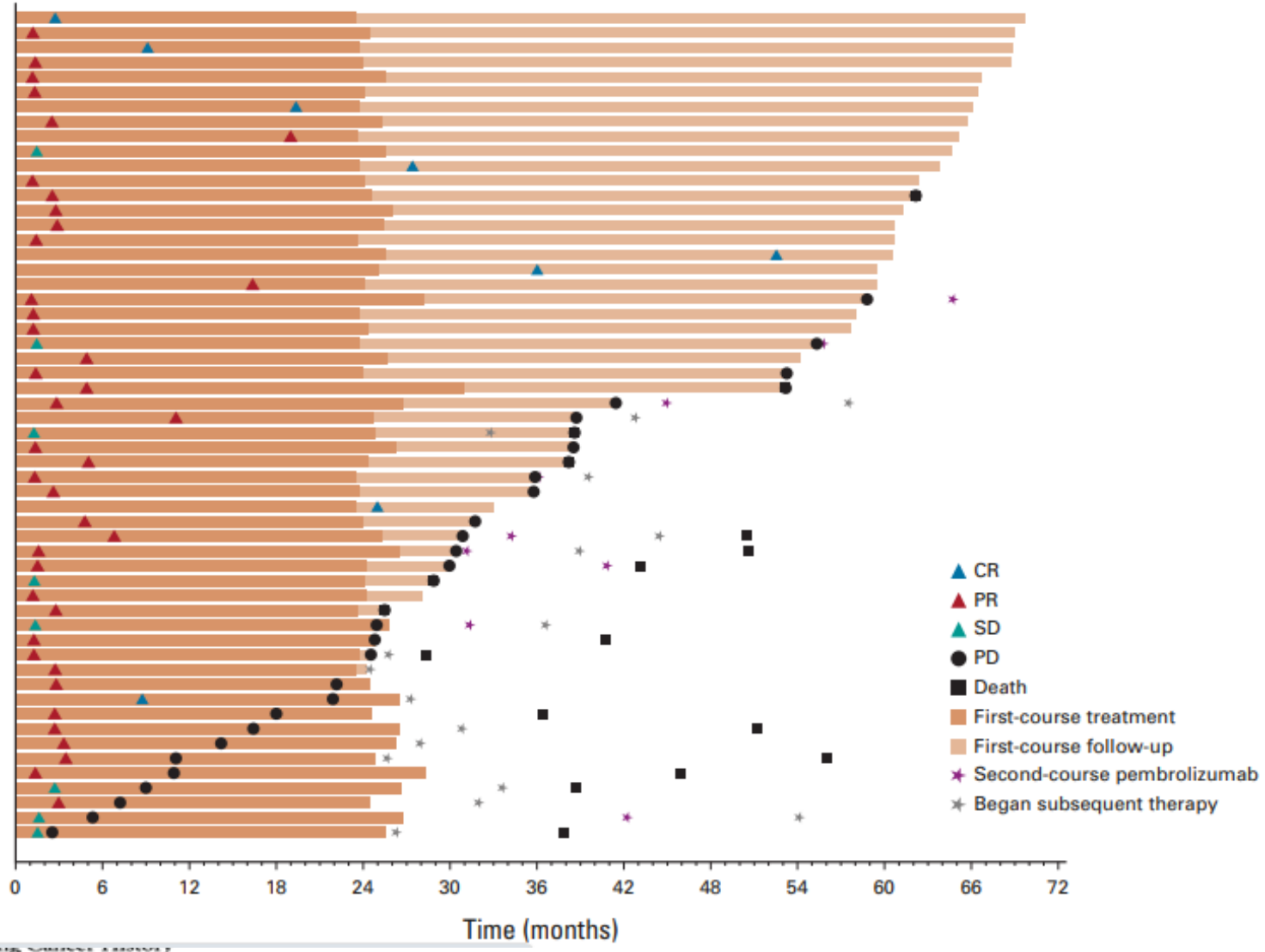
Garassino MC et al JCO 2023

Outcomes in Patients Who Completed 35 Cycles of Pembrolizumab



	n = 57
ORR (95% CI),[a] %	86.0 (74.2–93.7)
Best overall response, n (%)	
CR	8 (14.0)
PR	41 (71.9)
Median DOR (range),[b] mo	57.7 (4.2 to 68.3+)
3-y OS rate after completing 35 cycles[c]	71.9%
Alive without PD or subsequent therapy, n (%)	23 (40.4)

[a]Per RECIST version 1.1 by BICR. [b]Kaplan-Meier estimate. [c]Approximately 5 years after randomization. Data cutoff date: March 8, 2022.

Garassino MC et al JCO 2023

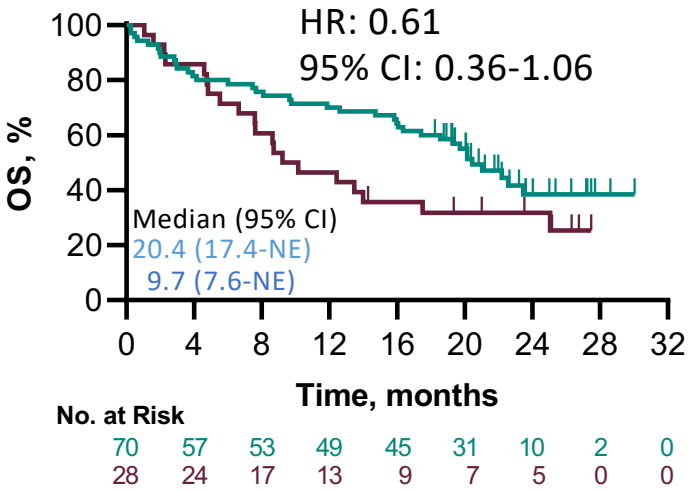
Clinical Utility of Prespecified bTMB Cutpoint of 15 mut/Mb: Pembro-CT improved outcomes vs PBO-CT for bTMB ≥15 and <15 mut/Mb

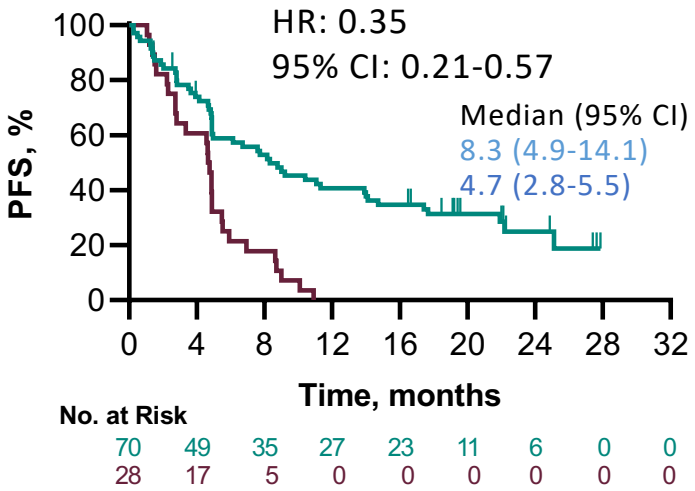
OS

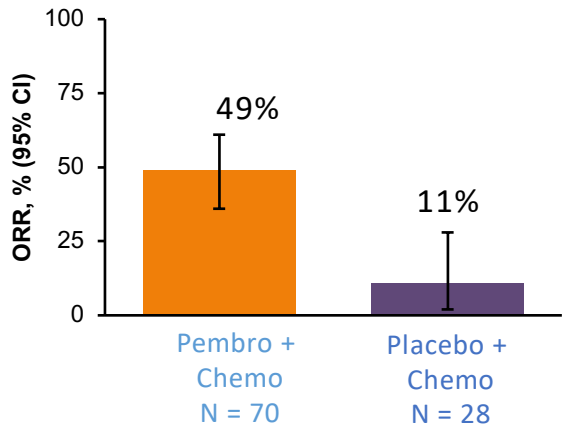
PFS

ORR

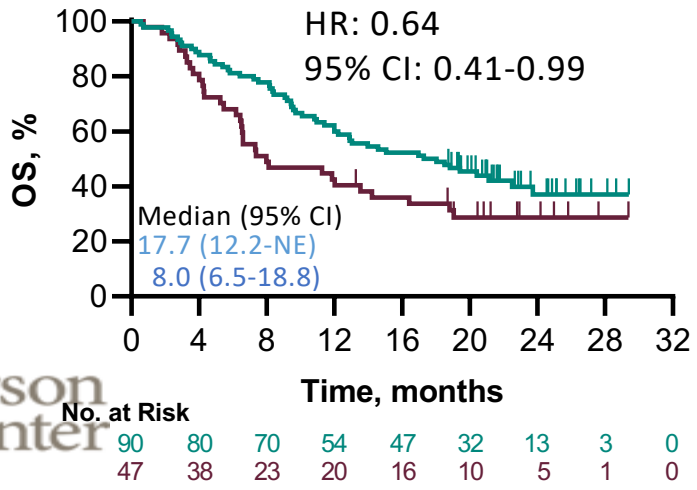
≥15 mut/Mb

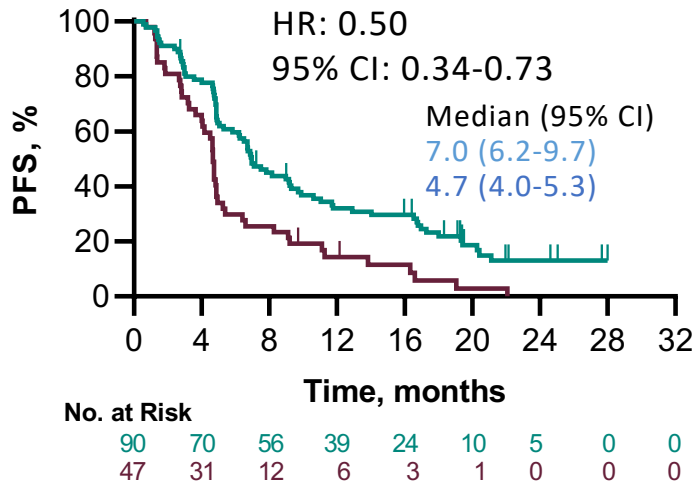


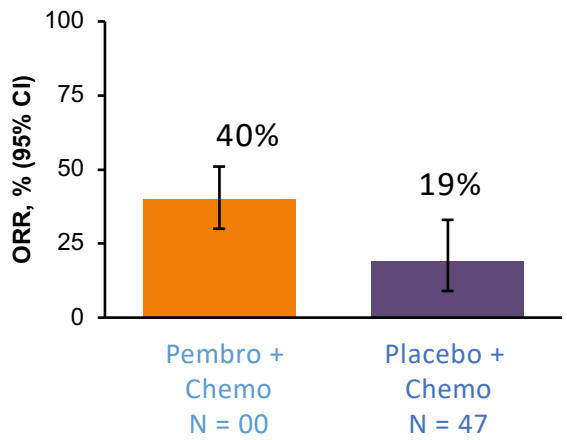




<15 mut/Mb







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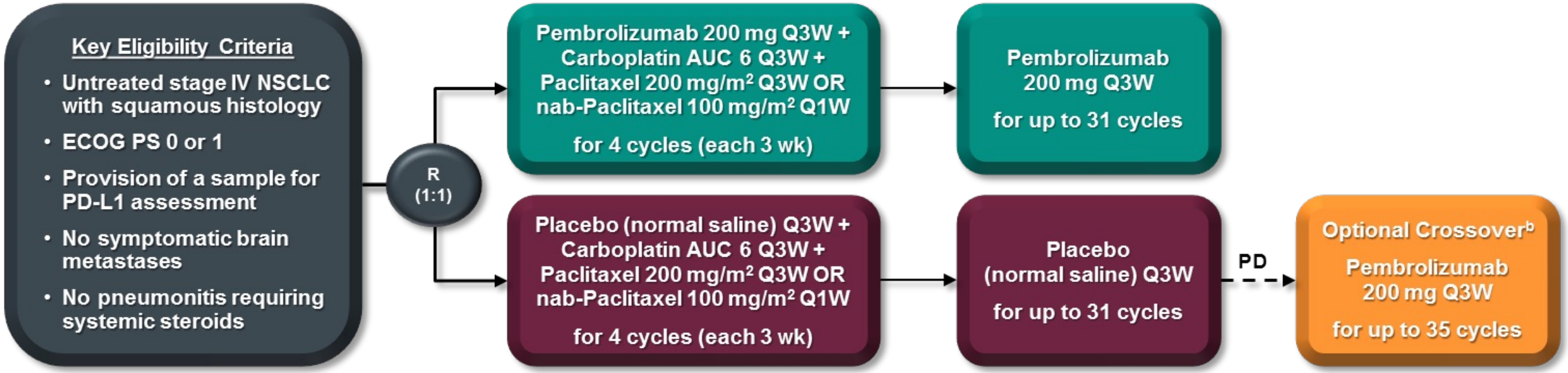
KEYNOTE-407 Study Design (NCT02775435)



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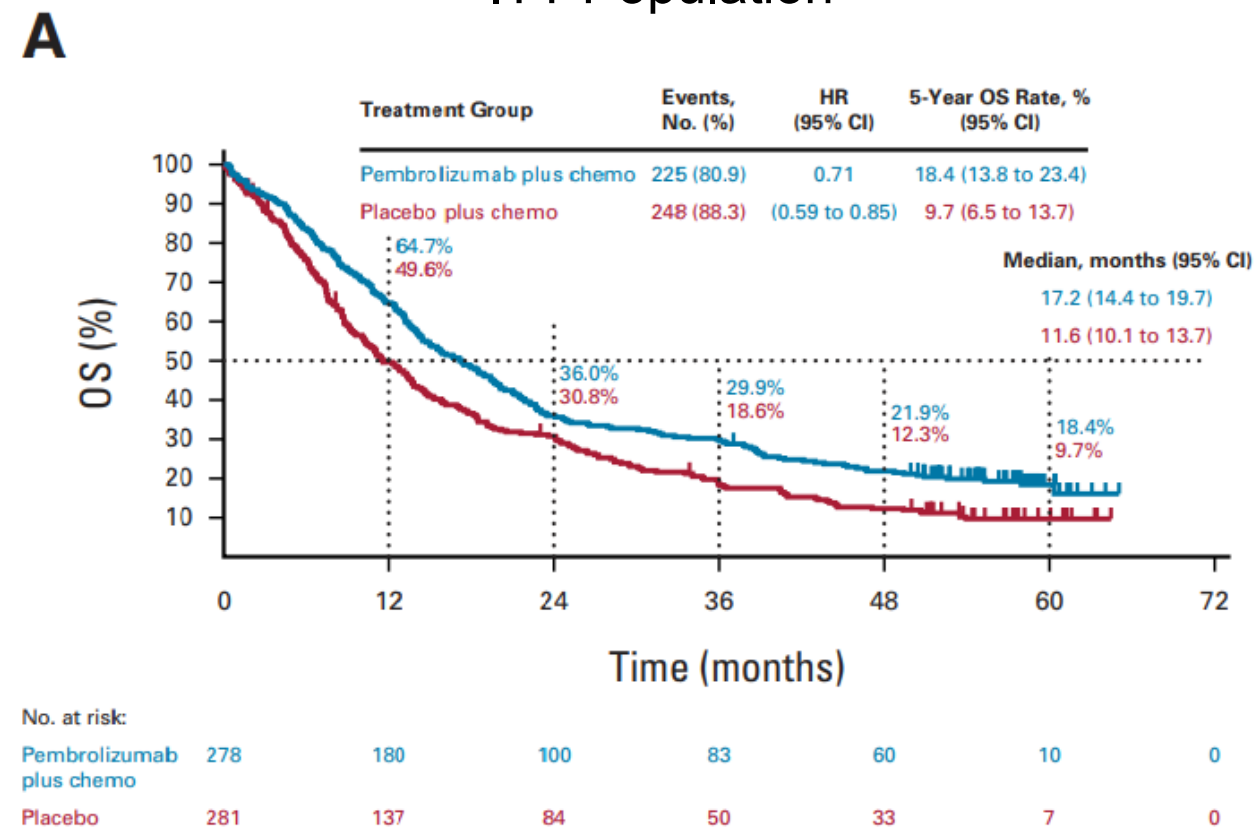
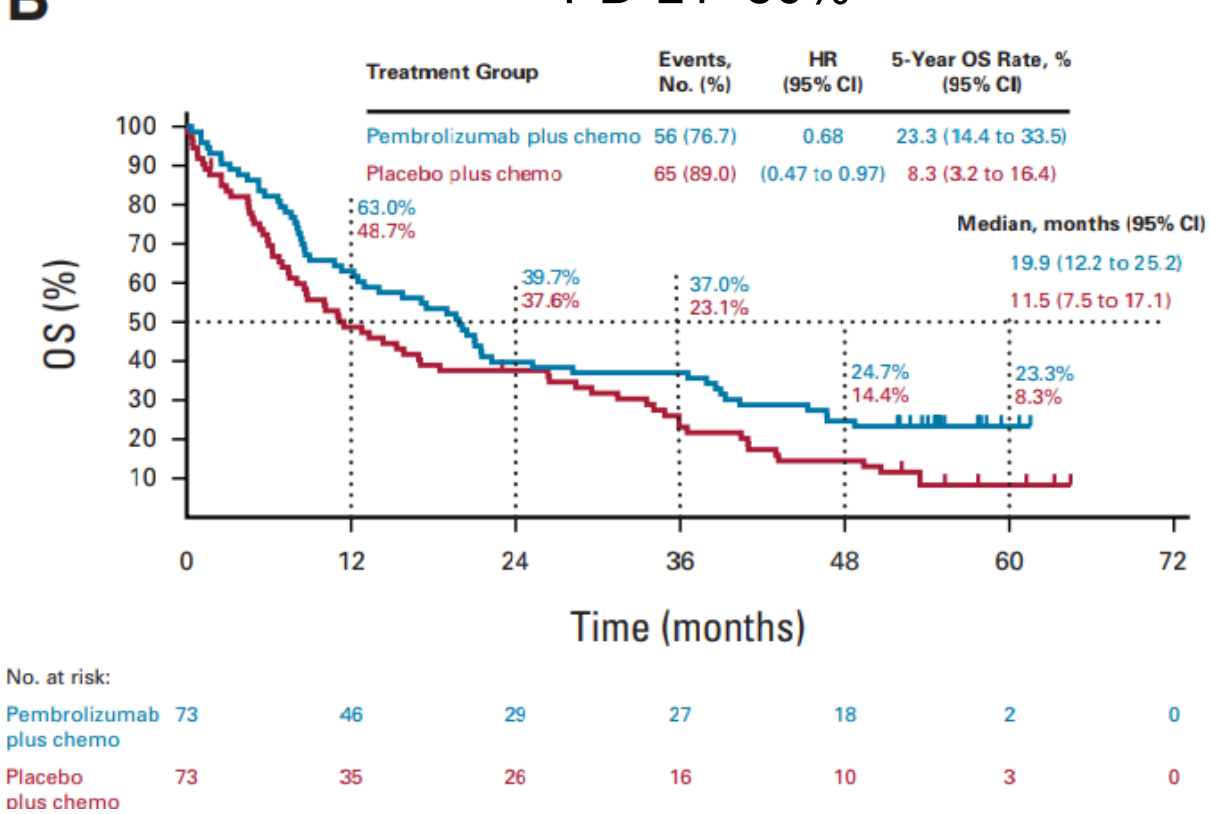
Paz-Ares L et al. *NEJM, 2018*

KEYNOTE-407 in ITT and PD-L1 >50% mNSCLC

ITT Population



PD-L1>50%



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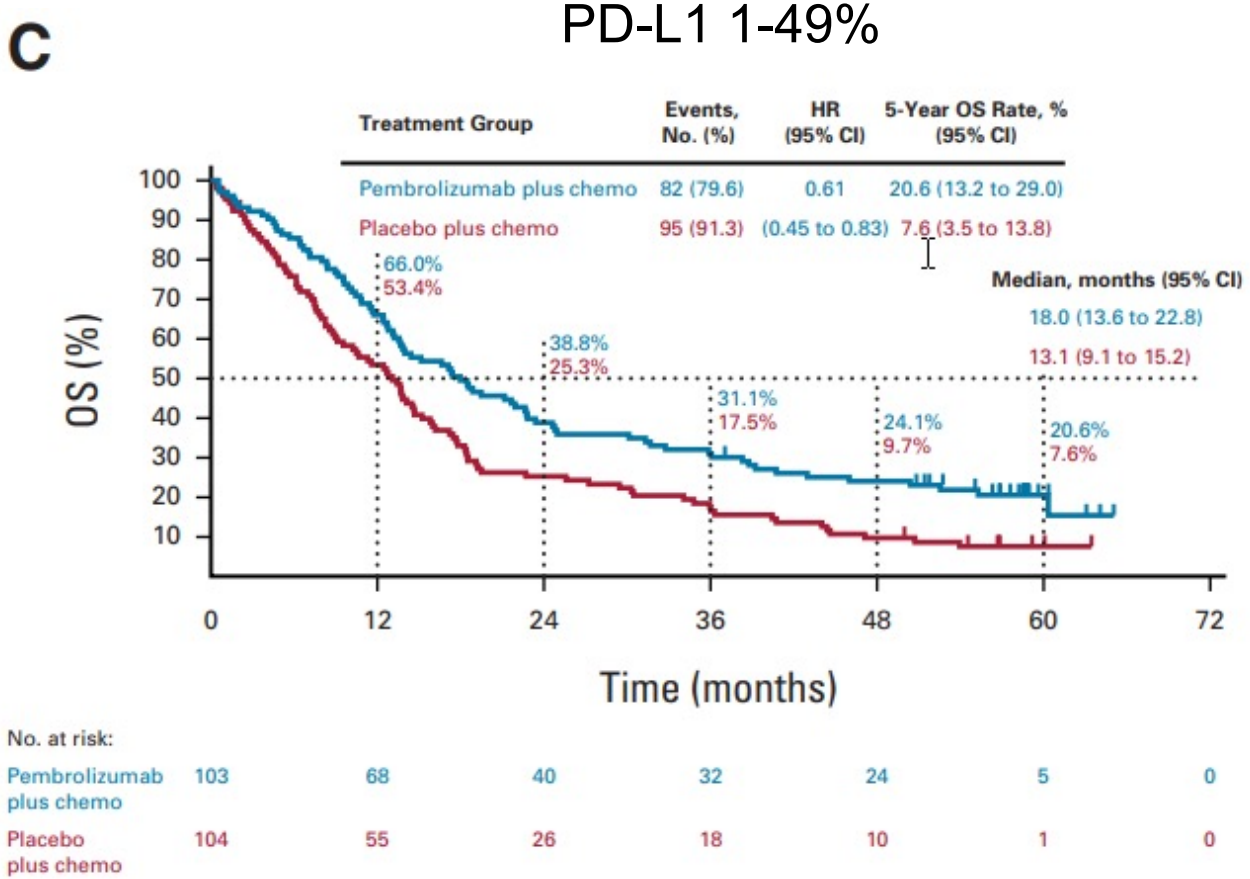
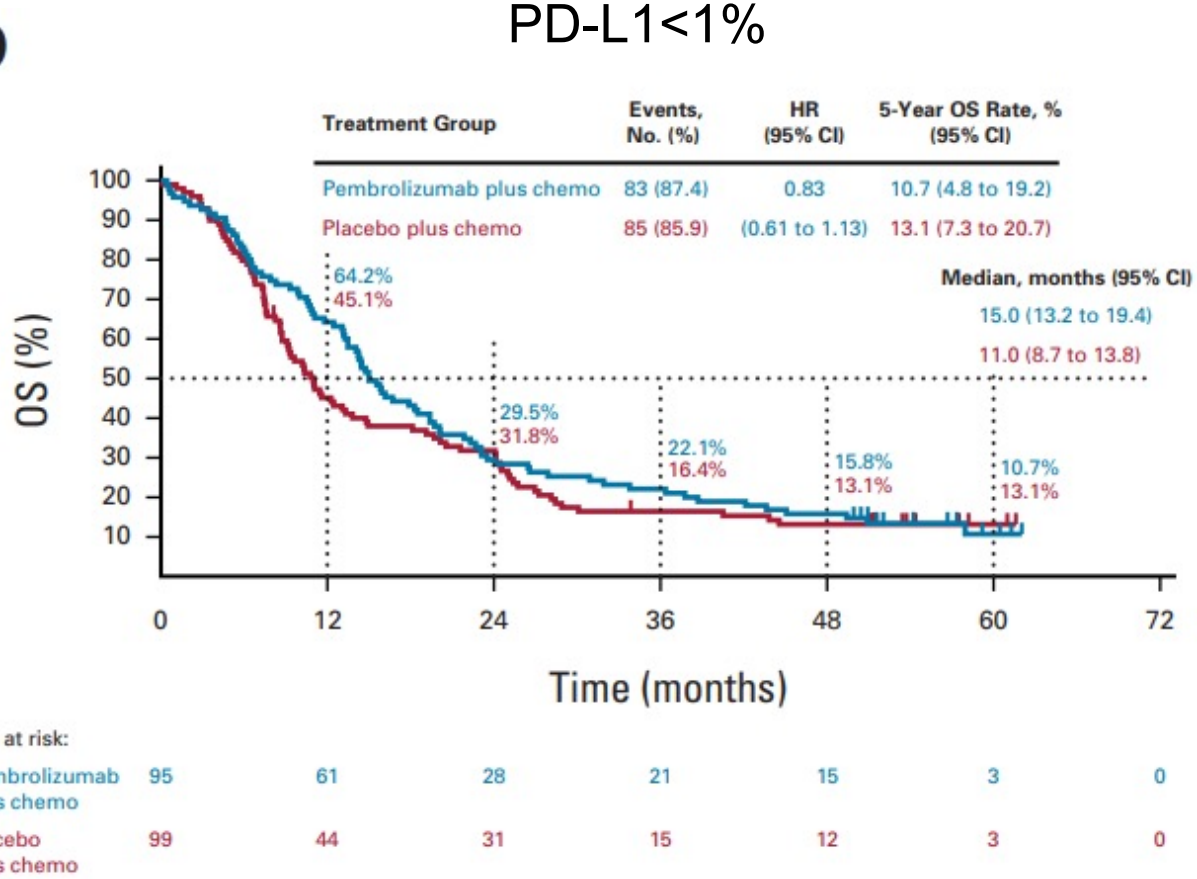
Novello S et al JCO 2023

KEYNOTE-407 in PD-L1 low and negative mNSCLC

PD-L1 1-49%



PD-L1<1%



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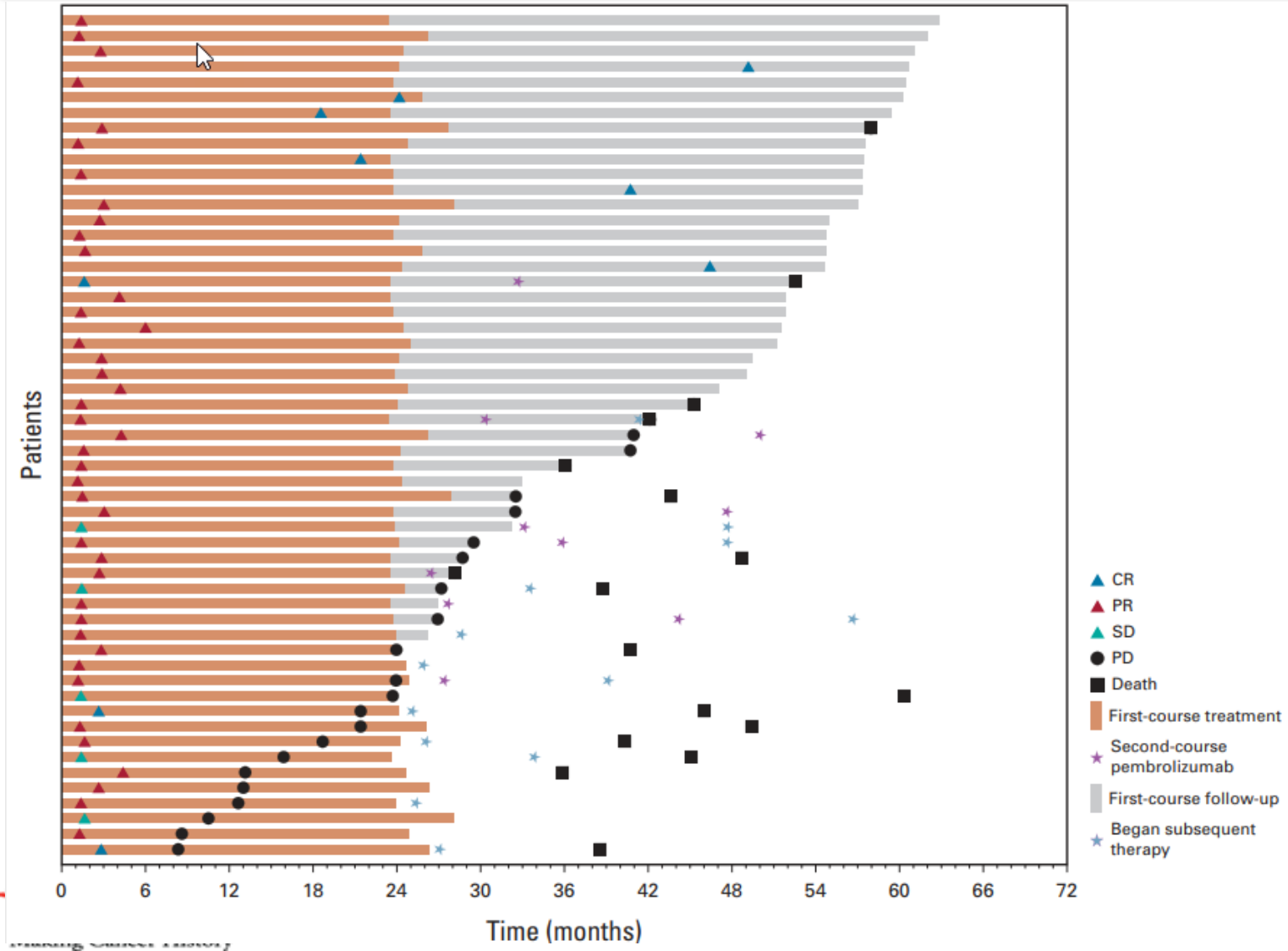
Outcomes in Patients Who Completed 35 Cycles of Pembrolizumab



	n = 55
ORR (95% CI),[a] %	90.9 (80.0–97.0)
Best overall response, n (%)	
CR	9 (16.4)
PR	41 (74.5)
Median DOR (range),[b] mo	NR (7.1 to 61.5+)
3-y OS rate after completing 35 cycles[c]	69.5%
Alive without PD or subsequent therapy, n (%)	24 (43.6)

Novello S et al JCO 2023

EMPOWER-Lung 3 (NCT03409614)

Background: Cemiplimab (a high-affinity, fully human anti–PD-1) is approved as first-line monotherapy for advanced NSCLC with PD-L1 ≥50% (EMPOWER-Lung 1 Study[1])

Key eligibility criteria
- Treatment-naive advanced NSCLC (non-squamous and squamous histology; Stage IIIb/c†, IV)
- Any PD-L1 expression
- No *EGFR*, *ALK*, or *ROS1* mutations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases‡

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 PRO

R 2:1

Arm A
Cemiplimab 350 mg Q3W + investigator's choice platinum-doublet chemo Q3W for 4 cycles§

Arm B
Placebo Q3W + investigator's choice platinum-doublet chemo Q3W for 4 cycles§

PD or 108 weeks

PD or 108 weeks

Follow-up

N=466

Two interim analyses were prespecified per protocol
Second interim analysis (14 June 2021) presented here

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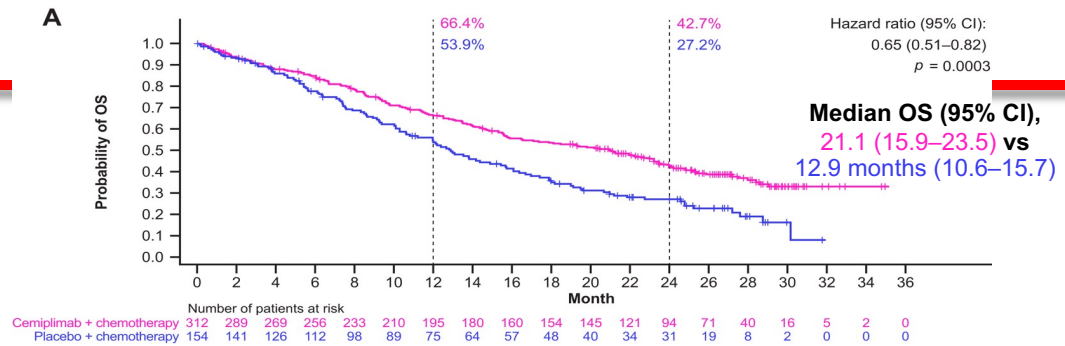
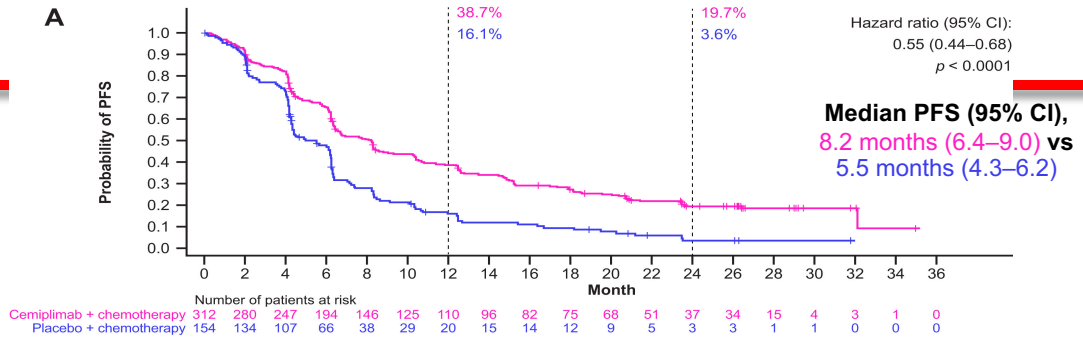
Gogishvili M, et al. *Nat Med*. 2022

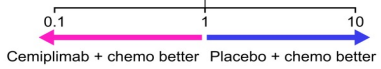
2-Yr Follow-Up EMPOWER-Lung 3 Part 2: OS and PFS





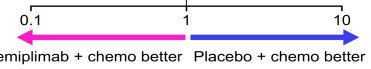
B

	Cemiplimab + chemo (OS events/patients)	Placebo + chemo (OS events/patients)	Hazard ratio (95% CI)
All patients	180/312	111/154	0.65 (0.51–0.82)
Age group			
<65 years	100/184	70/94	0.53 (0.39–0.72)
≥65 years	80/128	41/60	0.81 (0.55–1.18)
Sex			
Male	155/268	92/123	0.55 (0.42–0.71)
Female	25/44	19/31	0.98 (0.54–1.78)
Race			
White	155/267	102/138	0.61 (0.47–0.78)
Non-White	25/45	9/16	0.81 (0.38–1.74)
Histology			
Squamous	79/133	47/67	0.61 (0.42–0.87)
Nonsquamous	101/179	64/87	0.64 (0.47–0.88)
PD-L1 level			
<1%	66/95	34/44	0.94 (0.62–1.42)
1–49%	62/114	43/61	0.50 (0.34–0.74)
≥50%	52/103	34/49	0.56 (0.36–0.86)
ECOG performance status			
0	15/51	14/18	0.24 (0.12–0.51)
1	163/259	96/134	0.70 (0.54–0.90)
Geographic region			
Europe	157/270	102/138	0.61 (0.48–0.79)
Asia	23/42	9/16	0.78 (0.36–1.69)
Brain metastasis at baseline			
Yes	12/24	7/7	0.29 (0.11–0.75)
No	168/288	104/147	0.65 (0.51–0.83)
Cancer stage at screening			
Locally advanced	21/45	18/24	0.50 (0.27–0.95)
Metastatic	159/267	93/130	0.64 (0.49–0.83)
Smoking history			
Smokers	155/269	96/130	0.58 (0.45–0.75)
Non-smokers	25/43	15/24	0.85 (0.45–1.62)

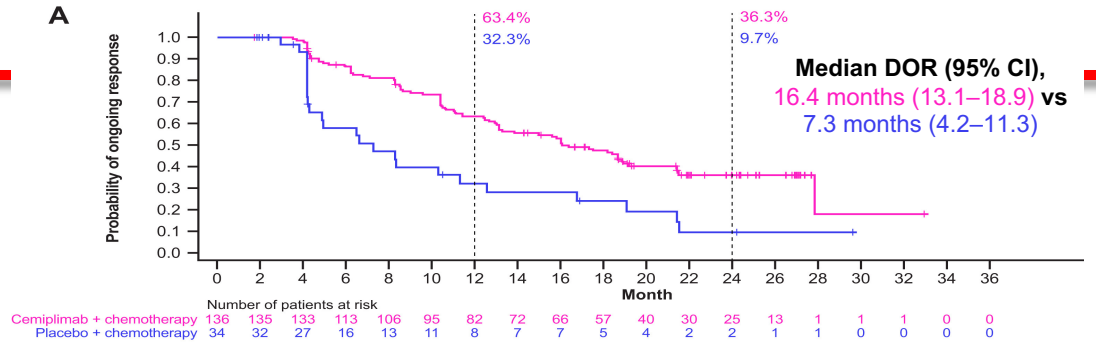


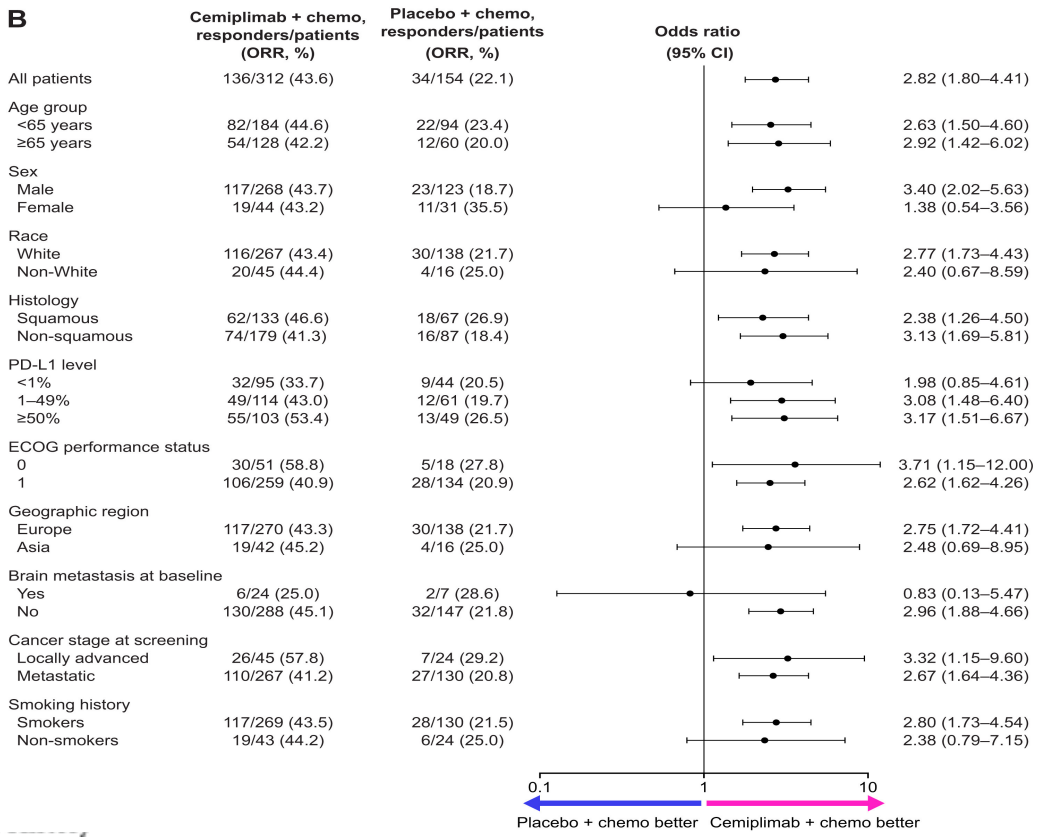
B

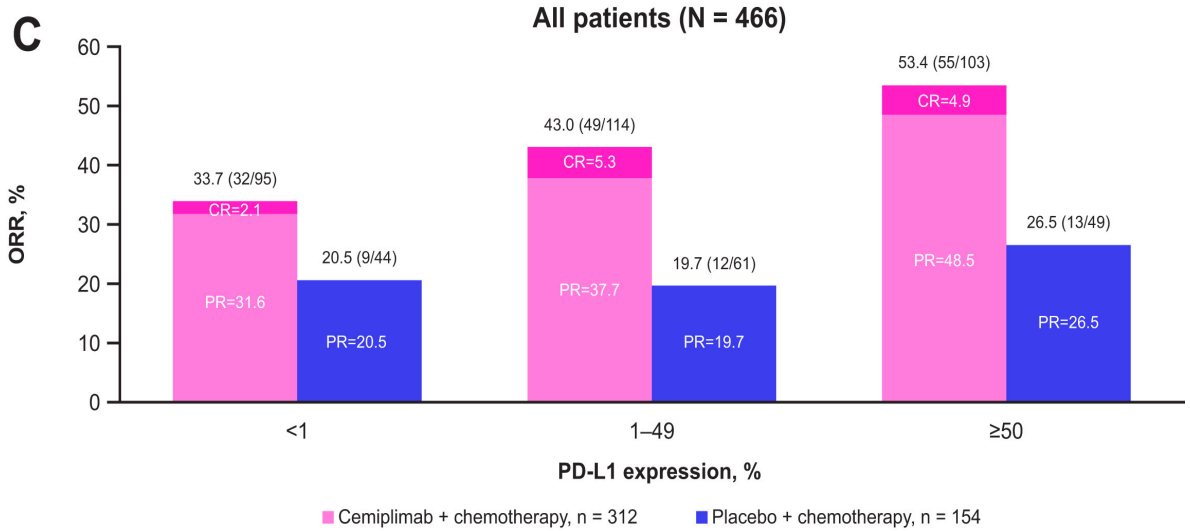
	Cemiplimab + chemo (PFS events/patients)	Placebo + chemo (PFS events/patients)	Hazard ratio (95% CI)
All patients	234/312	133/154	0.55 (0.44–0.68)
Age group			
<65 years	134/184	84/94	0.50 (0.38–0.66)
≥65 years	100/128	49/60	0.60 (0.42–0.85)
Sex			
Male	203/268	107/123	0.48 (0.38–0.62)
Female	31/44	26/31	0.71 (0.42–1.20)
Race			
White	208/267	119/138	0.55 (0.44–0.69)
Non-White	26/45	14/16	0.53 (0.28–1.02)
Histology			
Squamous	109/133	57/67	0.56 (0.41–0.78)
Nonsquamous	125/179	76/87	0.53 (0.39–0.71)
PD-L1 level			
<1%	77/95	39/44	0.73 (0.50–1.08)
1–49%	87/114	55/61	0.48 (0.34–0.68)
≥50%	70/103	39/49	0.48 (0.32–0.72)
ECOG performance status			
0	28/51	15/18	0.20 (0.10–0.42)
1	204/259	116/134	0.60 (0.48–0.76)
Geographic region			
Europe	211/270	119/138	0.55 (0.44–0.70)
Asia	23/42	14/16	0.48 (0.25–0.95)
Brain metastasis at baseline			
Yes	18/24	7/7	0.61 (0.25–1.48)
No	216/288	126/147	0.54 (0.43–0.70)
Cancer stage at screening			
Locally advanced	30/45	23/24	0.34 (0.19–0.61)
Metastatic	204/267	110/130	0.58 (0.46–0.74)
Smoking history			
Smokers	205/269	113/130	0.52 (0.41–0.66)
Non-smokers	29/43	20/24	0.66 (0.37–1.17)



2-Yr Follow-Up EMPOWER-Lung 3 Part 2: Tumor Response







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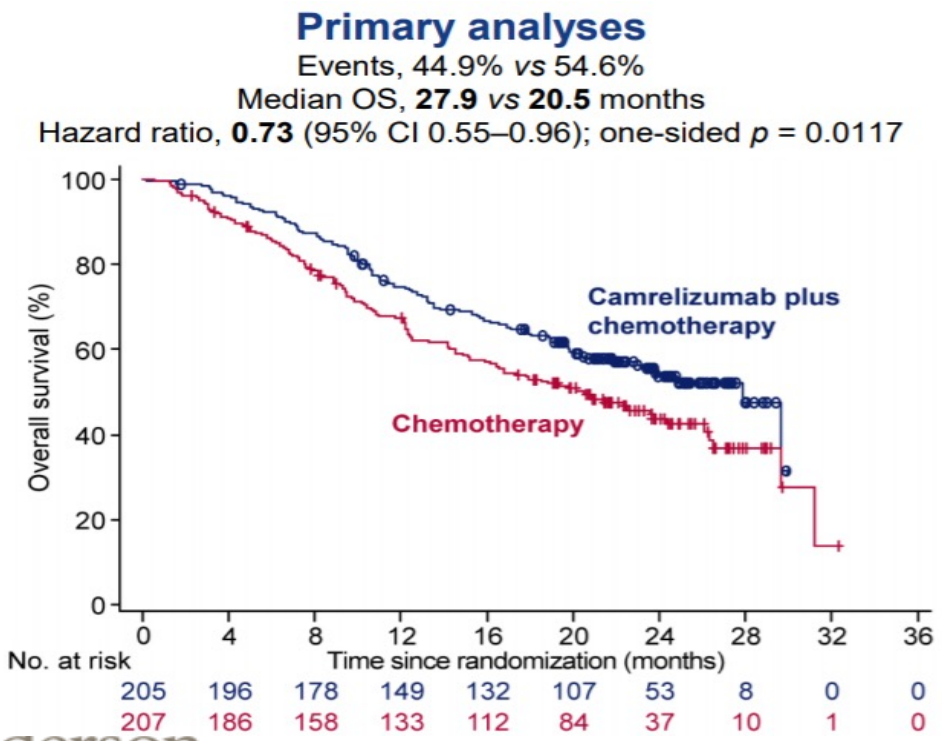
CameL: Camrelizumab + Chemo in 1L in Non-Squamous mNSCLC

Objective: CameL is a randomized, open-label, multicenter, phase 3 trial of camrelizumab + carboplatin and pemetrexed vs chemotherapy alone in chemotherapy-naive patients with advanced non-squamous NSCLC

Overall Survival (all patients)



Overall Survival in PD-L1 Positive Patients

	Camrelizumab plus chemotherapy	Chemotherapy
Events	38.4%	49.6%
Median OS	**NR**	**23.7** months
Hazard ratio	**0.70** (95% CI 0.48–1.02); one-sided p = 0.0318	

PFS2 (all patients)

	Camrelizumab plus chemotherapy	Chemotherapy
Events	60.0%	71.5%
Median PFS2	**18.9** months	**12.5** months
Hazard ratio	**0.66** (95% CI 0.52–0.84); one-sided p = 0.0004	

(Median follow-up: 19.3 months)

Zhou C, et al. WCLC 2020. Poster presentation P79.02.

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Tislelizumab + Chemo in 1L Advanced Squamous mNSCLC

Objective: Phase 3 randomized study of tislelizumab plus chemotherapy vs chemotherapy alone as 1L treatment for advanced squamous NSCLC

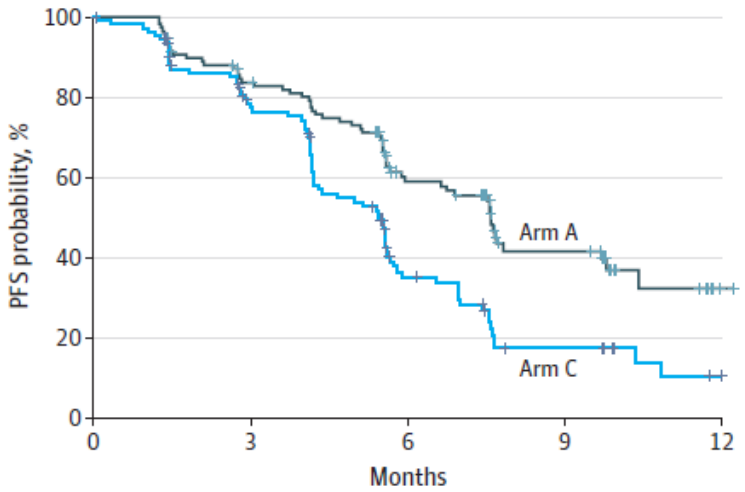
Arm A
Tislelizumab + paclitaxel + carboplatin

Arm B
Tislelizumab + nab-paclitaxel + carboplatin

Arm C
Paclitaxel + carboplatin

A Tislelizumab plus PC vs PC

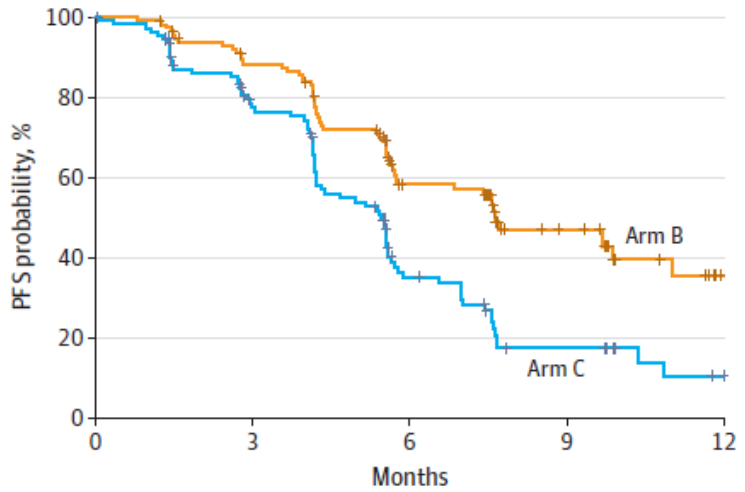
Source	Events, No. (%)	Median (95% CI)	Hazard ratio (95% CI)	*P* value
Arm A	60 (50.0)	7.6 (6.0-9.8)	0.52 (0.37-0.74)	<.001
Arm C	76 (62.8)	5.5 (4.2-5.7)		



No. at risk					
Arm A	120	95	50	23	1
Arm C	121	74	27	10	0

B Tislelizumab plus nab-PC vs PC

Source	Events, No. (%)	Median (95% CI)	Hazard ratio (95% CI)	*P* value
Arm B	56 (47.1)	7.6 (5.8-11.0)	0.48 (0.34-0.68)	<.001
Arm C	76 (62.8)	5.5 (4.2-5.7)		



No. at risk					
Arm B	119	98	47	23	1
Arm C	121	74	27	10	0

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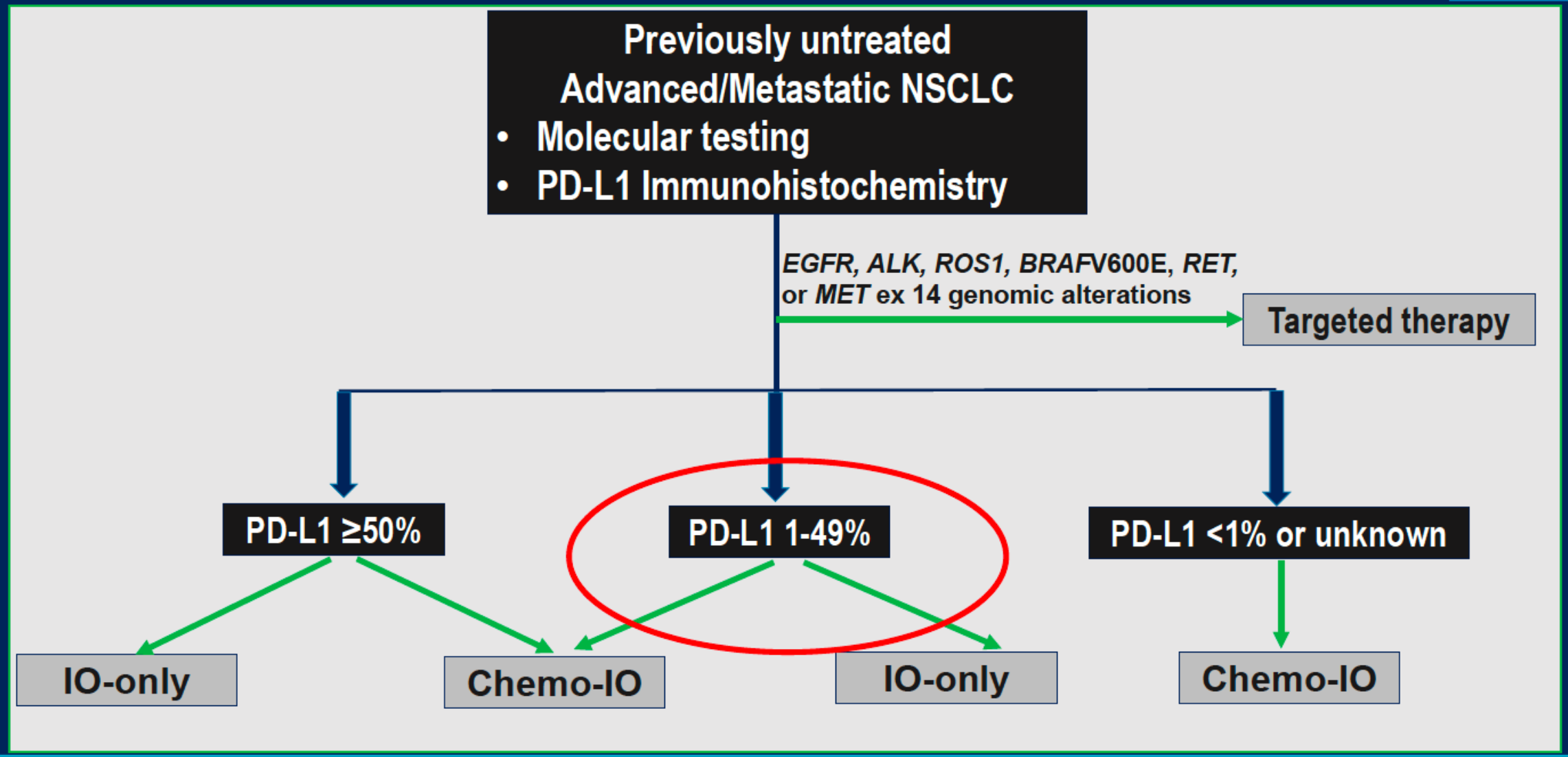
Wang J, et al. JAMA Oncol. 2021;e210366.

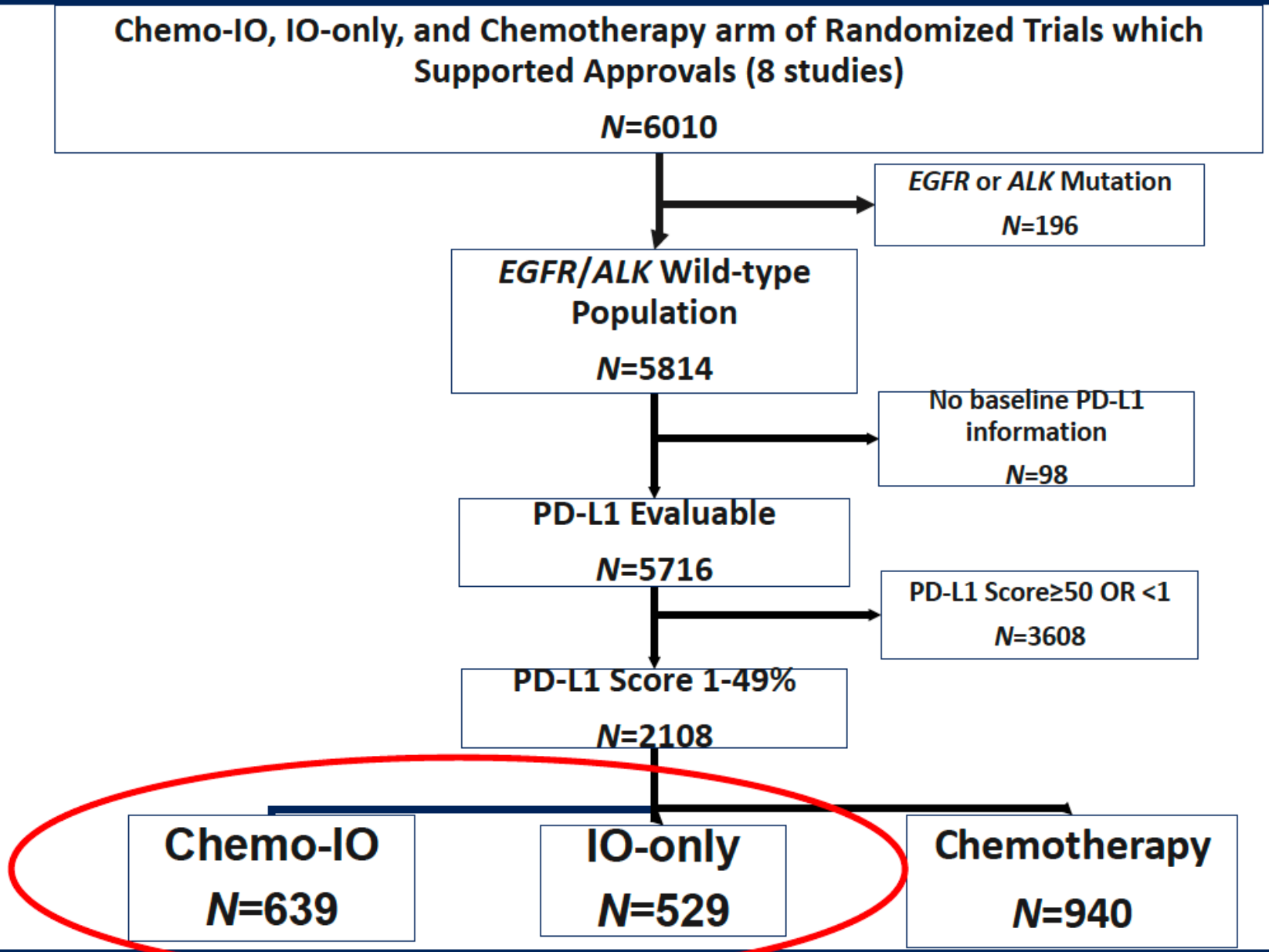
Background



Trials supporting FDA approval of first-line Chemo-IO and IO-only regimens

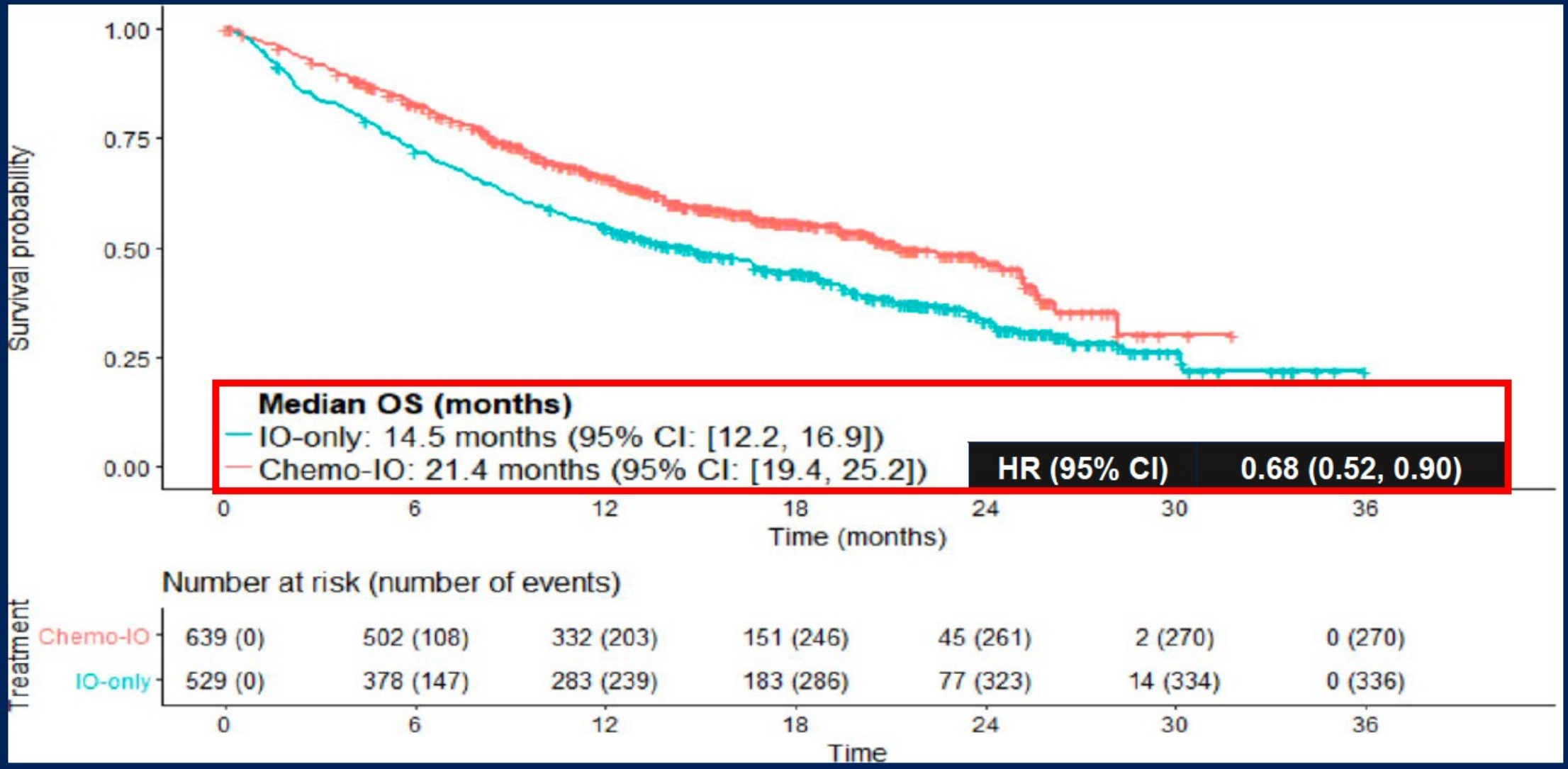
Trial*	Active treatment
Immunotherapy-only (PD-L1 ≥1%)	
KEYNOTE-042	**Pembrolizumab**
CHECKMATE-227	**Nivolumab plus Ipilimumab**
Chemo-immunotherapy	
KEYNOTE-189	**Pembrolizumab** plus Platinum-doublet chemo
KEYNOTE-407	**Pembrolizumab** plus Platinum-doublet chemo
KEYNOTE-021 (cohort G)	**Pembrolizumab** plus Platinum-doublet chemo
IMPOWER-150**	**Atezolizumab** plus Bevacizumab plus Platinum-doublet chemo
IMPOWER-130	**Atezolizumab** plus Platinum-doublet chemo
CA2099LA	**Nivolumab plus Ipilimumab** plus Platinum-doublet chemo

*Control arms: Platinum-doublet chemotherapy
**Control arm in IMPOWER-150: Bevacizumab plus Platinum-doublet chemotherapy



Exploratory OS: NSCLC PDL1 1-49%

FDA

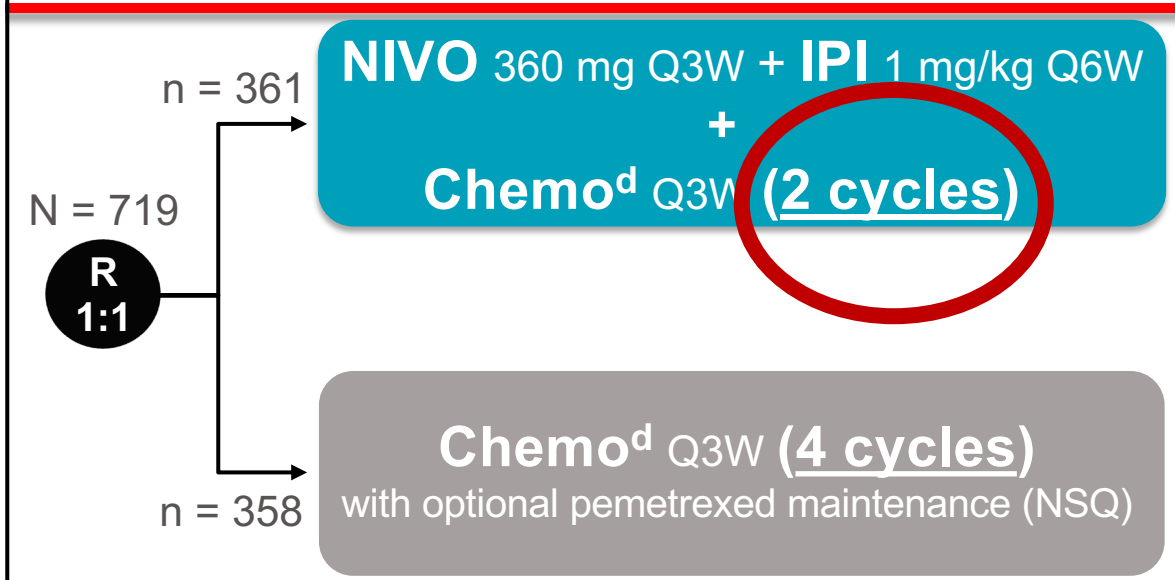


CheckMate 9LA study design[a]

Key eligibility criteria

- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No sensitizing *EGFR* mutations or known *ALK* alterations
- ECOG PS 0–1

Stratified by PD-L1[b] (< 1%[c] vs ≥ 1%), sex, and histology (SQ vs NSQ)



Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

Primary endpoint
- OS

Secondary endpoints
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

Exploratory endpoints
- Safety

DBL: February 18, 2021; minimum / median follow-up for OS: 24.4 months / 30.7 months.

[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

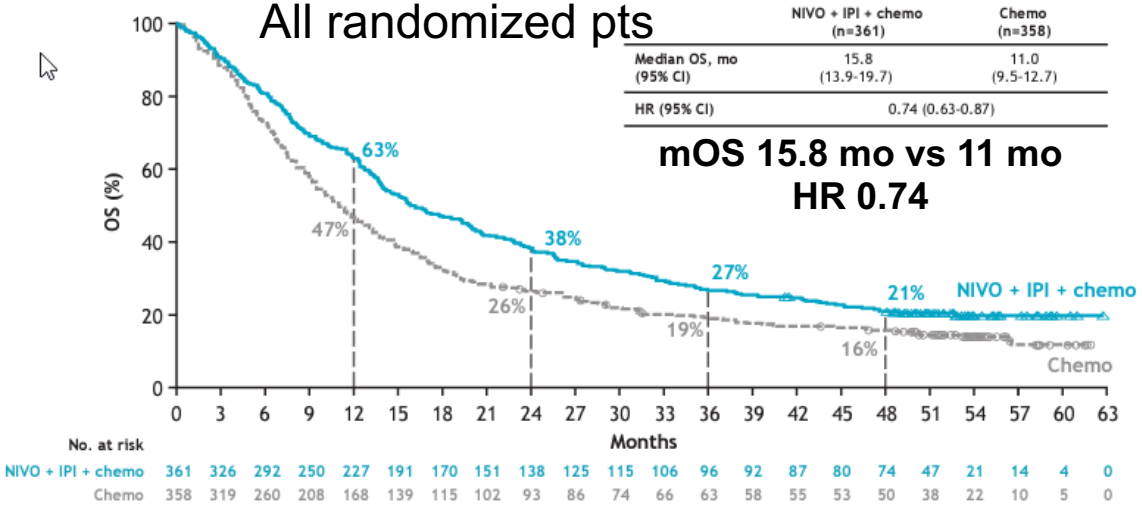
Reck Met al. *J Clin Oncol*. 2021;39(suppl_15):9000.

CM9LA with 4 yr follow up: OS by PD-L1 expression status

All randomized pts

	NIVO + IPI + chemo (n=361)	Chemo (n=358)
Median OS, mo (95% CI)	15.8 (13.9-19.7)	11.0 (9.5-12.7)
HR (95% CI)	0.74 (0.63-0.87)	

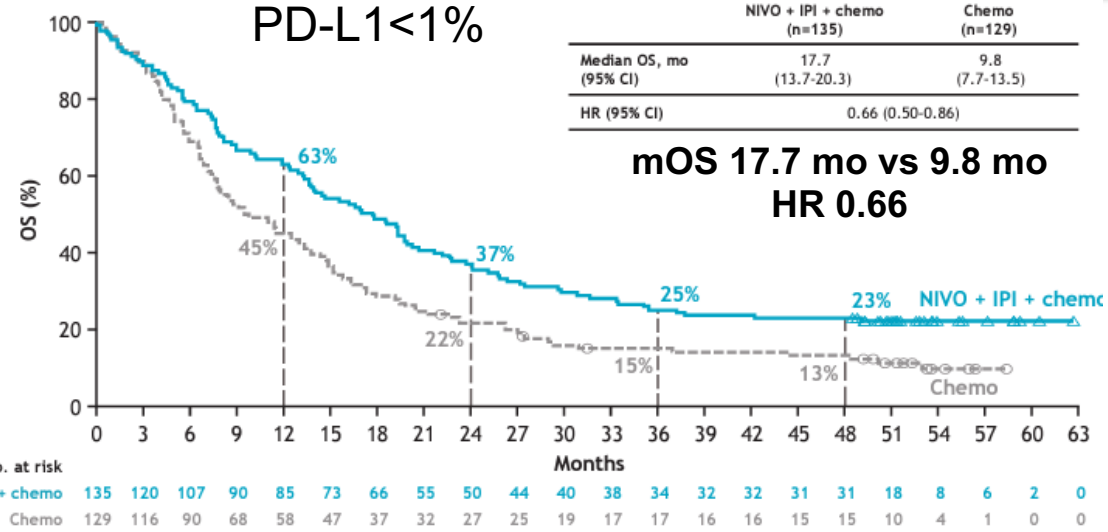
mOS 15.8 mo vs 11 mo
HR 0.74



PD-L1<1%

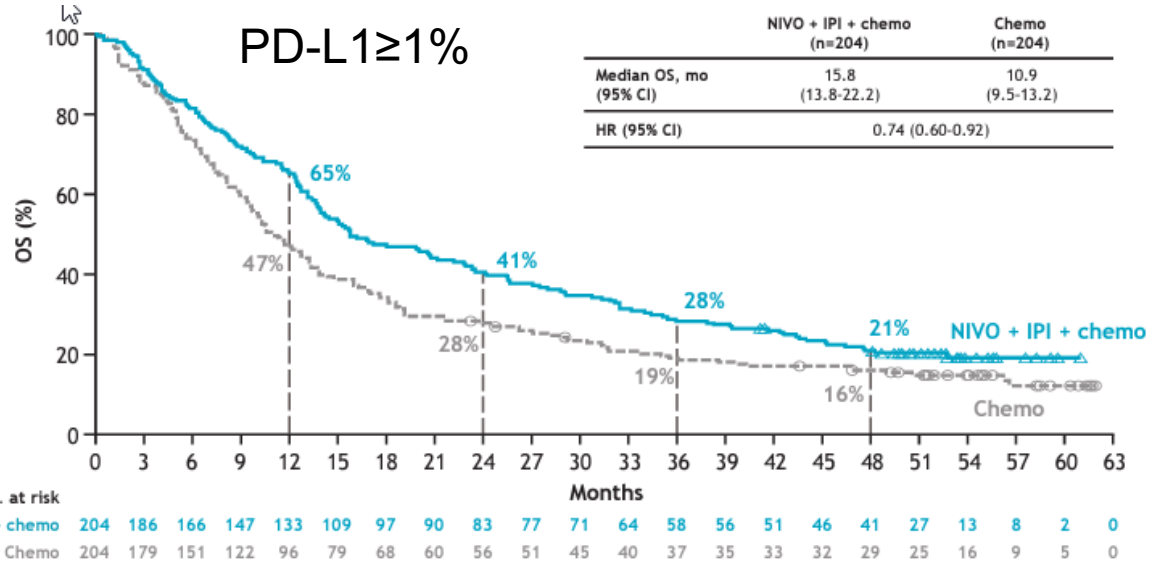
	NIVO + IPI + chemo (n=135)	Chemo (n=129)
Median OS, mo (95% CI)	17.7 (13.7-20.3)	9.8 (7.7-13.5)
HR (95% CI)	0.66 (0.50-0.86)	

mOS 17.7 mo vs 9.8 mo
HR 0.66



PD-L1≥1%

	NIVO + IPI + chemo (n=204)	Chemo (n=204)
Median OS, mo (95% CI)	15.8 (13.8-22.2)	10.9 (9.5-13.2)
HR (95% CI)	0.74 (0.60-0.92)	



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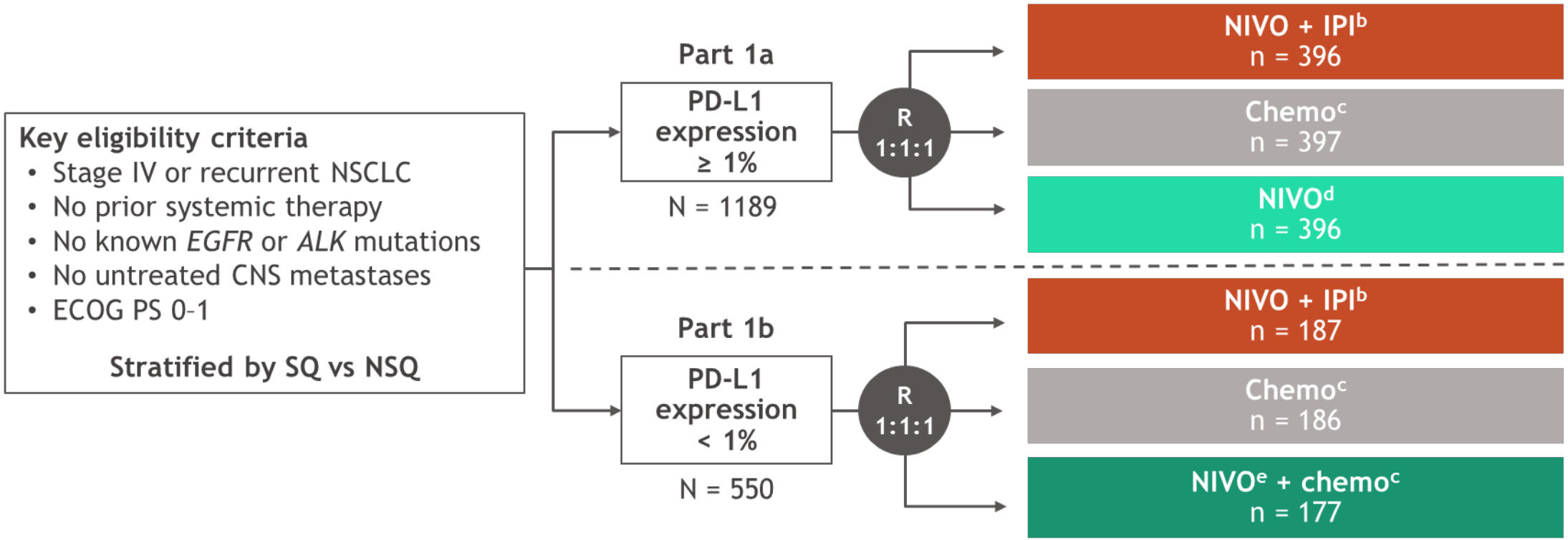
Carbone D et al, JITC 2023

CM227 trial: Nivo+Ipi in patients with mNSCLC



Independent primary endpoints (NIVO + IPI vs chemo)[f]
- PFS in patients with high TMB (≥ 10 mut/Mb)
- OS in patients with tumor PD-L1 ≥ 1%

Exploratory analyses
- OS by response[g] and tumor burden reduction[h]
- OS by baseline HRQoL[i]

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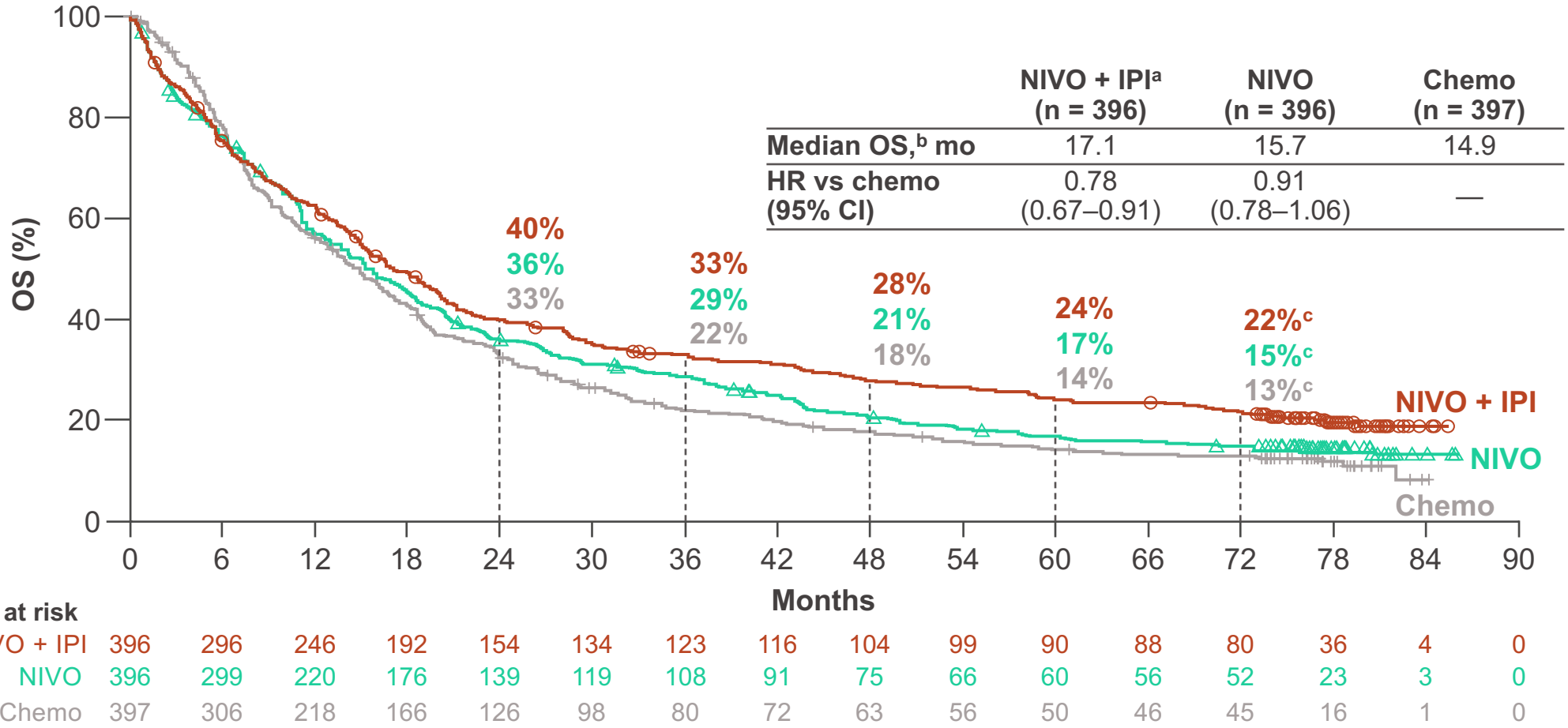
Ramalingam S, WCLC 2023

OS in patients with tumor PD-L1 ≥ 1%



	NIVO + IPI[a] (n = 396)	NIVO (n = 396)	Chemo (n = 397)
Median OS,[b] mo	17.1	15.7	14.9
HR vs chemo (95% CI)	0.78 (0.67–0.91)	0.91 (0.78–1.06)	—

No. at risk																
NIVO + IPI	396	296	246	192	154	134	123	116	104	99	90	88	80	36	4	0
NIVO	396	299	220	176	139	119	108	91	75	66	60	56	52	23	3	0
Chemo	397	306	218	166	126	98	80	72	63	56	50	46	45	16	1	0

– In an exploratory analysis of OS by histology in patients with tumor PD-L1 ≥ 1%, 6-year OS rates with NIVO + IPI vs chemo were 25% vs 16% (NSQ) and 14% vs 5% (SQ)[d]

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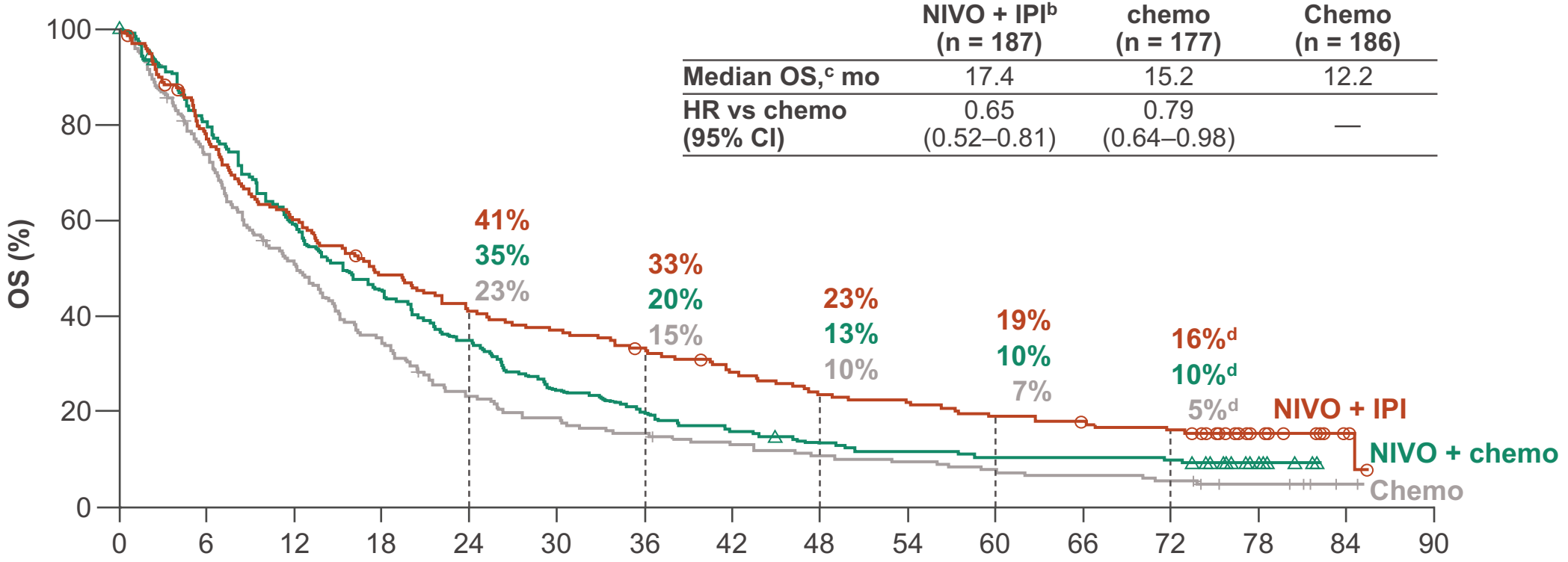
Ramalingam S, WCLC 2023

OS in patients with tumor PD-L1 < 1%[a]

	NIVO + IPI[b] (n = 187)	NIVO + chemo (n = 177)	Chemo (n = 186)
Median OS,[c] mo	17.4	15.2	12.2
HR vs chemo (95% CI)	0.65 (0.52–0.81)	0.79 (0.64–0.98)	—



No. at risk																
NIVO + IPI	187	142	110	88	74	67	59	49	41	38	33	30	27	11	3	0
NIVO + chemo	177	139	102	78	60	42	34	27	22	19	17	17	16	5	0	0
Chemo	186	135	92	62	41	33	27	22	18	16	12	11	9	5	1	0

- In an exploratory analysis of OS by histology in patients with tumor PD-L1 < 1%, 6-year OS rates with NIVO + IPI vs chemo were 15% vs 6% (NSQ) and 18% and 4% (SQ)[e]

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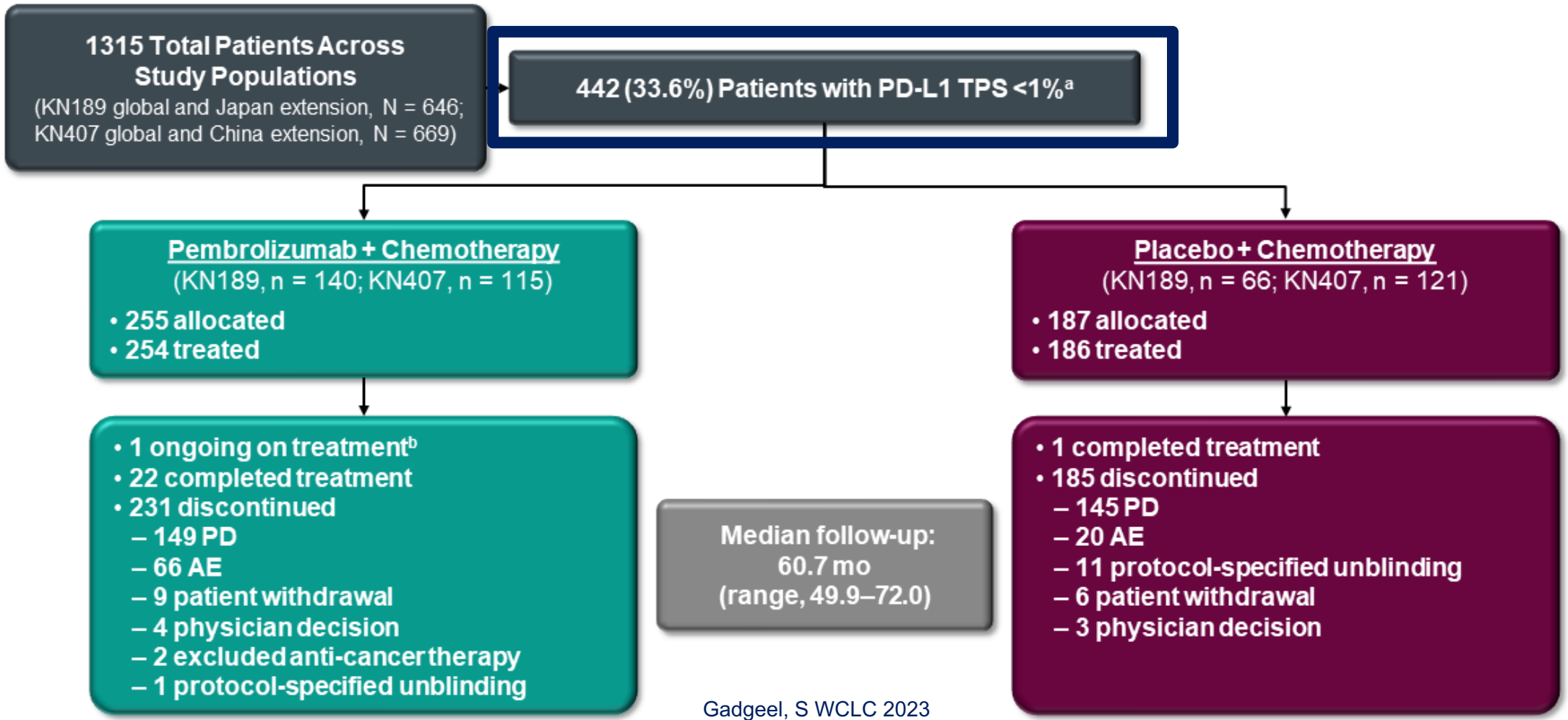
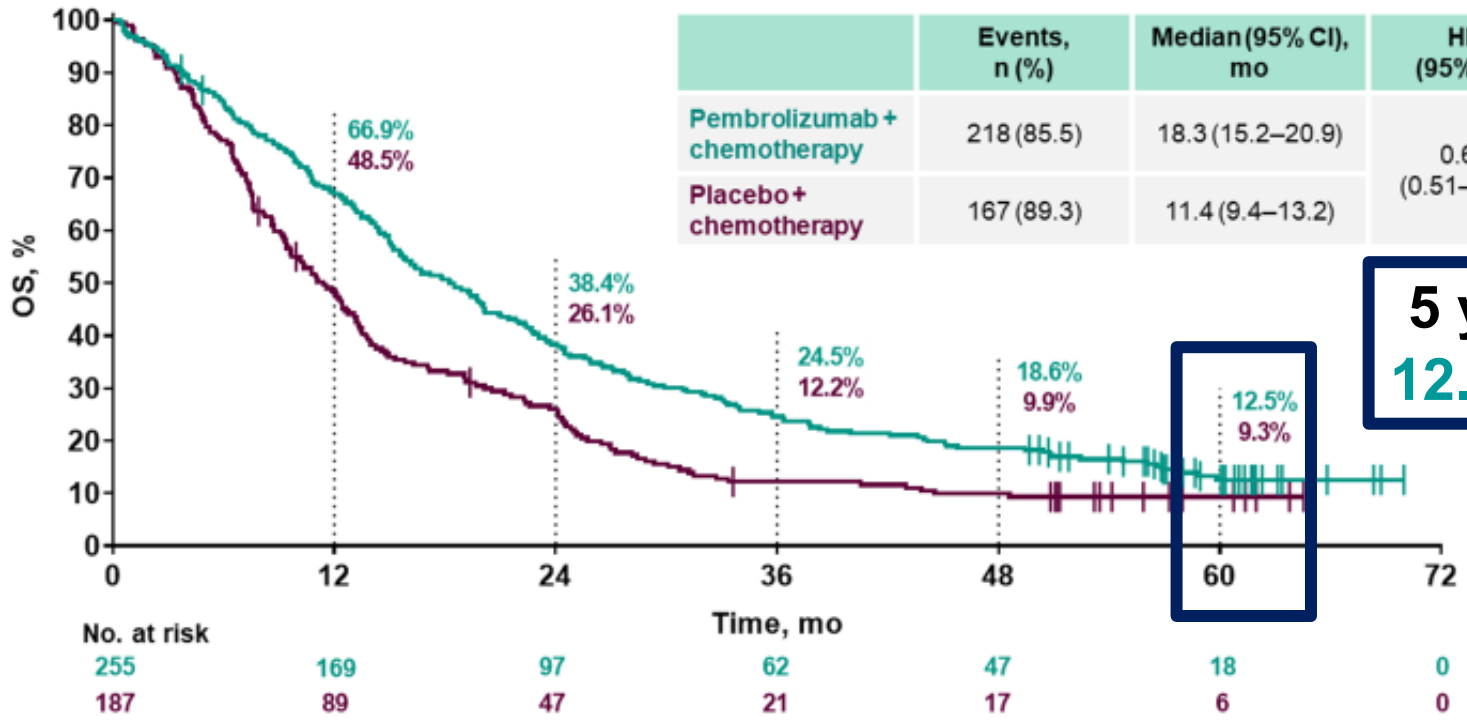
Ramalingam S, WCLC 2023

Pooled KN189 and KN407 pt population with PD-L1<1% mNSCLC



Gadgeel, S WCLC 2023

Pooled KN189 and KN407 5 yr OS in pts with PD-L1<1% mNSCLC



	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembrolizumab + chemotherapy	218 (85.5)	18.3 (15.2–20.9)	0.64 (0.51–0.79)
Placebo + chemotherapy	167 (89.3)	11.4 (9.4–13.2)	

5 yr OS rates
12.5% vs 9.3%

mOS 18.3 mo vs 11.4 mo
HR 0.64 (0.51-0.79)

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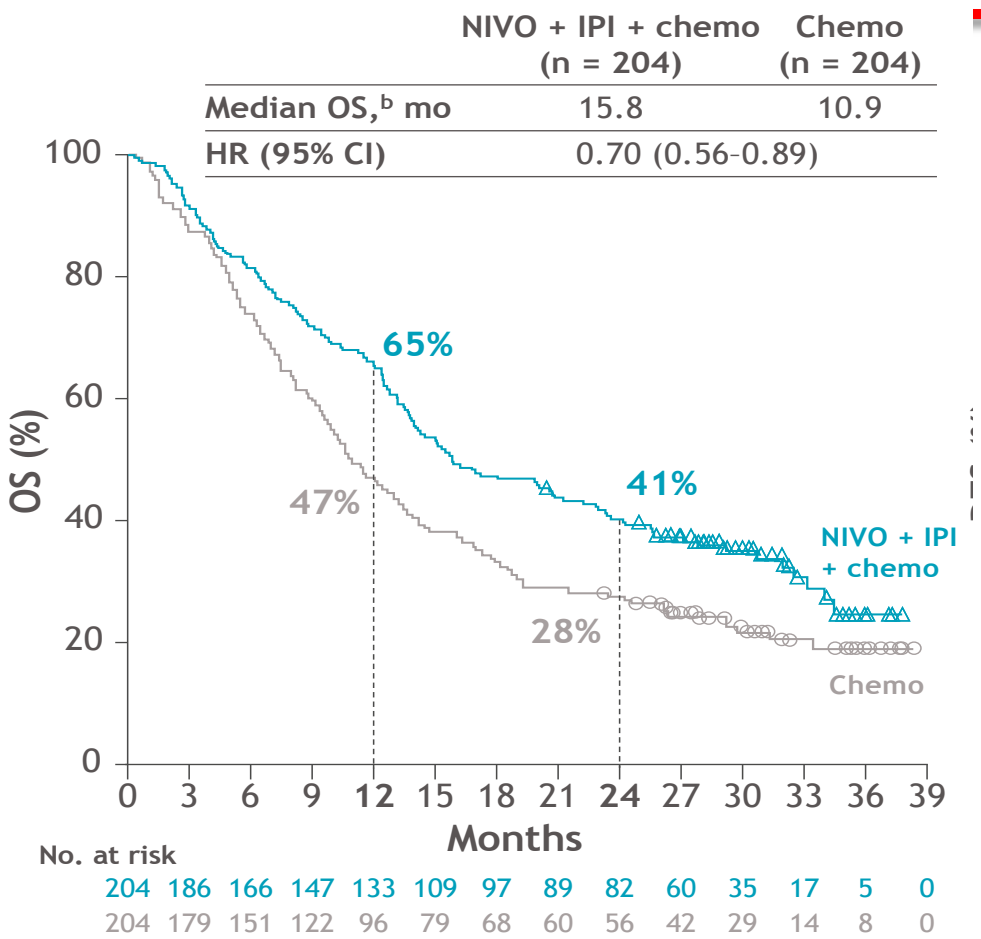
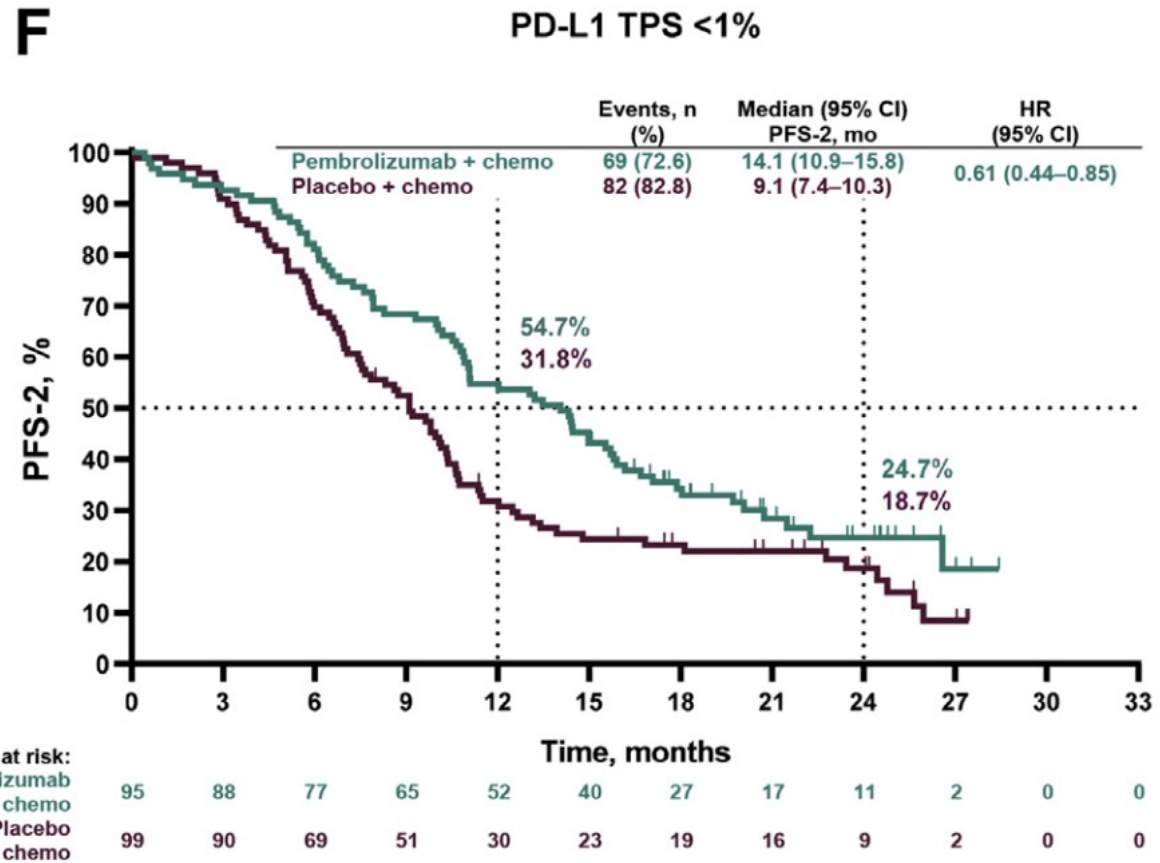
Gadgeel, S WCLC 2023

SQUAMOUS PD-L1 <1% 9LA vs 407

OS





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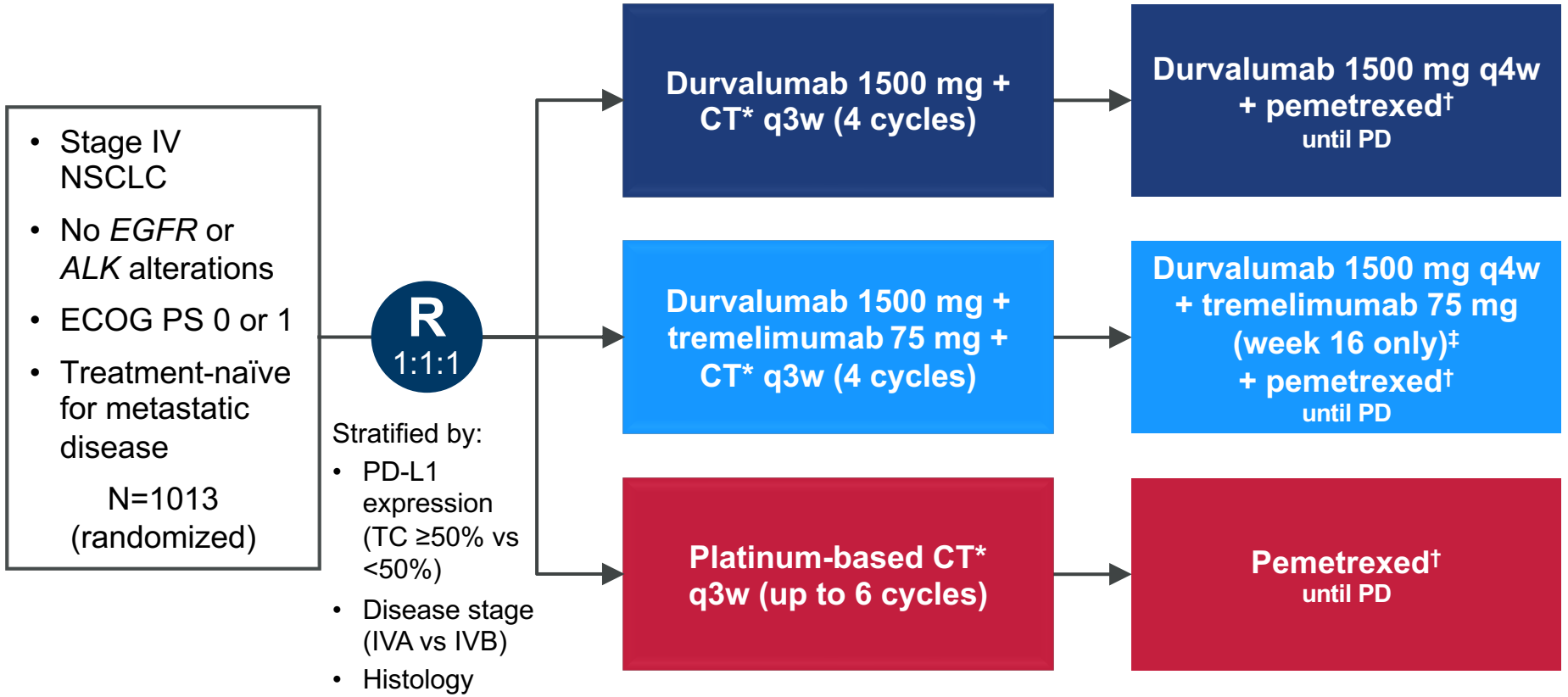
9LA **KN 407**

POSEIDON Study Design

Phase 3, global, randomized, open-label, multicenter study



Primary endpoints
- PFS by BICR (D+CT vs CT)
- OS (D+CT vs CT)

Key secondary endpoints
- PFS by BICR (D+T+CT vs CT)
- OS (D+T+CT vs CT)
- OS in patients with bTMB ≥20 mut/Mb (D+T+CT vs CT)

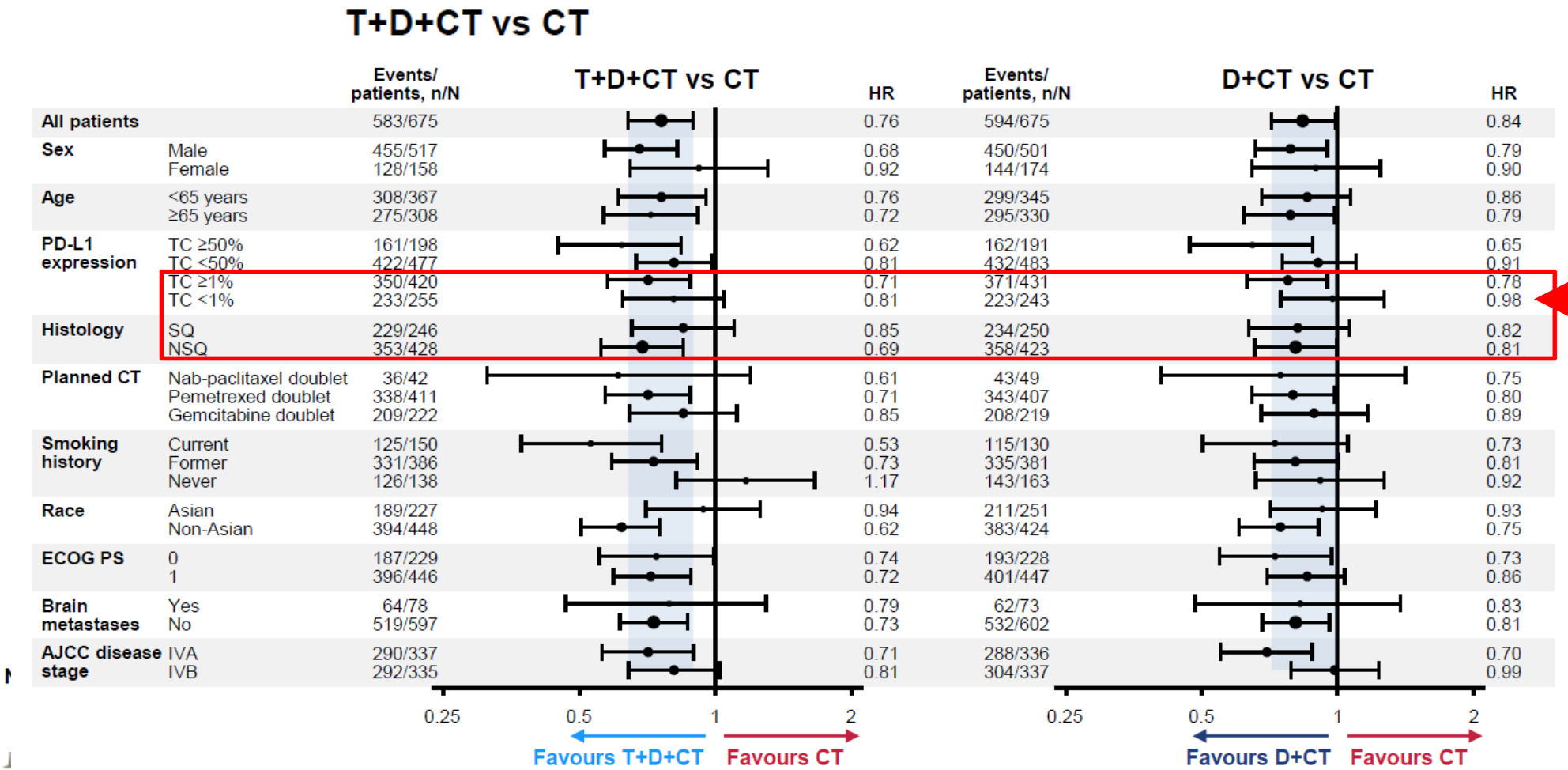
Additional secondary endpoints
- ORR, DoR, and BOR by BICR
- PFS at 12 months
- HRQoL
- Safety and tolerability

*CT options: gemcitabine + carboplatin/cisplatin (squamous), pemetrexed + carboplatin/cisplatin (non-squamous), or nab-paclitaxel + carboplatin (either histology);
†Patients with non-squamous histology who initially received pemetrexed during first-line treatment only (if eligible); ‡Patients received an additional dose of tremelimumab post CT (5th dose)

BICR, blinded independent central review; BOR, best objective response; bTMB, blood tumor mutational burden; D, durvalumab; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; Mb, megabase; mut, mutations; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; q4w, every 4 weeks; T, tremelimumab; TC, tumor cell

Rizvi NA, et al. *JAMA Oncol.* 2020;6(5):661-674.

POSEIDON 5 yr OS in pts with mNSCLC (ITT)



T+D+CT vs CT
PD-L1 <1%
HR 0.81

D+CT vs CT
PD-L1 <1%
HR 0.98

Median follow-up in censored patients at DCO: 63.4 months (range 0.0–73.9)

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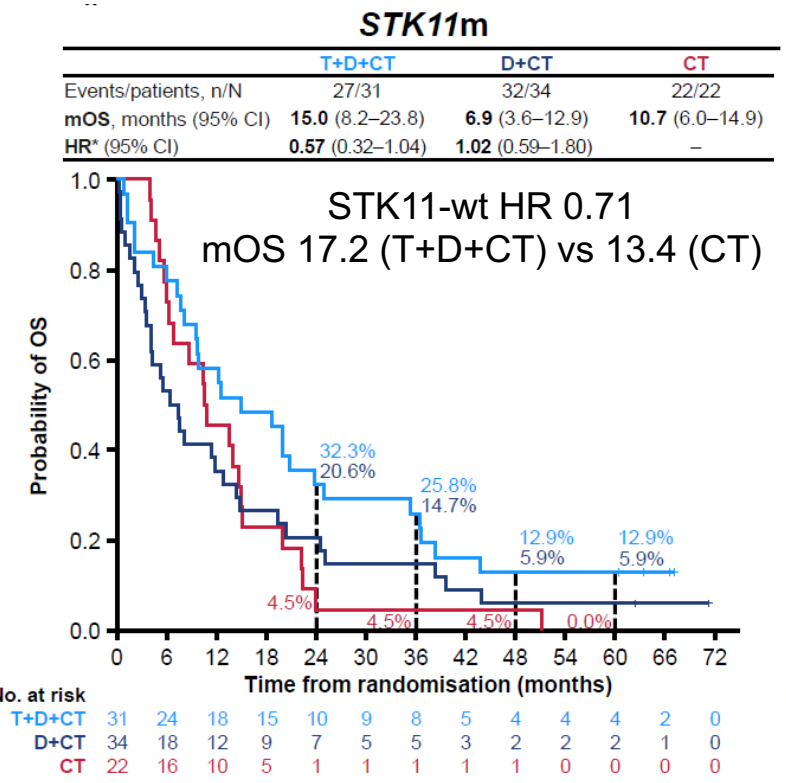
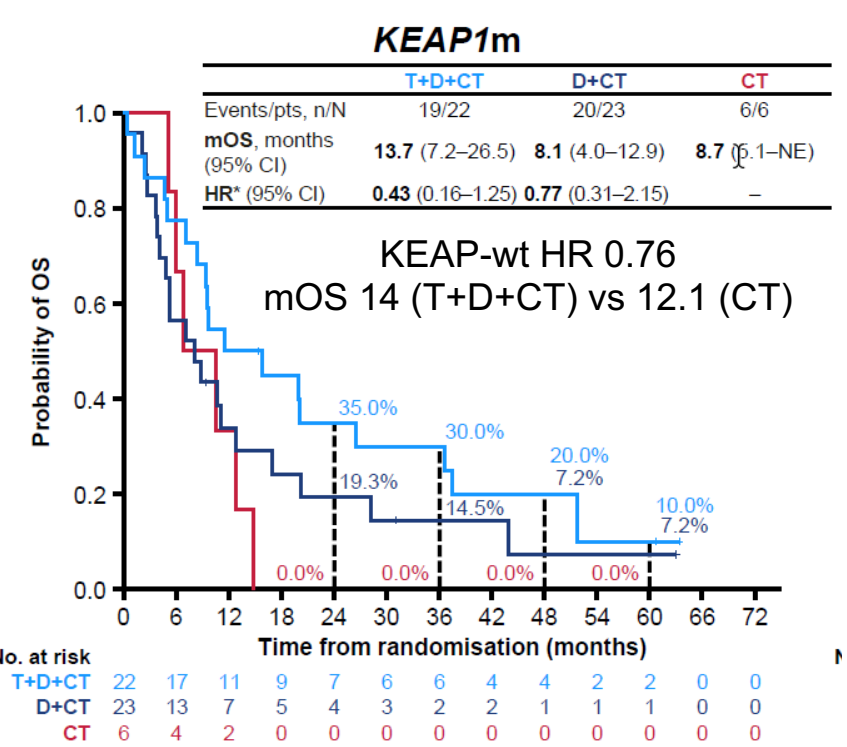
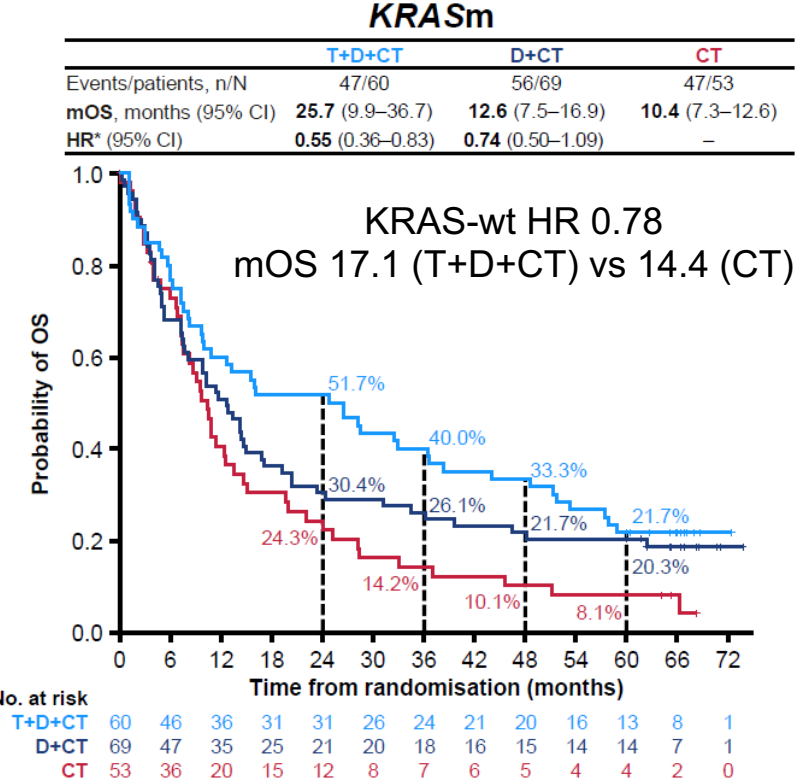
Peters S, ESMO-IO 2023

Some molecular subgroups enriched in PD-L1 <1% pts may benefit from dual IO: Prospective trials are needed







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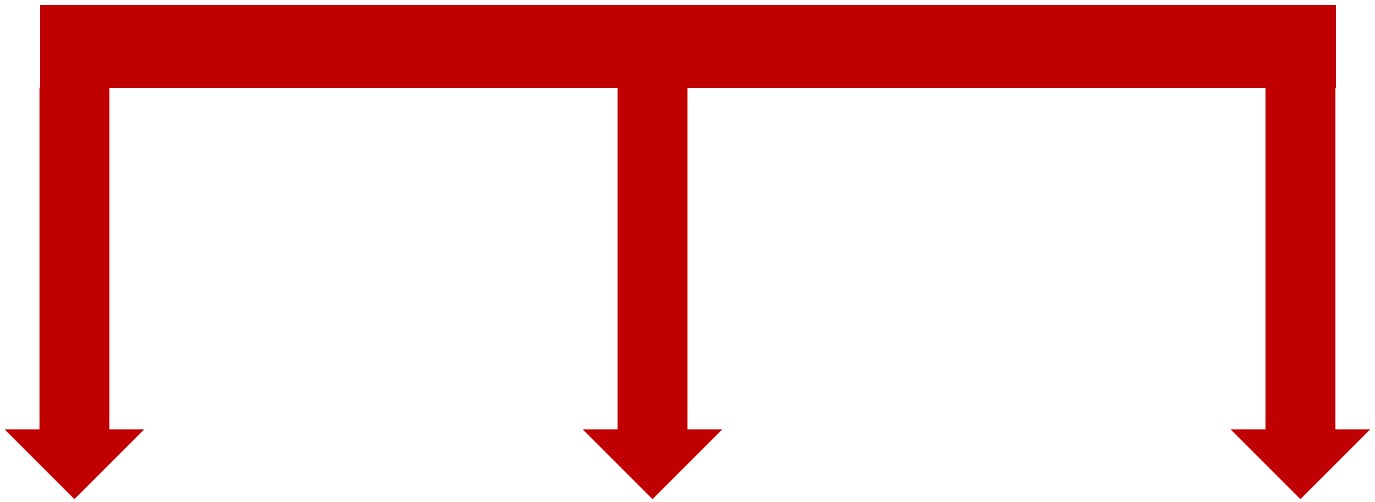
Conclusions

Patients with wilde-type tumor



PD-L1>50%	PD-L1 1-49%	PD-L1 <1%
Pembrolizumab Cemiplimab Atezolizumab	Chemotherapy+immunotherapy	Chemotherapy+immunotherapy (Consider anti CTLA4)

(Chemo+immunotherapy an option if high tumor burden/symptoms)

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