Memorial Sloan Kettering Cancer Center

Neoadjuvant v Adjuvant – Is the Debate Over?

November 7, 2026

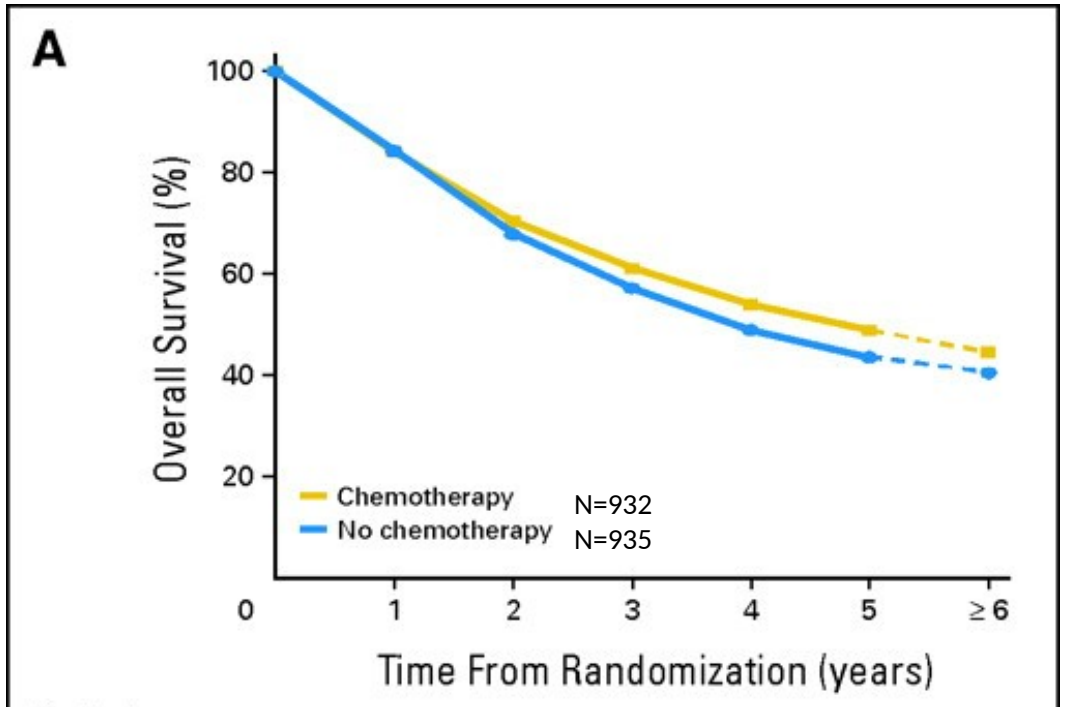
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Member, Memorial Sloan Kettering Cancer Center
Professor, Weill Cornell Medical College

Disclosures

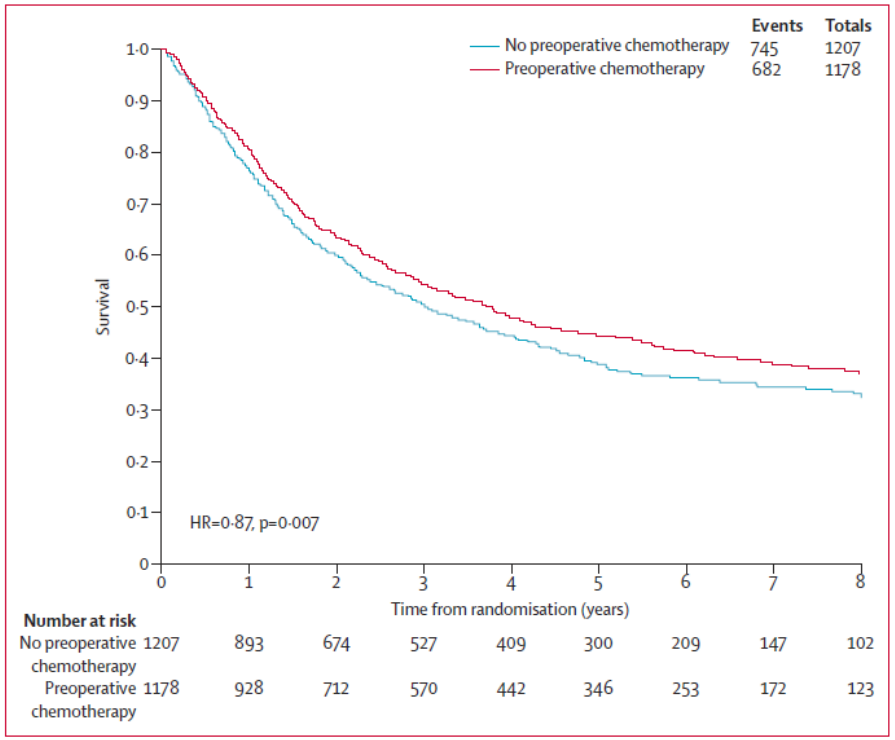
- Research grants
  - AZ, Lilly, Genentech, Biontech, Merck, BI, Taiho
- Consultant
  - AbbVie, AZ, BI, Genentech/Roche, Guardant health, Janssen, EMD-Serono, Exact Sciences, Lilly, Merck, Natera, NuvationBio, Pfizer, Revolutiom Medicine

2004…
Neoadjuvant v Adjuvant Chemotherapy - a historic perspective

IALT – adjuvant cis + vinca or etop



Neoadjuvant Meta-analysis



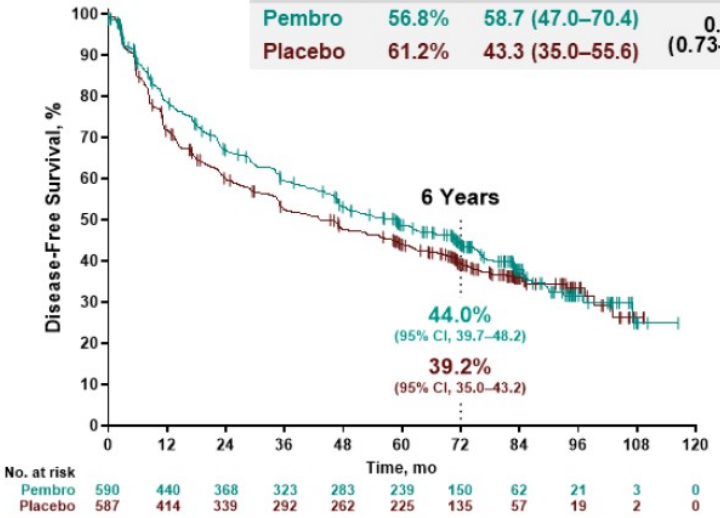
Arriagada R et al. *N Engl J Med*. 2004;350:351-360.

Preoperative chemotherapy for non-small-cell lung cancer: a systematic review and meta-analysis of individual participant data, The Lancet, Volume 383, Issue 9928, 2014, Pages 1561-1571

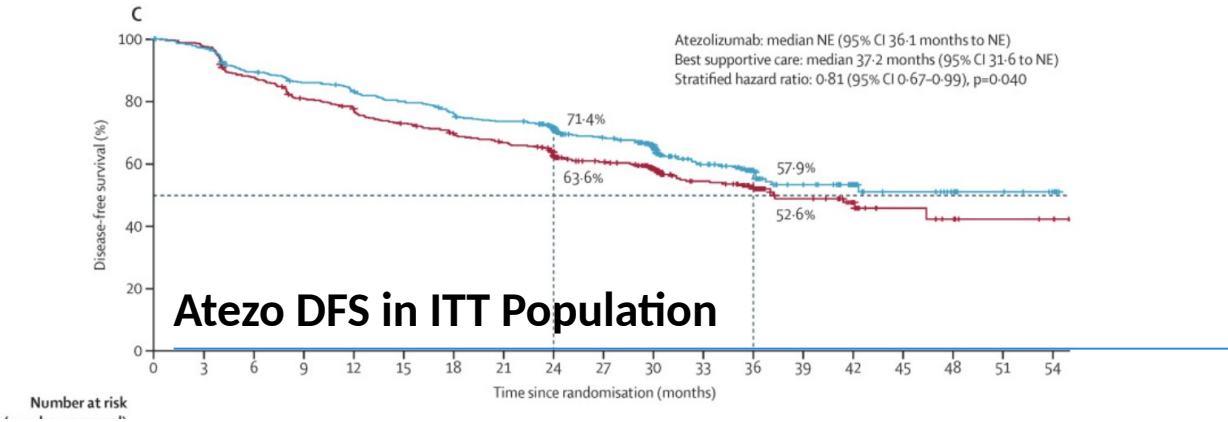
2012…
Along comes immunotherapy - added to the SOC, adjuvant chemo

Adj IO after chemo doesn't add much in all-comers

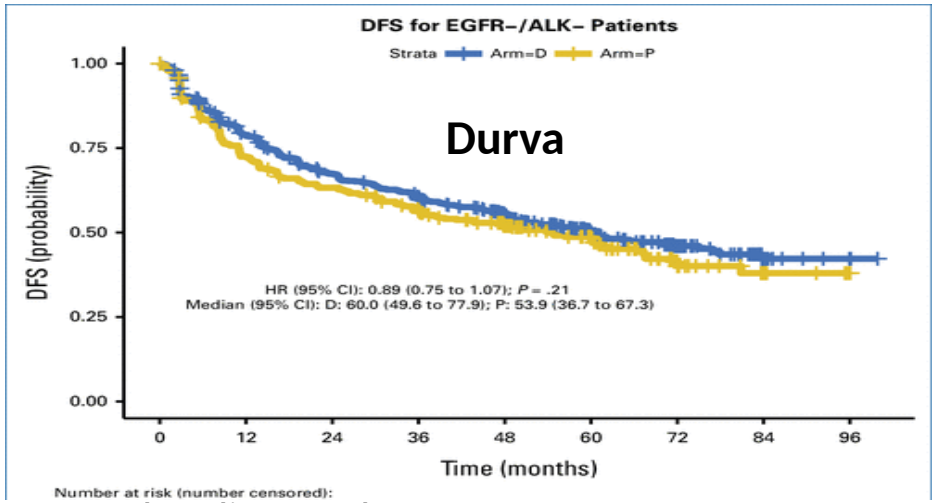
	Pts w/ Event	Median (95% CI), mo	HR[d] (95% CI)
Pembro	56.8%	58.7 (47.0–70.4)	0.85 (0.73–0.98)
Placebo	61.2%	43.3 (35.0–55.6)	



O'Brien M, ESMO 2026..



Felip E, *e al. Annals of Oncology* 2023 34907-919DOI: (10.1016/j.annonc.2023.07.001



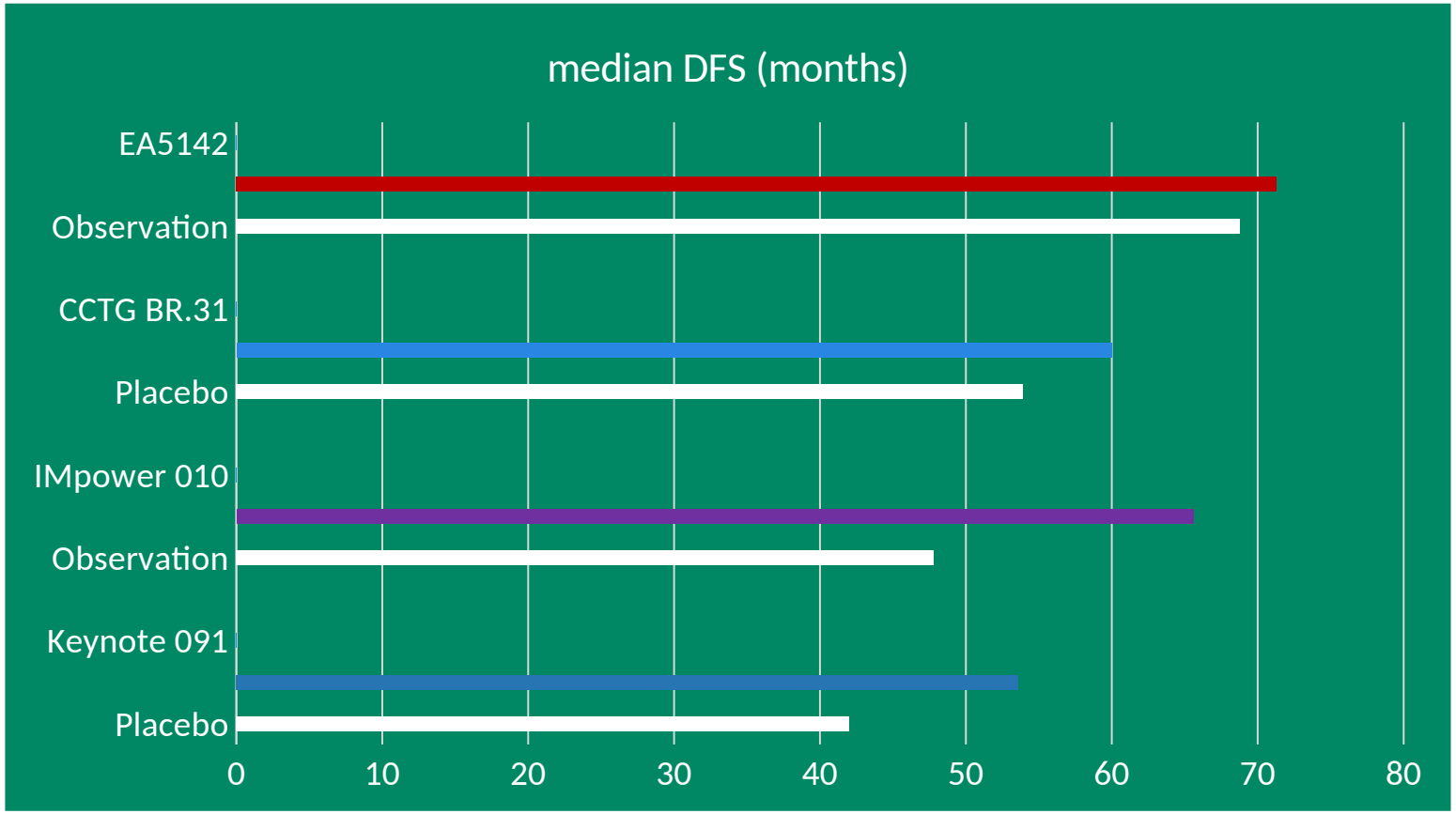
Goss G, et al. J Clin Oncol. 2026; 44: 553-564.

Nivo

Chaft J, et al. JAMA. 2026.

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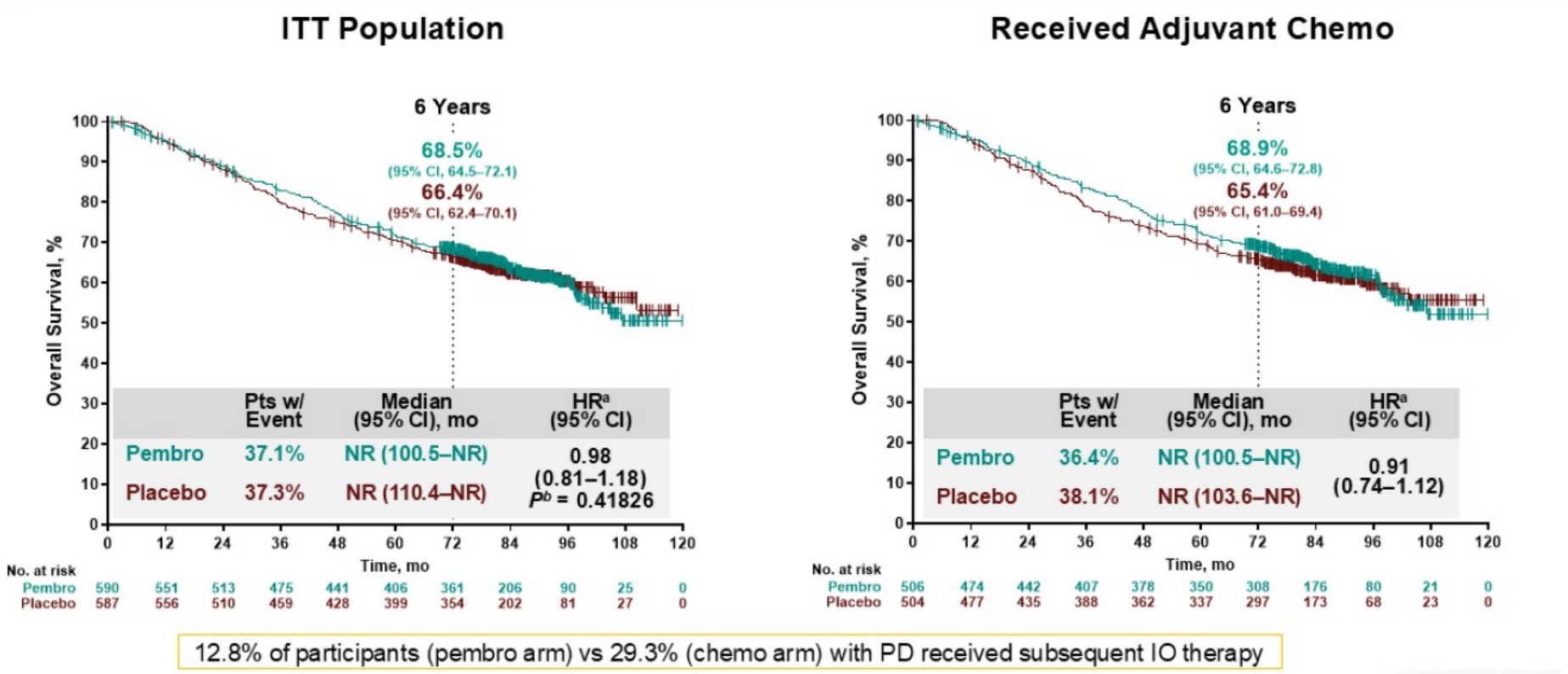
Adjuvant IO after chemotherapy, hasn't added much



Adapted from Chaft J. 2026 ASCO Annual Meeting

Adjuvant pembro – no OS Advantage

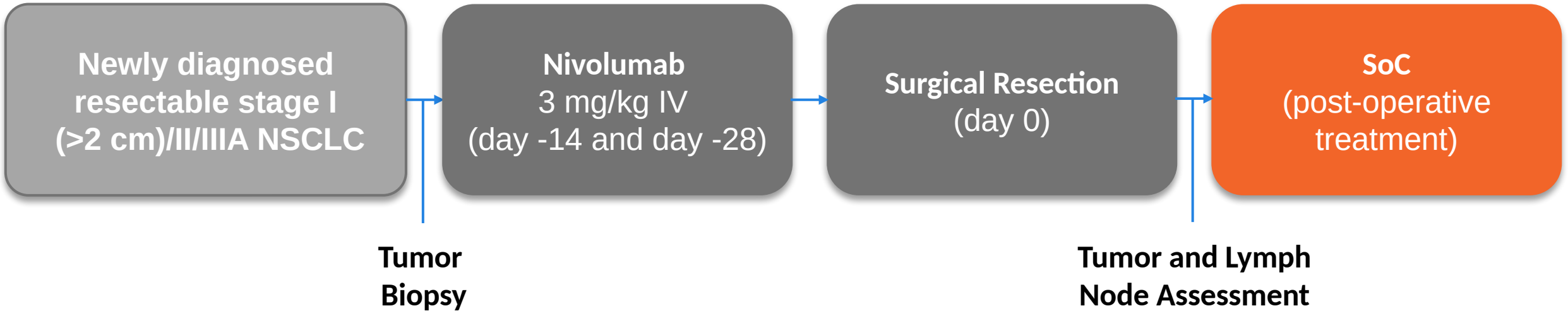
Final Analysis: Overall Survival



12.8% of participants (pembro arm) vs 29.3% (chemo arm) with PD received subsequent IO therapy

O'Brien M, et al. ESMO 2026. Madrid, Spain

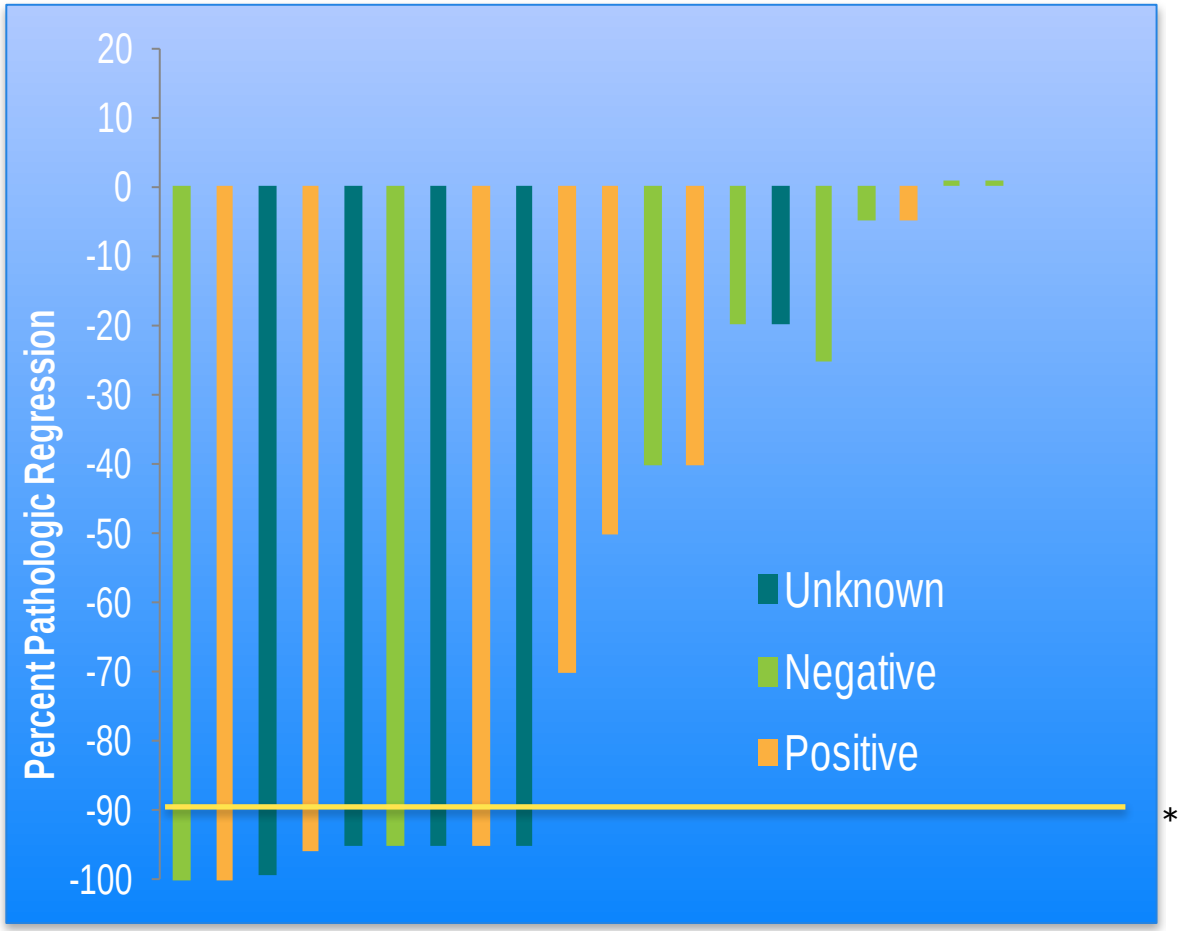
2016…
A pilot study that fueled the neoadjuvant vs adjuvant IO debate



- Primary endpoints: safety and feasibility
- Also evaluated: Tumor pathological response, expression of PD-L1, mutational burden, and mutation-associated, neoantigen-specific T-cell responses

Forde PM, Chaft JE, et al. *N Engl J Med*. 2018;378(21):1976-1986.

2 doses of neoadjuvant nivolumab induced path regression in most patients



*

- Major Pathologic Response (MPR) was seen in 9/21 cases [43% (95% CI 24-63%)]

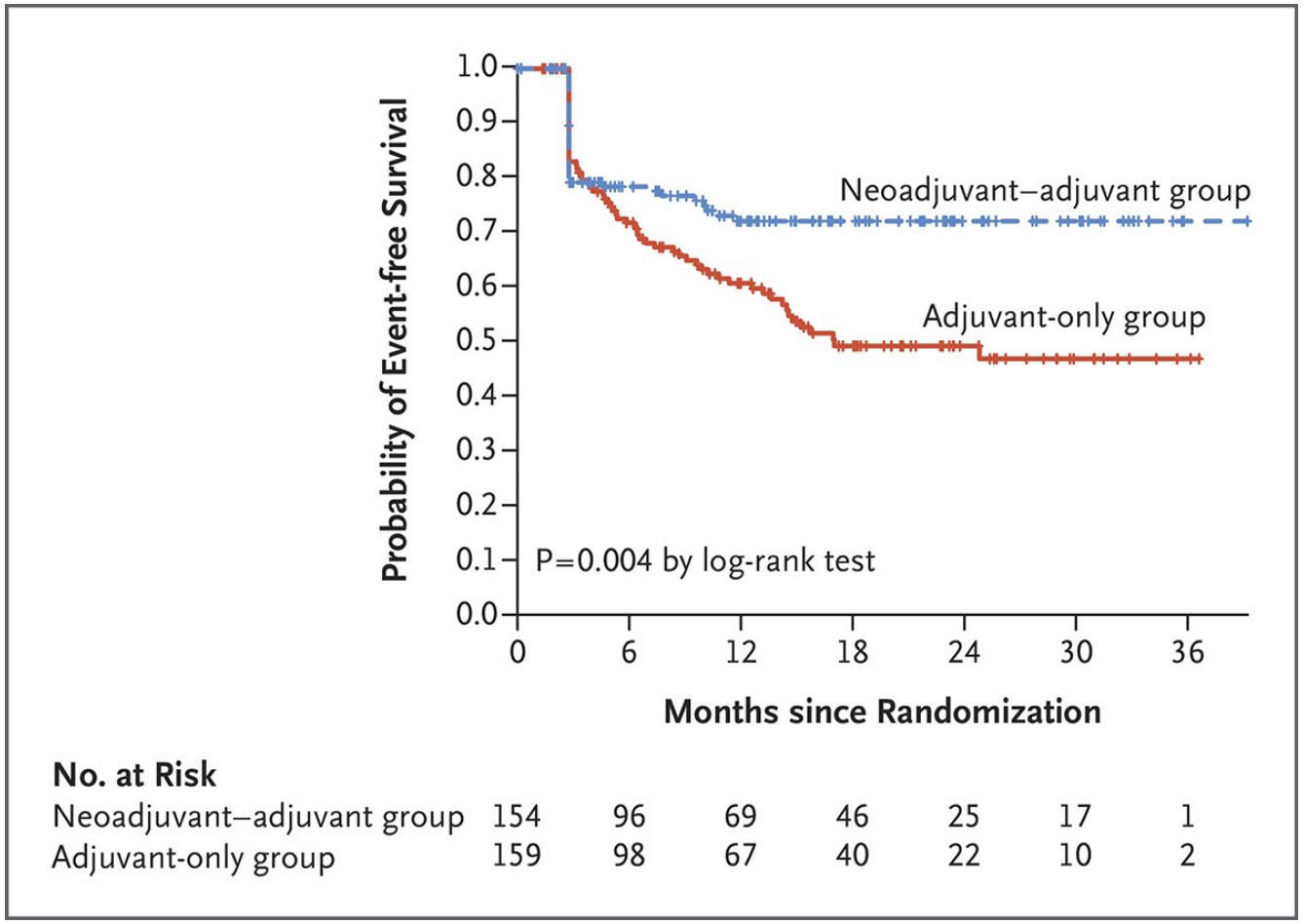
- Pre-treatment PD-L1 positivity [≥1% membranous staining (Dako 28-8)] did not correlate with MPR

*MPR is defined as ≤10% viable tumor cells
(Pataer, et al. JTO, 2012. Hellmann, et al. Lancet Oncol 2014.)

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Forde PM, Chaft JE, et al. *N Engl J Med*. 2018;378(21):1976-1986.

Further rationale for NEOADJUVANT IO
Periop IO vs adj IO in resectable melanoma



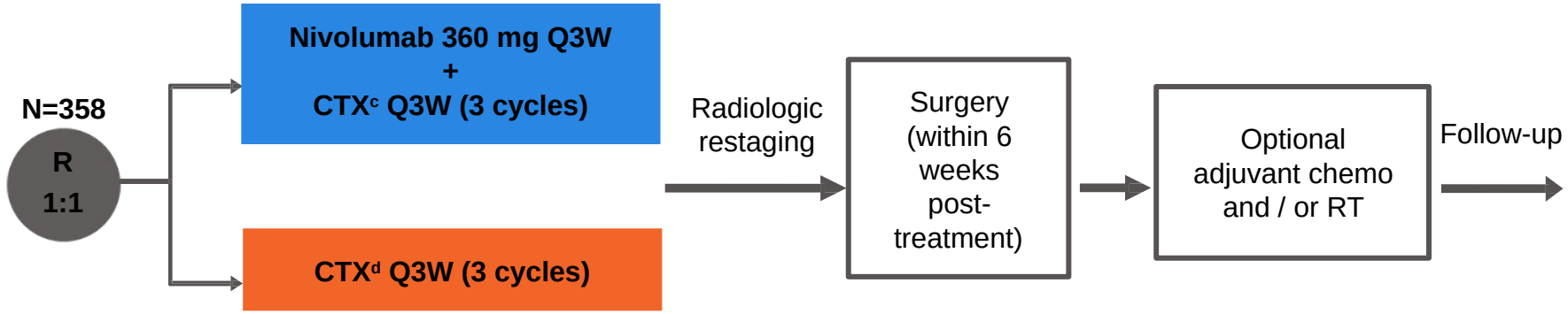
Patel, S. P. , et al. (2023). *The New England Journal of Medicine, 388* (9), 813-823.

CheckMate 816 study design

Key eligibility criteria

- Newly diagnosed, resectable, Stage IB (≥4 cm)–IIIA NSCLC (per AJCC TNM 7th edition)
- ECOG PS 0–1
- No known sensitizing *EGFR* mutations or *ALK* alterations

Stratified by stage (IB–II vs IIIA), PD-L1[a] (≥1% vs <1%[b]), and sex



Primary endpoints:

- pCR by BIPR
- EFS by BICR

Secondary endpoints:

- MPR by BIPR
- OS
- TTDM

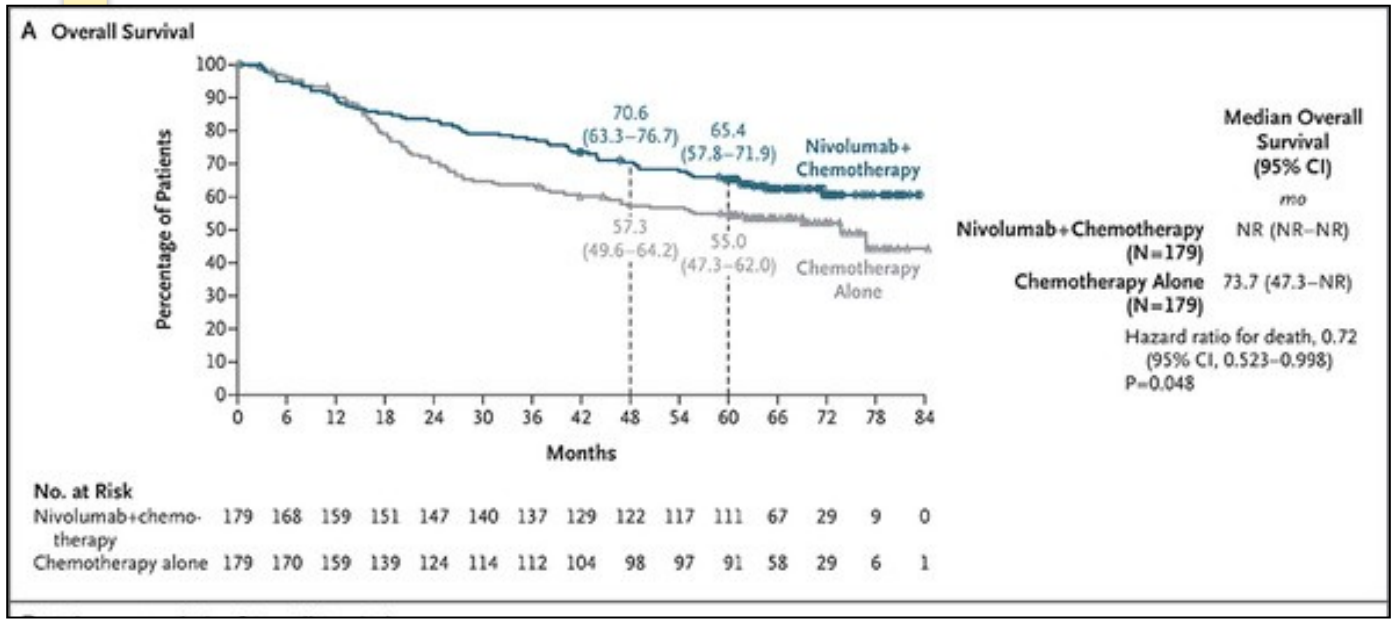
Exploratory analyses:

- EFS by surgical outcomes
- pCR and EFS by 4-gene inflammatory signature score

Girard N, et al. Oral presentation at: ELCC 2023; 29 March–1 April 2023; Copenhagen, Denmark. Abstract 84O

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Neoadj nivo + chemo



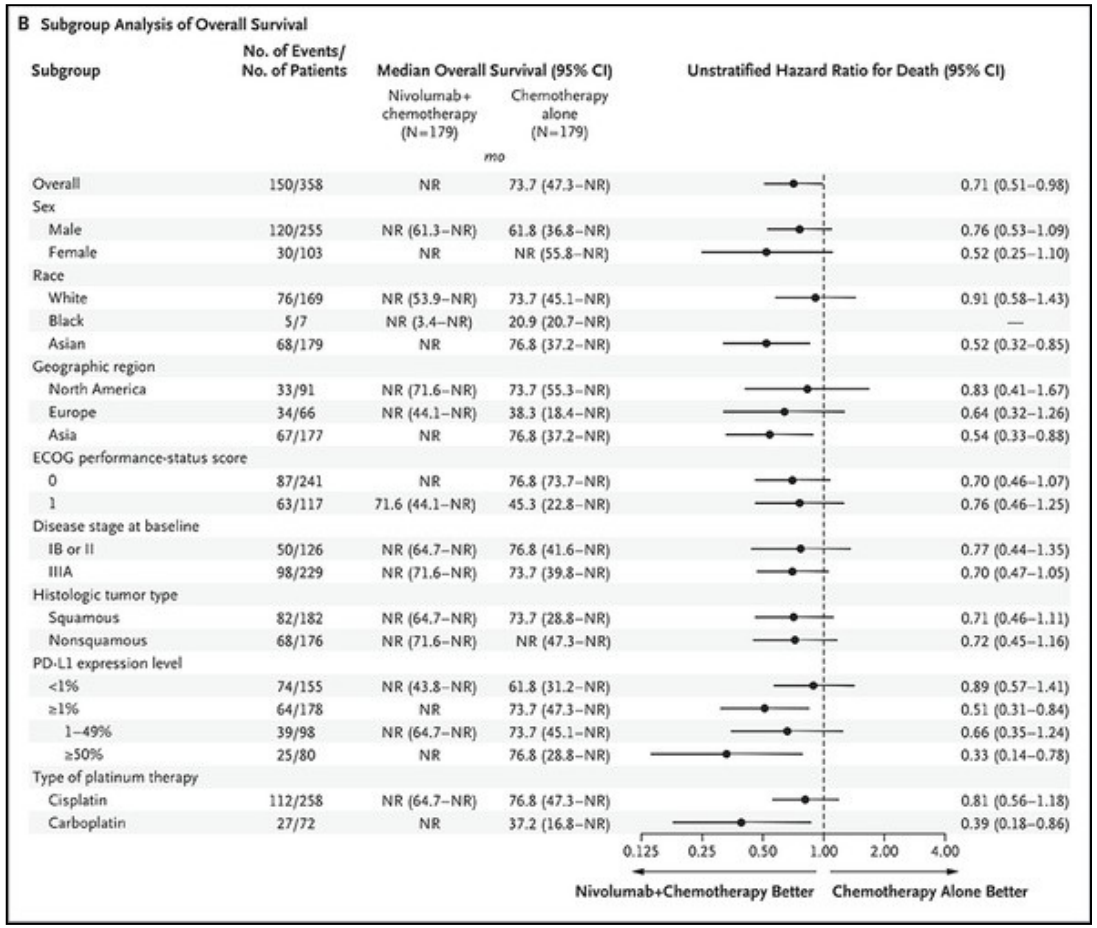
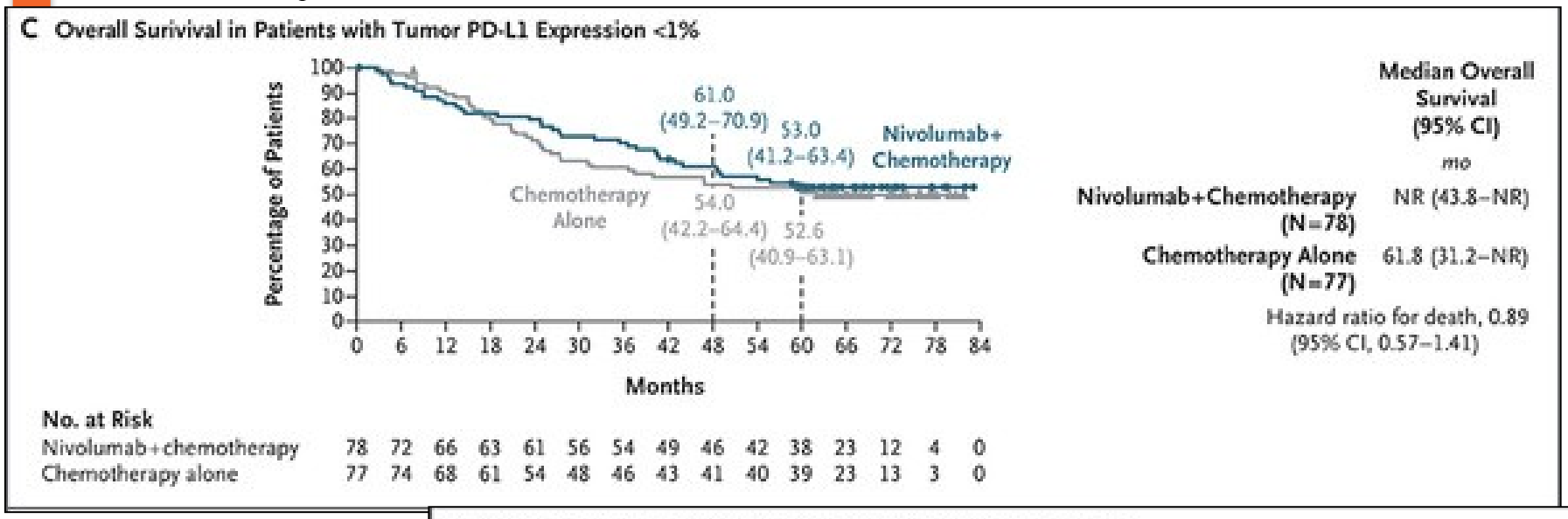


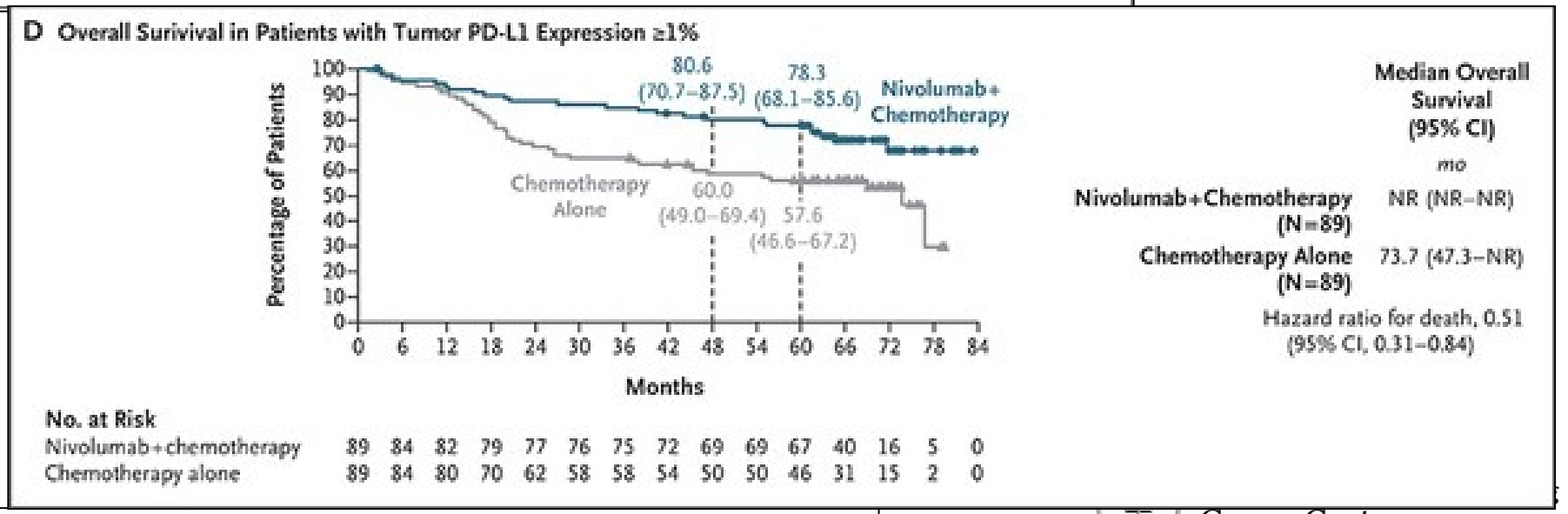
Figure 1 Overall Survival in All Patients and According to Prespecified Subgroups. Panel A shows overall survival among the patients who underwent concurrent randomization. Open circles and open triangles indicate censored data for the nivolumab-plus-chemotherapy group and the chemotherapy-alone group, respectively. The 1-year overall survival was 89.8% (95% confidence interval [CI], 84.3 to 93.5) and 90.4% (95% CI, 85.0 to 93.9) in the two groups, respectively; the 2-year overall survival was 83.1% (95% CI, 76.7 to 87.8) and 70.5% (95% CI, 63.2 to 76.6), respectively; and the 3-year overall survival was 77.4% (95% CI, 70.5 to 82.9) and 63.7% (95% CI, 56.1 to 70.3), respectively. Panel B shows overall survival in prespecified patient subgroups. In Panel B, the confidence intervals were not adjusted for multiplicity and should not be used for hypothesis testing; all subgroup analyses were prespecified. ECOG denotes Eastern Cooperative Oncology Group, NR not reached, and PD-L1 programmed death ligand 1.

Forde et al. New England Journal of Medicine. 393(8):741-752, August 21, 2025.

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OS by PD-L1 status





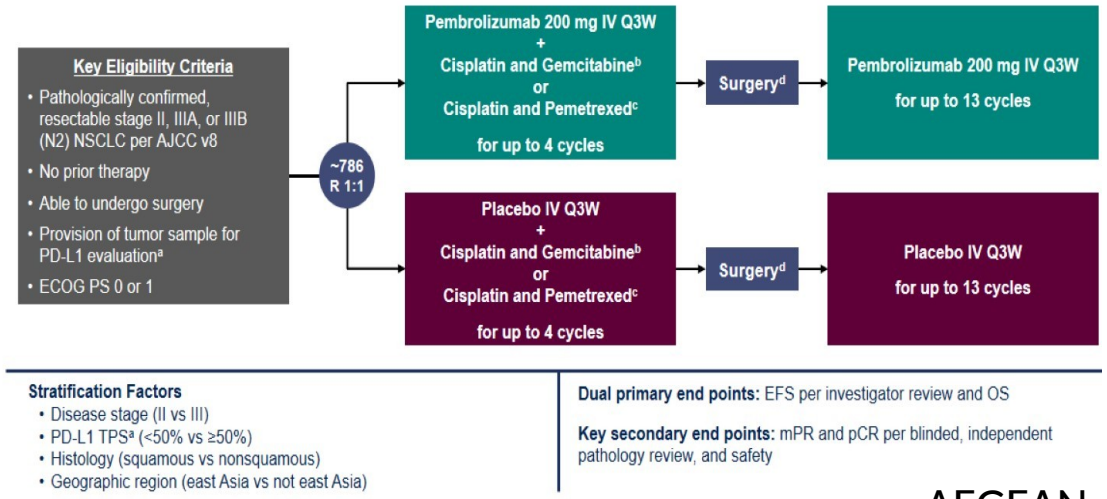
Forde et al. New England Journal of Medicine. 393(8):741-752, August 21, 2025.

1884 Cancer Center

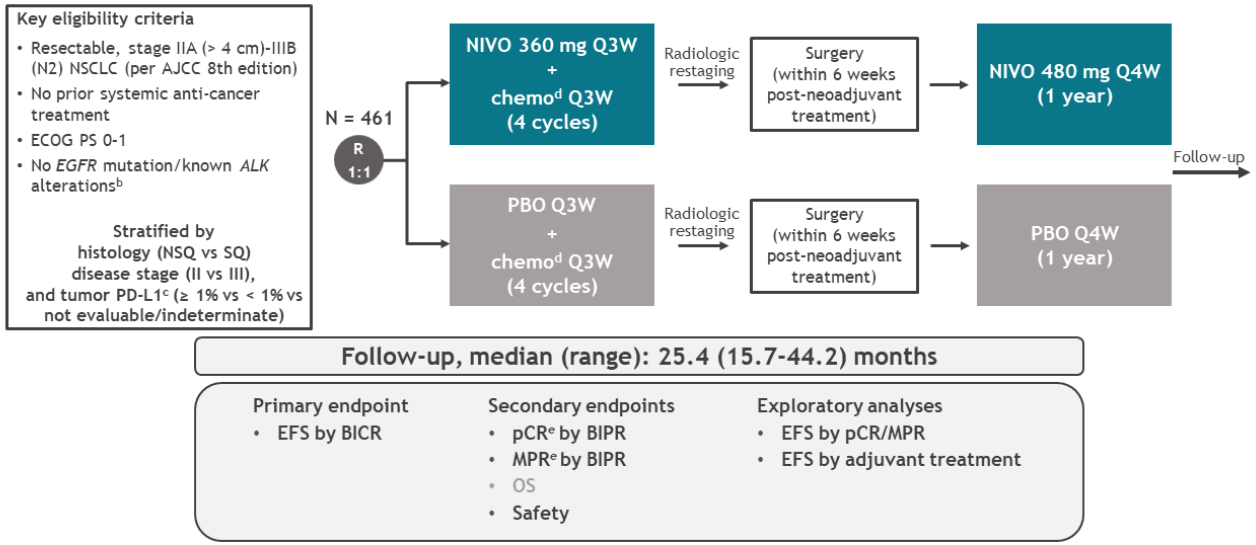
What now? Is more better? “Perioperative therapy”

Periop Study Schemas (3 of 6 available studies)

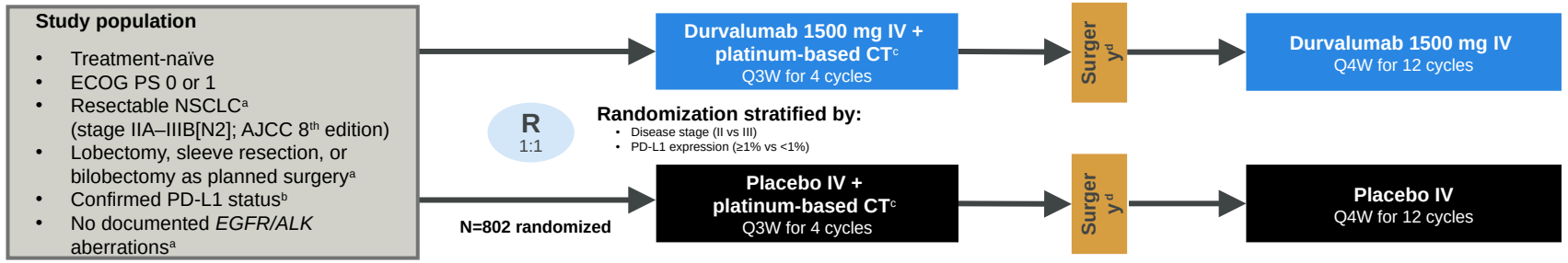
Keynote 671



Checkmate 77T



AEGEAN



Primary (in *EGFR/ALK* wildtype):

- pCR by central lab (per IASLC 2020)
- EFS using BICR (per RECIST v1.1)

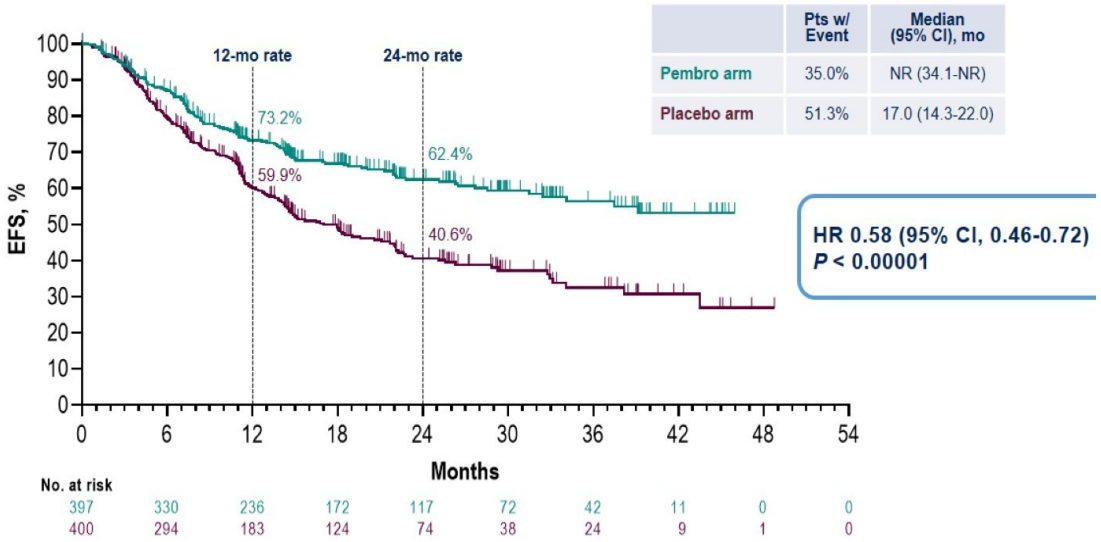
Key secondary:

- MPR by central lab (per IASLC 2020)
- DFS using BICR (per RECIST v1.1)
- OS

ering

EFS

Keynote 671

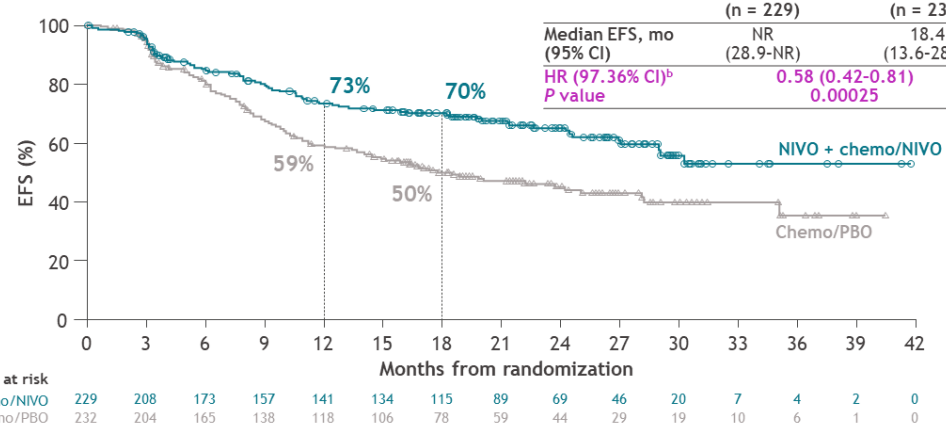


	Pts w/ Event	Median (95% CI), mo
Pembro arm	35.0%	NR (34.1-NR)
Placebo arm	51.3%	17.0 (14.3-22.0)

HR 0.58 (95% CI, 0.46-0.72)
P < 0.00001

Wakelee, H. (2023). *The New England Journal of Medicine, 389* (6), 491-503.

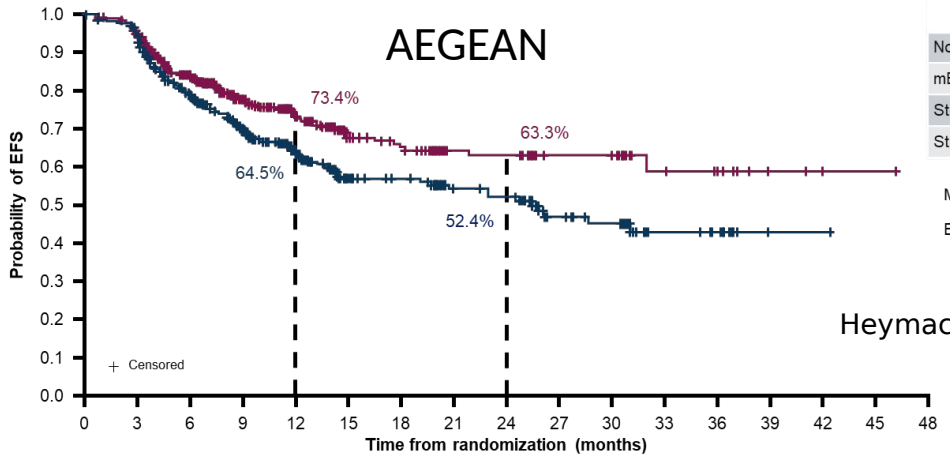
Checkmate 77T



	NIVO + chemo/NIVO (n = 229)	Chemo/PBO (n = 232)
Median EFS, mo (95% CI)	NR (28.9-NR)	18.4 (13.6-28.1)
HR (97.36% CI)[b]	0.58 (0.42-0.81)	
P value	0.00025	

Cascone, T. ESMO 2023.

AEGEAN



	D arm	P arm
No. events / no. patients (%)	98/366 (26.8)	138/374 (36.9)
mEFS, months (95% CI)	NR (31.9–NR)	25.9 (18.9–NR)
Stratified HR* (95% CI)	0.68 (0.53–0.88)	
Stratified log-rank P-value	0.003902	

Median follow-up (range) in censored patients: 11.7 months (0.0–46.1)

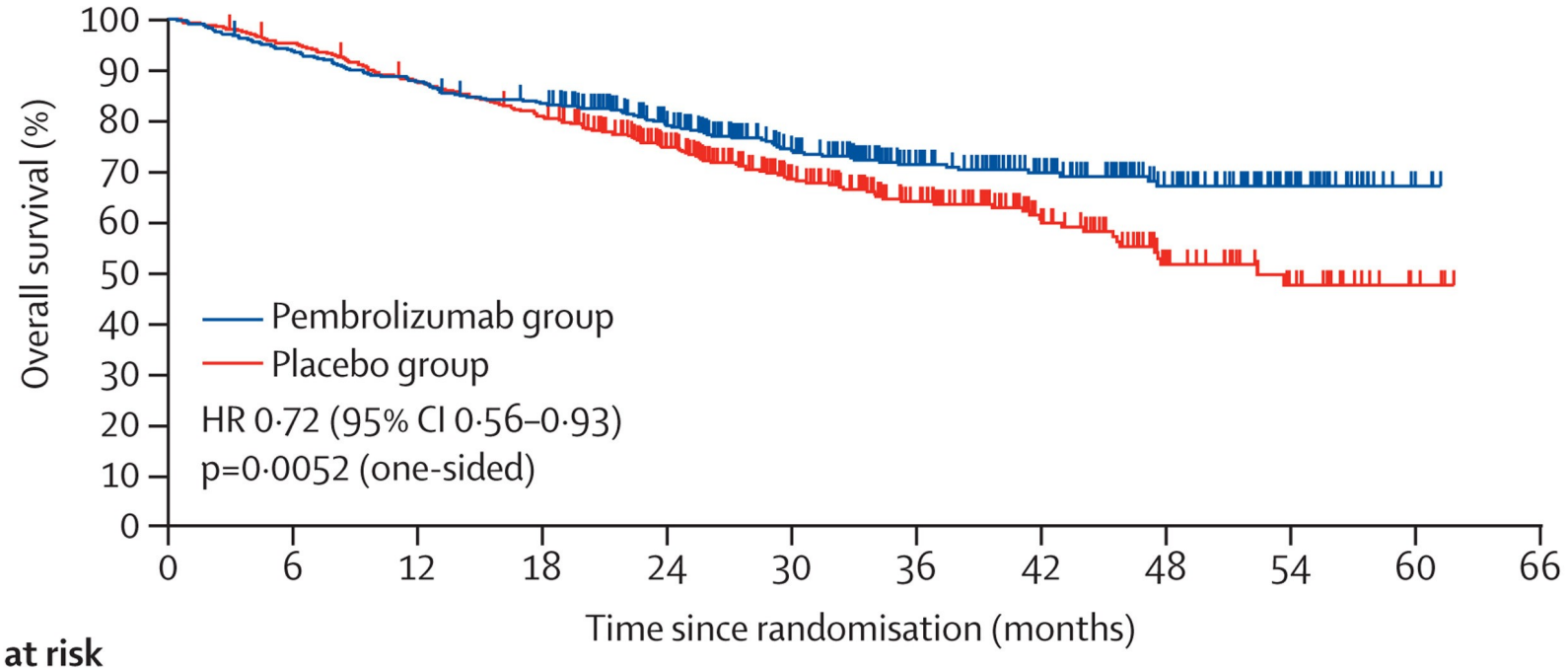
EFS maturity: 31.9%

Heymach, J. V. (2023). *The New England Journal of Medicine, 389* (18), 1672-1684.

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KN-671 OS

A

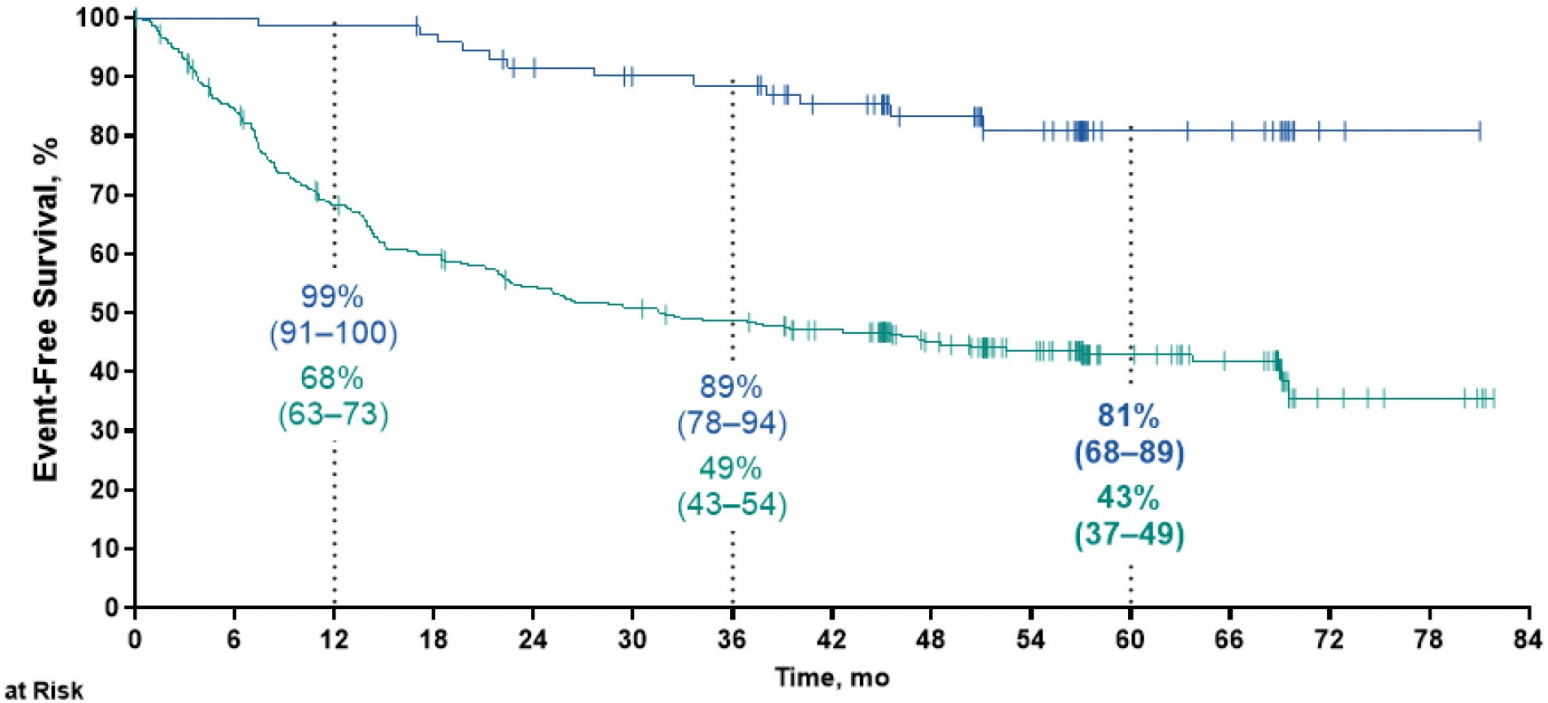


Number at risk (number censored)												
Pembrolizumab group	397 (0)	371 (1)	347 (1)	327 (4)	277 (38)	205 (95)	148 (145)	108 (182)	69 (218)	32 (255)	4 (283)	0 (287)
Placebo group	400 (0)	379 (2)	347 (4)	319 (5)	256 (45)	176 (106)	125 (147)	77 (190)	39 (219)	20 (236)	4 (252)	0 (256)

Spicer J, et al. The Lancet Oncology, e-pub Sept 14, 2024

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Exploratory Analysis of Event-Free Survival[a] in the Pembrolizumab Arm – Participants With vs Without pCR



No. at Risk															
With pCR	72	72	71	69	63	59	58	50	39	33	14	13	2	1	0
Without pCR	325	268	213	186	166	155	147	135	104	80	48	39	8	5	0

	Pts w/ Event	Median (95% CI), mo	HR (95% CI)
With pCR	17%	NR (NR–NR)	0.21 (0.12–0.38)
Without pCR	55%	31.9 (22.2–50.3)	

The Kaplan-Meier curve shows EFS rate (95% CI) at indicated timepoints.
[a]Per RECIST version 1.1 by investigator assessment. Data cutoff date: July 3, 2025 (median follow-up time: 60.2 [range, 42.6–85.8] months).

Reck M, et al. ELCC 2026. Copenhagen.

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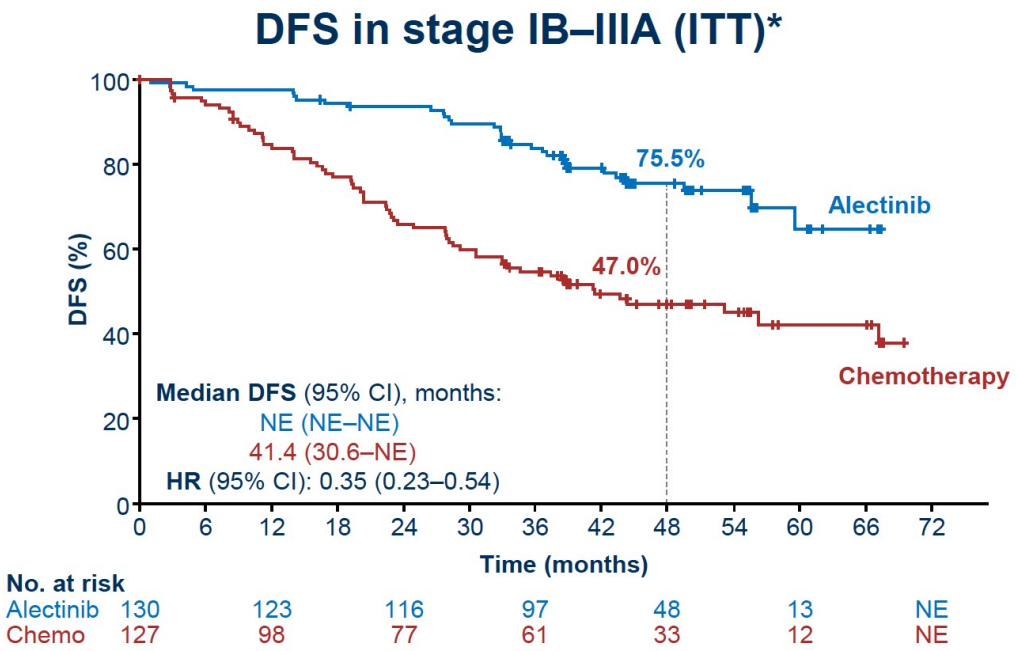
Neoadjuvant v Adjuvant Immunotherapy – Is the debate over?



Neoadjuvant vs Adjuvant targeted therapy?

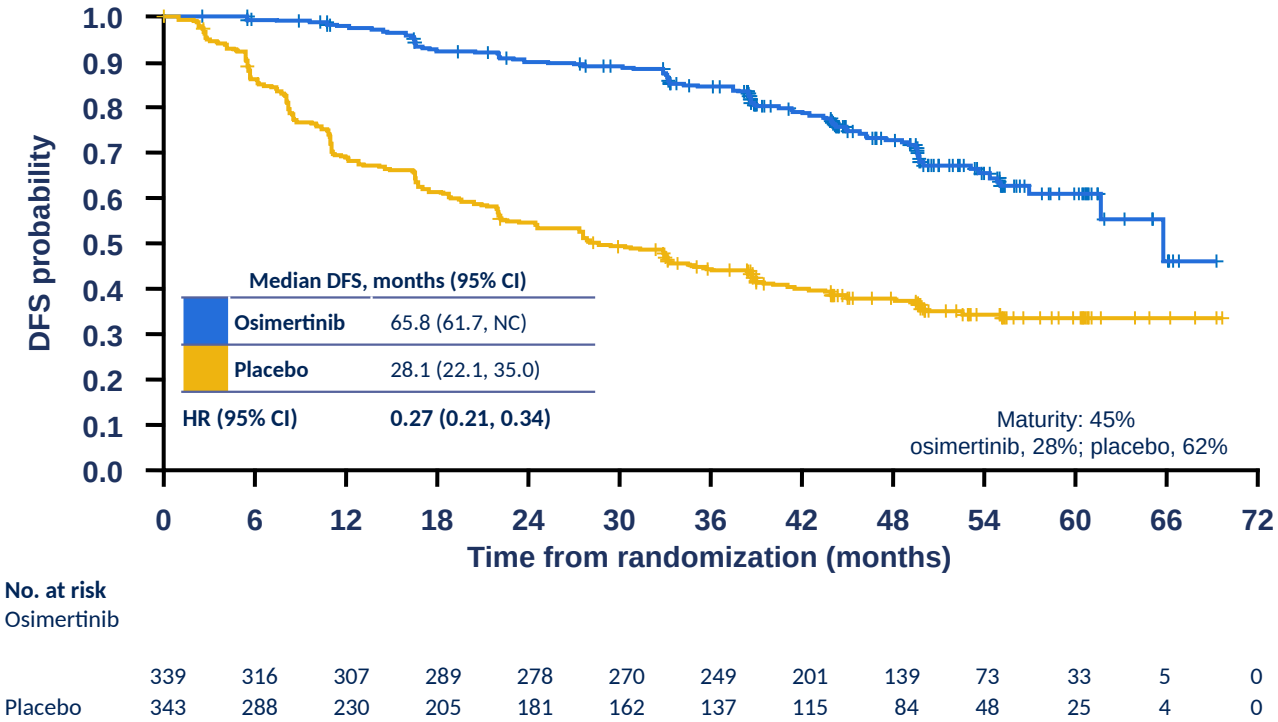
Adjuvant TKI data resected IB-III

ALINA - ALK+ alectinib vs chemotherapy



Solomon B et al. ESMO 2023. Abstract LBA2.
Update Dziadziuszko R. ESMO 2025

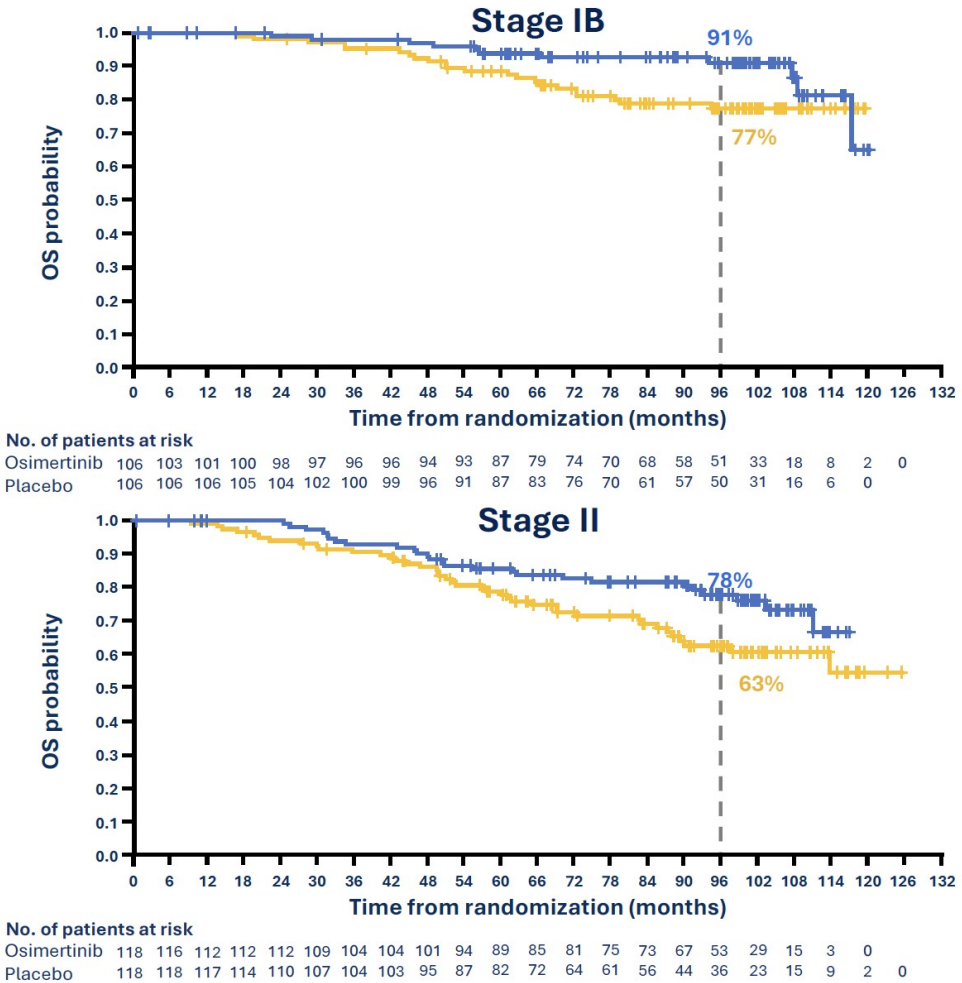
ADAURA – EGFR+ osimertinib vs placebo



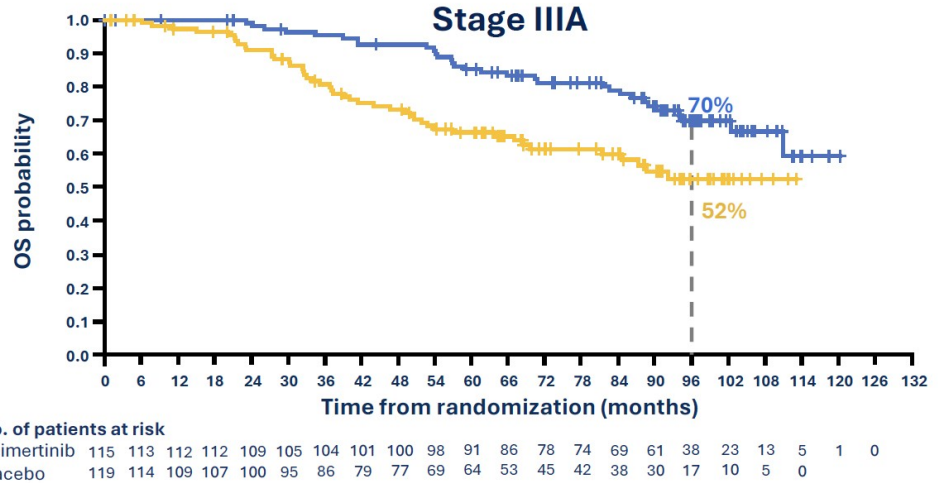
Herbst et al. J Clin Oncol 2023;41:1830–1840
Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract / oral LBA47.

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8-year ADAURA OS Update



	Stage IB	Stage II	Stage IIIA
8-year OS rate, % (95% CI)			
Osimertinib	91 (82, 95)	78 (68, 85)	70 (59, 78)
Placebo	77 (68, 85)	63 (52, 71)	52 (41, 63)
OS HR (95% CI)	**0.50 (0.23, 1.01)**	**0.60 (0.36, 0.97)**	**0.49 (0.31, 0.77)**

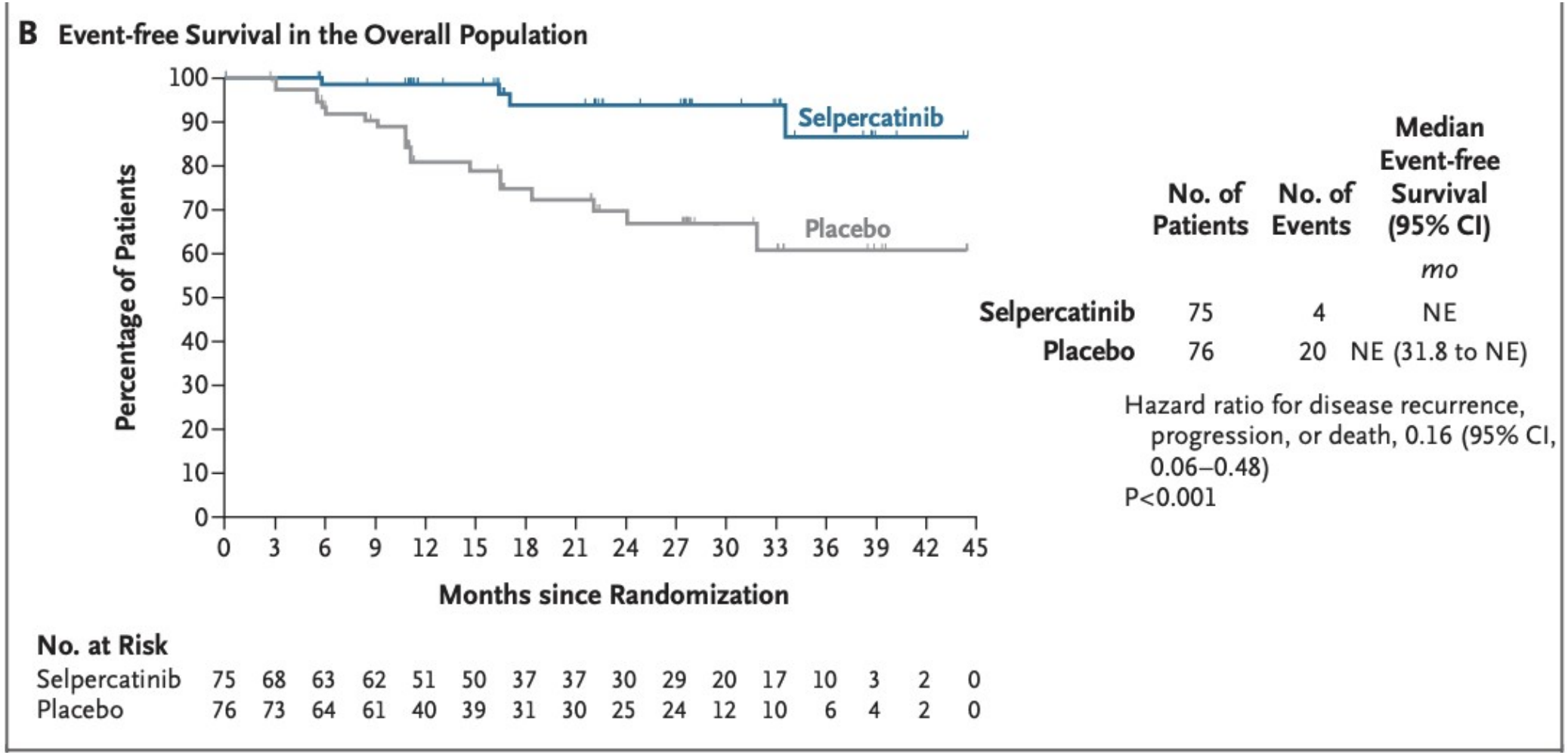


DCO: May 4, 2026. *AJCC / UICC 7th edition. AJCC, American Joint Committee on Cancer; CI, confidence interval; HR, hazard ratio; OS, overall survival; UICC, Union for International Cancer Control.

Herbst R, et al. WCLC 2026. Seoul, Korea

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Selpercatinib in definitively treated RET+ NSCLC

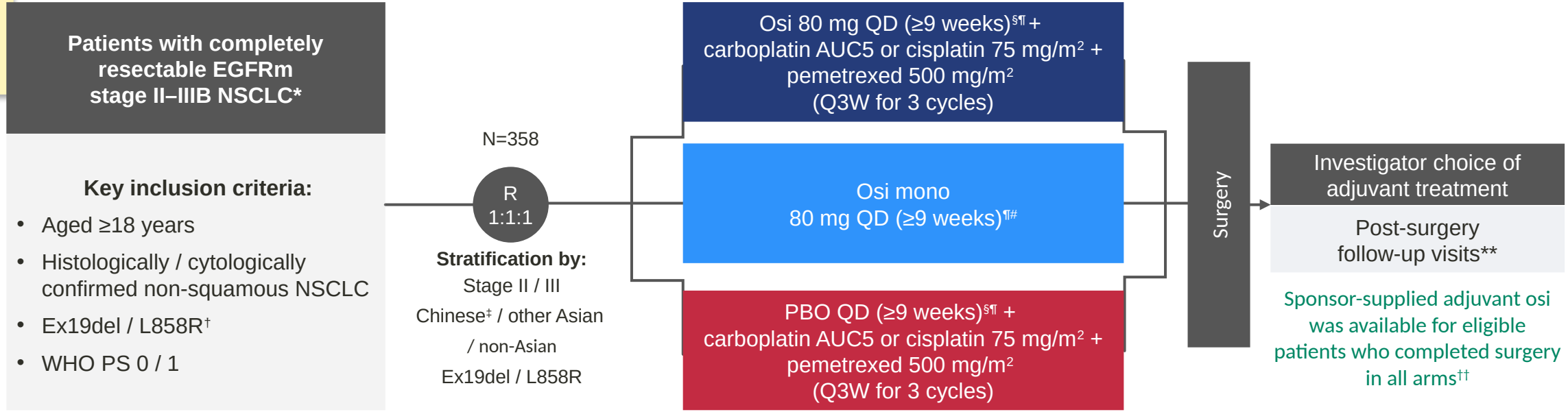


	No. of Patients	No. of Events	Median Event-free Survival (95% CI)
			mo
Selpercatinib	75	4	NE
Placebo	76	20	NE (31.8 to NE)

Hazard ratio for disease recurrence, progression, or death, 0.16 (95% CI, 0.06–0.48)
P<0.001

Wu Y, et al. NEJM 2026.

NeoADAURA: global, randomized, Phase 3 controlled study



Endpoints:

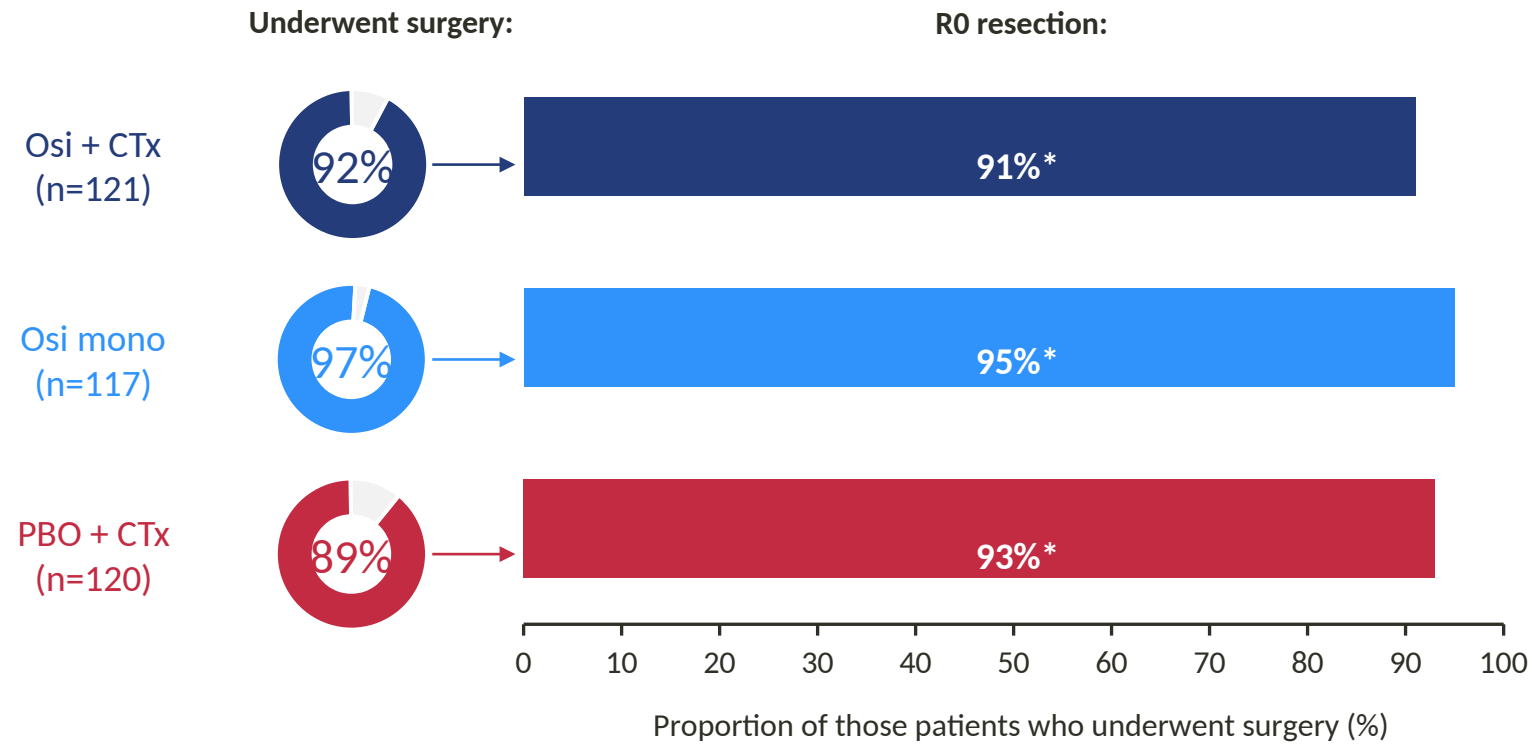
- **Primary: major pathological response (MPR; by blinded central pathology review)**
- Secondary: event-free survival, pathological complete response, nodal downstaging and safety

NCT04351555. Figure borrowed from "*Neoadjuvant osimertinib with/without chemotherapy versus chemotherapy alone for EGFR-mutated resectable non-small-cell lung cancer: NeoADAURA*", Tsuboi M et al. Published online July 19, 2021 in *Future Oncology* and reprinted by permission of the publisher Informa UK Limited trading as Taylor & Francis Ltd, http://www.tandfonline.com. The figure was adapted with permission from the authors.

*AJCC Staging Manual 8th edition.†Confirmed by sponsor pre-approved local or central tissue testing. ‡Chinese living in mainland China. §Double-blind; ¶Osi or PBO could be continued up to the date of surgery, at the discretion of the investigator. #Open-label, sponsor-blinded. **At weeks 12 and 24 post-surgery, then every 24 weeks until 5 years, and then every 48 weeks until disease recurrence or other withdrawal criteria were met. ††Adjuvant osi could be given for a maximum 3-year treatment period, or until unacceptable toxicity or disease recurrence.

AJCC, American Joint Committee on Cancer; AUC, area under the curve; CTx, chemotherapy; del, deletion; EGFRm, epidermal growth factor receptor-mutated; Ex19del, Exon 19 deletion; mono, monotherapy; NSCLC, non-small cell lung cancer; osi, osimertinib; PBO, placebo; Q3W, once every 3 weeks; QD, once daily; R, randomization; WHO PS, World Health Organisation performance status

Surgery summary



In each arm, **91%** of patients who completed surgery received sponsor-supplied adjuvant osi†

- SAEs causally related to surgery occurred in 10%, 5% and 7% of patients
- No patients died within 30 days post-surgery

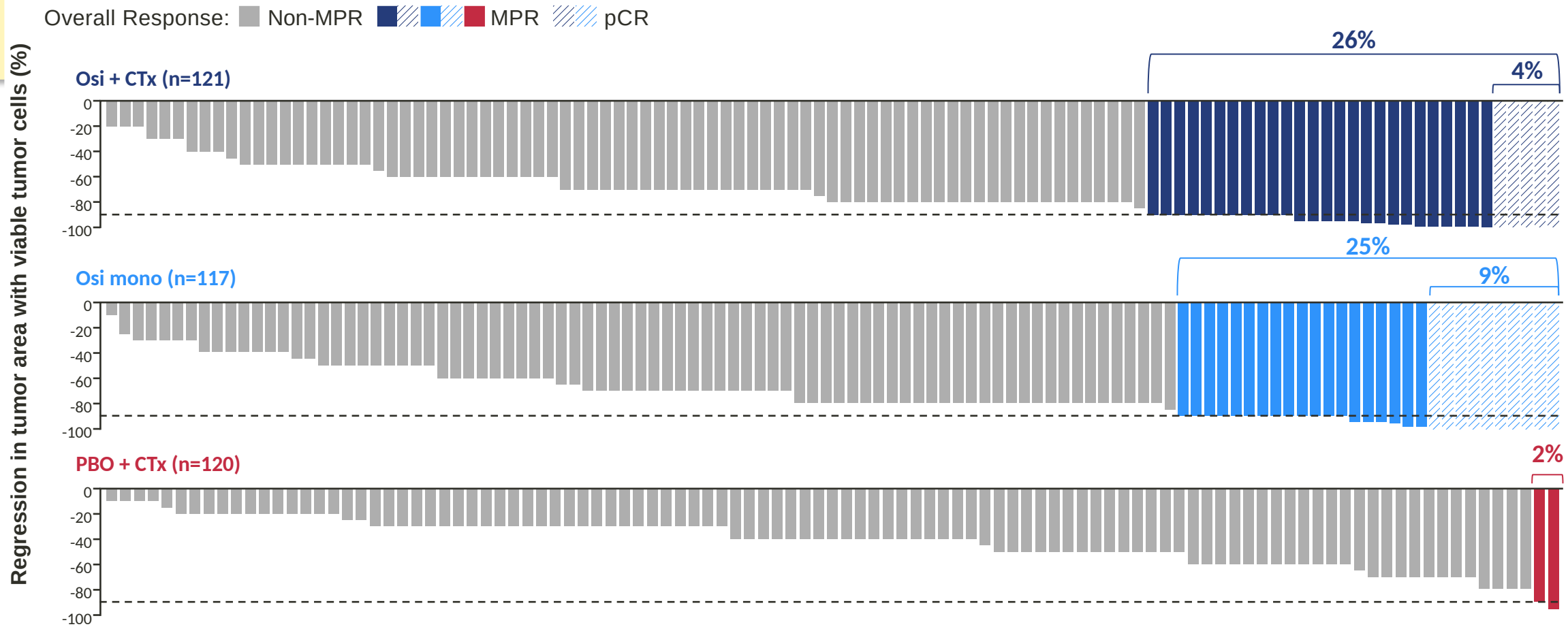
Data cut-off: October 15, 2024.

*One patient in the osi + CTx arm, two patients in the osi mono arm and one patient in the PBO + CTx arm had missing R status data. One patient in the osi + CTx arm and one patient in the PBO + CTx arm had an R2 resection. †In addition to patients who received sponsor-supplied adjuvant osi, two patients in the osi + CTx arm, one patient in the osi mono arm and two patients in the PBO + CTx arm received commercial supplied osi.

CTx, chemotherapy; mono, monotherapy; osi, osimertinib; PBO, placebo

Depth of pathological response

Depth of pathological response was greater with the osi-containing regimens



Data cut-off: October 15, 2024.

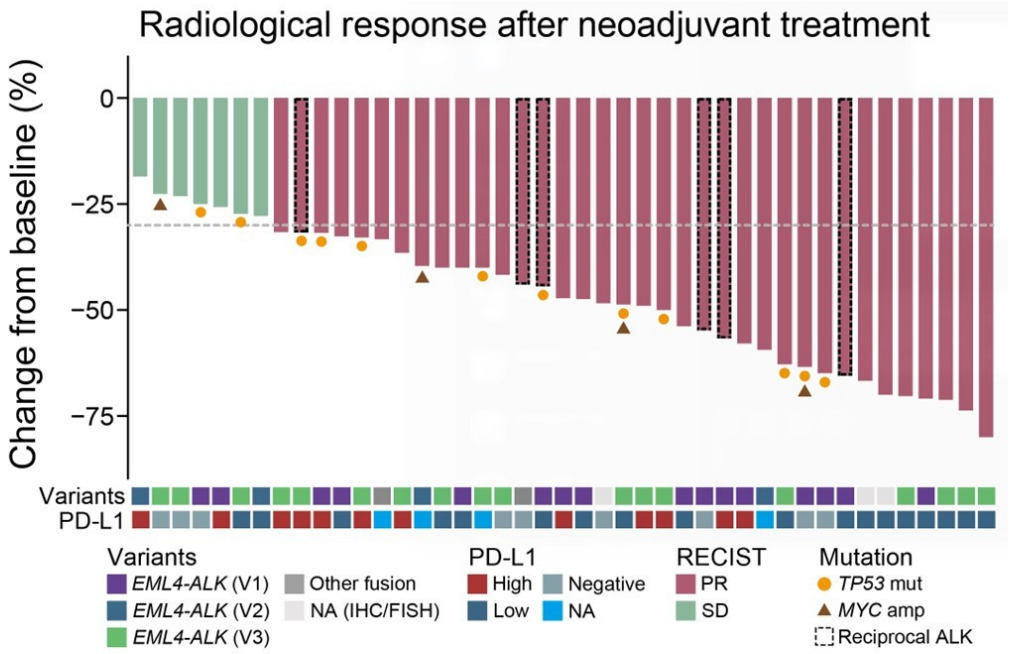
MPR defined as ≤10% residual viable tumor cells in the lung primary tumor at resection, dotted line at −90% denotes the MPR cut-off. pCR defined as no residual viable tumor in surgical specimens including primary tumors and lymph nodes. Patients had to have an R0 result to be classified as responders. MPR and pCR assessed using the IASLC method. Pathological regression is summarized based on patients with evaluable % residual viable tumor, osi + CTx: n=109; osi mono: n=110; PBO + CTx: n=105. Rates of MPR / pCR are calculated based on the full analysis set.

CTx, chemotherapy; mono, monotherapy; IASLC, International Association for the Study of Lung Cancer; MPR, major pathological response; osi, osimertinib; PBO, placebo

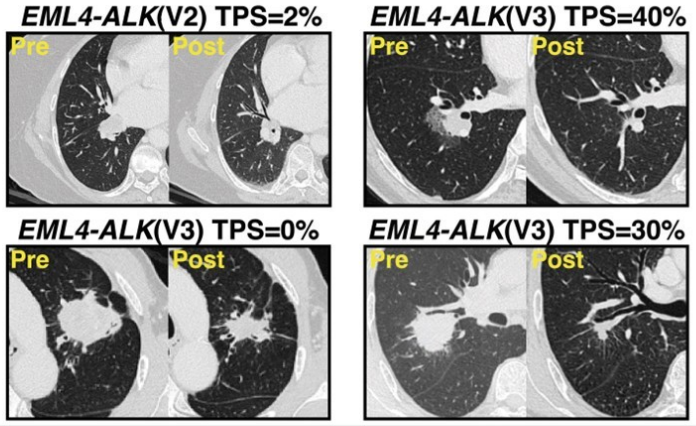
Memorial Sloan Kettering Cancer Center

LORIN

Results Secondary Endpoints—ORR and survival



Objective response	N=43
CR, n (%)	0 (0)
PR, n (%)	36 (84)
SD, n (%)	7 (16)
PD, n (%)	0 (0)
ORR, n (%)	**36 (84)**



After a median follow-up of 13 months (range 2.6-34.1months), 3 patients experienced local disease relapse without distant metastasis. The 1-year EFS rate was 97.1% (95% CI, 91.5-100). Median EFS and OS were not reached.

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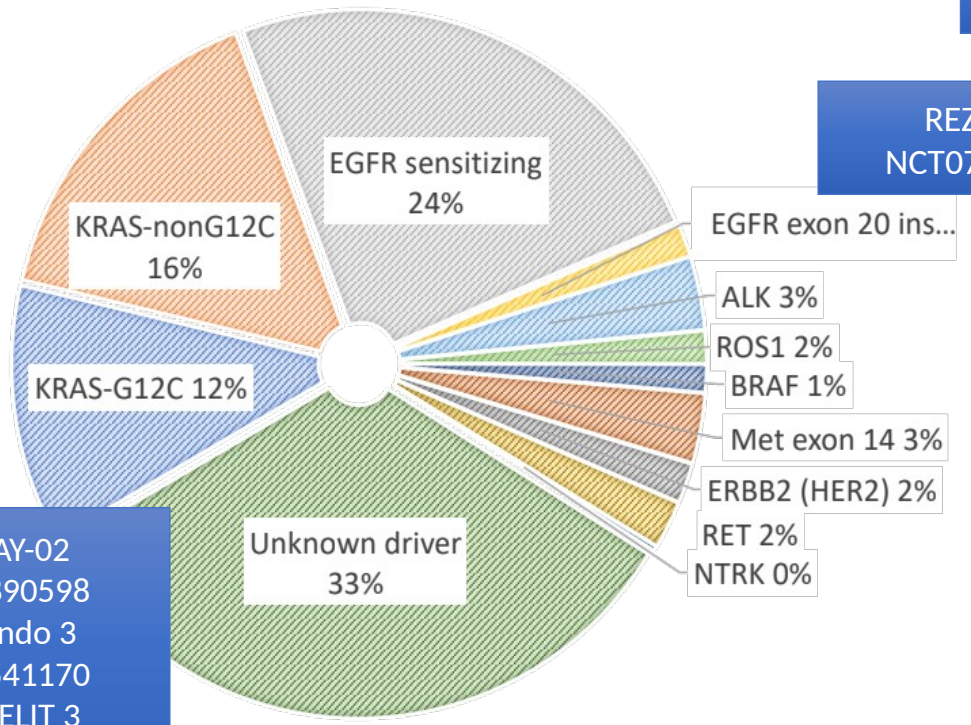
Neoadjuvant vs Adjuvant Targeted Therapy – Is the debate over?



Ongoing Trials of Targeted Therapy in Resectable NSCLC

- 38 % • Actionable Oncogene
- 3 % • taletrectinib
- 2+ % • zipalertinib
- 12 % • olomorasib
- 2 % • zongertinib

~18% unmet need



WU-KONG16
NCT071282682

REZILIENT
NCT071281994

ELEVATE

TRUST-IV
NCT07154706

BEAMION-Lung 3
NCT07195695

SUNRAY-02
NCT06890598
Krascendo 3
NCT07541170
KANDLELIT 3
NCT07431827

Jamie E. Chaft, MD

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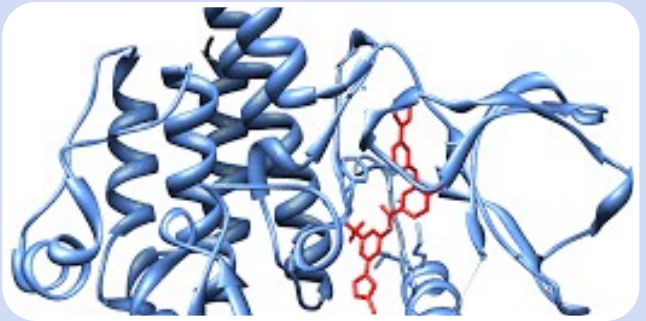
Neoadjuvant v Adjuvant – the debateS are evolving



Tabled



Neoadjuvant Wins



Adjuvant standard with more to come