Updates in Immunotherapy for Lung Cancer (What's new in 2022?)

Presented By: Jorge Nieva MD

July 29th 2022

Themes of 2022

- FDA approvals and deferrals
- Long term follow-up of older clinical trial in metastatic disease
- Improving on PD-1/PD-L1 blockade

FDA Approvals

- Adjuvant Atezolizumab
- Neoadjuvant Nivolumab
- 1st line Cemiplimab in patients with PD-L1 > 50%

Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIA non-small-cell lung cancer (IMpower010): a randomized multicentre, open-label, phase 3 trail

Population	PD-L1 >1% n=476		II-IIIA n=882		IB-IIIA (intent to treat) n=1005	
3 year PFS	48.2%	60%	55.7 %	49.4%	57.9%	52.6%
P-value	.0039		.020		.040	

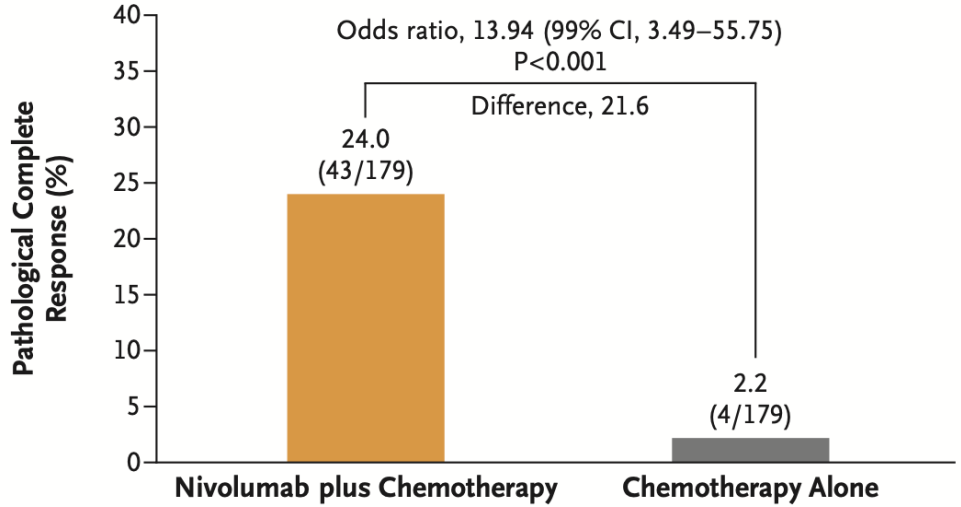
	Atezolizumab group (n=495)	Best supportive care group (n=495)
Adverse event		
Any grade	459 (93%)	350 (71%)
Grade 3–4	108 (22%)	57 (12%)
Serious	87 (18%)	42 (8%)
Grade 5	8 (2%)*	3 (1%)†
Led to dose interruption of atezolizumab	142 (29%)	..
Led to atezolizumab discontinuation	90 (18%)	..
Immune-mediated adverse events		
Any grade	256 (52%)	47 (9%)
Grade 3–4	39 (8%)	3 (1%)
Required the use of systemic corticosteroids‡	60 (12%)	4 (1%)
Led to discontinuation	52 (11%)	0

Data are n (%). *Interstitial lung disease, multiple organ dysfunction syndrome, myocarditis, and acute myeloid leukaemia (all four events related to atezolizumab), and pneumothorax, cerebrovascular accident, arrhythmia, and acute cardiac failure. †Pneumonia; pulmonary embolism; and cardiac tamponade and septic shock in the same patient. ‡Atezolizumab-related.

Table 2: **Safety summary in the safety evaluable population**

Lancet. 2021 Oct 9;398(10308):1344-1357.

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer



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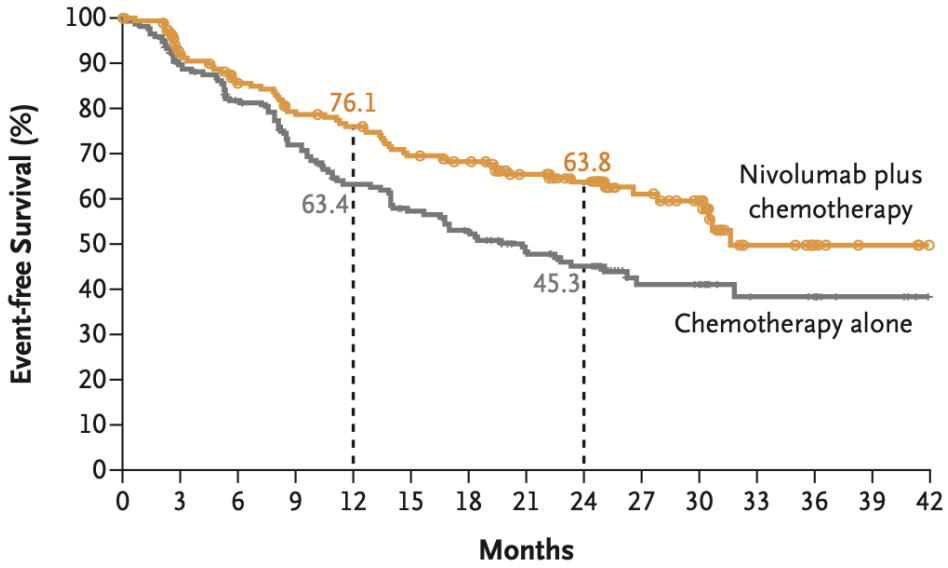


No. at Risk															
Nivolumab plus chemotherapy	179	151	136	124	118	107	102	87	74	41	34	13	6	3	0
Chemotherapy alone	179	144	126	109	94	83	75	61	52	26	24	13	11	4	0

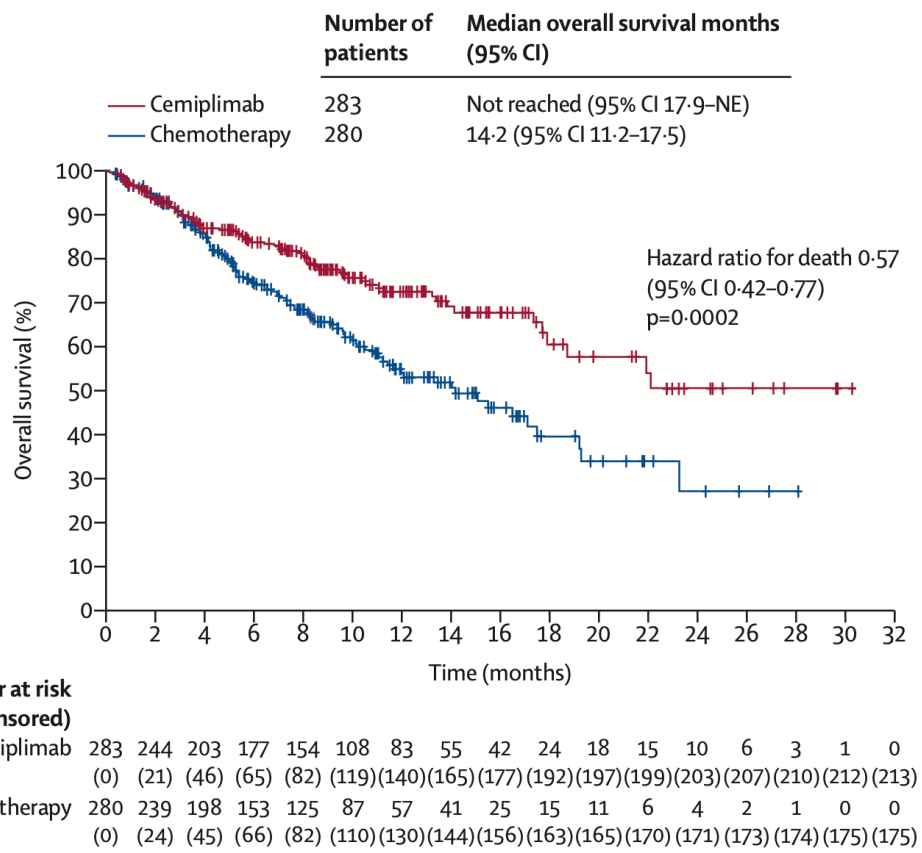
	No. of Patients	Median Event-free Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

Hazard ratio for disease progression, disease recurrence, or death, 0.63 (97.38% CI, 0.43–0.91)
P=0.005

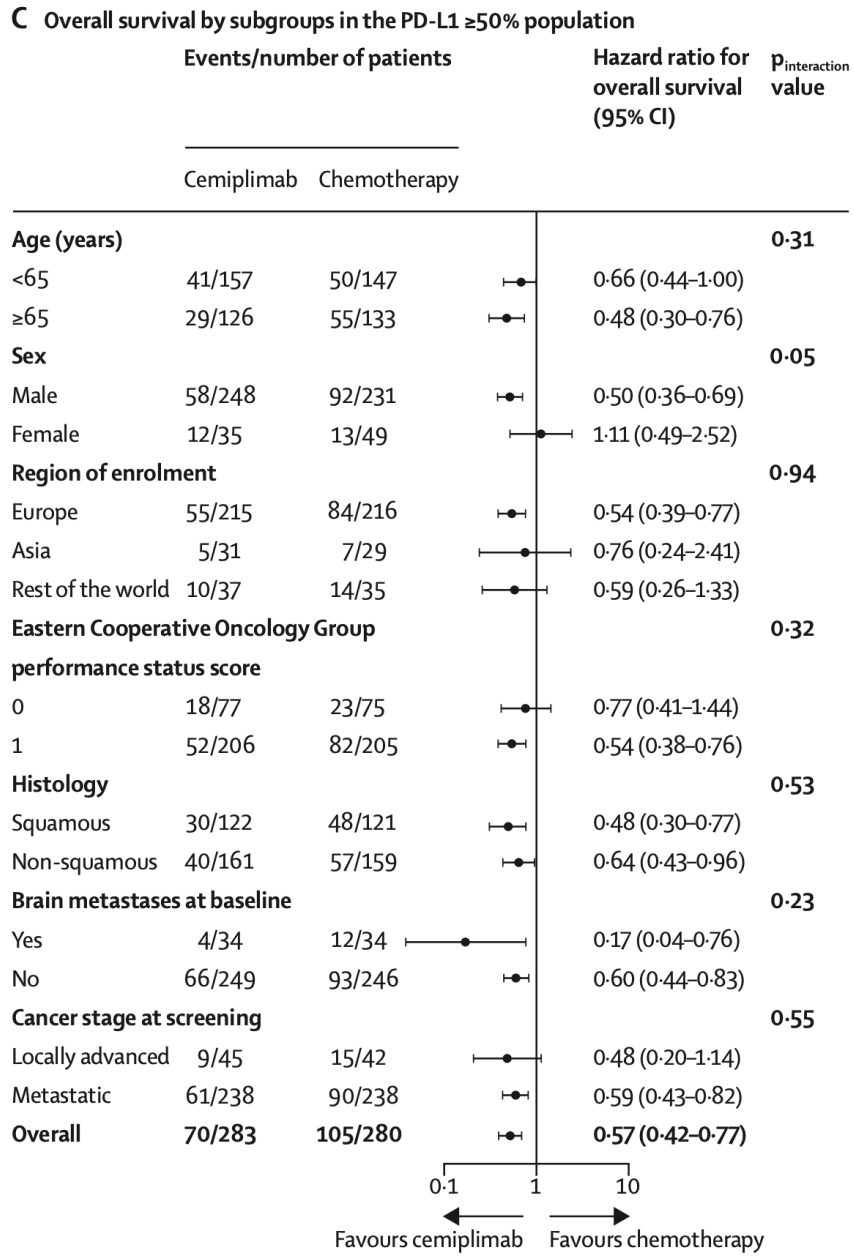
N Engl J Med 2022 May 26;386(21):1973-1985

Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial.

A Overall survival in the PD-L1 ≥50% population



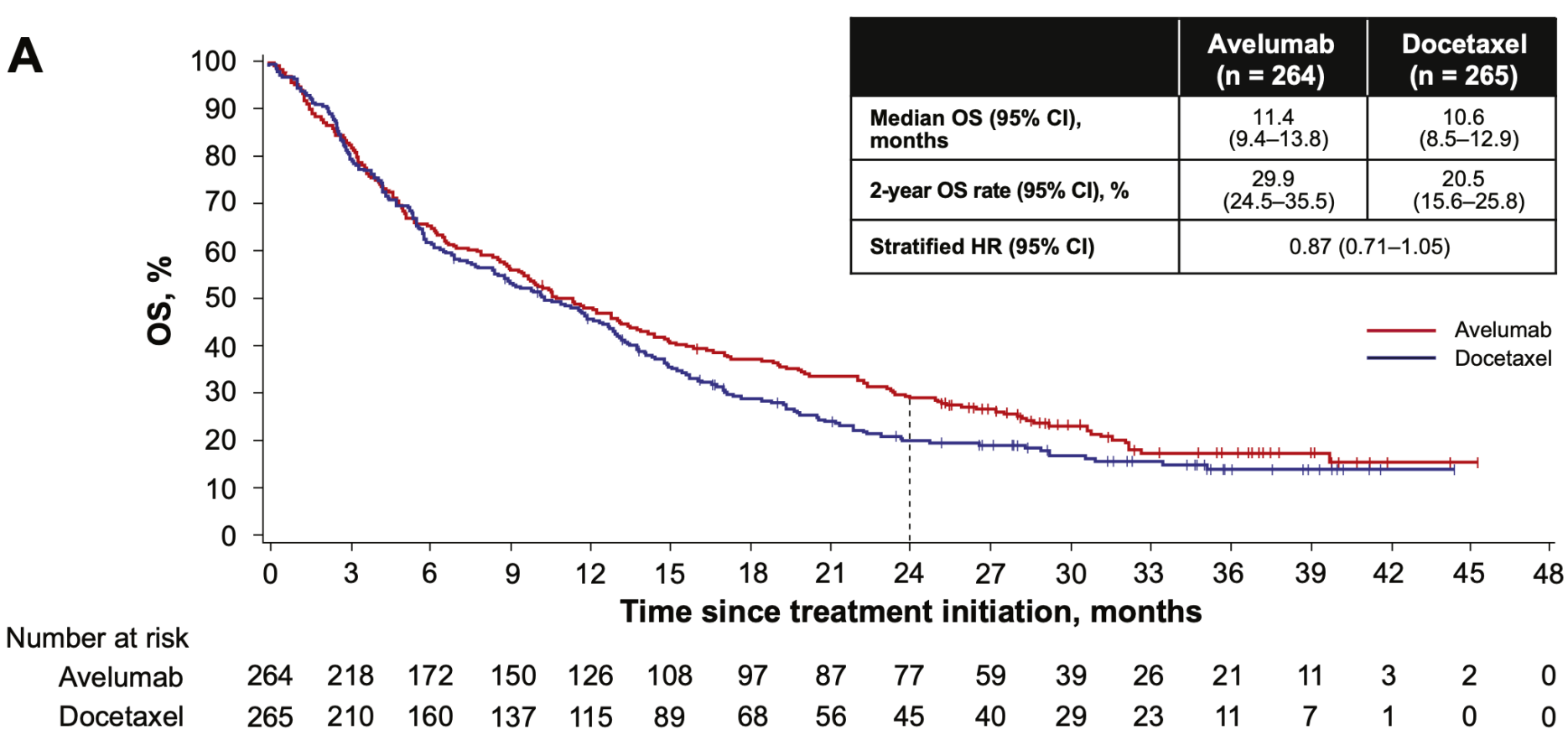
C Overall survival by subgroups in the PD-L1 ≥50% population



Lancet. 2021 Feb 13;397(10274):592-604.

Not FDA approved

Avelumab Versus Docetaxel in Patients With Platinum-Treated Advanced NSCLC: 2-Year Follow-Up From the JAVELIN Lung 200 Phase 3 Trial.

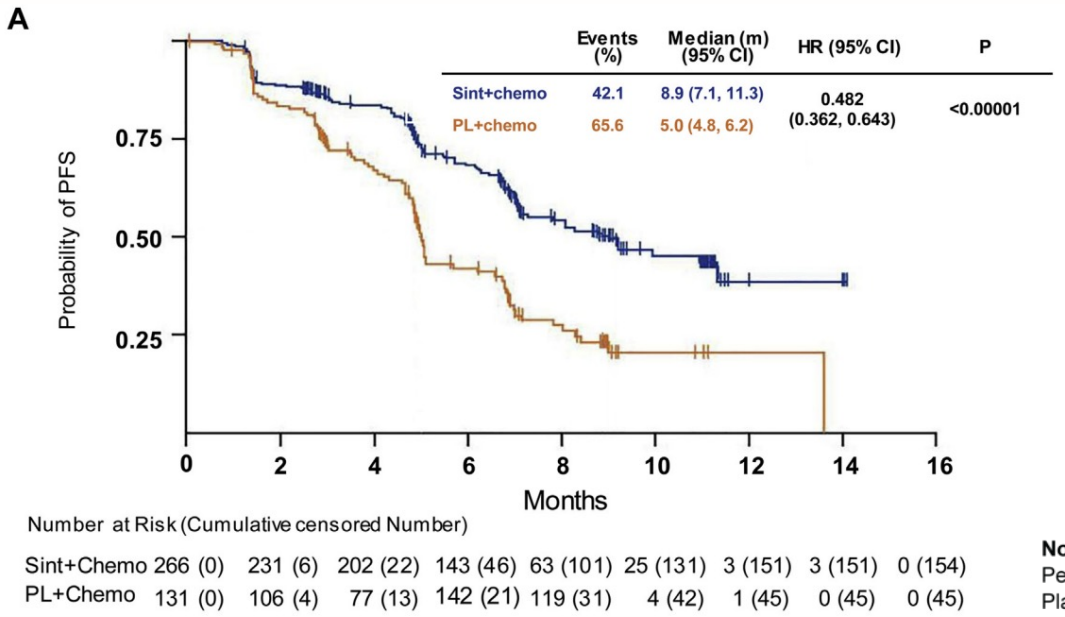


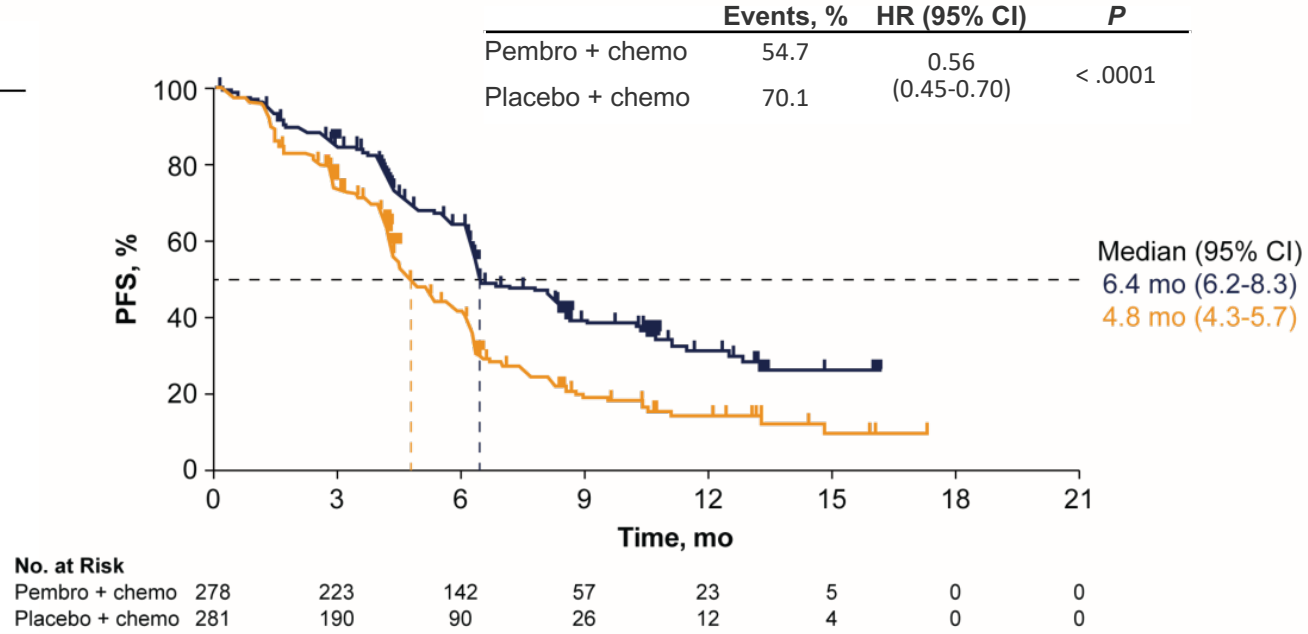
	Avelumab (n = 264)	Docetaxel (n = 265)
Median OS (95% CI), months	11.4 (9.4–13.8)	10.6 (8.5–12.9)
2-year OS rate (95% CI), %	29.9 (24.5–35.5)	20.5 (15.6–25.8)
Stratified HR (95% CI)	0.87 (0.71–1.05)	

J Thorac Oncol. 2021 Aug;16(8):1369-1378.

No approval for Sintilimab

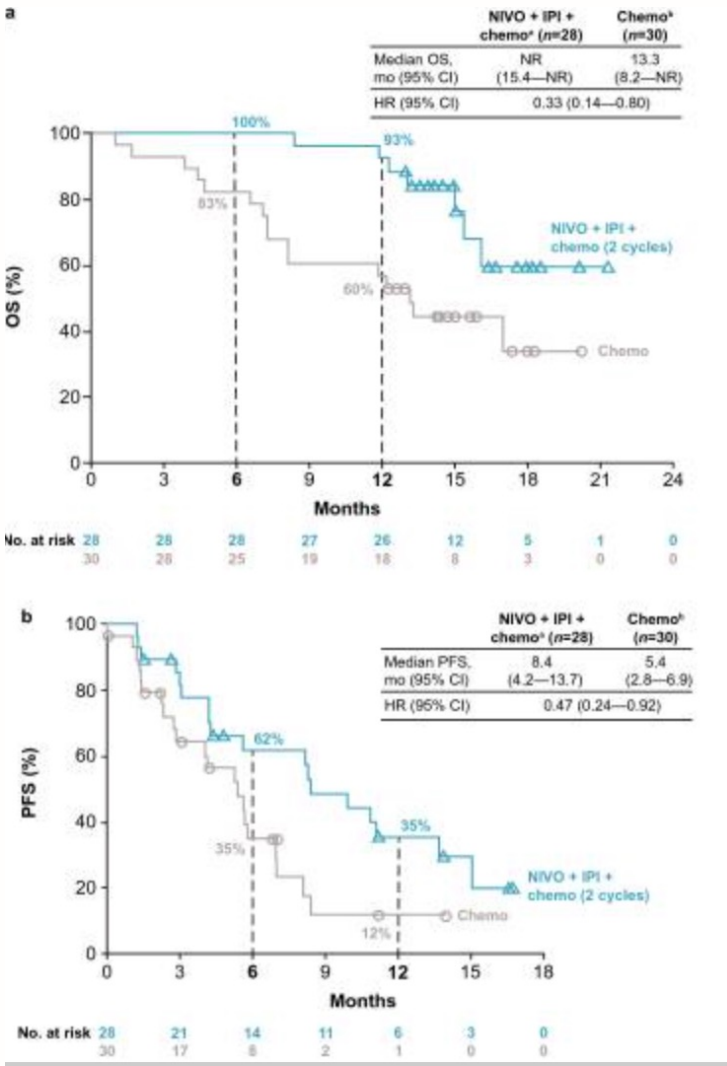
- Sintilimab Orient 11
- Pembrolizumab Keynote 407





Subset analysis of Asian patients in CheckMate 9LA

	NIVO + IPI + chemo[a] (*n* = 28)		Chemo[b] (*n* = 30)	
	Any grade	Grade 3–4	Any grade	Grade 3–4
Total patients with an event,[c] *n* (%)	28 (100)	16 (57)	29 (97)	18 (60)
TRAEs occurring in ≥ 15% of patients in either treatment arm, *n* (%)				
Decreased appetite	13 (46)	2 (7)	12 (40)	3 (10)
Constipation	12 (43)	0	17 (57)	0
Nausea	11 (39)	0	18 (60)	0
Neutrophil count decreased	10 (36)	5 (18)	8 (27)	5 (17)
Fatigue	8 (29)	1 (4)	7 (23)	0
Malaise	8 (29)	0	8 (27)	0
Maculopapular rash	8 (29)	3 (11)	2 (7)	0
Anemia	8 (29)	1 (4)	15 (50)	7 (23)
Rash	7 (25)	2 (7)	0	0
Alopecia	6 (21)	0	8 (27)	0
White blood cell count decreased	6 (21)	3 (11)	6 (20)	2 (7)
Diarrhea	5 (18)	0	3 (10)	1 (3)
Pyrexia	5 (18)	0	2 (7)	0
Platelet count decreased	4 (14)	1 (4)	7 (23)	1 (3)
Peripheral sensory neuropathy	3 (11)	0	9 (30)	0
Hiccups	3 (11)	0	8 (27)	0
TRAEs leading to treatment discontinuation[d], *n* (%)	6 (21)	3 (11)	5 (17)	2 (7)



Int J Clin Oncol. 2022 Apr;27(4):695-706.

Camrelizumab Plus Carboplatin and Paclitaxel as First-Line Treatment for Advanced Squamous NSCLC (CameL-Sq): A Phase 3 Trial.

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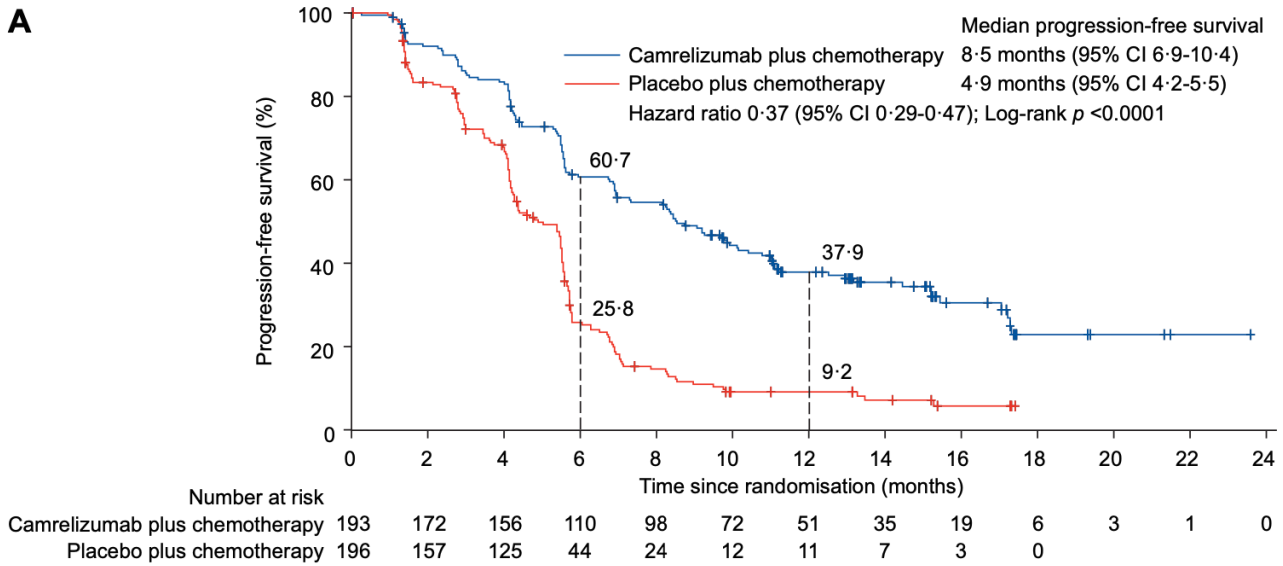

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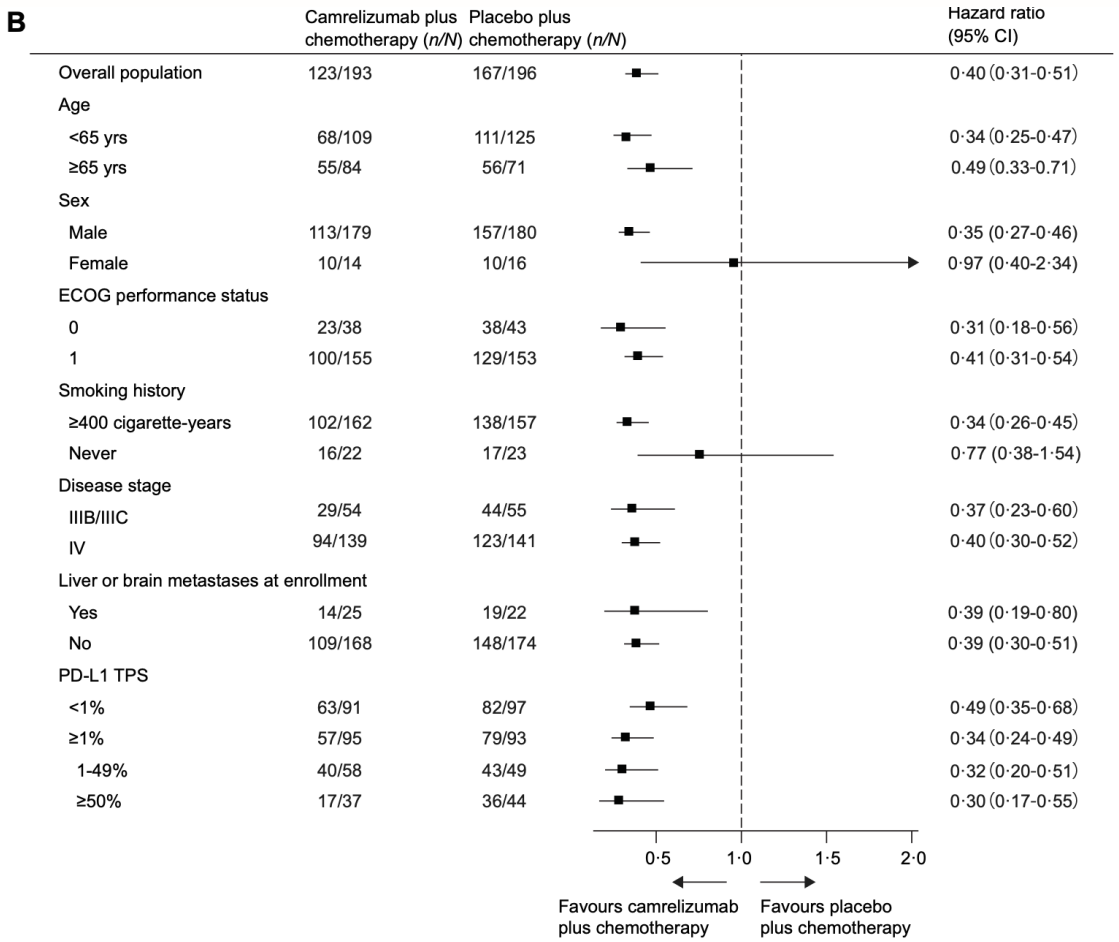
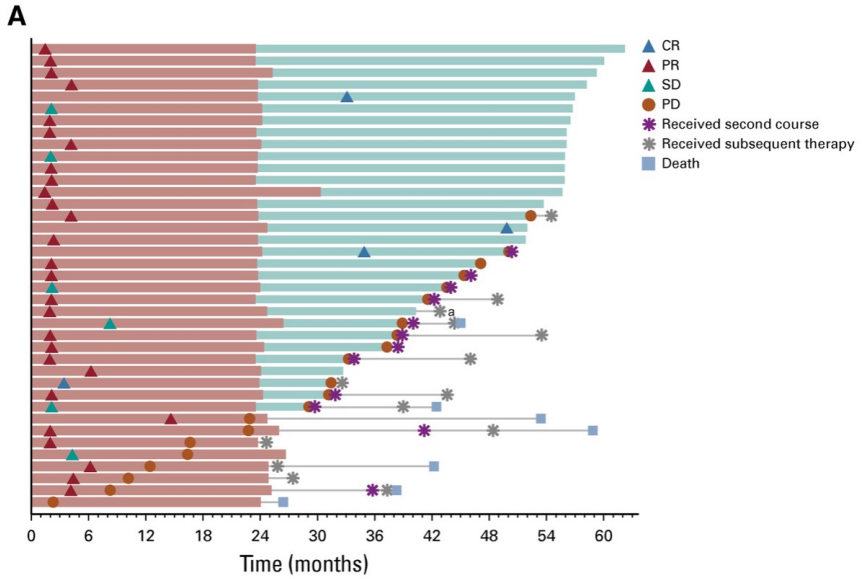


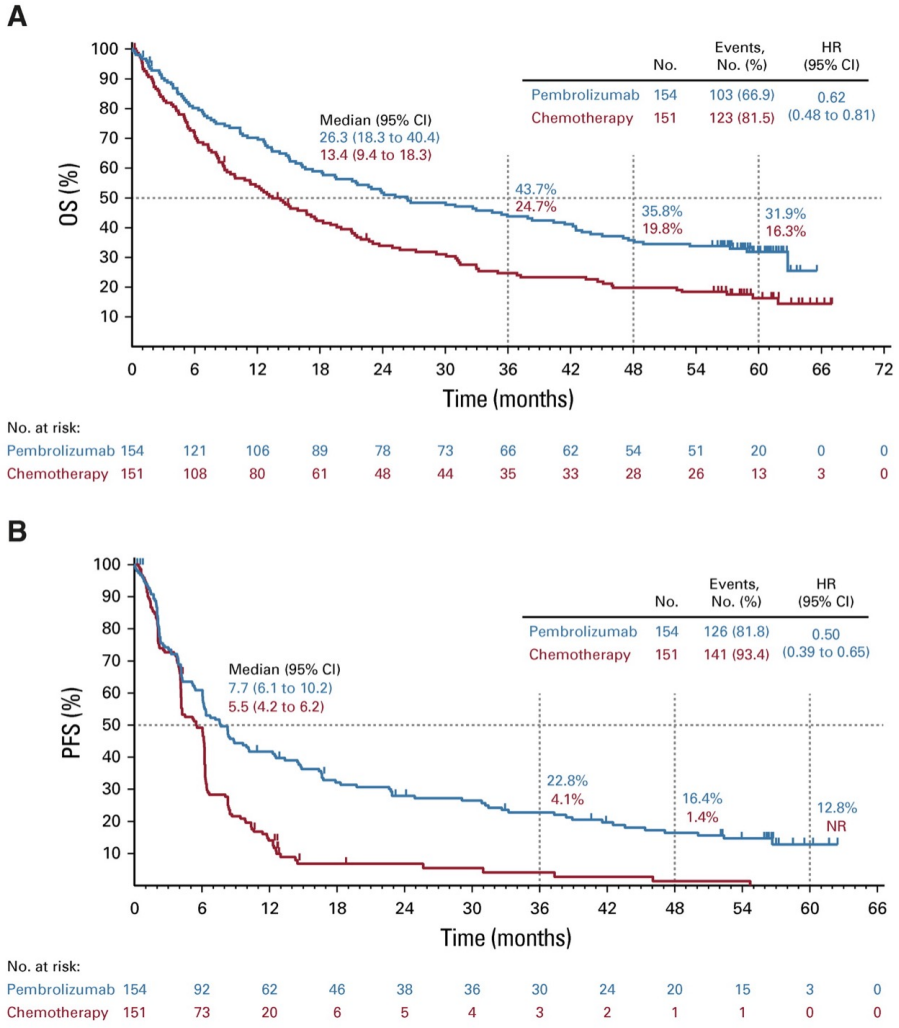
J Thorac Oncol. 2022 Apr;17(4):544-557.

Long Term Follow-up

Five-Year Outcomes from Keynote 024 With Pembrolizumab Versus Chemotherapy for Metastatic NSCLCWith PD-L1 TP≥ 50

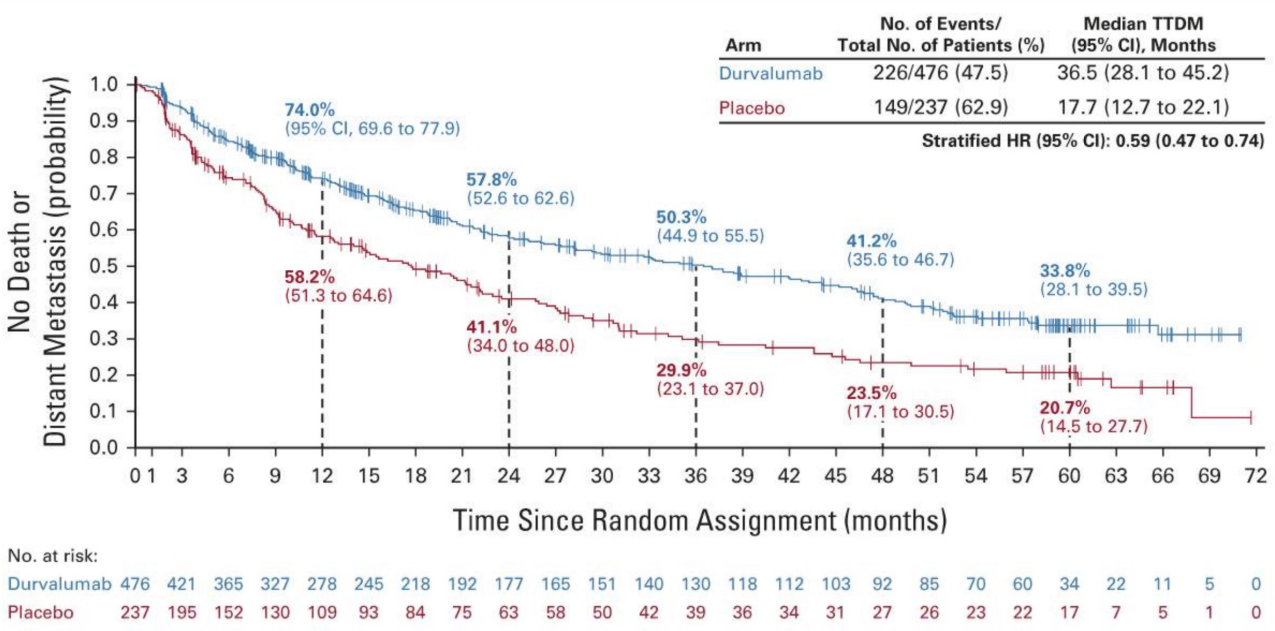
After 35 cycles given

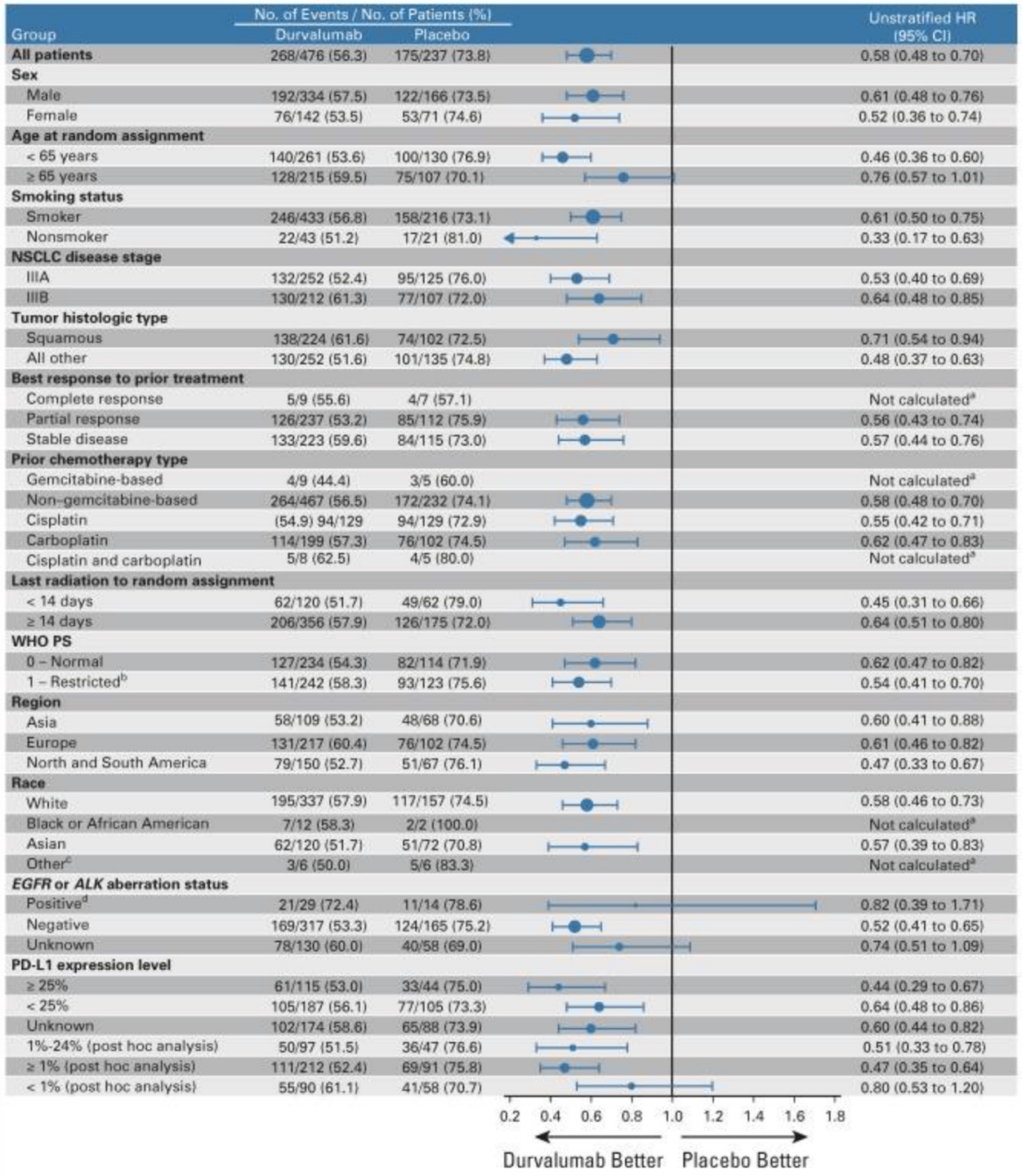




Journal of Clinical Oncology 39, no. 21 (July 20, 2021) 2339-2349

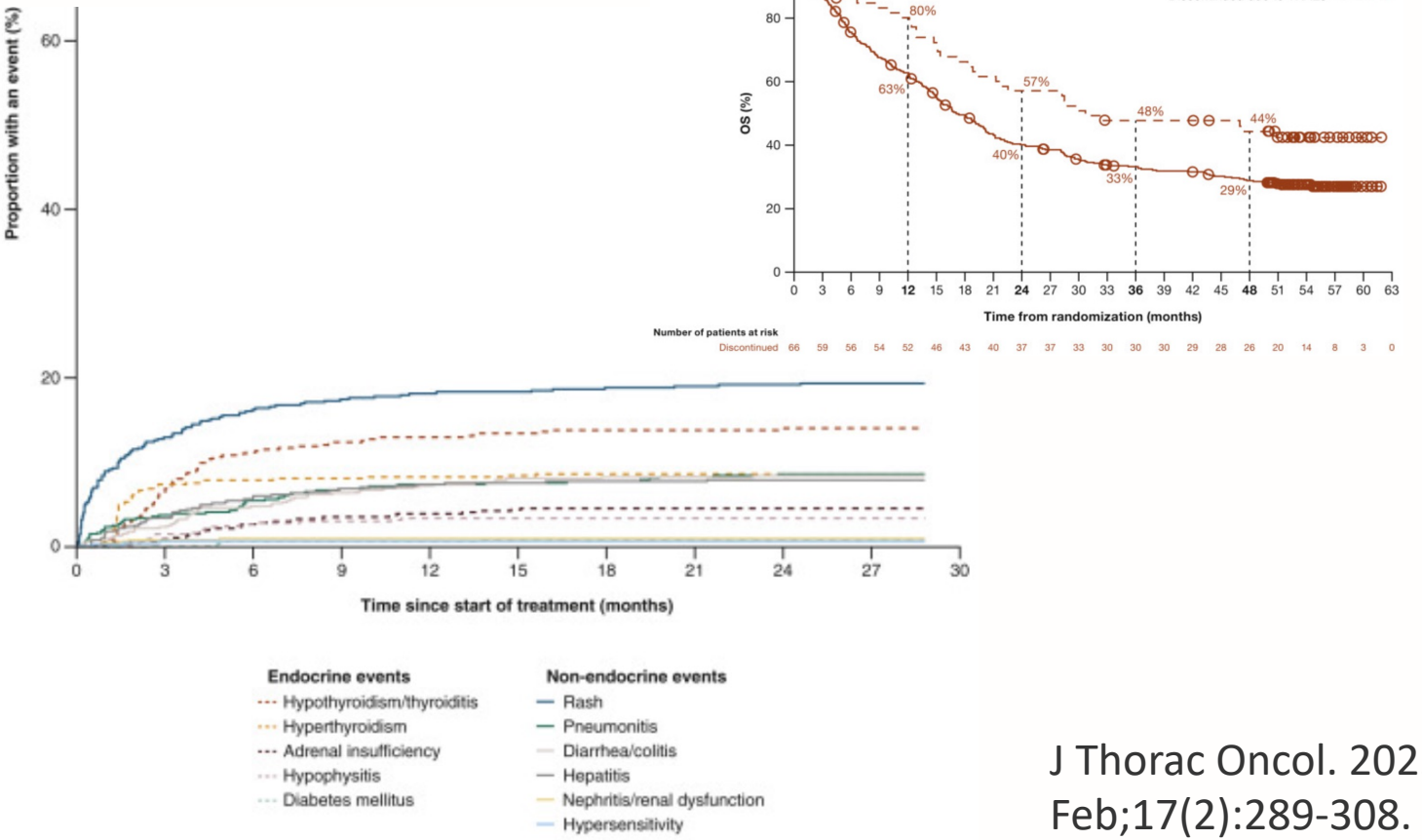
Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer



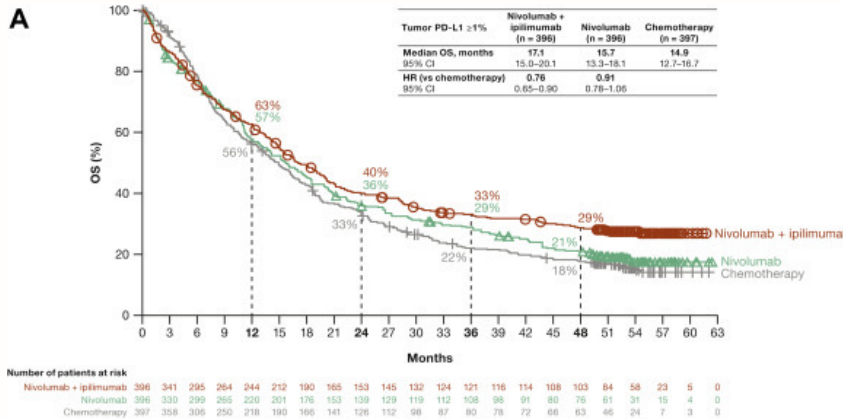


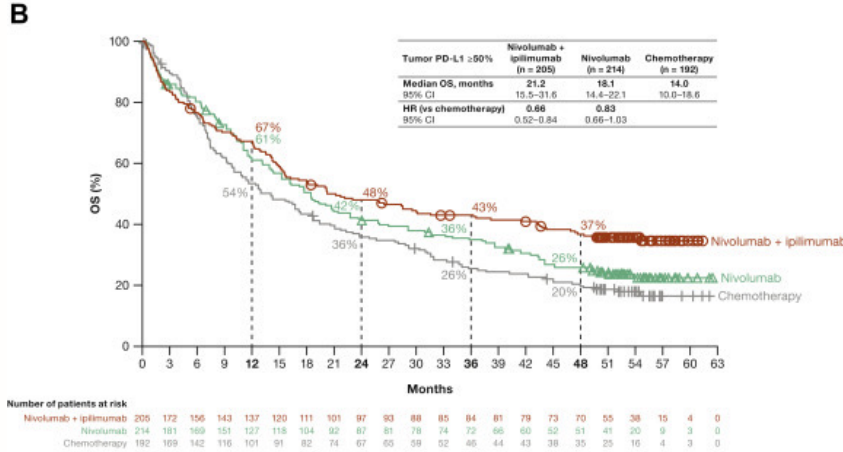
J Clin Oncol. 2022 Apr 20;40(12):1301-1311.

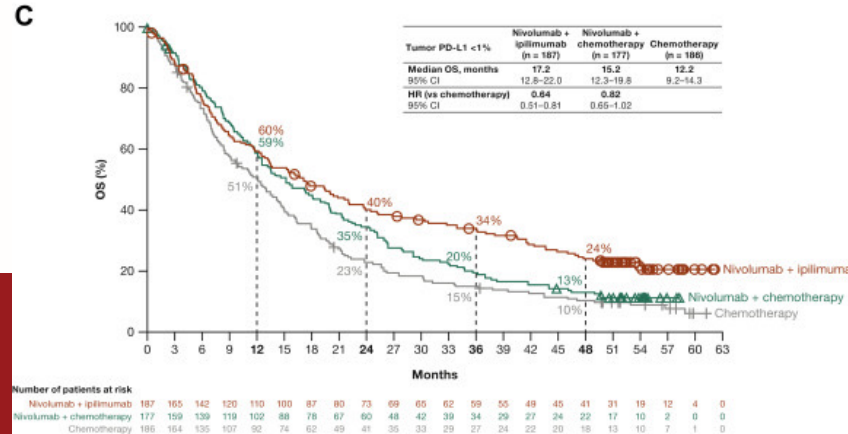
First-Line Nivolumab Plus Ipilimumab in Advanced NSCLC: 4-Year Outcomes From the Randomized, Open-Label, Phase 3 CheckMate 227



J Thorac Oncol. 2022 Feb;17(2):289-308.



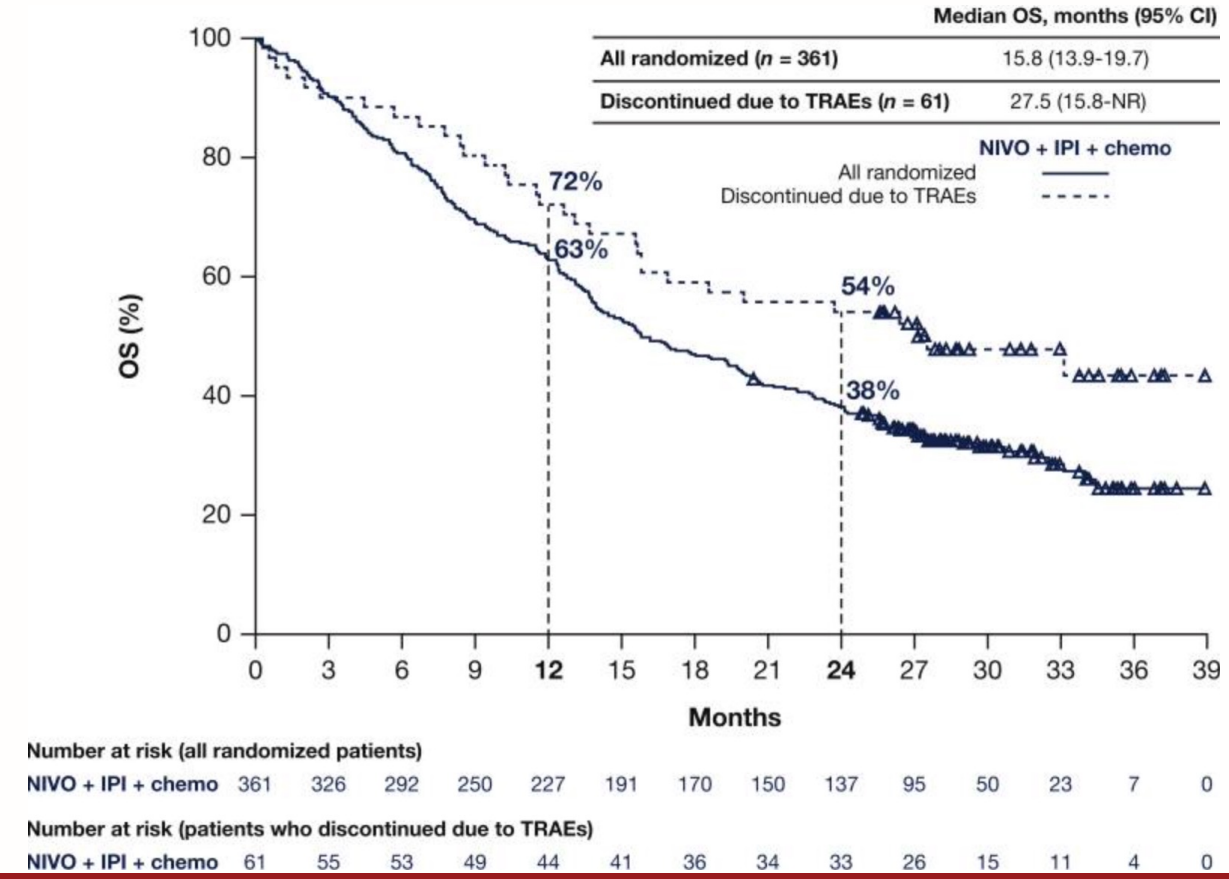


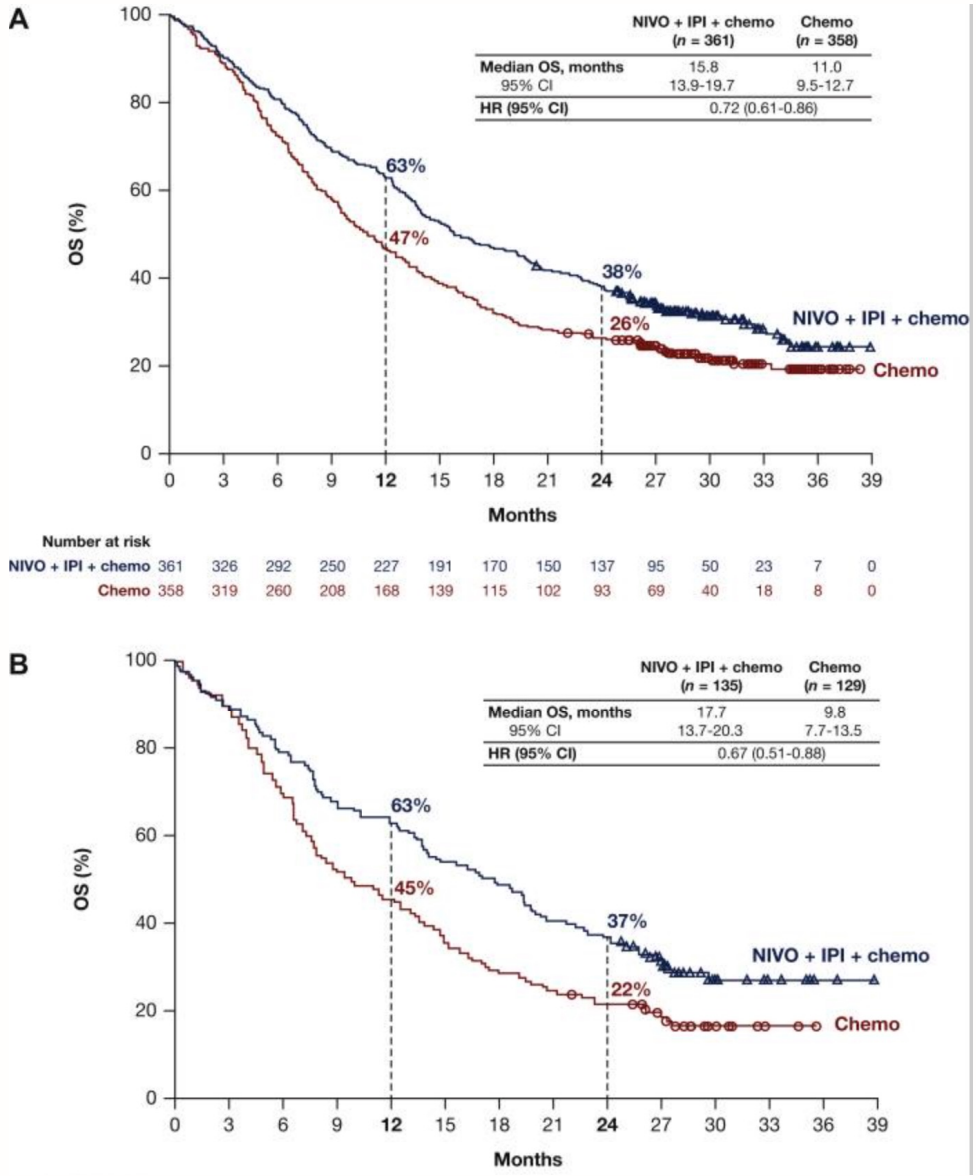


J Thorac Oncol. 2022 Feb;17(2):289-308.

First-line nivolumab plus ipilimumab with two cycles of chemotherapy versus chemotherapy alone (four cycles) in advanced non-small-cell lung cancer: CheckMate 9LA 2-year update

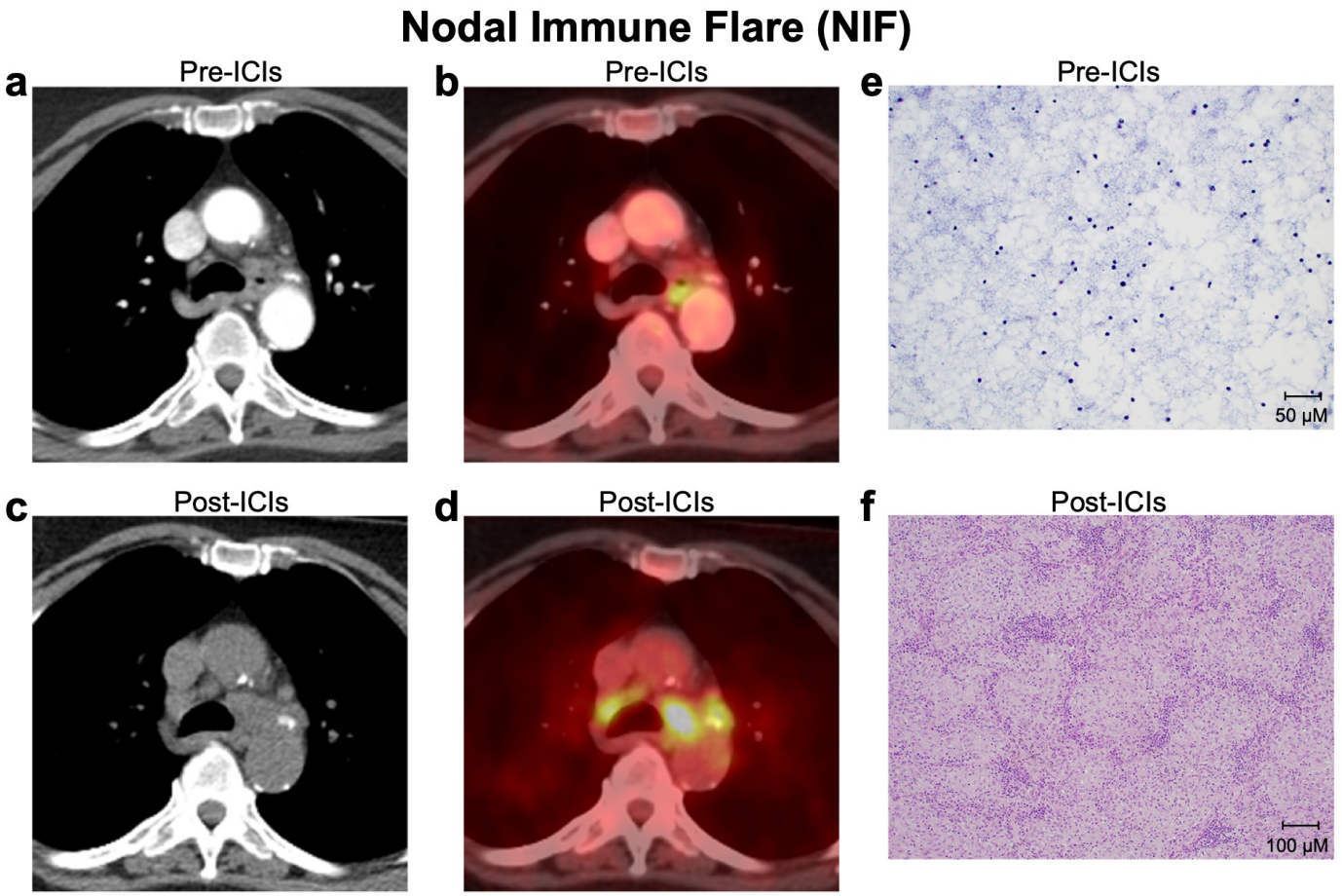
AE's may be good!

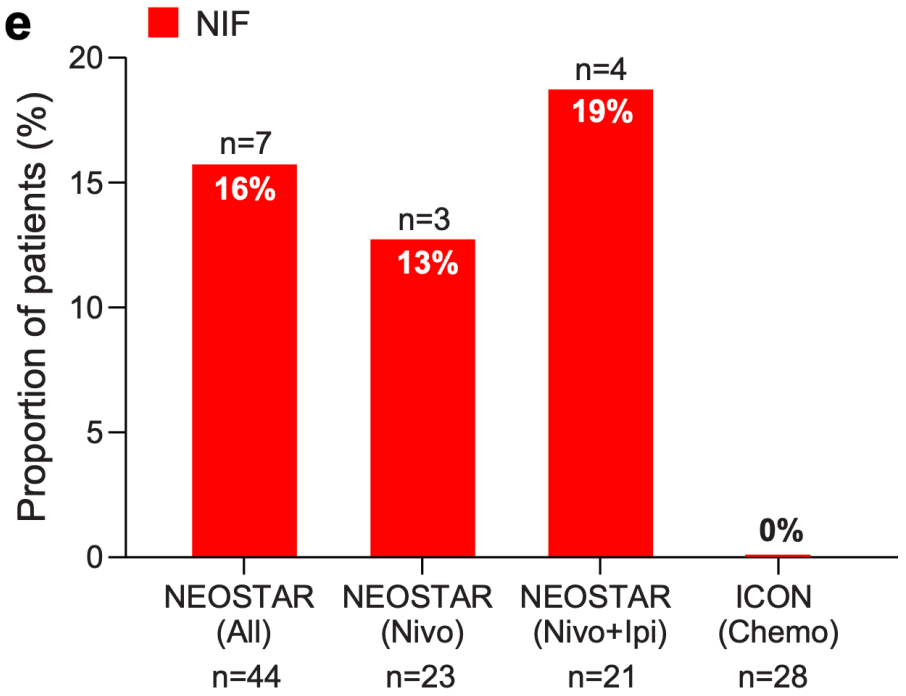




ESMO Open. 2021 Oct;6(5):100273.

Nodal immune flare mimics nodal disease progression following neoadjuvant immune checkpoint inhibitors in non-small cell lung cancer

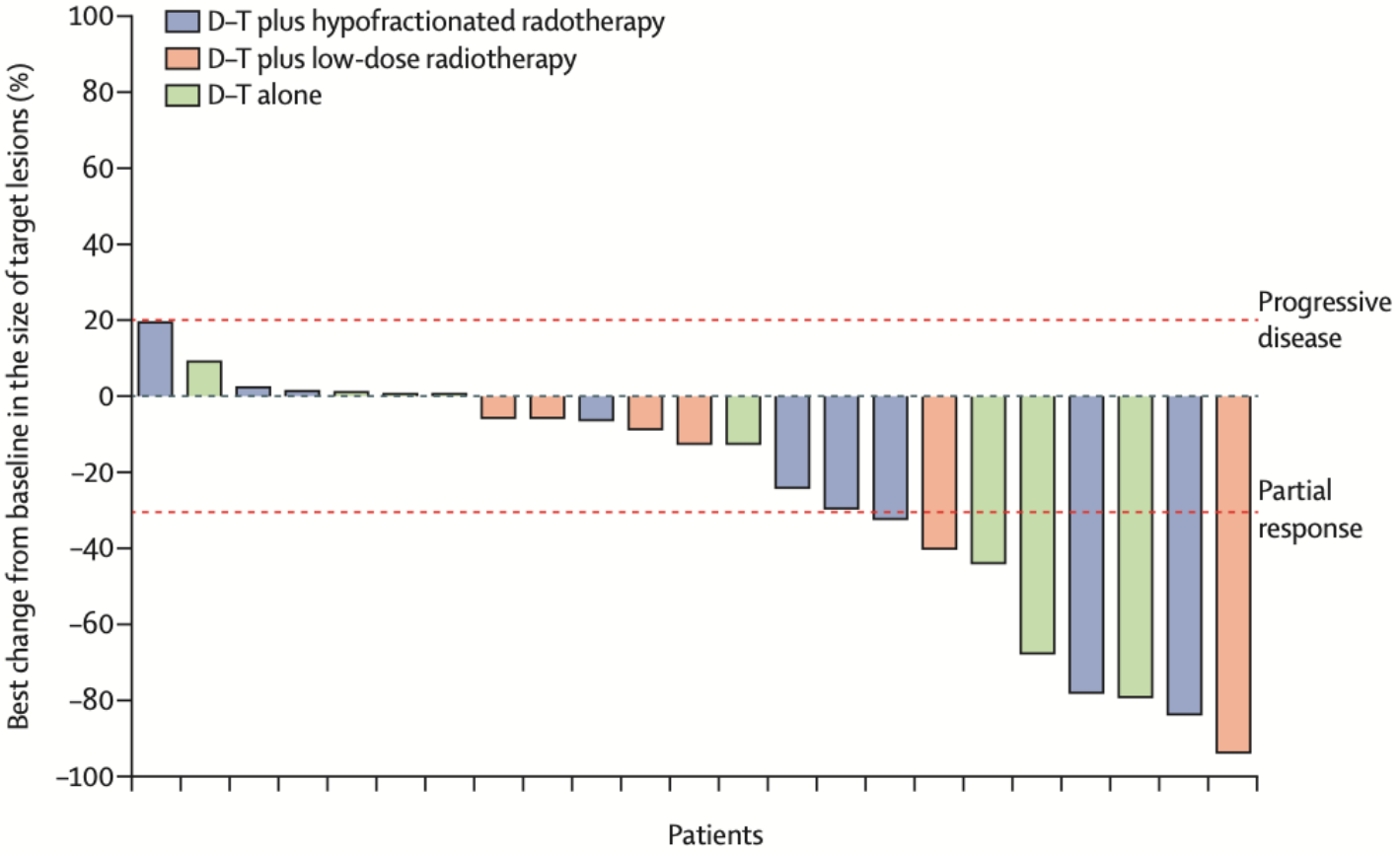


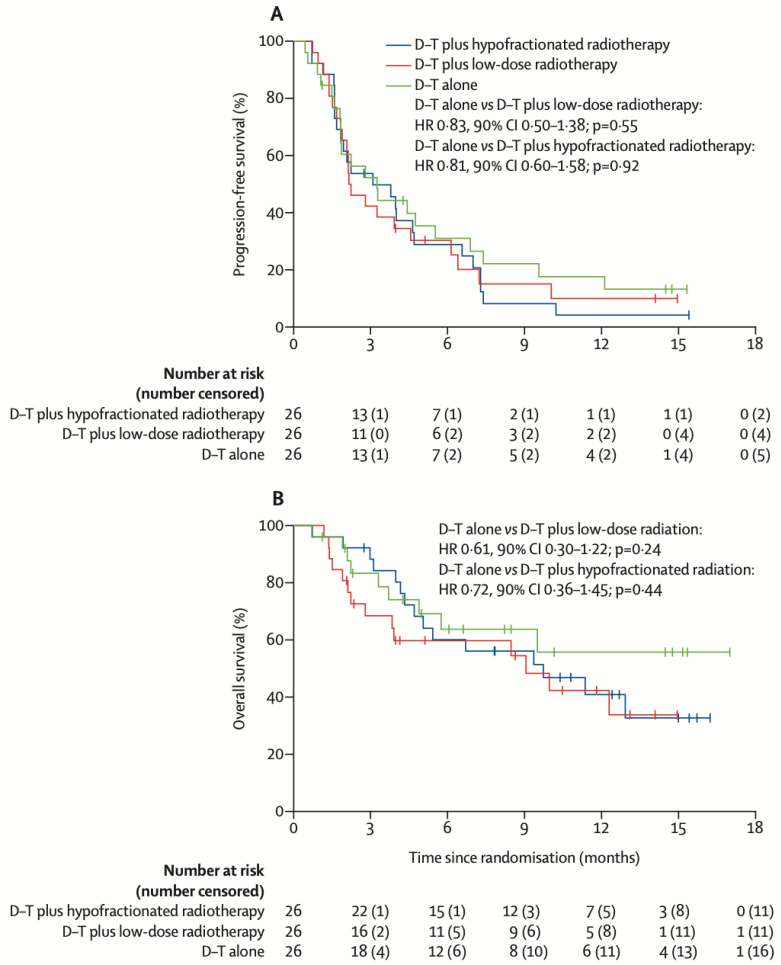


NIF is associated with an inflamed nodal immune microenvironment and with fecal abundance of genera belonging to the family Coriobacteriaceae of phylum Actinobacteria

Nat Commun. 2021 Aug 19;12(1):5045.

Durvalumab plus tremelimumab alone or in combination with low-dose or hypofractionated radiotherapy in metastatic non-small-cell lung cancer refractory to previous PD(L)-1 therapy: an open-label, multicentre, randomised, phase 2 trial.





Lancet Oncol. 2022 Feb;23(2):279-291.

Improving on PD-L1 blockade

CCTG BR34: A Randomized Phase 2 Trial of Durvalumab and Tremelimumab With or Without

C

Subgroup	No. of Patients	Median OS (months): Durvalumab + Tremelimumab + Chemotherapy (n = 151)	Median OS (months): Durvalumab + Tremelimumab (n = 150)	Hazard Ratio for Death (90% CI)
OS – Overall	**301**	**16.6**	**14.1**	**0.88 (0.67–1.16)**
Age				
<65	155	16.7	14.8	0.73 (0.49–1.06)
≥65	146	15.3	10.6	0.85 (0.58–1.23)
Sex				
Female	139	18.7	12.9	0.67 (0.45–1.02)
Male	162	12.0	14.0	1.01 (0.72–1.42)
CNS Metastases				
No	252	15.3	12.9	0.87 (0.66–1.16)
Yes	49	NR	18.3	0.58 (0.28–1.17)
Liver Metastases				
No	241	18.7	16.8	0.81 (0.60–1.11)
Yes	60	7.9	8.7	0.81 (0.48–1.35)
Histology				
Squamous	55	8.4	10.5	1.11 (0.65–1.88)
Nonsquamous	246	18.7	16.0	0.76 (0.56–1.03)
Smoking Status				
Never	30	16.7	14.8	0.72 (0.31–1.65)
Former	201	15.3	12.9	0.91 (0.66–1.25)
Current	70	NR	14.2	0.67 (0.38–1.17)
Disease Stage				
IVA	103	18.7	17.5	0.99 (0.60–1.62)
IVB	198	14.6	11.5	0.79 (0.58–1.07)

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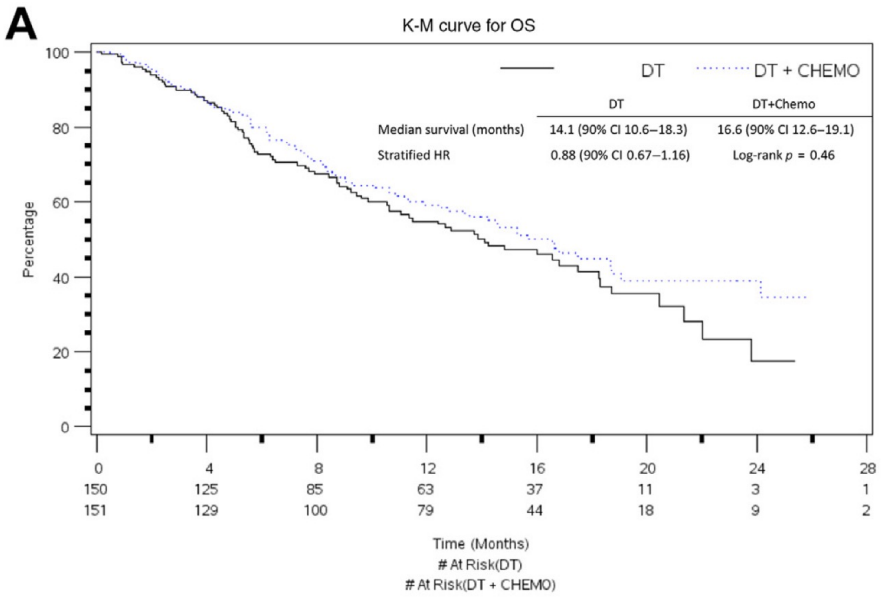

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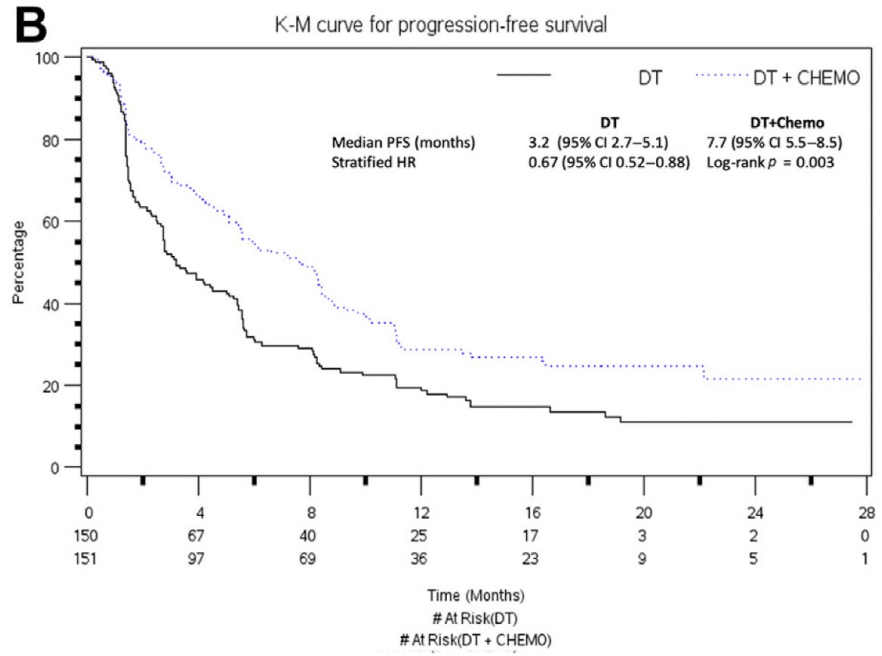


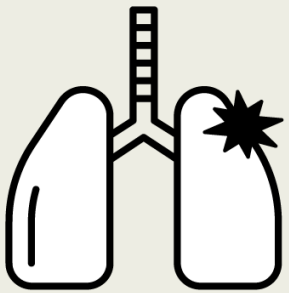
J Thorac Oncol. 2022 Mar;17(3):434-445.

JAMA Oncology

RCT: Nivolumab Plus Ipilimumab vs Nivolumab for Previously Treated Patients With Stage IV Squamous Cell Lung Cancer

POPULATION

169 Men, 83 Women



Pretreated, immunotherapy-naive stage IV or recurrent squamous cell non-small cell lung cancer

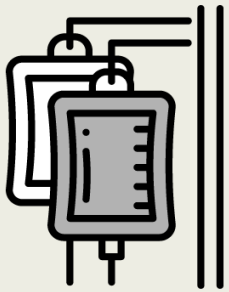
Median age, 67.5 y (range, 41.8-90.3 y)

SETTINGS / LOCATIONS

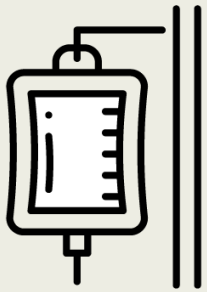
58 Institutions in the US through the National Clinical Trials Network

INTERVENTION

252 Patients randomized and analyzed



125 Nivolumab plus ipilimumab
Nivolumab, 3 mg/kg, intravenously every 2 wk with ipilimumab, 1 mg/kg, intravenously every 6 wk



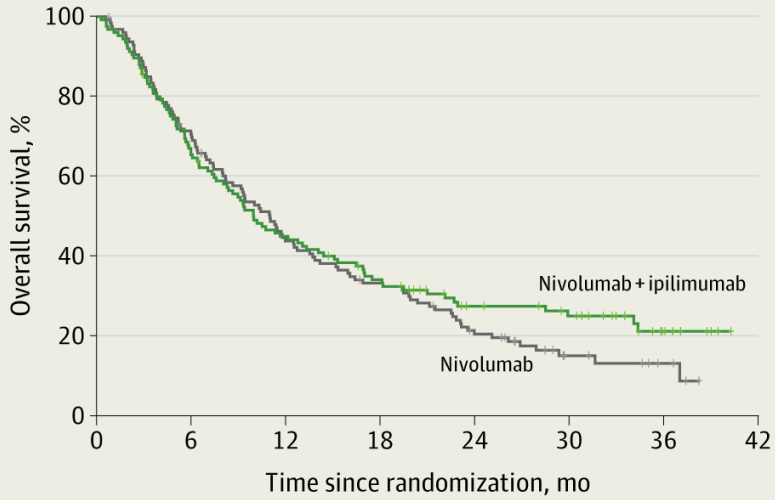
127 Nivolumab
Nivolumab, 3 mg/kg, intravenously every 2 wk until disease progression or intolerable toxic effects

PRIMARY OUTCOME

Overall survival, defined as time from randomization to death due to any cause

FINDINGS

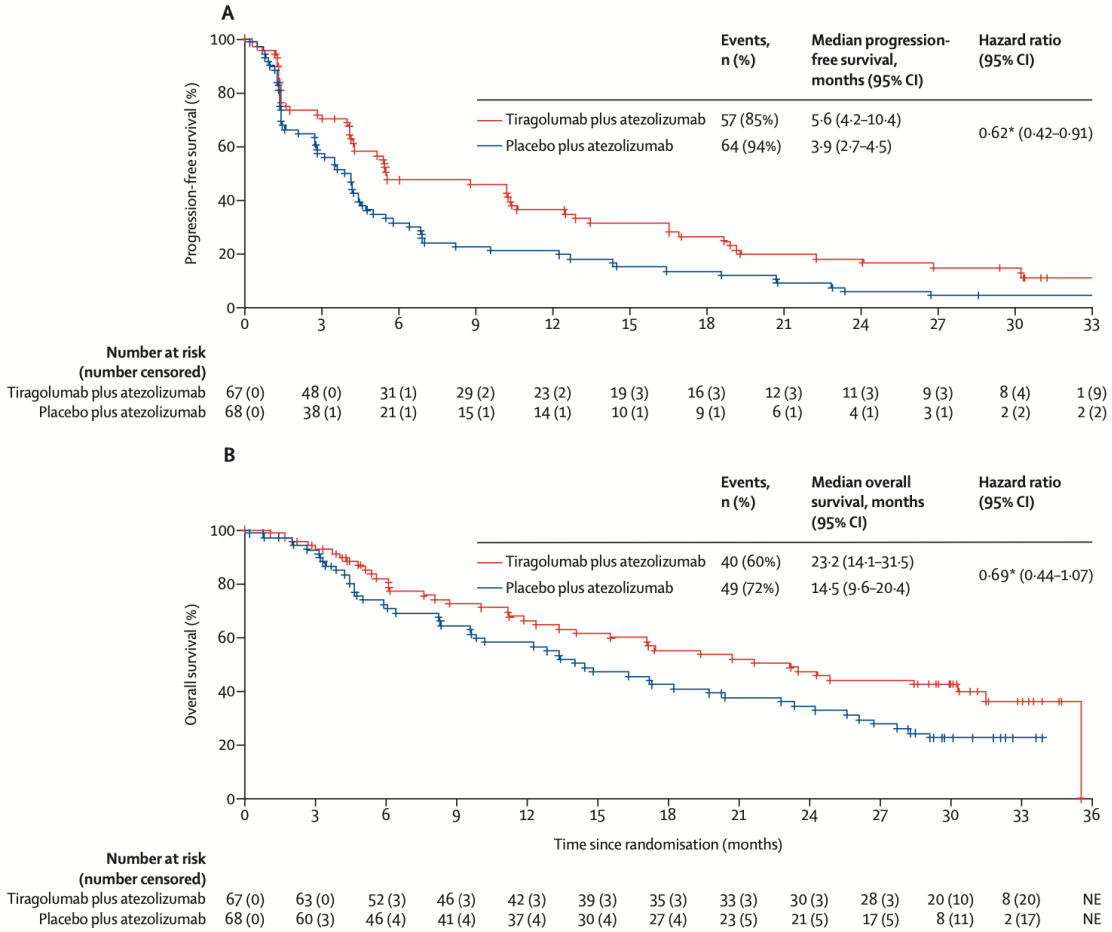
Ipilimumab added to nivolumab did not improve outcomes in patients with pretreated immunotherapy-naive squamous cell non-small cell lung cancer (HR, 0.87 [95% CI, 0.66-1.16]; *P* = .34)

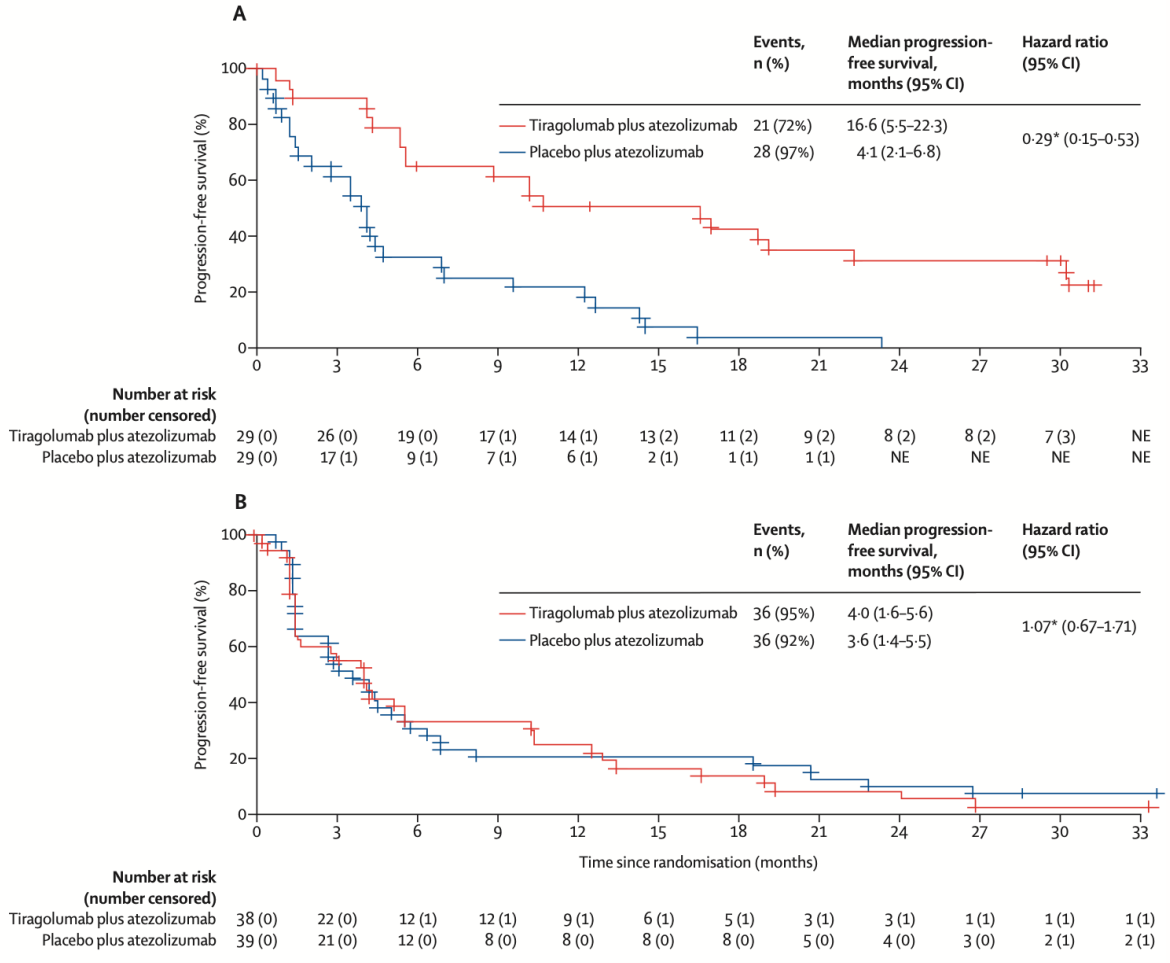


Median overall survival, mo:
Nivolumab plus ipilimumab: 10 (95% CI, 8.0-14.4)
Nivolumab: 11 (95% CI, 8.6-13.7)

Gettinger SN, Redman MW, Bazhenova L, et al. Nivolumab plus ipilimumab vs nivolumab for previously treated patients with stage IV squamous cell lung cancer: the Lung-MAP S1400I phase 3 randomized clinical trial. *JAMA Oncol.* Published online July 15, 2021. doi:10.1001/jamaoncol.2021.2209

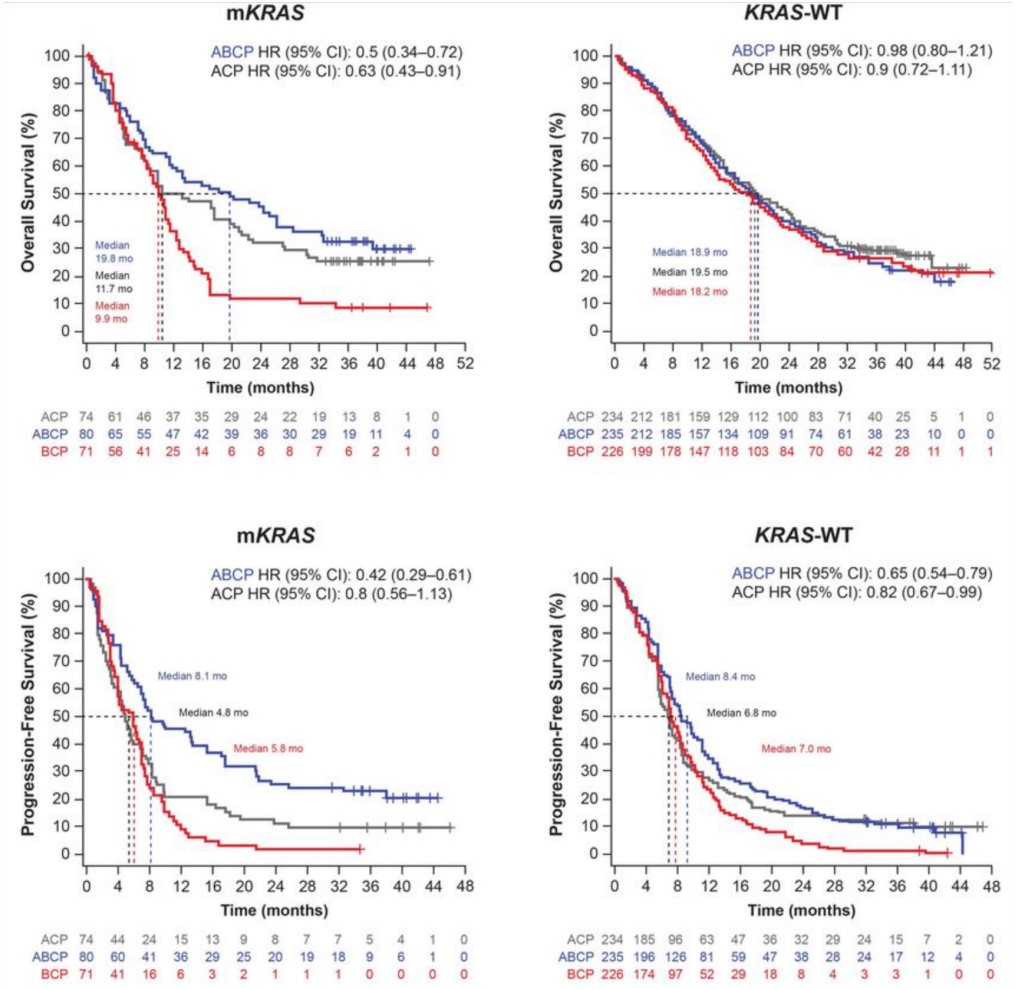
Tiragolumab plus atezolizumab versus placebo plus atezolizumab as a first-line treatment for PD-L1-selected non-small-cell lung cancer (CITYSCAPE): primary and follow-up analyses of a randomised, double-blind, phase 2 study.

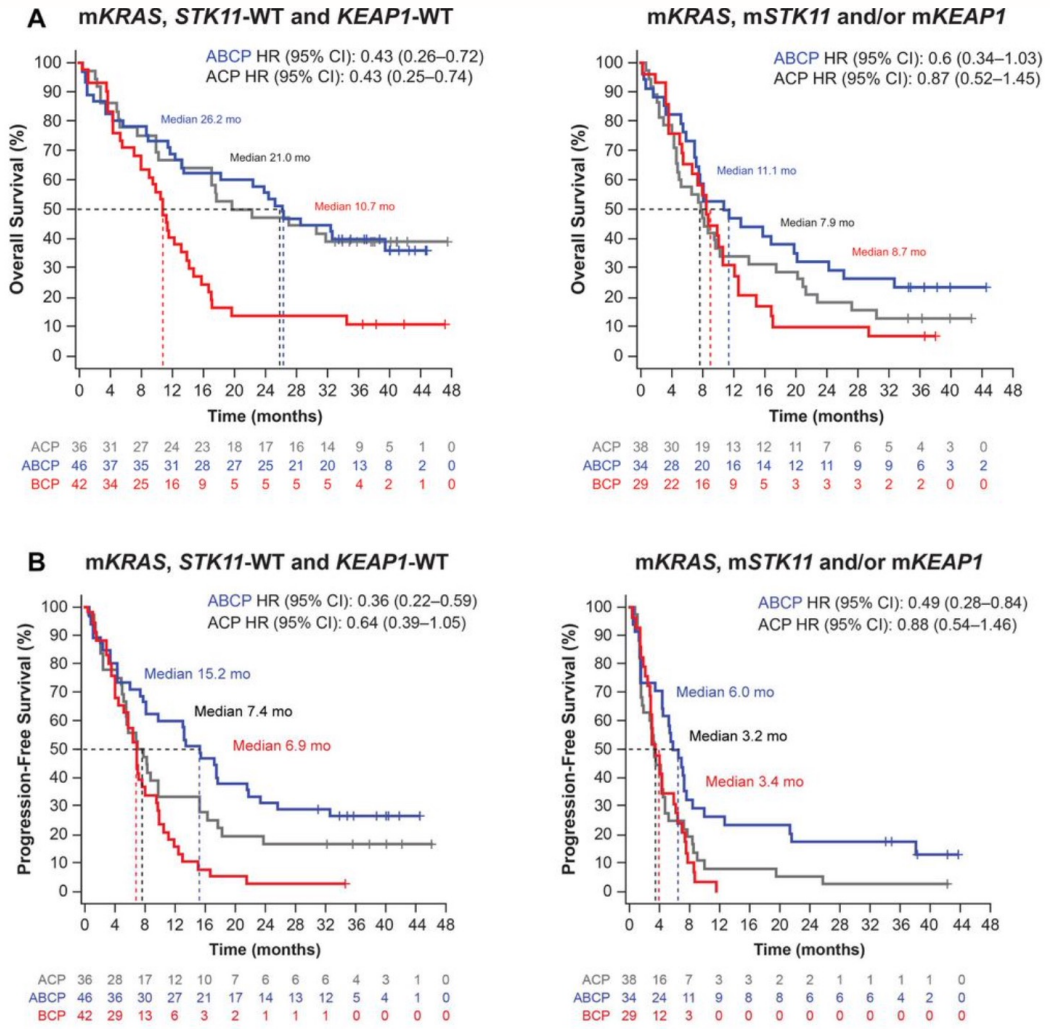




Lancet Oncol. 2022 Jun;23(6):781-792.

Clinical efficacy of atezolizumab plus bevacizumab and chemotherapy in *KRAS*-mutated non-small cell lung cancer with *STK11*, *KEAP1,* or *TP53* comutations: subgroup results from the phase III IMpower150 trial.

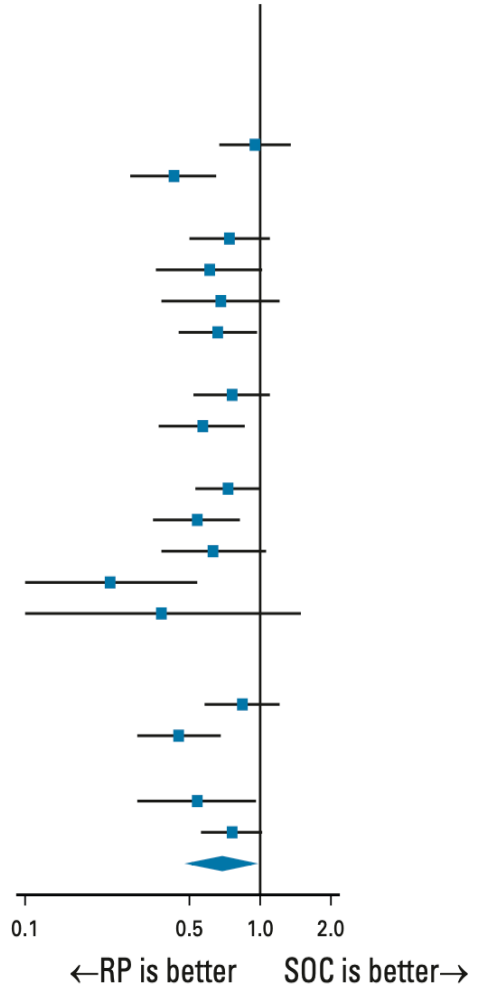


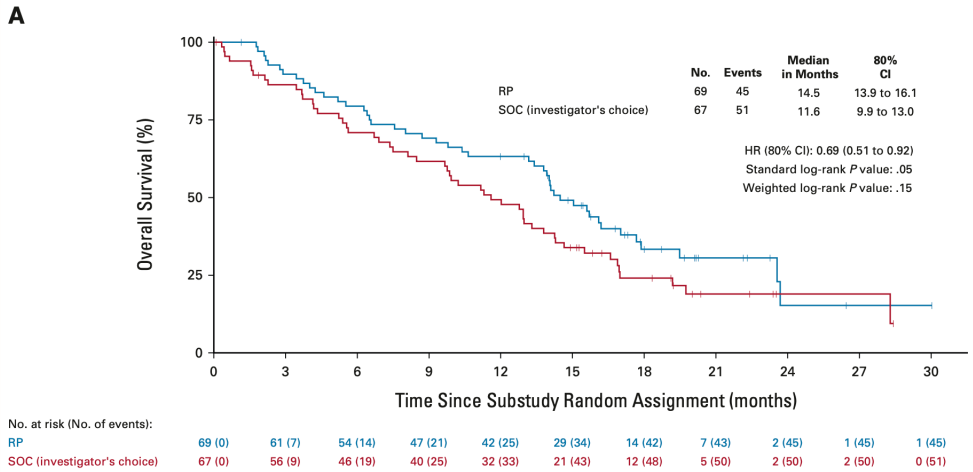


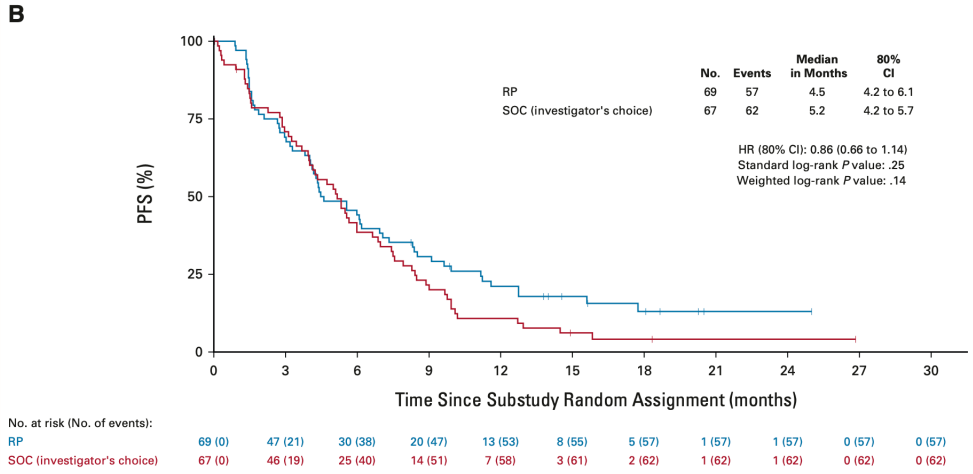
J Immunother Cancer. 2022 Feb;10(2):e003027.

Phase II Randomized Study of Ramucirumab and Pembrolizumab Versus Standard of Care in Advanced Non-Small-Cell Lung Cancer Previously Treated With Immunotherapy-Lung-MAP S1800A

	RP Events/n	SOC Events/n	HR (80% CI)	*P*
Histology				
Nonsquamous	27/40	27/39	0.95 (0.67 to 1.35)	.43
Squamous/mixed	18/29	24/28	0.43 (0.28 to 0.65)	.005
PD-L1				
0	21/29	21/26	0.74 (0.50 to 1.10)	.16
1-49	11/21	15/22	0.61 (0.36 to 1.02)	.11
≥ 50	8/12	12/16	0.68 (0.38 to 1.21)	.20
≥ 1	19/33	27/38	0.66 (0.45 to 0.97)	.08
TMB				
< 10	23/32	28/38	0.76 (0.52 to 1.10)	.17
≥ 10	18/33	20/25	0.57 (0.37 to 0.86)	.04
Biomarker				
TP53	31/48	35/48	0.73 (0.53 to 1.00)	.10
CDKN2A	18/27	21/24	0.54 (0.35 to 0.82)	.03
KRAS	12/21	13/16	0.63 (0.38 to 1.06)	.13
STK11	4/7	10/10	0.23 (0.10 to 0.54)	.01
KEAP1	1/3	7/10	0.38 (0.10 to 1.49)	.18
Prior Treatment				
IO + Chemotherapy combination	20/32	32/42	0.84 (0.58 to 1.21)	.27
Chemotherapy→IO	25/36	18/23	0.45 (0.30 to 0.68)	.006
PS				
0	15/23	8/9	0.54 (0.30 to 0.96)	.08
1	30/46	43/58	0.76 (0.56 to 1.02)	.12
Overall	45/69	51/67	0.69 (0.51 to 0.92)	.05







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