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Frontline treatment of advanced NSCLC without actionable driver mutations

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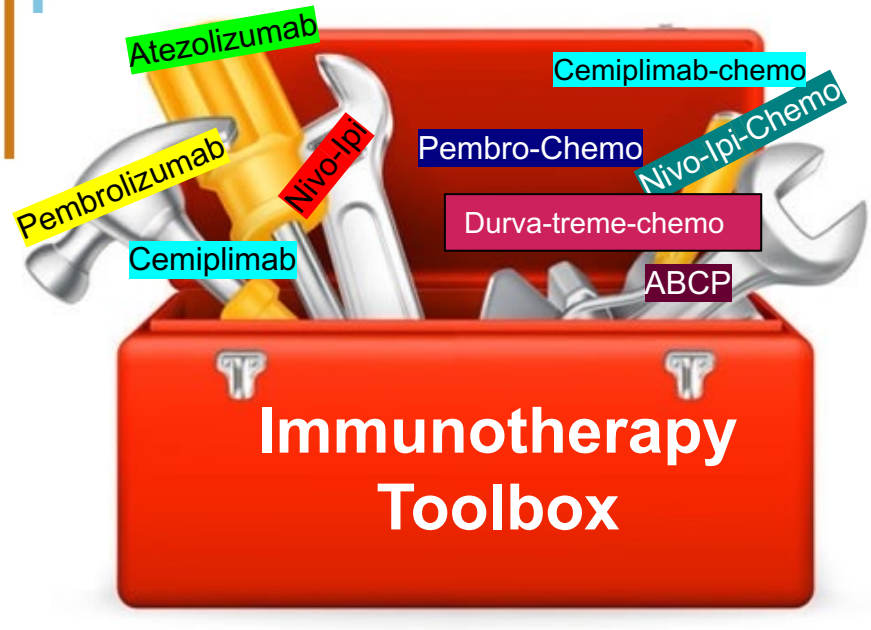
Immunotherapy in advanced NSCLC: An Ever-Evolving Landscape



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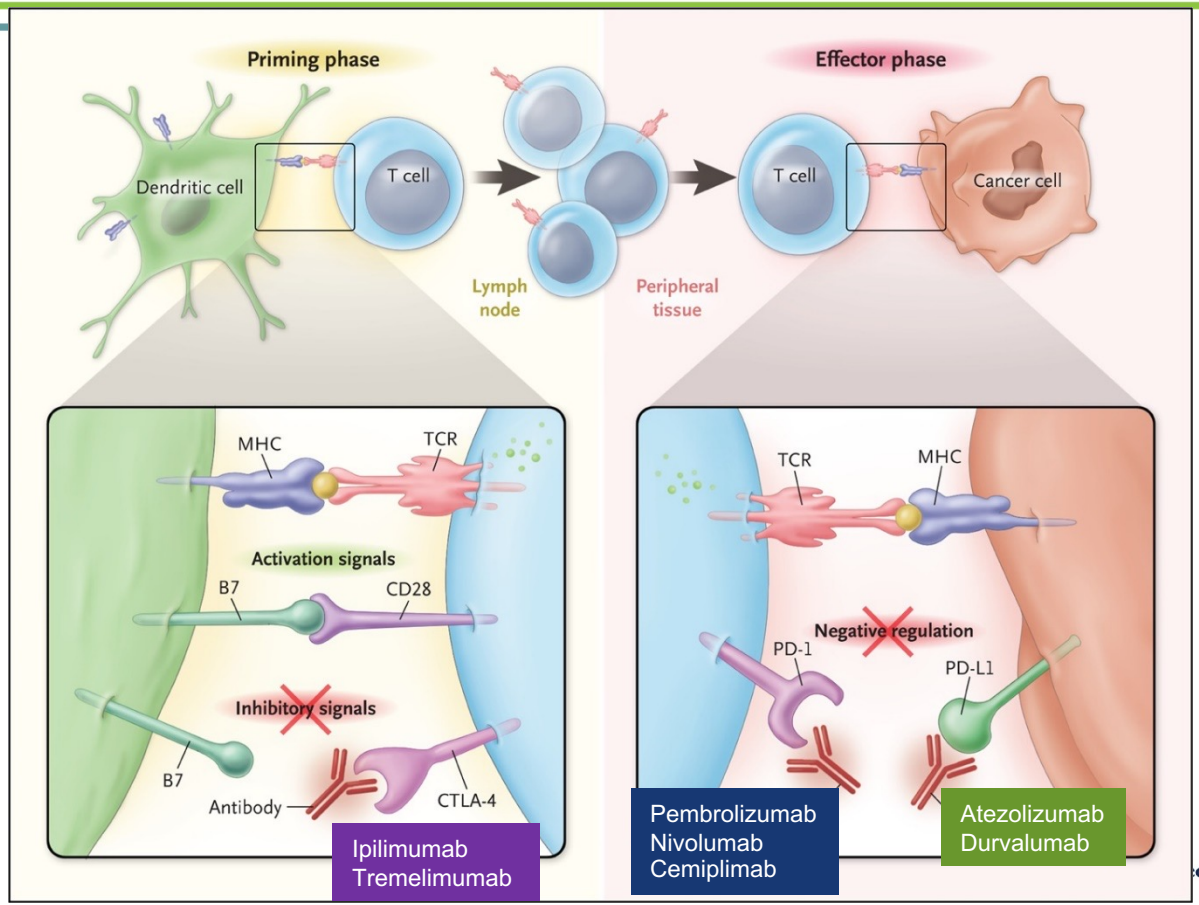
Platinum-based doublet chemotherapy

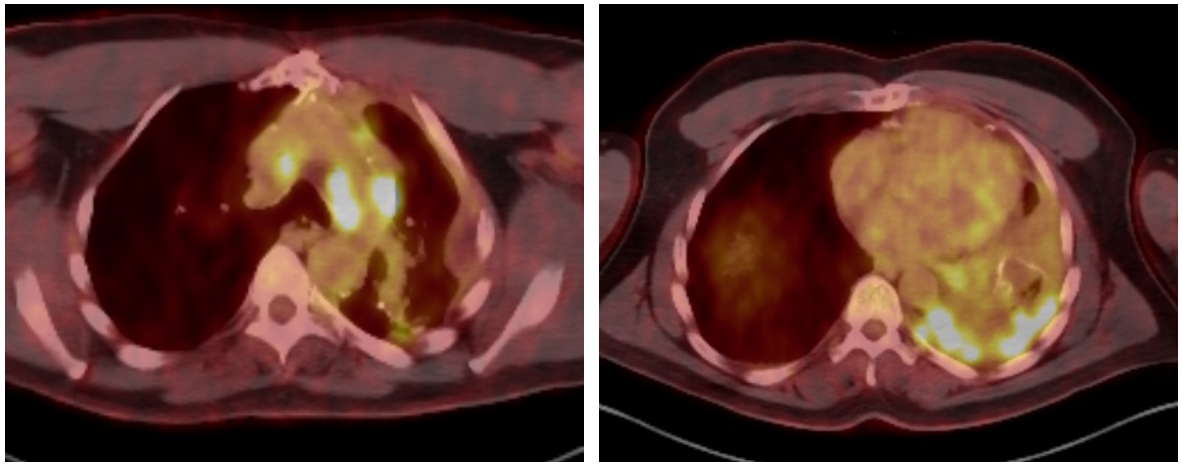
Mechanisms of PD-1 and CTLA-4 Immunotherapy



Ribas *et al.* N Engl J Med. 2012

76-year-old male with stage IV NSCLC

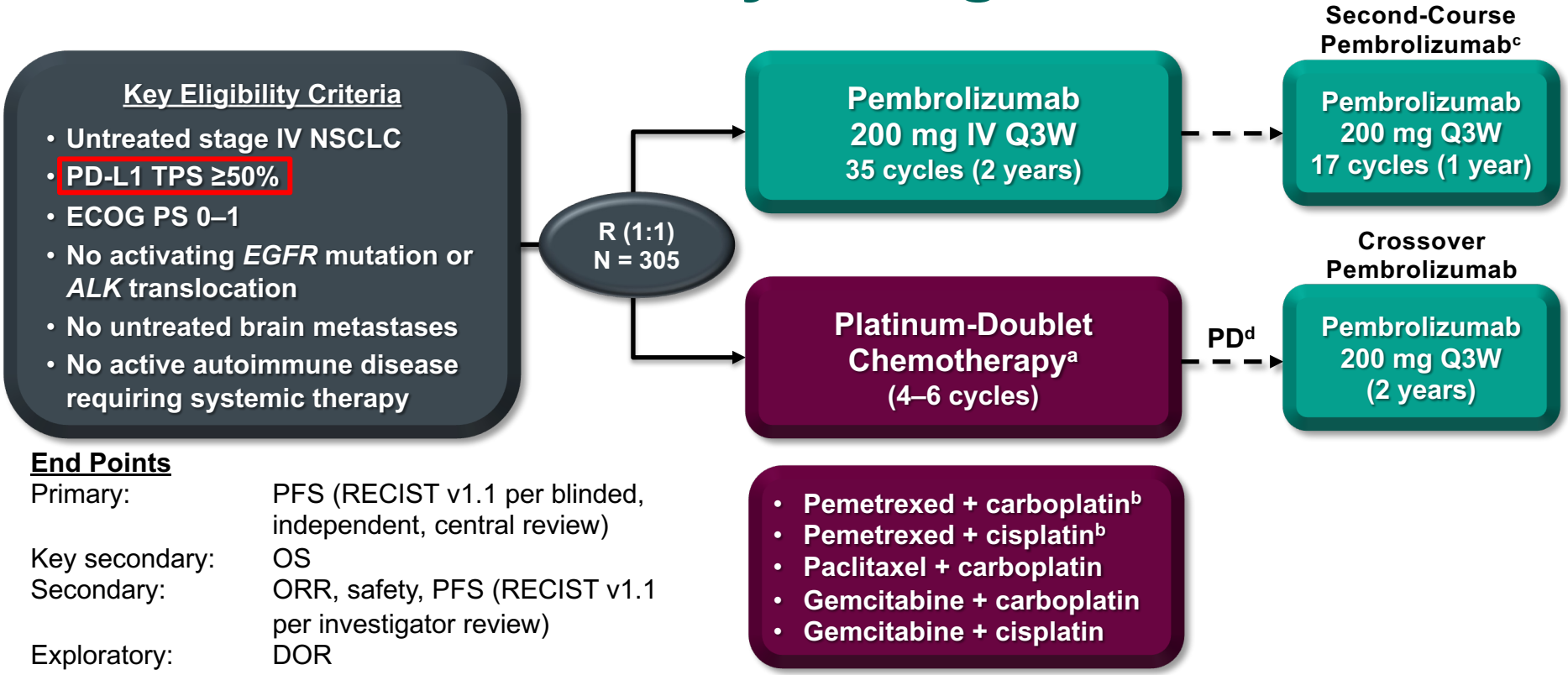
- Has a history of stage IIIA (T4N0M0) NSCLC in 2015 s/p left lower lobectomy, left upper wedge resection, 4 cycles of adjuvant chemotherapy
- Development respiratory symptoms in 2019
- Imaging showed left pleural effusion and pleural nodules/thickening
- Bronchoscopic evaluation revealed recurrence of lung adenocarcinoma
- Molecular profiling: PD-L1 50% (22C3), *KRAS* G12C



Anti-PD-(L)1 Monotherapy

KEYNOTE-024

KEYNOTE-024 Study Design



End Points

Primary:	PFS (RECIST v1.1 per blinded, independent, central review)
Key secondary:	OS
Secondary:	ORR, safety, PFS (RECIST v1.1 per investigator review)
Exploratory:	DOR

[a]Optional pemetrexed maintenance therapy for nonsquamous disease. [b]Permitted for nonsquamous disease only. [c]Patients randomized to pembrolizumab who completed 2 years of therapy or who stopped pembrolizumab after achieving CR and then had PD were eligible for a second course of pembrolizumb monotherapy. [d]Before the DMC recommendation and amendment 8, which permitted those in the chemotherapy arm to be offered pembrolizumab (based on interim analysis 2 data), patients were eligible for crossover when PD was confirmed by blinded, independent, central radiology review.

Brahmer *et al.* ESMO 2020

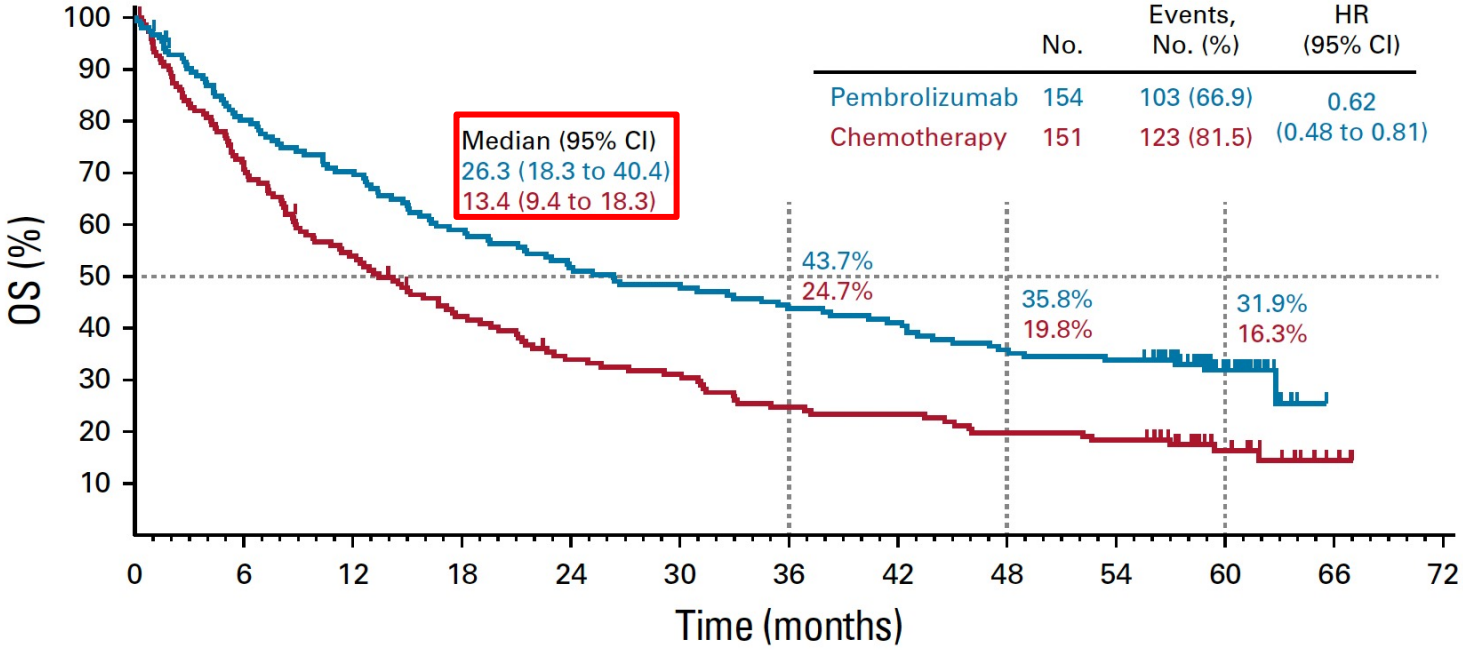
KEYNOTE-024 Objective Response
By RECIST v1.1 per Investigator Review

	Pembrolizumab N = 154	Chemotherapy N = 151
Objective response, n (%)	71 (46.1)	47 (31.1)
Best objective response, n (%)		
Complete response	7 (4.5)	0
Partial response	64 (41.6)	47 (31.1)
Stable disease	37 (24.0)	60 (39.7)
Progressive disease	35 (22.7)	25 (16.6)
Not evaluable	0	1 (0.7)
No assessment	11 (7.1)	18 (11.9)
Time to response, median (range), mo	2.1 (1.4–14.6)	2.1 (1.1–12.2)
DOR, median (range), mo	29.1 (2.2–60.8+)	6.3 (3.1–52.4)

"+", indicates response duration is censored; DOR, duration of response.
ITT population.
Data cutoff: June 1, 2020.

Brahmer *et al.* ESMO 2020

KEYNOTE-024: 5-Year Overall Survival



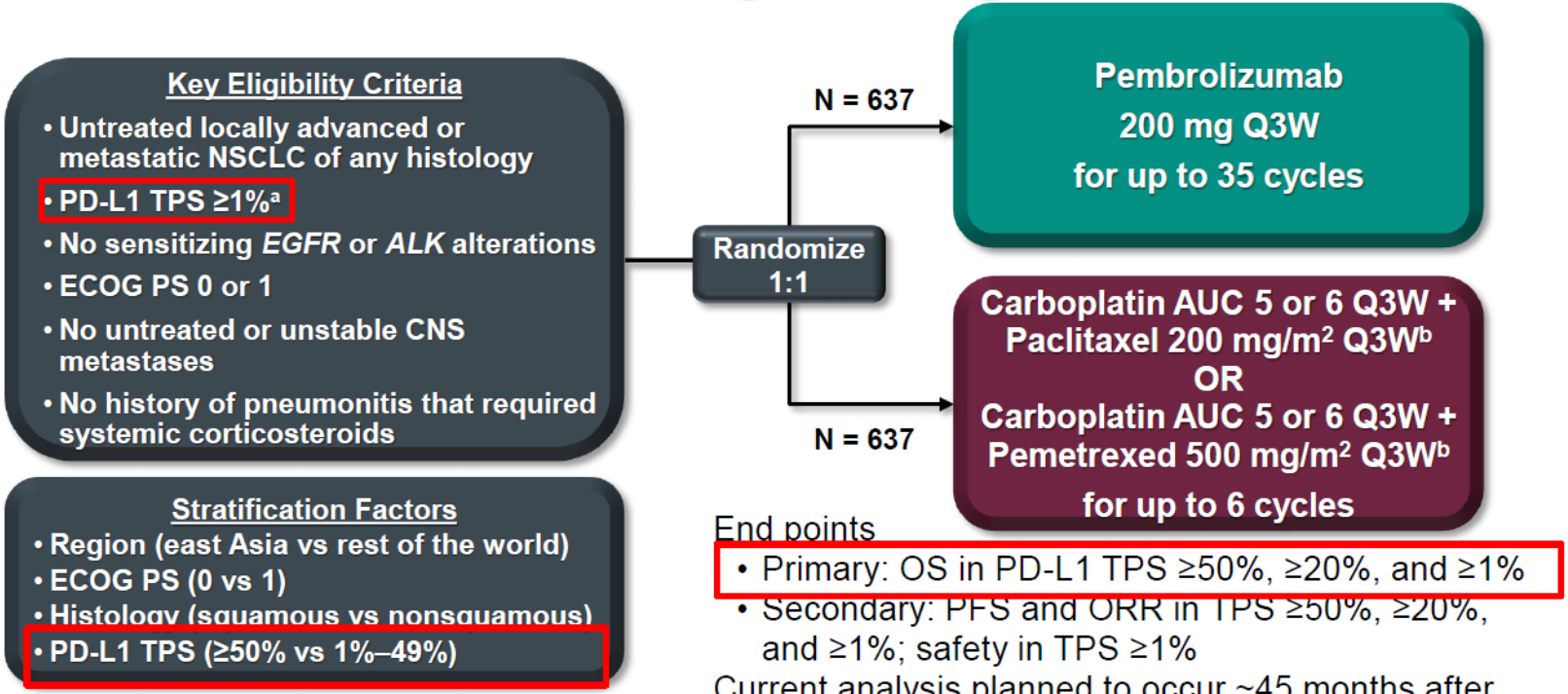
ITT population.

[b]Effective crossover rate from chemotherapy to anti–PD-L1 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-L1 therapy outside of crossover; patients may have received >1 subsequent anti–PD-L1 therapy). Data cutoff: June 1, 2020.

Reck *et al.* JCO 2021

KEYNOTE - 042

KEYNOTE-042 Study Design



End points
- Primary: OS in PD-L1 TPS ≥50%, ≥20%, and ≥1%
- Secondary: PFS and ORR in TPS ≥50%, ≥20%, and ≥1%; safety in TPS ≥1%

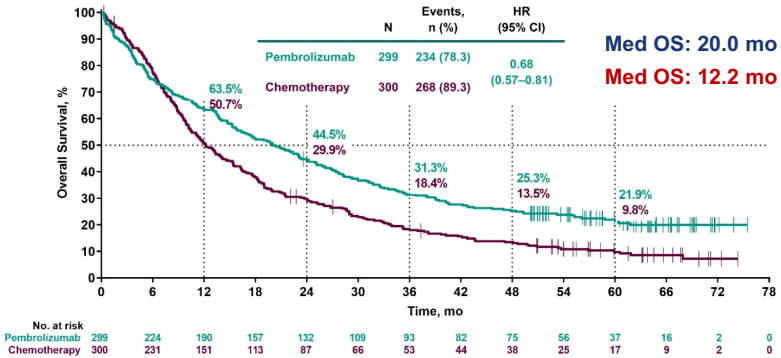
Current analysis planned to occur ~45 months after study start

CNS, central nervous system.
[a]Assessed in formalin-fixed tumor samples using PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies, Carpinteria, CA, USA), with expression measured using TPS (defined as the percentage of tumor cells with membranous PD-L1 staining).
[b]Pemetrexed maintenance therapy was optional but strongly encouraged for patients with nonsquamous histology.

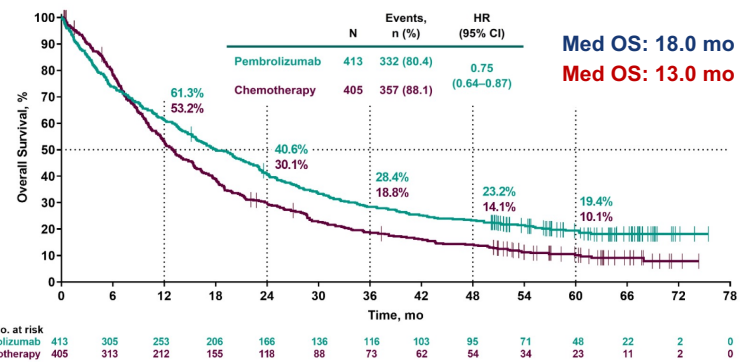
Mok *et al.* ESMO 2019

KEYNOTE-042: Overall Survival Analysis

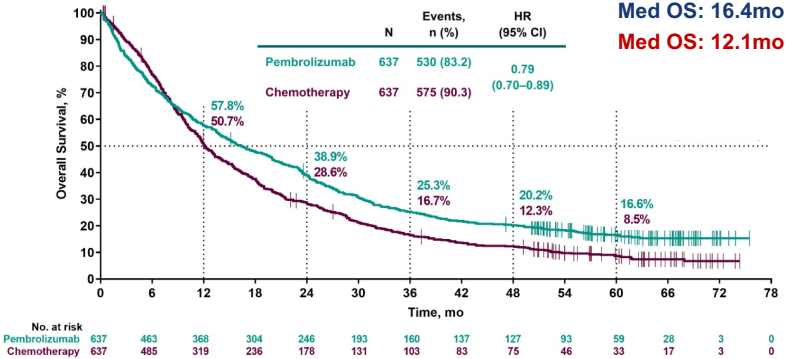
PD-L1 TPS ≥ 50%



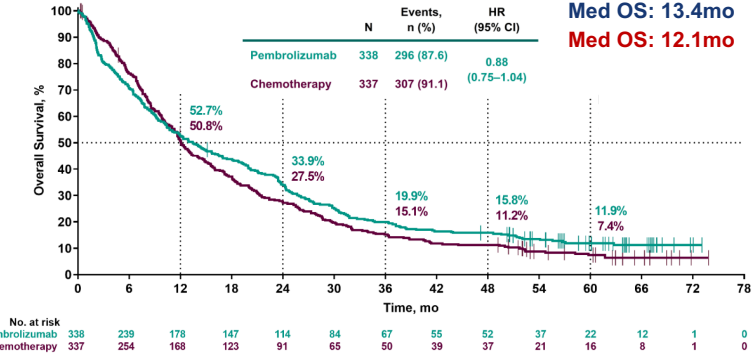
PD-L1 TPS ≥ 20%



PD-L1 TPS ≥ 1%



PD-L1 TPS 1-49%



De Castro Jr *et al.* J Clin Oncol 2023

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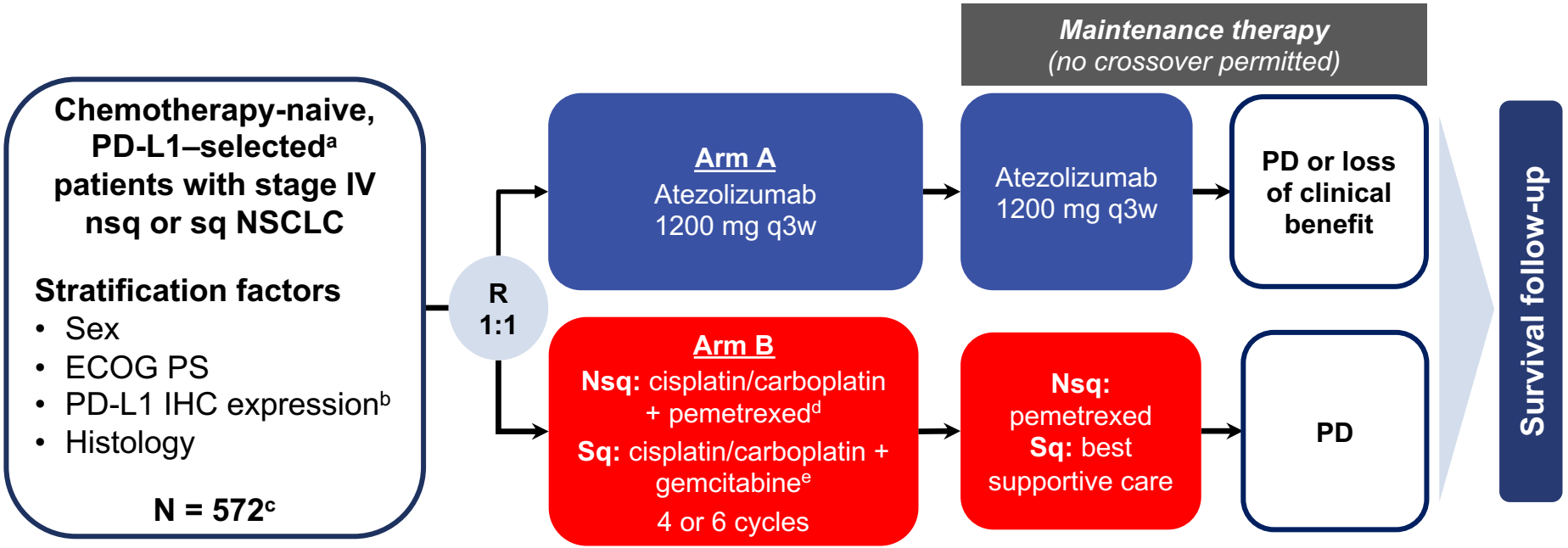
IMpower110

IMpower110 Study Design



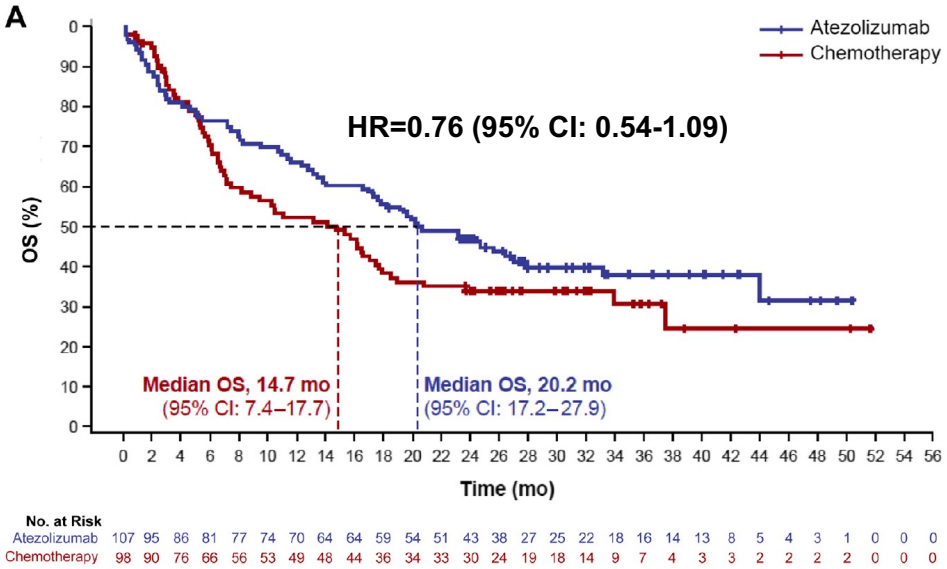
- Primary endpoint: OS in WT population[f]
- Key secondary endpoints: investigator-assessed PFS, ORR and DOR (per RECIST version 1.1)

IC, tumour-infiltrating immune cells; IHC, immunohistochemistry; nsq, non-squamous; PD, progressive disease; q3w, every 3 weeks; R, randomised; sq, squamous; TC, tumour cells; WT, wild-type. [a] PD-L1 expression (VENTANA SP142 IHC assay) ≥ 1% on TC or IC. [b] TC1/2/3 and any IC vs TC0 and IC1/2/3. [c] 554 patients in the WT population. [d] Cisplatin 75 mg/m^2 or carboplatin area under the curve (AUC) 6 + pemetrexed 500 mg/m^2 IV q3w. [e] Cisplatin 75 mg/m^2 + gemcitabine 1250 mg/m^2 or carboplatin AUC 5 + gemcitabine 1000 mg/m^2 IV q3w. [f] WT population excludes patients with *EGFR*+ and/or *ALK*+ NSCLC.

Spigel et al. IMpower110 Interim OS Analysis https://bit.ly/2lxRNHQ

IMpower110: Overall Survival Analysis

PD-L1 ≥ 50% on TC or ≥ 10% on IC by SP142 IHC

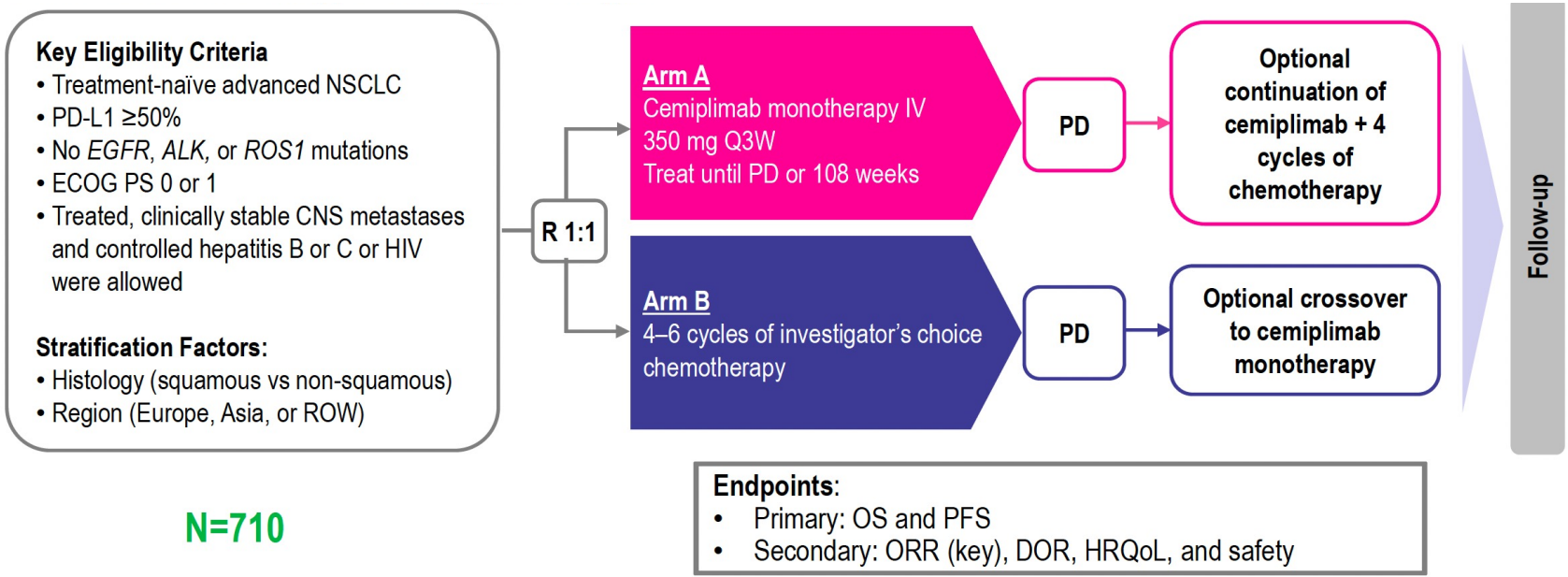


PD-L1 high	Atezolizumab (N=107)	Chemo (N=98)
ORR	40.2%	28.6%
Median DOR	38.9 mo	8.3 mo
Median OS	20.2 mo	14.7 mo
Median PFS	8.2 mo	5.0 mo

Jassem *et al.* J Thorac Oncol 2021

EMPOWER-Lung 1

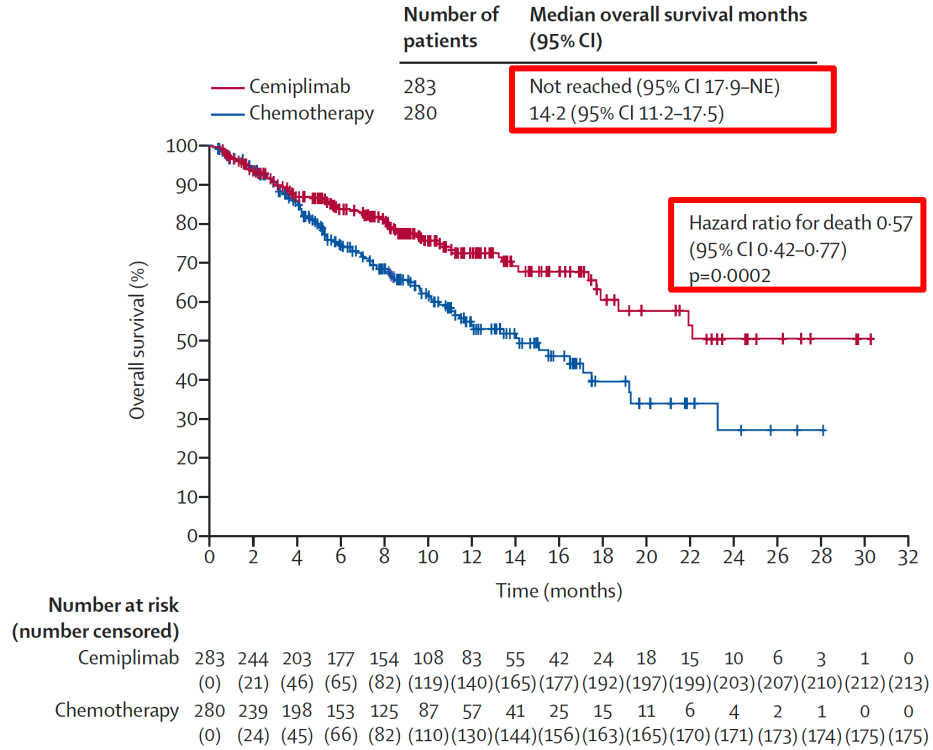
EMPOWER-Lung 1: Study design

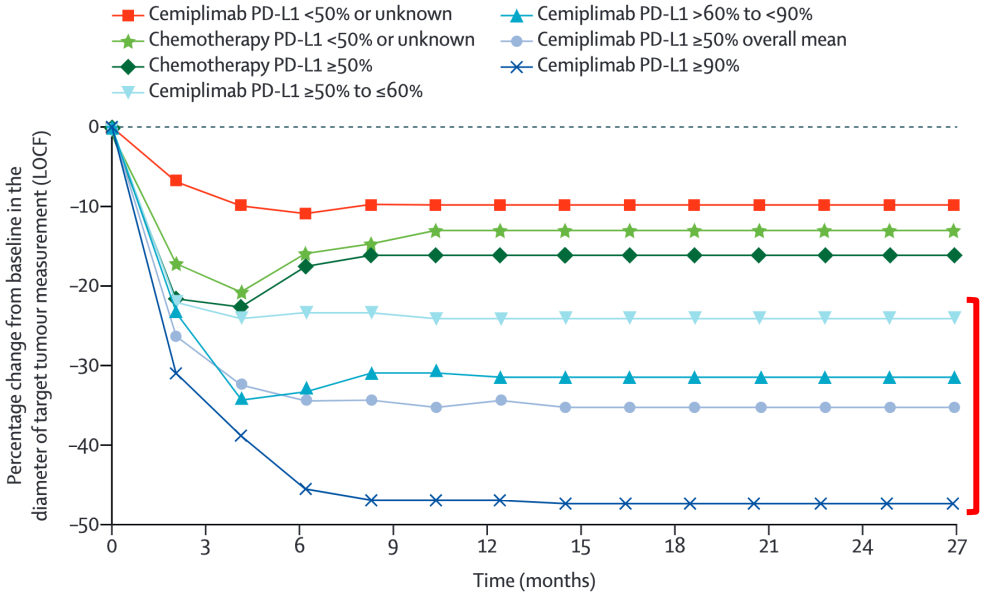


ALK, anaplastic lymphoma kinase; CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HIV, human immunodeficiency virus; HRQoL, health-related quality of life; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomized; ROS1, c-ros oncogene 1; ROW, rest of the world.

Kilickap *et al.* WCLC 2020

EMPOWER-Lung 1: Overall Survival Analysis





Sezer *et al.* Lancet 2021

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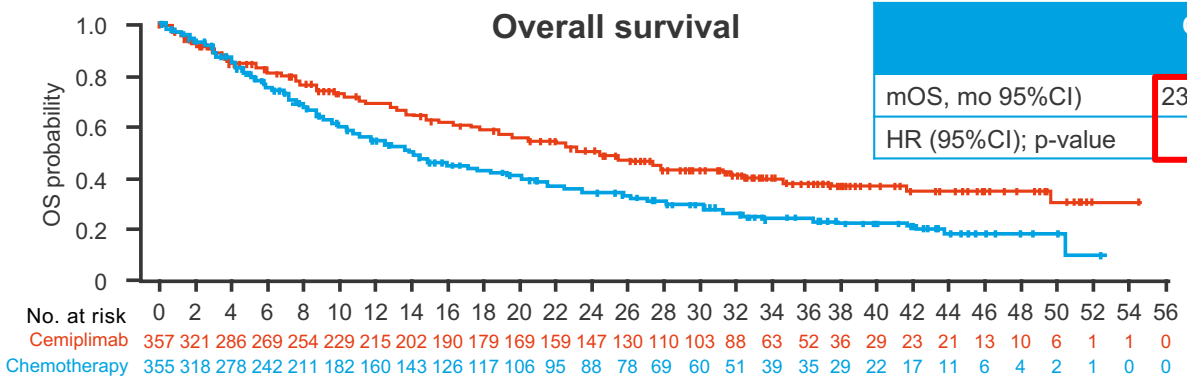
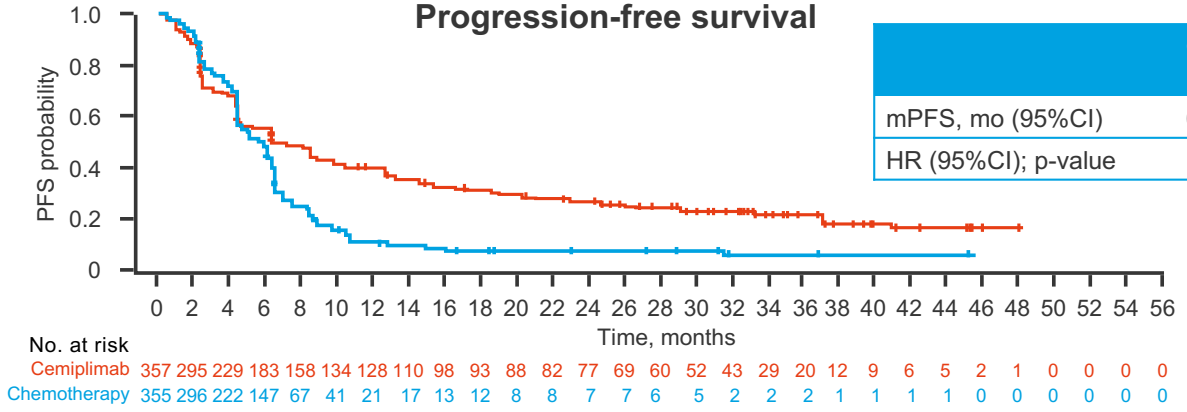
EMPOWER-Lung 1: Updated Survival Data



	Cemiplimab (n=357)	Chemotherapy (n=355)
mOS, mo 95%CI)	23.4 (19.4, 27.4)	13.7 (11.2, 16.2)
HR (95%CI); p-value	0.63 (0.52, 0.77); 0.0001	



	Cemiplimab (n=357)	Chemotherapy (n=355)
mPFS, mo (95%CI)	6.3 (4.6, 8.3)	5.3 (4.3, 6.0)
HR (95%CI); p-value	0.56 (0.47, 0.67); 0.0001	

Özgüroğlu *et al.* ESMO 2022

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Summary of immunotherapy monotherapy trials in treatment-naïve advanced NSCLC

Study	Patient PD-L1 status	Regimen	Primary Endpoint	ORR	Median DoR (mo)	Median PFS (mo)	Median OS (mo)	OS HR (95% CI)
KN-024[1] (n=305)	TPS ≥ 50%	Pembrolizumab vs platinum-doublet	PFS	46.1% vs 31.1%	29.1 vs 6.3	7.7 vs 5.5	26.3 vs 13.4	0.62 (0.48-0.81)
KN-042[2] (n=1274)	TPS ≥ 1%	Pembrolizumab vs platinum-doublet	OS: ≥ 50% ≥ 20% ≥ 1%	 39% vs 32% 33% vs 29% 27% vs 27%	 28.1 vs 10.8 27.7 vs 10.8 26.5 vs 8.4	 6.5 vs 6.5 6.2 vs 6.9 5.6 vs 6.8	 20.0 vs 12.2 18.0 vs 13.0 16.4 vs 12.1	 0.68 (0.57-0.81) 0.75 (0.64-0.87) 0.79 (0.70-0.89)
IMpower110[3] (n=572)	TC/IC ≥ 1%	Atezolizumab vs platinum-doublet	OS: TC/IC 3 TC/IC 2/3 TC/IC1/2/3	 40.2% vs 28.6% 33.7% vs 32.1% 31.4% vs 32.1%	 38.9 vs 8.3 38.9 vs 5.8 26.3 vs. 5.7	 8.2 vs 5.0 7.3 vs 5.5 5.8 vs 5.6	 20.2 vs 14.7 19.9 vs 16.1 18.9 vs 14.7	 0.76 (0.54-1.09) 0.87 (0.66-1.14) 0.85 (0.69-1.04)
EMPOWER-Lung 1[4,5]	TPS ≥ 50%	Cemiplimab vs platinum-doublet	OS and PFS	39% vs 20%	16.7 vs. 6.0	6.3 vs. 5.3	23.4 vs 13.7	0.63 (0.52-0.77)

TC/IC3: PD-L1 expression on ≥50% tumor cells (TC3) or immune cells (IC3); TC/IC 2/3: PD-L1 expression on ≥5% tumor cells or immune cells; TC/IC 1/2/3 PD-L1 expression on ≥1% tumor cells or immune cells

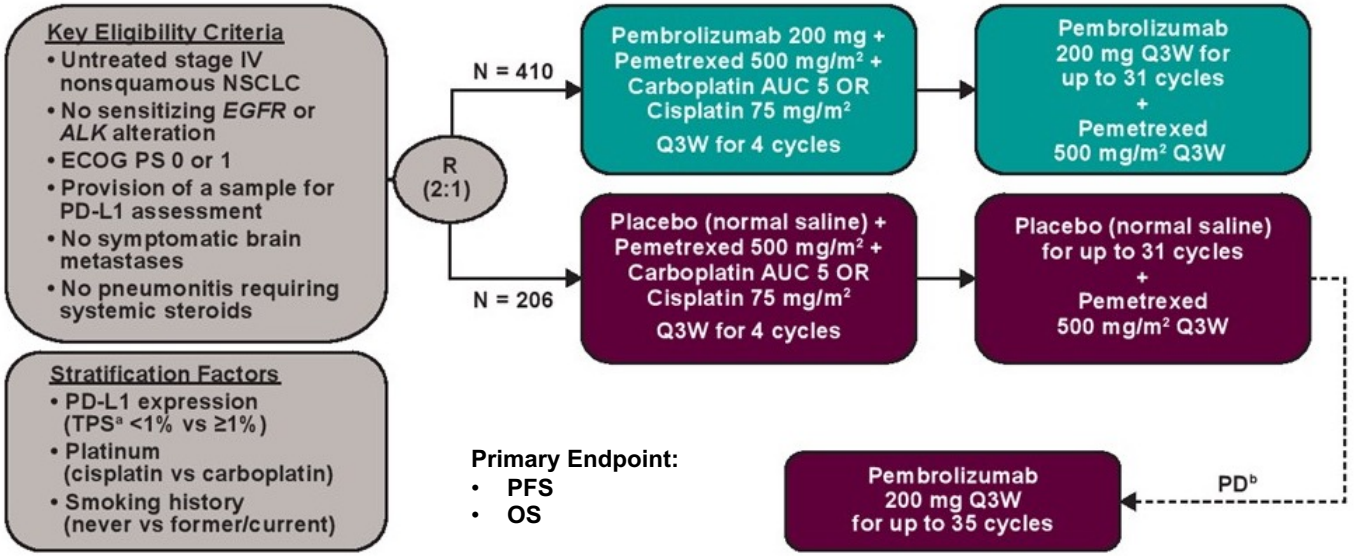
[1]Brahmer *et al.* ESMO 2020; [2]de Castro Jr *et al.* J Clinic Oncol 2023; [3]Jassem *et al.* J Thorac Oncol 2021; [4]Sezer *et al.* Lancet 2021; [5]Özgüroğlu et al. ESMO 2022

Anti-PD-(L)1 monotherapy has shown significant OS benefit and durable response in advanced NSCLC harboring high PD-L1

Chemoimmunotherapy

KEYNOTE-189

KEYNOTE-189: Study Design



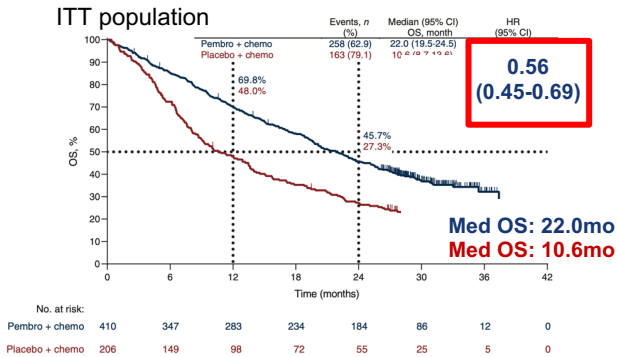
AUC, area under the concentration–time curve; ECOG PS, Eastern Cooperative Oncology Group performance status; PD, progressive disease; Q3W, every 3 weeks; R, randomized.

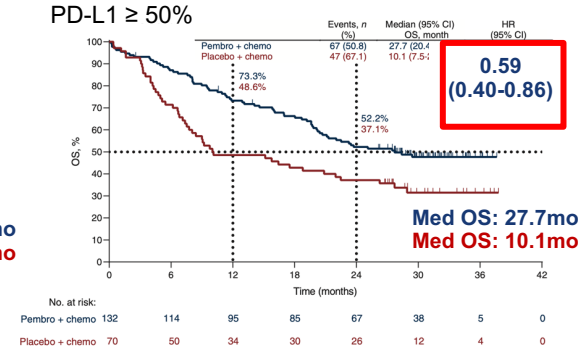
[a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay.

[b]Patients could cross over 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.

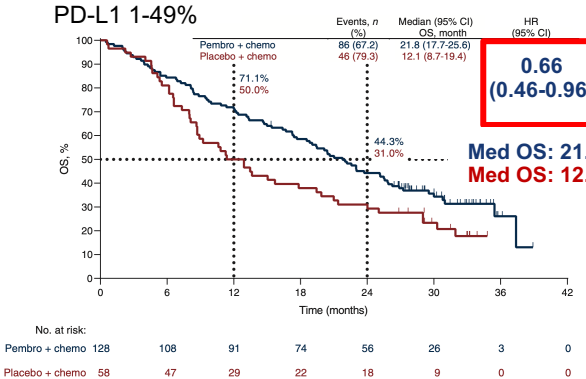
Gandhi *et al.* N Engl J Med. 2018

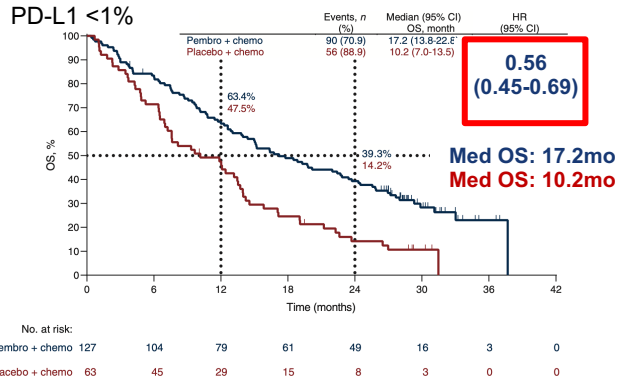
KEYNOTE-189: Protocol Specified Final Analyses





ITT (n=410)	Pembro + Chemo	Chemo
ORR	48.3%	19.9%
Median DOR	12.5 mo	7.1 mo
Median PFS	9.0 mo	4.9 mo

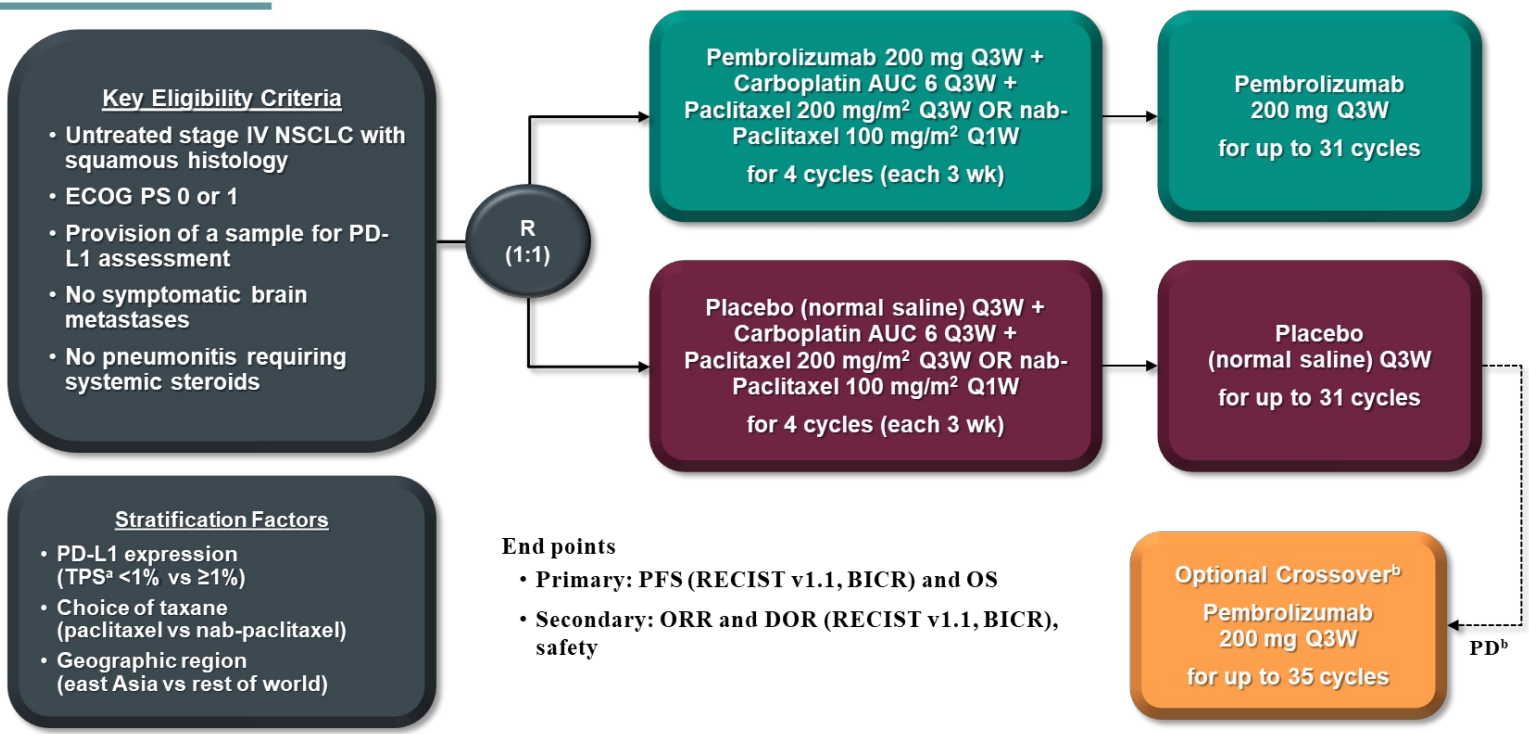




Rodriguez-Abreu *et al.* Ann Oncol. 2021

KEYNOTE-407

KEYNOTE-407: Study Design

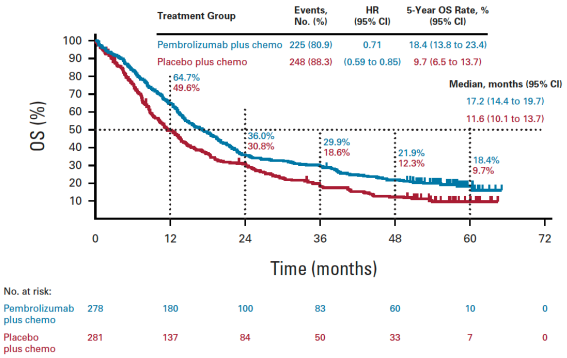


BICR, blinded independent central radiologic review. [a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay. [b]Patients could crossover during combination therapy or monotherapy. To be eligible for crossover, PD must have been verified by BICR and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

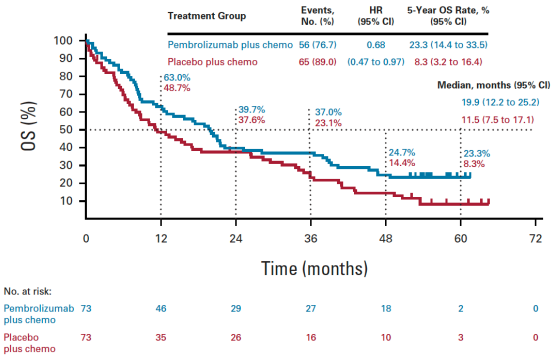
Paz-Ares *et al.* N Engl J Med. 2018

KEYNOTE-407: 5-Year OS Update

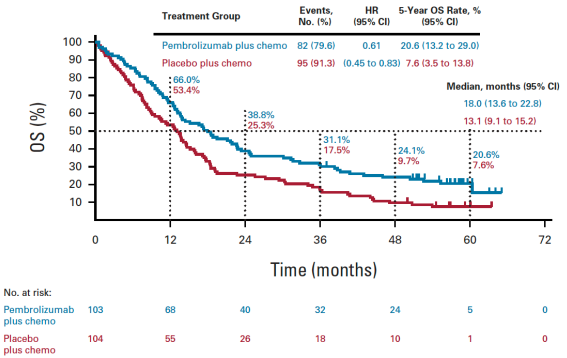
ITT population HR=0.71 (95% CI: 0.59-0.85)



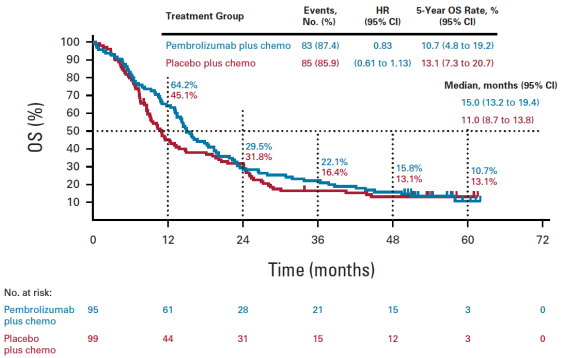
PD-L1 ≥ 50% HR=0.68 (95% CI: 0.47-0.97)



PD-L1 1-49 % HR=0.61 (95% CI: 0.45-0.83)



PD-L1 <1% HR=0.83 (95% CI: 0.61-1.13)



ITT (n=559)	Pembro + chemo	Chemo
ORR	62.2%	38.8%
Median DOR	9.0 mo	4.9 mo
Median OS	17.2 mo	11.6 mo
Median PFS	8.0 mo	5.1 mo

Novello *et al.* JCO 2023

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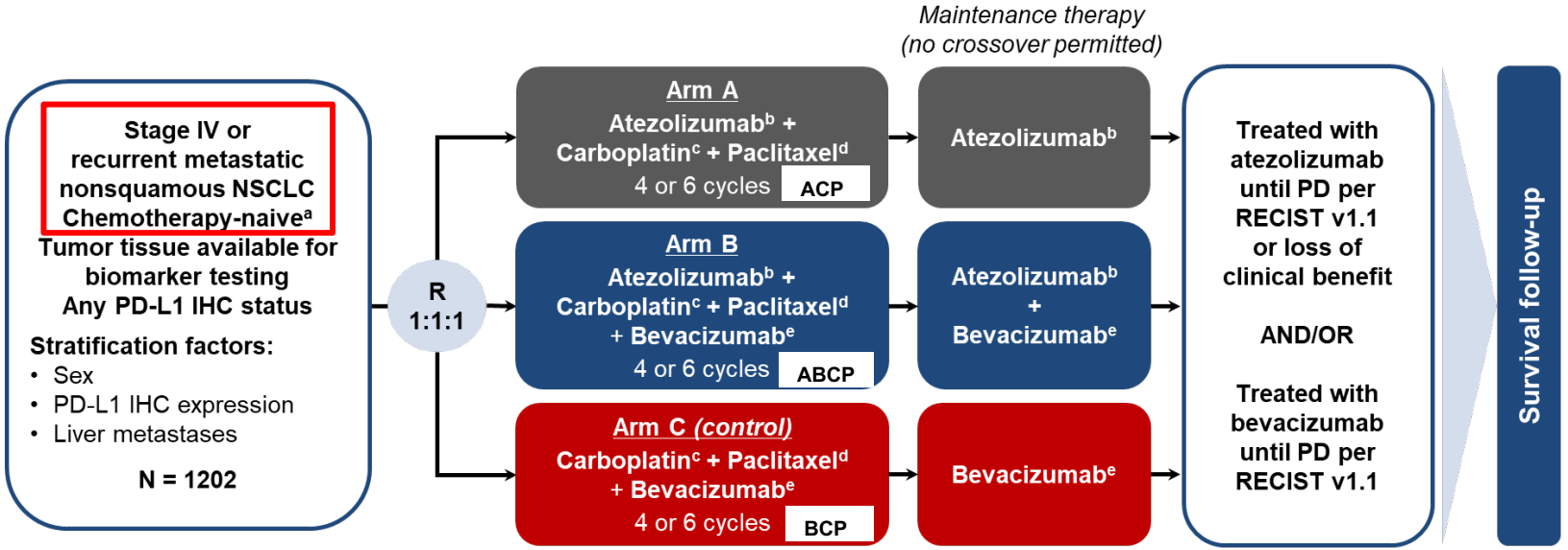
IMpower150

IMpower150: Study Design

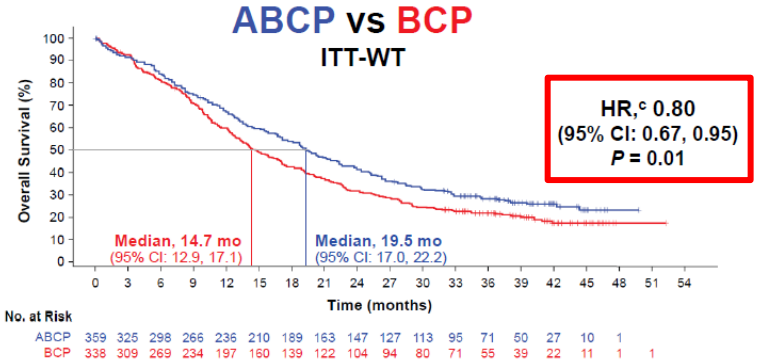


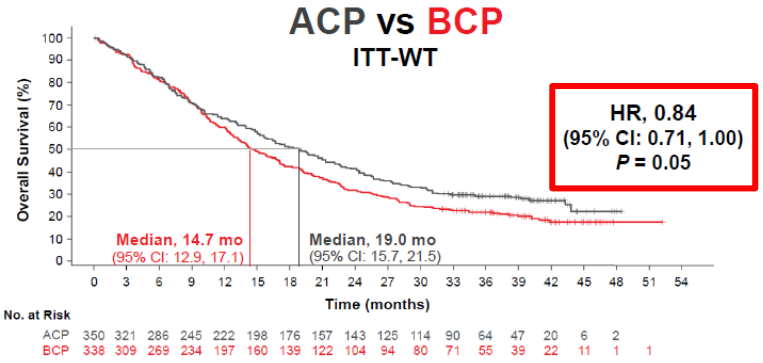
[a] Patients with a sensitizing *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies.
[b] Atezolizumab: 1200 mg IV q3w. [c] Carboplatin: AUC 6 IV q3w. [d] Paclitaxel: 200 mg/m^2 IV q3w. [e] Bevacizumab: 15 mg/kg IV q3w.

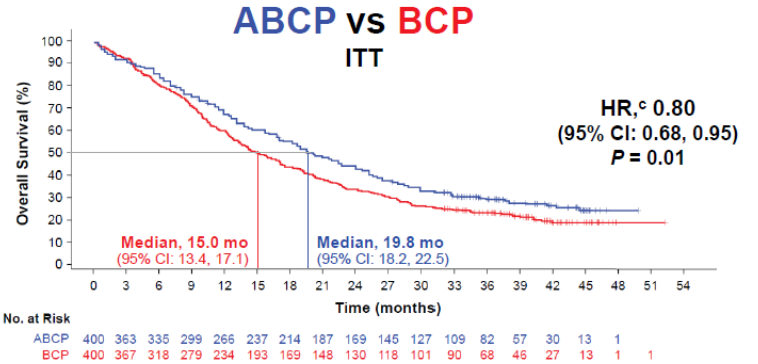
Primary Endpoints
- PFS in "wild-type" ITT population
- OS in "wild-type" ITT population
- PFS in "wild-type" population w/ high effector T-cell gene signature

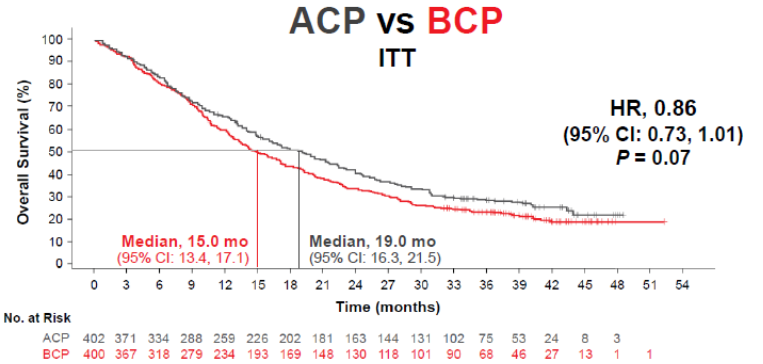
Socinski *et al.* NEJM. 2018

IMpower150: Updated OS Analyses





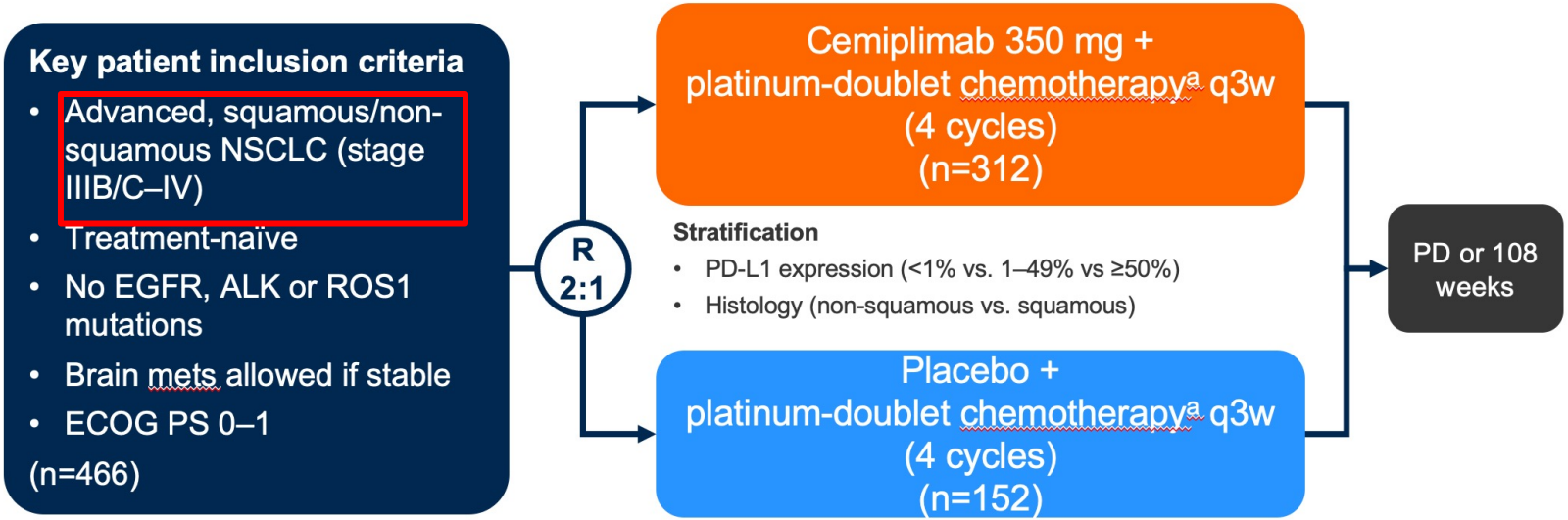




Median follow-up (ITT-WT): Arm B vs Arm C, 39.8 mo; Arm A vs Arm C, 39.3 mo. Median follow-up (ITT): Arm B vs Arm C, 39.8 mo; Arm A vs Arm C, 39.3 mo; minimum follow-up (ITT; all arms), 32.4 mo. [a] ITT-WT population excluded patients with *EGFR* or *ALK* genetic alterations. [b] Stratified analyses. [c] OS analysis for Arm B vs Arm C was considered final at the second interim OS analysis; data are shown for descriptive purposes only. Data cutoff: September 13, 2019.

Socinski *et al.* AACR 2020
Socinski *et al.* JTO 2021

EMPOWER-Lung 3



Primary endpoint

- OS

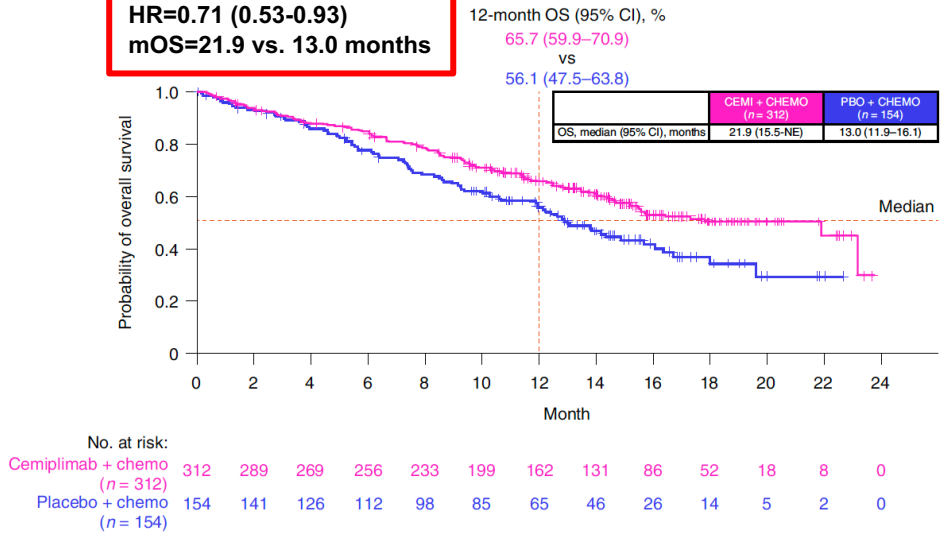
Secondary endpoints

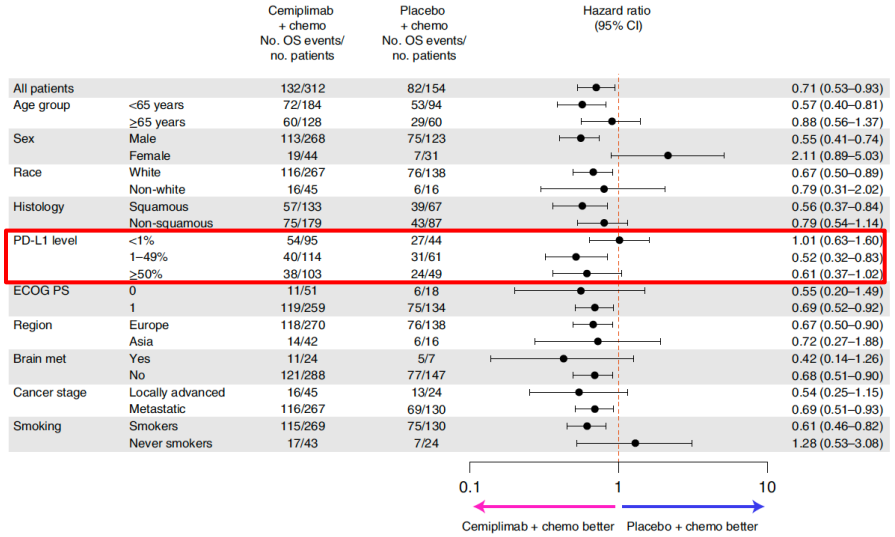
PFS, ORR, DoR, BOR, PROs, safety

Gogishvili *et al.* ESMO 2021

EMPOWER-Lung 3: Overall Survival

HR=0.71 (0.53-0.93)
mOS=21.9 vs. 13.0 months





Gogishvili *et al.* Nat Med 2022

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Summary of landmark chemo-immunotherapy trials in treatment-naïve advanced NSCLC

Study	Patient Pop	Regimen	Primary Endpt	ORR (%)	Median DoR (mo)	Median PFS (mo)	Median OS (mo)	OS HR (95% CI)
KN-189[1] (n=616)	Non-squamous	Platinum/pem/ pembrolizumab vs platinum/pem/placebo	PFS; OS	48.3% vs 19.9%	12.5 vs 7.1	9.0 vs 4.9	22.0 vs 10.6	0.56 (0.46-0.69)
KN-407[2] (n=559)	Squamous	Carbo/(nab)pac/ pembro vs carbo/ (nab)pac/placebo	PFS; OS	62.2% vs 38.8%	8.0 vs 5.1	8.0 vs 5.1	17.2 vs 11.6	0.71 (0.59-0.85)
IMpower150[3] (n=1202)	Non-squamous	ABCP ACP BCP	PFS*; OS	56% 40% 41%	11.5 8.3 6.0	8.3 - 6.8	19.5 19.0 14.7	0.80 (0.68-0.95) 0.84 (0.71-1.00) 1^
IMpower130[4] (n=723)	Non-squamous	Atezo/carbo/nab-paclitaxel vs carbo/ nab-paclitaxel	PFS; OS	49.2% vs 31.9%	8.4 vs 6.1	7.0 vs 5.5	18.6 vs 13.9	0.79 (0.64-0.98)
EMPOWER-Lung 3[5]	All	Cemiplimab/platinum-doublet vs platinum doublet	OS	43.3% vs 22.7%	15.6 vs 7.3	8.2 vs 5.0	21.9 vs 13.0	0.71 (0.53-0.93)

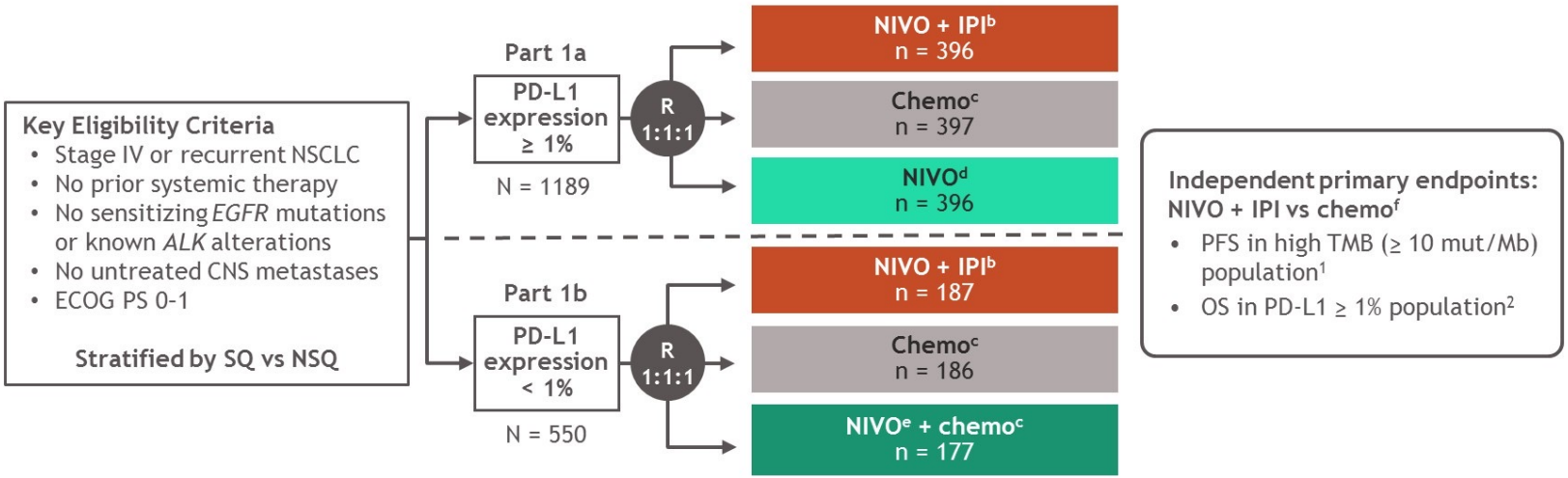
*PFS assessed in both wild-type ITT population and wild-type population with high effector T-cell gene signature.
^HR comparisons made to BCP as reference arm
ABCP: atezolizumab/bevacizumab/carboplatin/paclitaxel; ACP: atezolizumab/carboplatin/paclitaxel; BCP: bevacizumab/carboplatin/paclitaxel
[1]Rodriguez-Abreu et al. Ann Oncol 2021; [2]Novello *et al.* J Clin Oncol 2023; [3]Socinski *et al.* AACR 2020; [4]West *et al.* Lancet Oncol 2019; [5]Gogishvili *et al.* Nat Med 2022

Chemoimmunotherapy has shown significant OS benefit and high ORRs in patients with advanced NSCLC regardless of PD-L1 levels

Dual immune checkpoint blockade +/- chemotherapy

CheckMate 227

CheckMate 227[a] Part 1 study design



Database lock: February 28, 2020; minimum / median follow-up for OS: 37.7 months / 43.1 months.

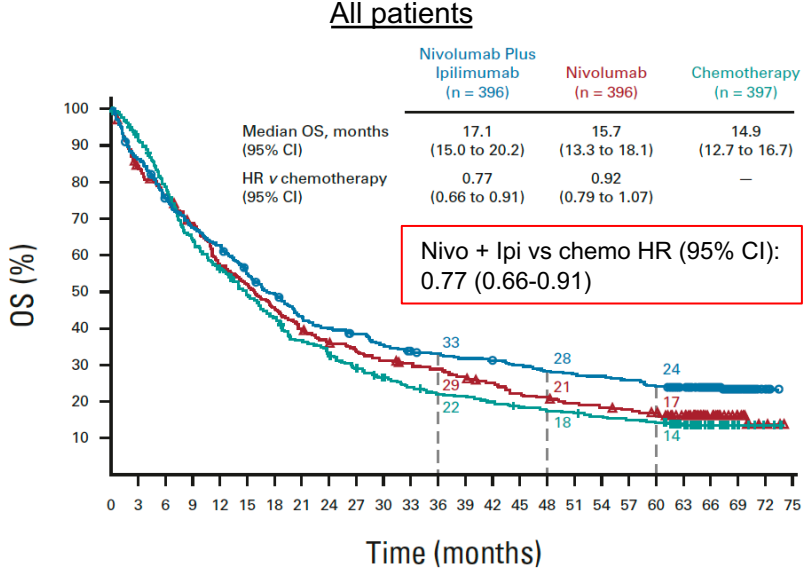
Treatment was continued until disease progression, unacceptable toxicity, or for 2 years for immunotherapy; [a]NCT02477826; [b]NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W); [c]**NSQ:** pemetrexed + cisplatin or carboplatin, Q3W for ≤ 4 cycles, with optional pemetrexed maintenance following chemo or NIVO + pemetrexed maintenance following NIVO + chemo; **SQ:** gemcitabine + cisplatin, or gemcitabine + carboplatin, Q3W for ≤ 4 cycles; [d]NIVO (240 mg Q2W); [e]NIVO (360 mg Q3W); [f]Both endpoints were met; results were previously reported.

1. Hellmann MD, et al. *N Engl J Med* 2018;378(22):2093-2104; 2. Hellmann MD, et al. *N Engl J Med* 2019;381(21):2020-2031.

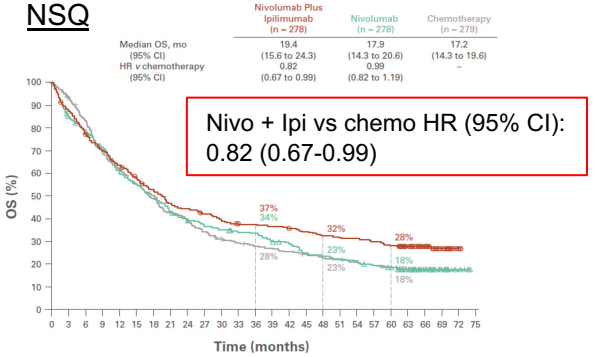
Paz-Ares *et al.* ASCO 2021

5-year OS in patients with PD-L1 ≥ 1%

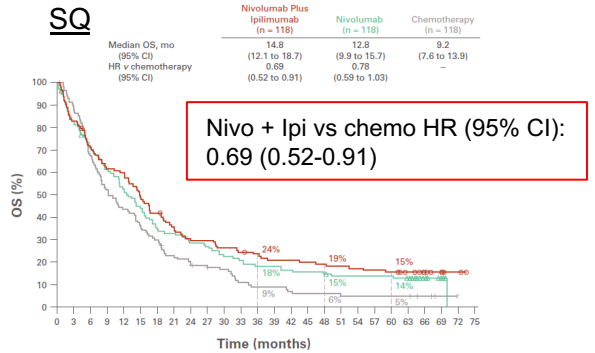
All patients



NSQ



SQ



Brahmer *et al*. JCO 2022

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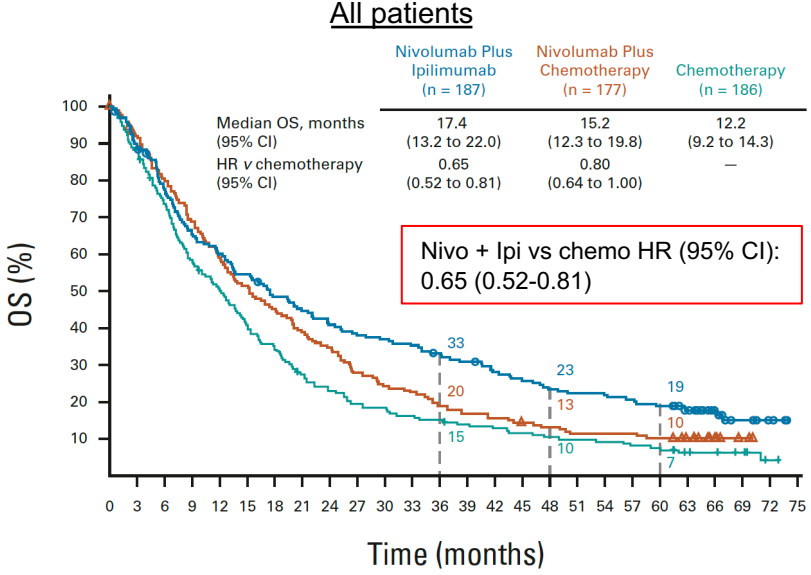
5-year OS in patients with PD-L1 < 1%

All patients

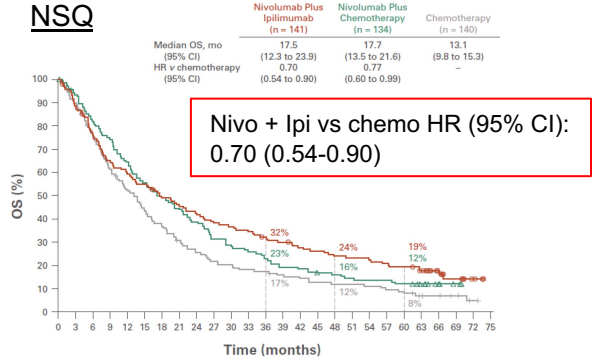


Nivo + Ipi vs chemo HR (95% CI): 0.65 (0.52-0.81)

No. at risk:

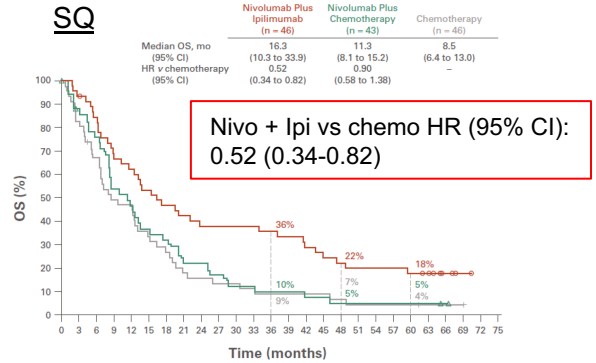
Nivolumab plus ipilimumab	187	165	142	120	110	100	88	81	74	69	67	64	59	55	49	45	41	39	38	36	33	27	15	8	3	0
Nivolumab plus chemotherapy	177	159	139	119	102	88	78	67	60	48	42	39	34	29	27	24	22	19	19	19	17	14	7	2	0	0
Chemotherapy	186	164	135	107	92	74	62	49	41	35	33	29	27	24	22	20	18	17	16	14	12	8	7	5	1	0

NSQ



Nivo + Ipi vs chemo HR (95% CI): 0.70 (0.54-0.90)

SQ



Nivo + Ipi vs chemo HR (95% CI): 0.52 (0.34-0.82)

Brahmer *et al*. JCO 2022

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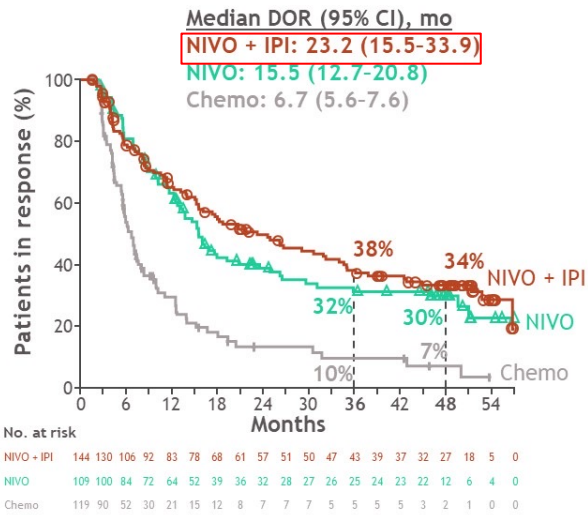
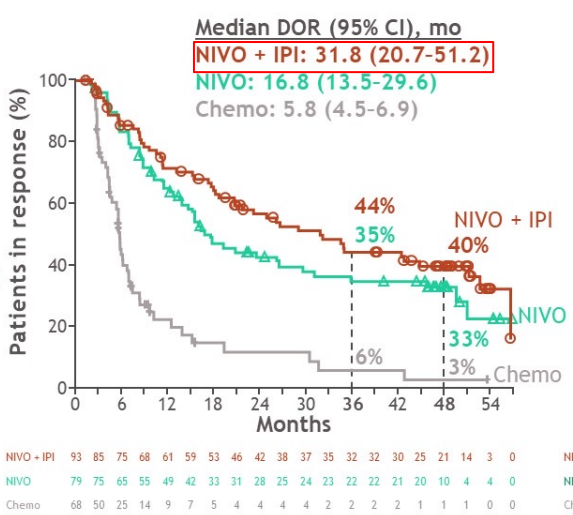
4-year update: DOR

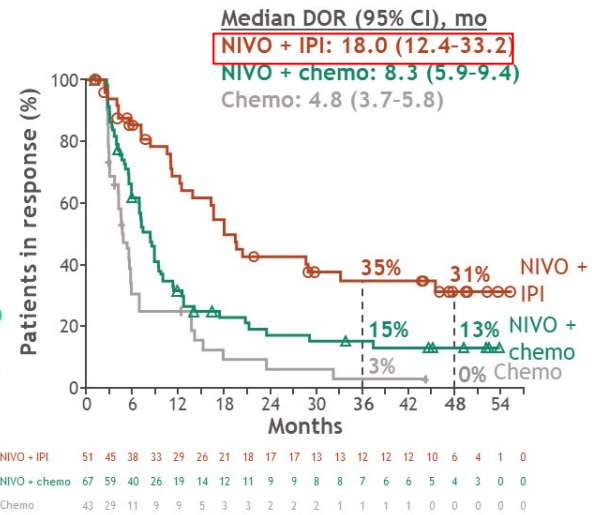
PD-L1 ≥ 1%



PD-L1 ≥ 50%



PD-L1 < 1%



Paz-Ares *et al.* ASCO 2021

CheckMate 9LA

CheckMate 9LA study design[a]

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

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

N = 719

R 1:1

n = 361

NIVO 360 mg Q3W + IPI 1 mg/kg Q6W + Chemo[d] Q3W (2 cycles)

n = 358

Chemo[d] Q3W (4 cycles) with optional pemetrexed maintenance (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

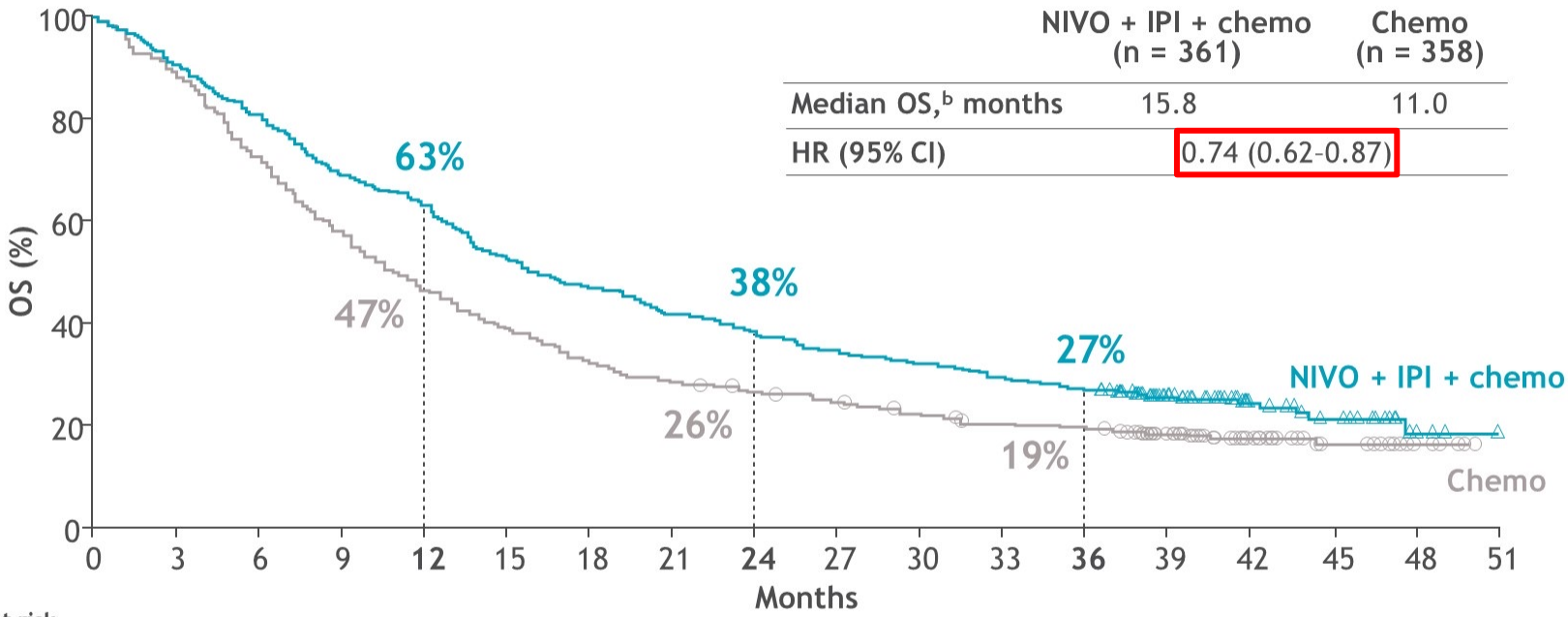
Exploratory endpoint
- Efficacy by oncogenic driver mutation status (*KRAS*, *TP53*, *STK11*, *KEAP1*)

Database lock: February 15, 2022; minimum/median follow-up for OS: 36.1/42.6 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.

1. Paz-Ares L, et al. *Lancet Oncol* 2021;22:198-211; 2. Reck M, et al. *ESMO Open* 2021;6:100273.

3-year update: OS in all randomized patients[a]



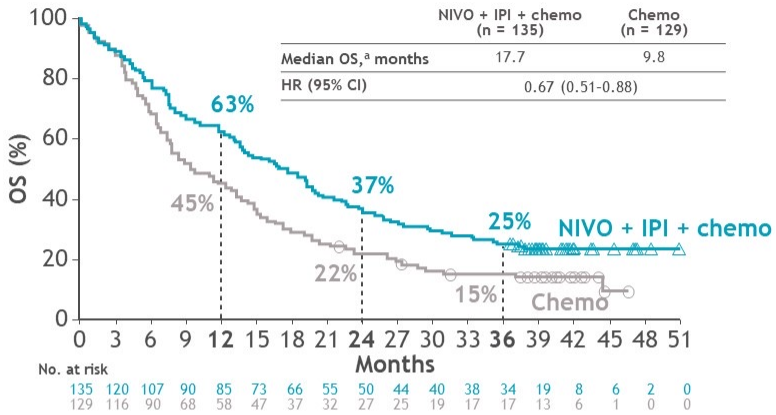
Paz-Ares *et al.* ASCO 2022

Database lock: February 15, 2022; minimum follow-up: 36.1 months.

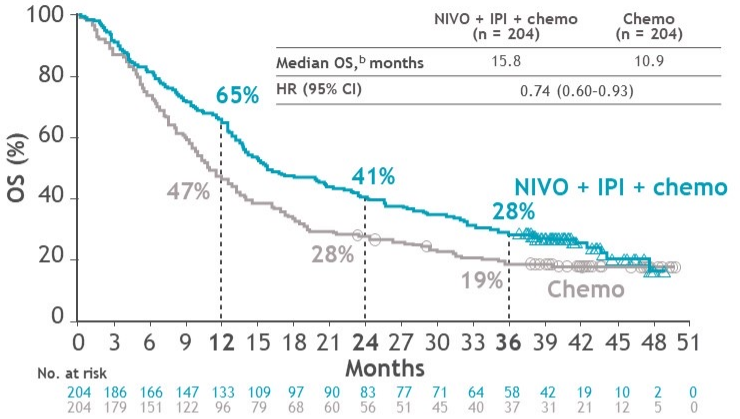
[a]In the all randomized population, subsequent systemic therapy was received by 37% (NIVO + IPI + chemo) and 49% (chemo) of patients, subsequent immunotherapy by 8% and 36%, and subsequent platinum-doublet chemo by 19% and 6%, respectively; [b]95% CI, 13.9-19.7 (NIVO + IPI + chemo) and 9.5-12.7 (chemo).

OS by PD-L1 expression

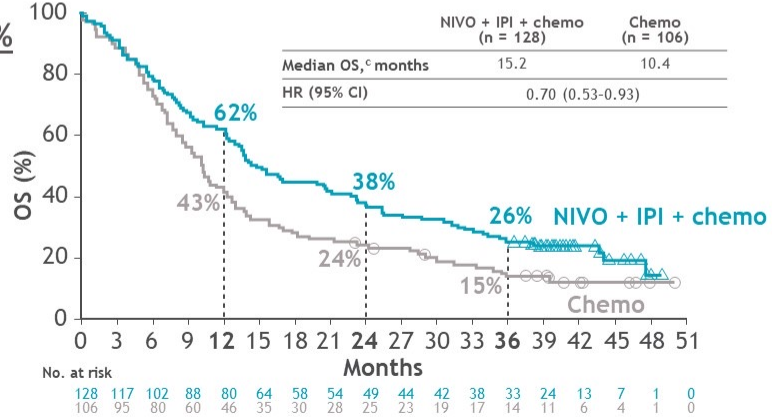
PD-L1 < 1%



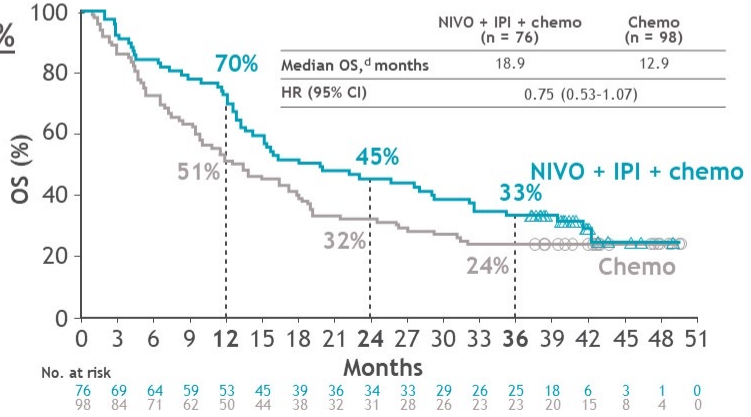
PD-L1 ≥ 1%



PD-L1 1-49%



PD-L1 ≥ 50%

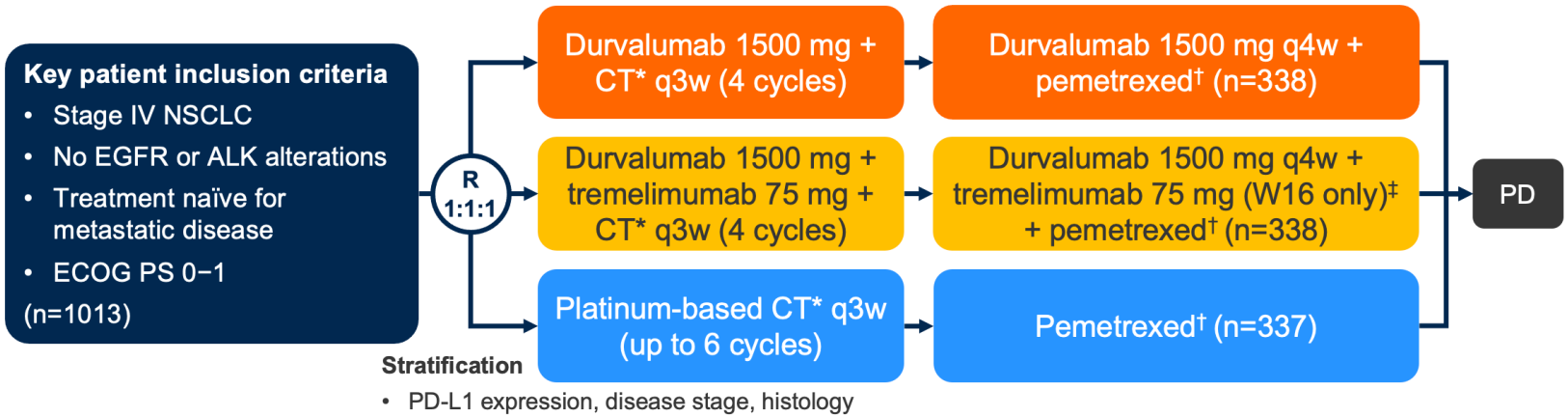


Database lock: February 15, 2022; minimum follow-up: 36.1 months.

[a]95% CI, 13.7-20.3 (NIVO + IPI + chemo) and 7.7-13.5 (chemo); [b]95% CI, 13.8-22.2 (NIVO + IPI + chemo) and 9.5-13.2 (chemo); [c]95% CI, 12.6-21.2 (NIVO + IPI + chemo) and 8.7-12.4 (chemo); [d]95% CI, 13.1-29.1 (NIVO + IPI + chemo) and 9.4-17.6 (chemo).

POSEIDON

POSEIDON: Study Design



Primary endpoints

- PFS (BICR), OS

Secondary endpoint

- ORR, DoR, BOR, HRQoL, safety

Johnson *et al.* WCLC 2021

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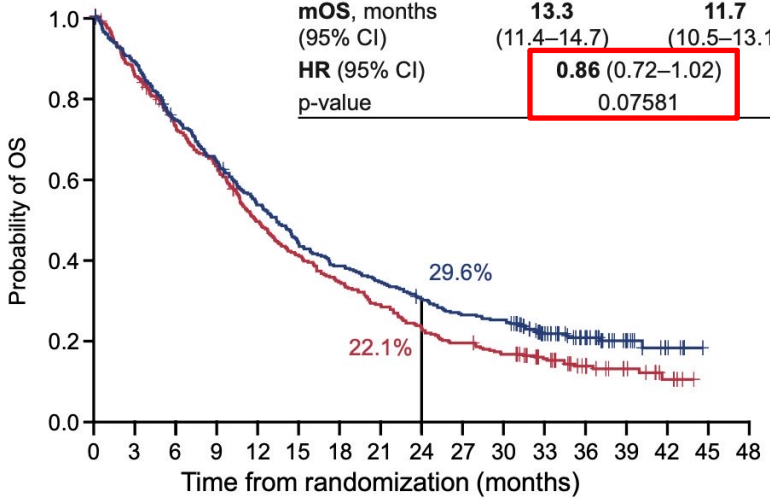
POSEIDON: Overall Survival Analyses

Durvalumab + CT vs. CT: OS

	D+CT	CT
Events, n/N (%)	264/338 (78.1)	285/337 (84.6)
mOS, months (95% CI)	**13.3** (11.4–14.7)	**11.7** (10.5–13.1)
HR (95% CI)	**0.86** (0.72–1.02)	
p-value	0.07581	

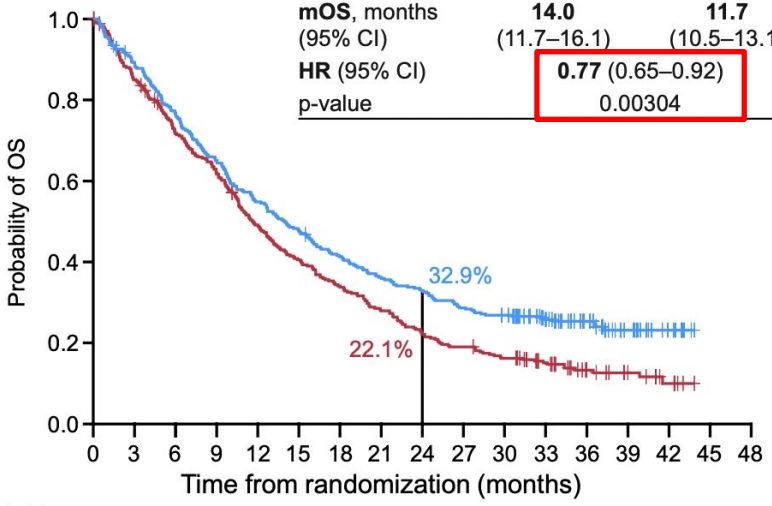


No. at risk																	
D+CT	338	296	247	212	176	142	126	112	97	85	81	51	33	15	5	0	0
CT	337	284	236	204	160	132	111	91	72	62	52	38	21	13	6	0	0

- Median follow-up in censored patients at DCO: 34.9 months (range 0–44.5)

Durvalumab + Tremelimumab + CT vs. CT: OS

	D+T+CT	CT
Events, n/N (%)	251/338 (74.3)	285/337 (84.6)
mOS, months (95% CI)	**14.0** (11.7–16.1)	**11.7** (10.5–13.1)
HR (95% CI)	**0.77** (0.65–0.92)	
p-value	0.00304	



No. at risk																	
D+T+CT	338	298	256	217	183	159	137	120	109	95	88	64	41	20	9	0	0
CT	337	284	236	204	160	132	111	91	72	62	52	38	21	13	6	0	0

- Median follow-up in censored patients at DCO: 34.9 months (range 0–44.5)

Johnson *et al.* J Clin Oncol 2022

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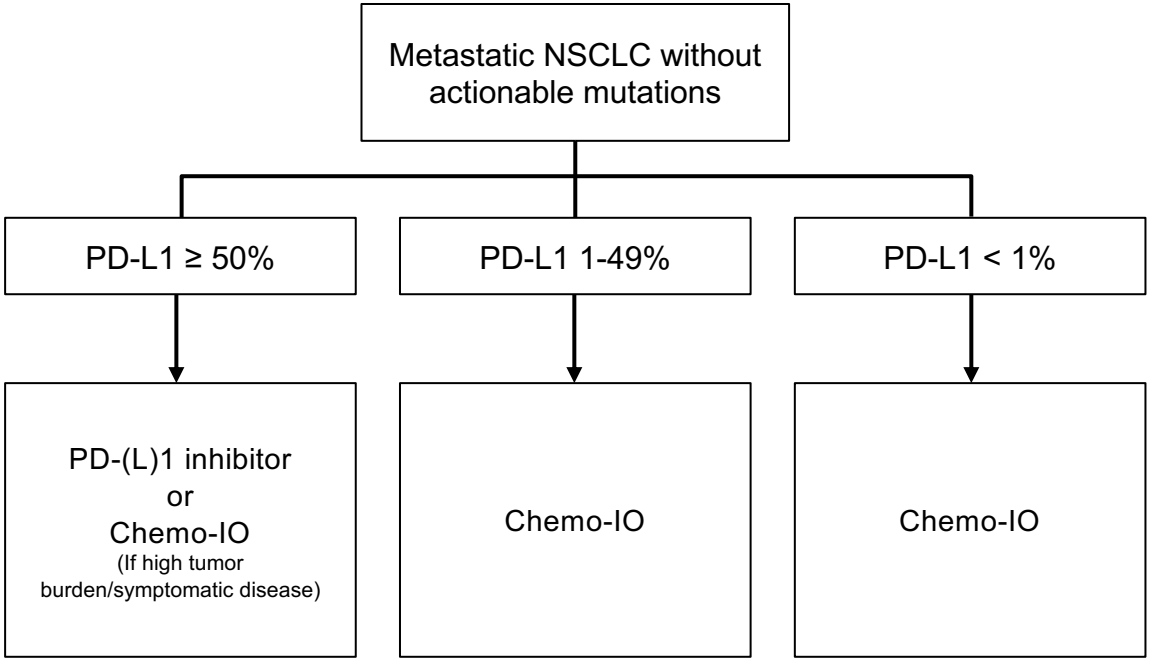
Study	Regimen	Study size	Median OS (months)	HR for OS (95% CI)	PD-L1
KEYNOTE 024[1]	Pembrolizumab	305	26.3 vs. 13.4	0.62 (0.48-0.81)	≥ 50%
KEYNOTE 042[2]	Pembrolizumab	1274	20.0 vs. 12.2 18.0 vs. 13.0 16.4 vs. 12.1	0.68 (0.57-0.81) 0.75 (0.64-0.87) 0.79 (0.70-0.89)	≥ 50% ≥ 20% ≥ 1%
IMpower110[3]	Atezolizumab	572	20.2 vs. 14.7 18.9 vs. 14.7	0.76 (0.54-1.09) 0.85 (0.69-1.04)	TC3 or IC3* ≥ 1%
EMPOWER-Lung 1[4]	Cemiplimab	710	23.4 vs. 13.7	0.63 (0.52-0.77)	≥ 50%
KEYNOTE 189[5] (non-Sq-NSCLC)	Pembrolizumab/ pemetrexed/platinum	616	22.0 vs. 10.7 27.7 vs. 10.1 21.8 vs. 12.1 17.2 vs. 10.2	0.56 (0.46-0.69) 0.59 (0.40-0.86) 0.66 (0.46-0.96) 0.56 (0.45-0.69)	All comers ≥ 50% 1-49% < 1%
KEYNOTE 407[6] (Sq-NSCLC)	Pembrolizumab/ taxane/carboplatin	559	17.2 vs. 11.6 19.9 vs. 11.5 18.0 vs. 13.1 15.0 vs. 11.0	0.71 (0.59-0.85) 0.68 (0.47-0.97) 0.61 (0.45-0.83) 0.83 (0.61-1.13)	All comers ≥ 50% 1-49% < 1%
IMpower150[7] (non-Sq-NSCLC)	Atezolizumab/ bevacizumab/ carboplatin/paclitaxel	1202	19.5 vs. 14.7	0.80 (0.67-0.95)	All comers
EMPOWER-Lung 3[8]	Cemiplimab/platinum-doublet	466	21.9 vs. 13.0	0.71 (0.53-0.93) 0.61 (0.37-1.02) 0.52 (0.32-0.83) 1.01 (0.63-1.60)	All comers ≥ 50% 1-49% < 1%
CHECKMATE 227[9]	Nivolumab/ Ipilimumab	1189/550 (Part 1A/B)	17.1 vs. 14.9 20.6 vs. 14.0 17.4 vs. 12.2	0.77 (0.66-0.91) 0.69 (0.54-0.86) 0.65 (0.52-0.81)	≥ 1% ≥ 50% < 1%
CHECKMATE 9LA[10]	Nivolumab/ Ipilimumab/ Platinum doublet (2 cycles)	719	15.8 vs. 11.0 18.9 vs. 12.9 15.4 vs. 10.4 17.7 vs. 9.8	0.74 (0.62-0.87) 0.75 (0.53-1.07) 0.70 (0.53-0.93) 0.67 (0.51-0.88)	All comers ≥ 50% 1-49% < 1%
POSEIDON[11]	Durvalumab/ Tremelimumab (5 doses)/ Platinum doublet	1013	14.0 vs. 11.7	0.77 (0.65-0.92) 0.65 (0.47-0.89) 0.76 (0.61-0.95) 0.77 (0.58-1.00)	All comers ≥ 50% ≥1 % < 1%

[1]Reck *et al.* JCO 2021; [2]de Castro Jr *et al.* J Clin Oncol 2023; [3]Jassem *et al.* J Thorac Oncol 2021; [4]Özgüroğlu *et al.* ESMO 2022; [5]Rodriguez-Abreu *et al.* Ann Oncol 2021; [6]Novello *et al.* J Clin Oncol 2023; [7]Socinski *et al.* JTO 2021; [8]Gogishvili et al. Nat Med 2022; [9]Brahmer *et al.* JCO 2022; [10]Paz-Ares *et al.* ASCO 2022; [11]Johnson *et al.* JCO 2022

Treatment algorithm for advanced NSCLC in the front-line setting

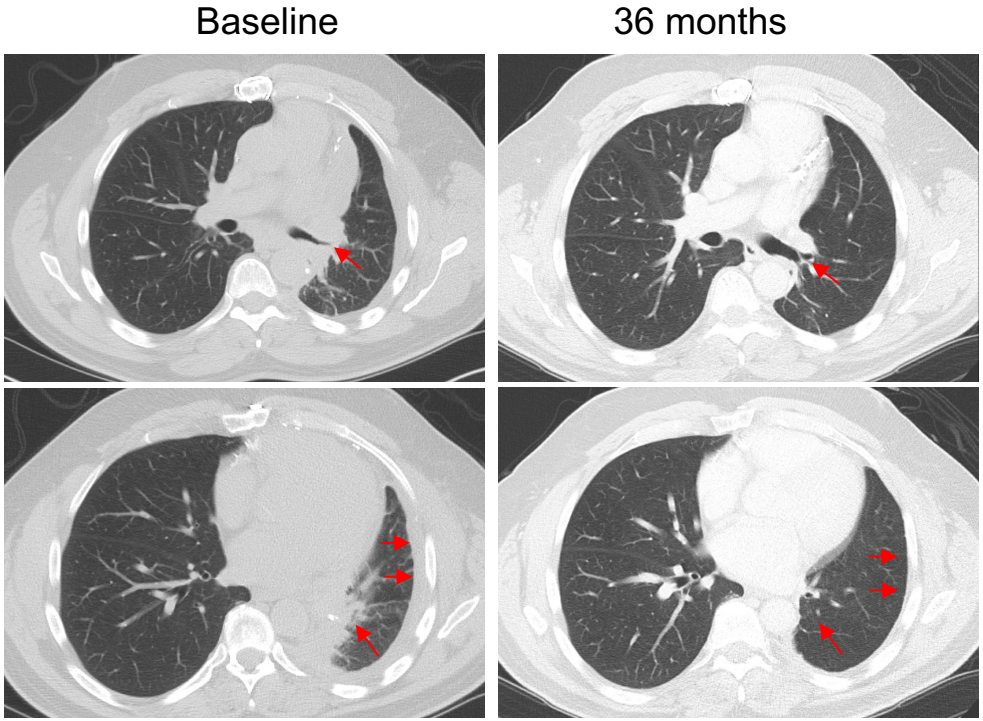


Dual immune checkpoint blockade

- Nivolumab/ipilimumab is a viable option for PD-L1 ≥1% (FDA label). Note clinical activity in PD-L1 <1%.

Back to the case

- Received pembrolizumab for 2 years. Now off treatment for 1 year.



Thank you for your attention.

@chulkimMD

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