16th CONGRESS Lung ON CANCER

BARCELONA 27 / 28 NOVEMBER 2025

GECP lung cancer research

Value of adjuvant therapy after neoadjuvant therapy

Dr. Enric Carcereny,
Institut Català d'Oncologia Badalona
Hospital Univ. Germans Trias i Pujol, Badalona,
BARGO Group
Barcelona

Disclosures

- **Advisory / Consultancy :** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Roche, Takeda, Pfizer, Johson&Johnson

- **Speaker Bureau / Expert testimony:** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Pfizer, Roche, Takeda, Pierre-Fabre, Regeneron

- **Travel / Accommodation / Expenses** :Bristol-Myers Squibb, Pfizer, Roche, Takeda, Astra Zeneca.

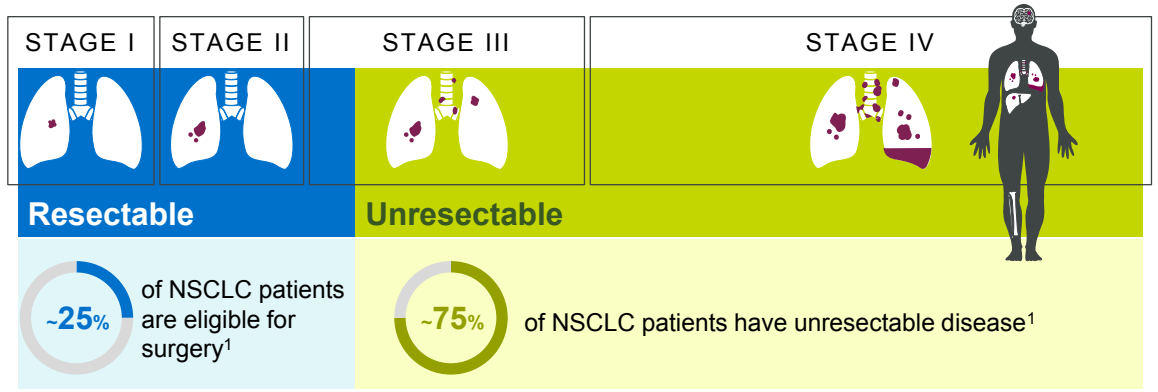
Outline

- Introduction.
- Can Efficacy Data Guide Adjuvant Therapy After Neoadjuvant Treatment?
- Tailoring Treatment: Subgroup Analyses by Disease Stage.
- Key Concerns After Prior Neoadjuvant Therapy.

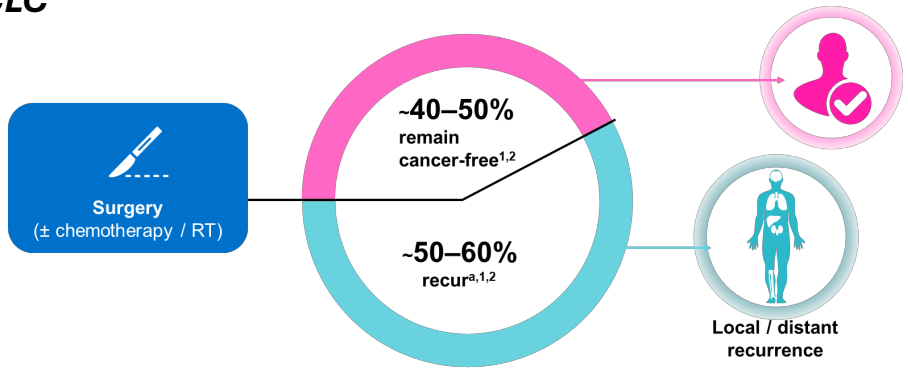
Introduction

Locally Advanced Lung Cancer: Where Surgery Alone Falls Short

NSCLC Staging and Surgical Eligibility

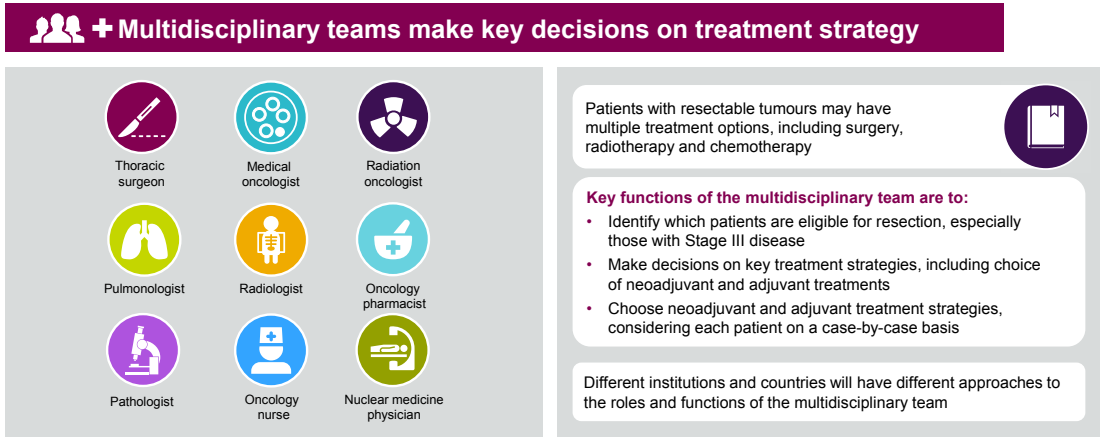


Recurrence Rates After Initial Treatment of Resectable NSCLC

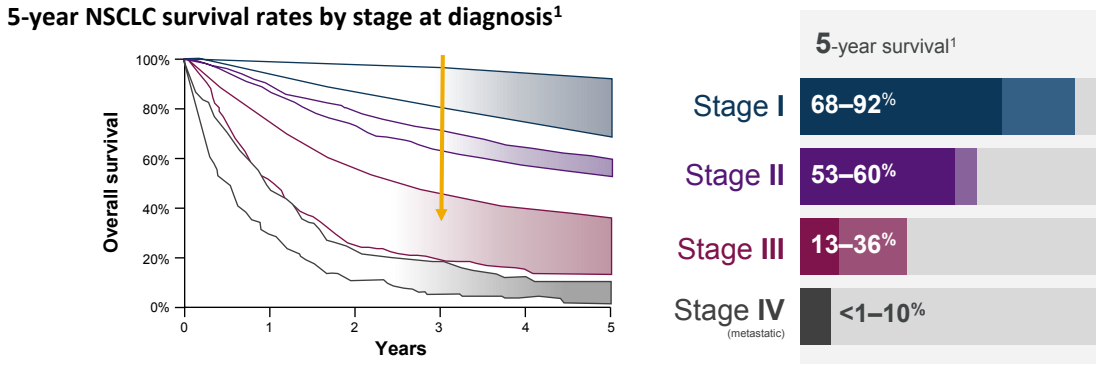


After initial treatment, more than half of patients with resectable NSCLC experience recurrence within 5 years

Role of the Multidisciplinary Team in Treatment Decisions



Five-Year Survival Rates by NSCLC Stage at Diagnosis

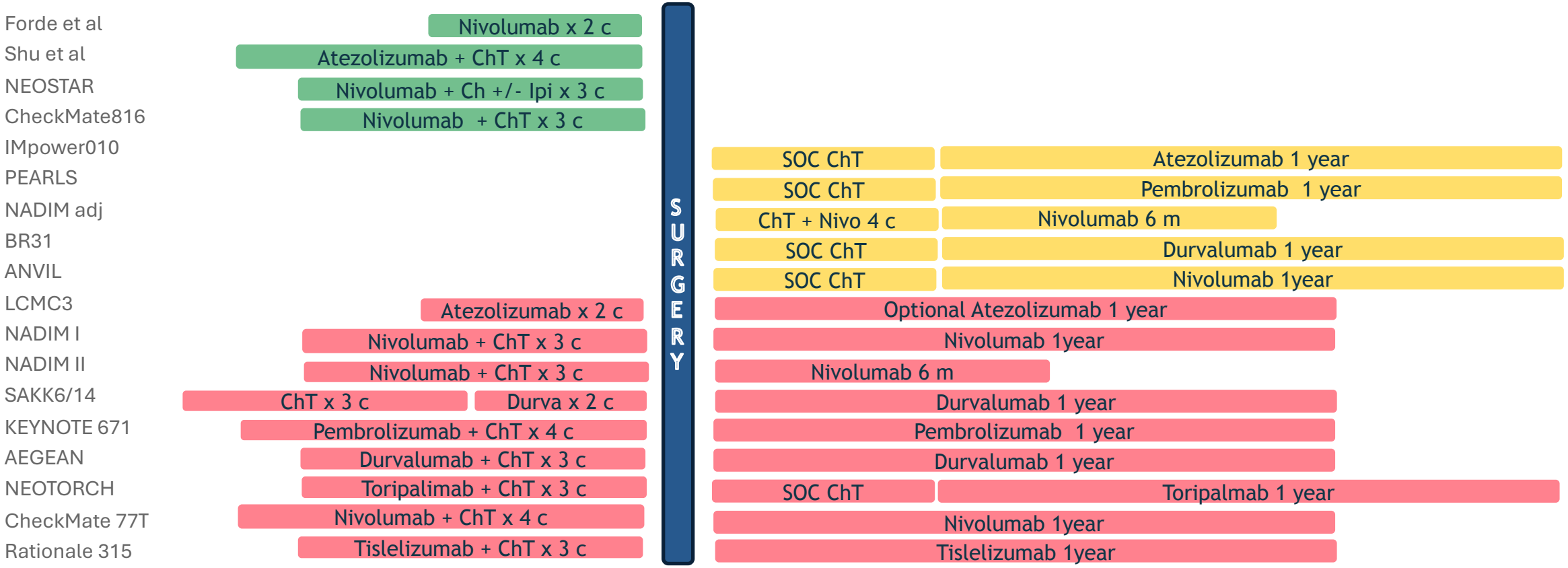


Adapted from Global Data. 2016. [a]Diagnosis statistics based on 7 major market countries (EU5, US, and Japan).

Deslypere G. Ther Adv Med Oncol. 2018 Postmus PE Ann Oncol. 2017 Goldstraw P J Thorac Oncol 2016 Boyd JA J Thorac Oncol 2010 McMurry TL Ann Surg 2018. Sekihara K Eur J Cardiothorac Surg 2017

Can Efficacy Data Guide Adjuvant Therapy After Neoadjuvant Treatment?

Summary of Key Neoadjuvant, Perioperative, and Adjuvant Studies in Operable NSCLC



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Can Efficacy Data Guide Adjuvant Therapy After Neoadjuvant Treatment?

What Works: Efficacy Data from Modern Resectable NSCLC Trials

Trial	Setting	Drug	n	Primary endpoint	STAGES	HR (EFS/DFS)	Median EFS/DFS (ICI vs placebo)	pCR	OS
CM-816	Neoadj	Nivolumab	358	EFS /pCR	IB-IIIA	0.63 (0.43-0.91) p=0.005	43.8 vs 18,4 m	24% vs 2.2%	65.4% vs 55% (5 y)
KN-671	Periop	Pembrolizumab	797	EFS/OS	II-IIIB	0.58 (0.46-0.72) p < 0.00001	47.2 vs 18.3 m	18,1% vs 4%	67.1% vs 51.5% (4 y)
AEGEAN	Periop	Durvalumab	802	EFS/pCR	II-III	0.68 (0.53-0.88) p= 0.004	NR vs 30 m	17,2% vs 4.3%	Not reported
CM-77T	Periop	Nivolumab	735	EFS	IIA-IIIB	0.58 (0.42-0.81) p=0.00025	NR vs 18.4 m	25,3% VS 4.7%	Not reported
NEOTORCH	Periop	Toripalimab	501	EFS/MPR	II-IIIB	0.40 (0.28-0.57) p < 0.001	NR vs 15.1 m	24,8% vs 1%	81% 2 y
RATIONALE 315	Periop	Tislelizumab	453	MPR	II-IIIA	0.56 (0.40-0.79) p=0.0003		41% vs 6%	89% 2 y
IMpower010	Adj	Atezolizumab	1269	DFS	IB-IIIA	(Stage IB-IIIA): 0.81(0.67, 0.99)p=040	65,6 vs 47,8 m	NA	ITT 79% 3 y
PEARLS	Adj	Pembrolizumab	1177	DFS	II-IIIA	0.76 (0.63-0.91) p= 0.0014	53.6 VS 42 m	NA	2% (1.5 y)
BR31	Adj	Durvalumab	1360	DFS PDL1 >25%	IB-IIIA	PD-L1 25%: 0.935 (0.70-1.247)	-	NA	Not reported

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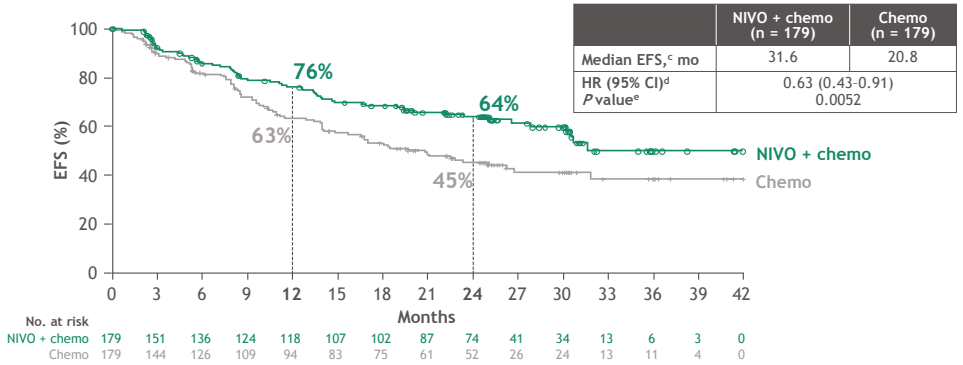
Can Efficacy Data Guide Adjuvant Therapy After Neoadjuvant Treatment?

2 years Event Free Survival

CheckMate 816



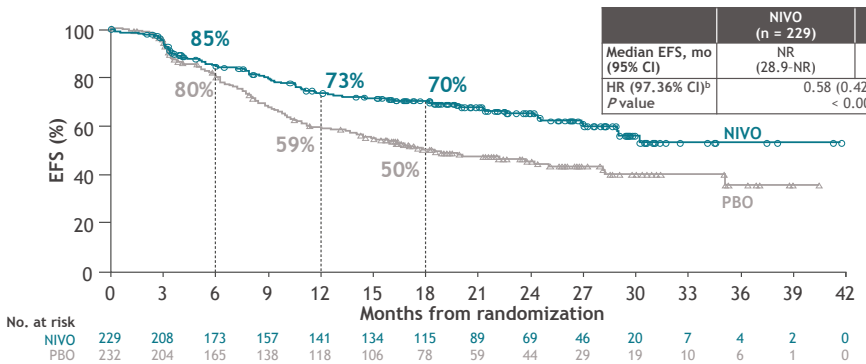
	NIVO + chemo (n = 179)	Chemo (n = 179)
Median EFS,[c] mo	31.6	20.8
HR (95% CI)[d] *P* value[e]	0.63 (0.43-0.91) 0.0052	

Forde N Engl J Med. 2022

9 weeks neoadjuvant chemo-IO

2 y EFS – 65%

Checkmate 77T



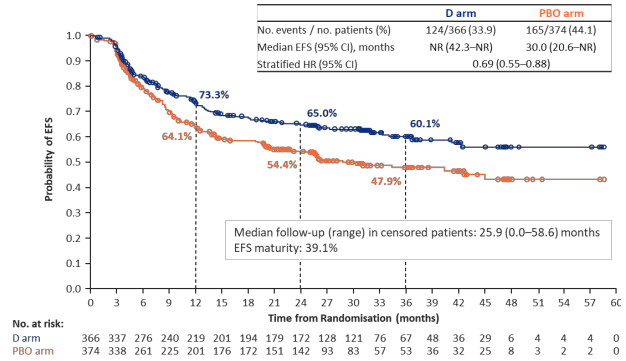
	NIVO (n = 229)	PBO (n = 232)
Median EFS, mo (95% CI)	NR (28.9-NR)	18.4 (13.6-28.1)
HR (97.36% CI)[b] *P* value	0.58 (0.42-0.81) < 0.001	

Cascone T N Engl J Med. 2024.

12 weeks neoadjuvant chemo-IO + 52 weeks adjuvant IO

2 y EFS – ~65%

AEGEAN



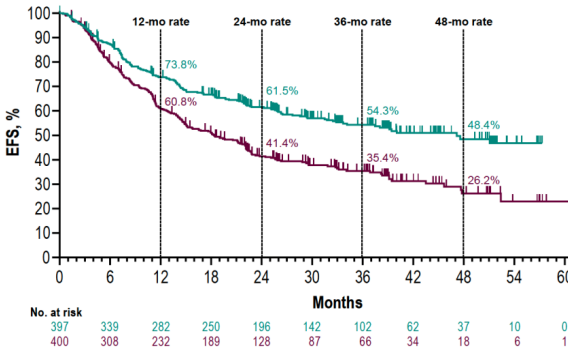
	D arm	PBO arm
No. events / no. patients (%)	124/366 (33.9)	165/374 (44.1)
Median EFS (95% CI), months	NR (42.3–NR)	30.0 (20.6–NR)
Stratified HR (95% CI)	0.69 (0.55–0.88)	

12 weeks neoadjuvant chemo-IO + 52 weeks of adjuvant IO

2 y EFS – 63.3%

Cascone T N Engl J Med. 2024.

KeyNote 671



12 weeks neoadjuvant chemo-IO + 39 weeks adjuvant IO

2 y EFS – 61.5%

Spicer JD Lancet. 2024

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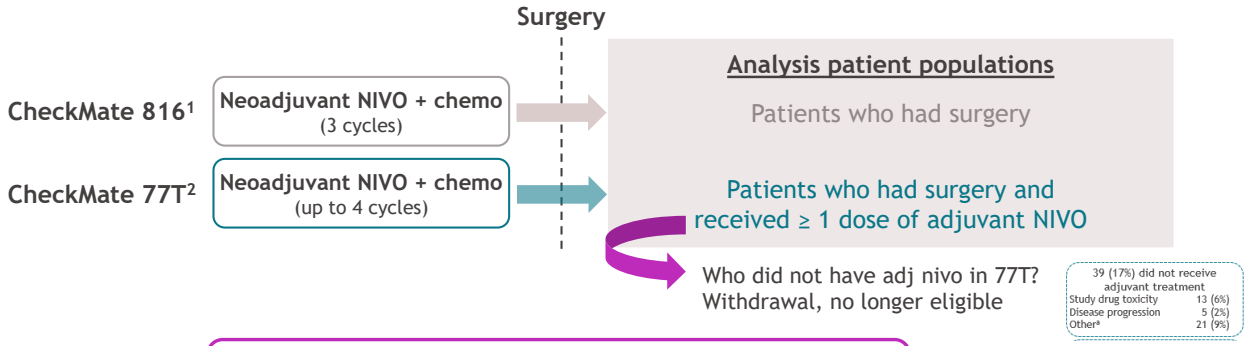
Can Efficacy Data Guide Adjuvant Therapy After Neoadjuvant Treatment?

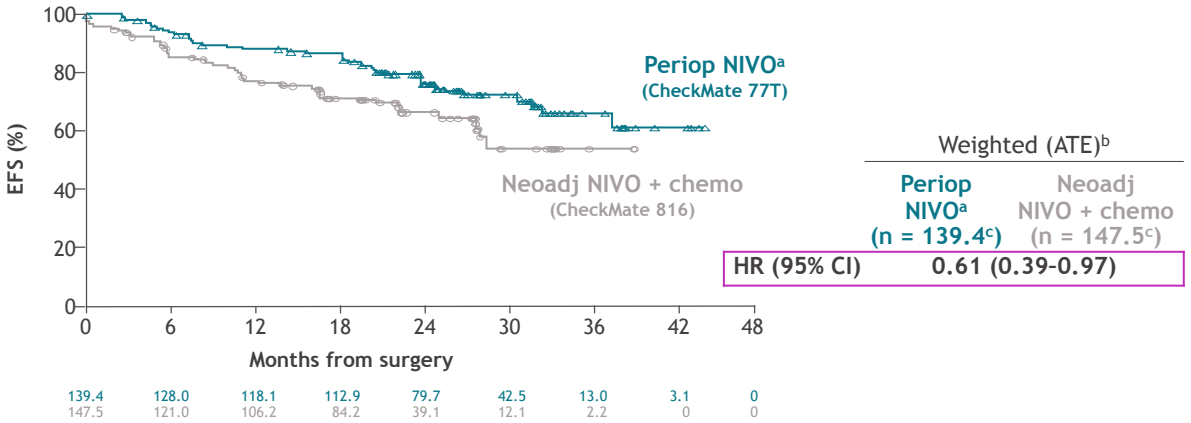
Individual Patient Level Analysis of CM816 and CM77T

Perioperative NIVO vs Neoadjuvant NIVO + chemo



Endpoint
EFS (BICR) landmarked from time of surgery

EFS (BICR) from definitive surgery



	Weighted (ATE)[b]	
	Periop NIVO[a] (n = 139.4[c])	Neoadj NIVO + chemo (n = 147.5[c])
HR (95% CI)	0.61 (0.39-0.97)	

- HR (95% CI): ATT[d] weighted analysis, 0.56 (0.35-0.90); unweighted analysis, 0.59 (0.38-0.92)

Baseline characteristics: analysis populations

	Unweighted	
	Perioperative NIVO (n = 139), %	Neoadjuvant NIVO + chemo (n = 147), %
Age < 65 years	48	52
Male	73	69
Asian	27	50
ECOG PS ≥ 1	33	25
Disease stage		
Stage IB-II	35	37
Stage III non-N2	24	16
Stage III N2	40	47
Squamous NSCLC	50	46
Current/former smoker,[b]	94	90
Tumor PD-L1 expression ≥ 1%	58	50

- In lieu of a head-to-head trial, exploratory propensity score weighting analyses (ATTa and ATEb) were performed to allow simplified reproduction of a randomized trial by adjusting for clinically relevant baseline demographics and disease characteristicsc between study populations and reducing the confounding effects of these factors
- Median duration of follow-upd: 29.5 months (CheckMate 816) and 33.3 months (CheckMate 77T)

Approximately 40% reduction in risk of disease recurrence or death after surgery was observed in patients who received ≥ 1 dose of adjuvant NIVO following neoadjuvant NIVO + chemo treatment and surgery compared with those who did not receive adjuvant NIVO

Forde PM WCLC 2024

Tailoring Treatment: Subgroup Analyses by Disease Stage

EFS and DFS by Patient Stages Subgroup in Phase 3 Trials of ICI-CT in Early NSCLC

Study	Treatment Approach	Treatment Regimen	Stage II HR (95% CI)	Stage IIIA HR (95% CI)	Stage IIIB HR (95% CI)
NEOADJUVANT					
CheckMate 816	Neoadjuvant	Nivolumab + CT (3 cycles)	0.87 (0.48-1.56)[a]	0.54 (0.37-0.80)	NA
PERIOPERATIVE					
AEGEAN	Perioperative	Durvalumab + CT (4 cycles)	0.76 (0.43-1.34)	0.57 (0.39-0.83)	0.83 (0.52-1.32)
KEYNOTE-671	Perioperative	Pembrolizumab + CT (4 cycles)	0.65 (0.42-1.01)	0.54 (0.41-0.72)[b]	0.52 (0.31-0.88)
CheckMate 77T	Perioperative	Nivolumab + CT (4 cycles)	0.81 (0.46-1.43)	0.51 (0.36-0.72)	0.73 (0.47-1.15)
Neotorch	Perioperative	Toripalimab + CT (3 cycles)	NA	0.44 (0.29-0.66)	0.30 (0.15-0.56)
RATIONALE-315	Perioperative	Tislelizumab + CT (3-4 cycles)	0.47 (0.26-0.87)	0.62 (0.42-0.94)	NR
ADJUVANT					
IMpower010	Adjuvant	CT → Atezolizumab vs. BSC	0.75 (0.47-1.18)	0.87 (0.43-1.76)	0.66 (0.47-0.93)
PEARLS/KEYNOTE-091	Adjuvant	Optional CT → Pembrolizumab vs. placebo	0.70 (0.55-0.91)	0.92 (0.69-1.24)	0.78 (0.58-1.03)
BR.31	Adjuvant	Optional CT → Durvalumab vs. placebo	0.95 (0.74-1.21)	0.84 (0.65-1.11)	NA

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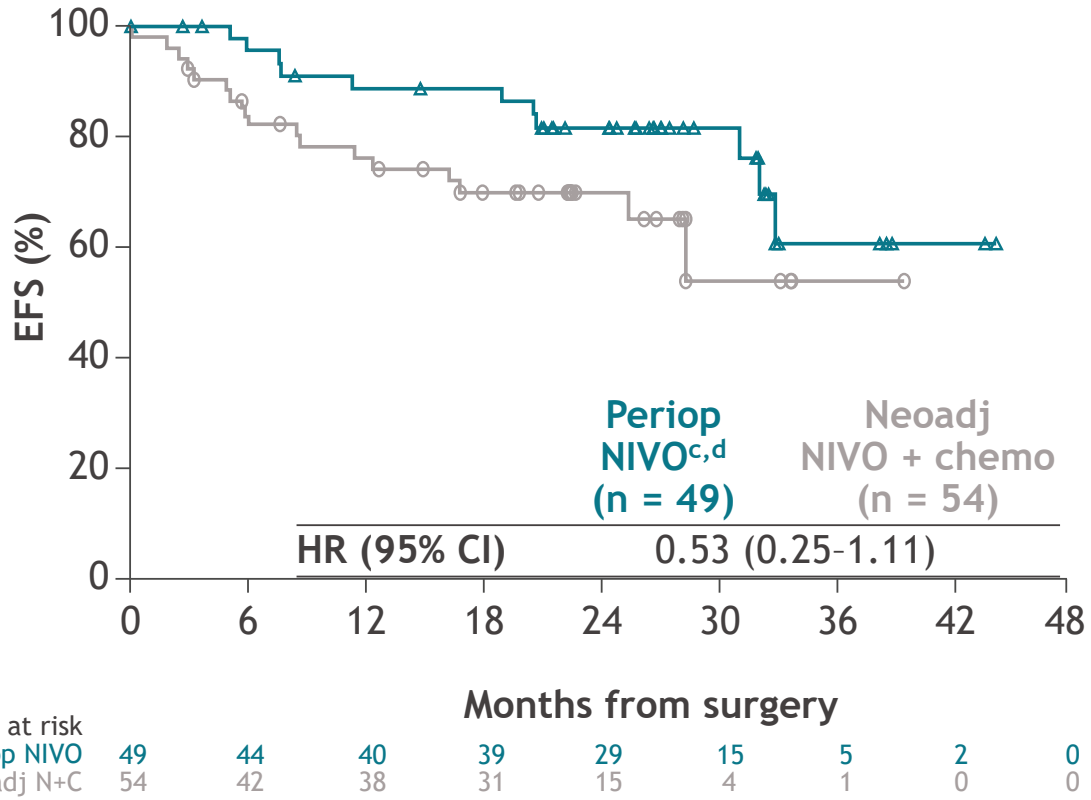
Tailoring Treatment: Subgroup Analyses by Disease Stage

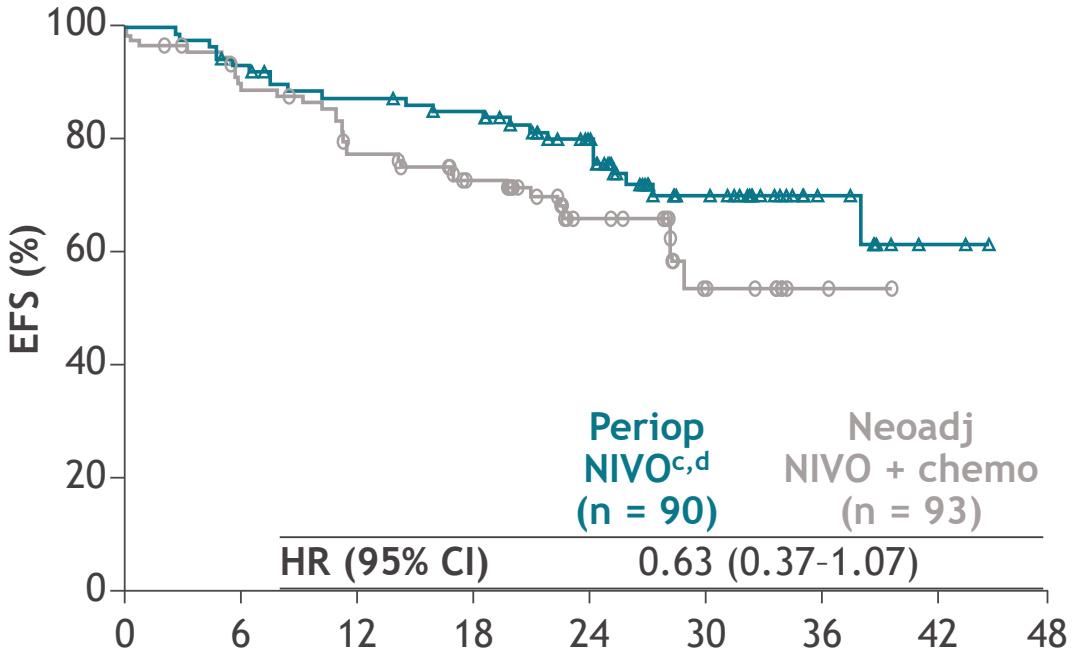
Individual Patient Level Analysis of CM816 and CM77T

Stage IB-II



No. at risk									
Periop NIVO	49	44	40	39	29	15	5	2	0
Neoadj N+C	54	42	38	31	15	4	1	0	0

Stage III



Periop NIVO	90	83	76	72	50	29	9	2	0
Neoadj N+C	93	80	68	55	26	9	2	0	0

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Tailoring Treatment: Subgroup Analyses by Histology

EFS and DFS by Histology in Phase 3 Trials of ICI-CT in Early NSCLC

Study	Treatment Approach	Treatment Regimen	SQ HR (95% CI)	Non-SQ HR (95% CI)
NEOADJUVANT				
CheckMate 816	Neoadjuvant	Nivolumab + CT (3 cycles)	0.77 (0.49-1.22)	0.50 (0.32-0.79)
PERIOPERATIVE				
AEGEAN	Perioperative	Durvalumab + CT (4 cycles)	0.71 (0.49-1.03)	0.69 (0.48-1.99)
KEYNOTE-671	Perioperative	Pembrolizumab + CT (4 cycles)	0.57 (0.41-0.77)	0.58 (0.43-0.78)
CheckMate 77T	Perioperative	Nivolumab + CT (4 cycles)		0.72 (0.49-1.07)
Neotorch	Perioperative	Toripalimab + CT (3 cycles)	0.35 (0.24-0.53)	0.54 (0.27-1.10)
RATIONALE-315	Perioperative	Tislelizumab + CT (3-4 cycles)	0.56 (0.38-0.83)	0.64 (0.32-1.26)
ADJUVANT				
IMpower010	Adjuvant	CT → Atezolizumab vs. BSC	0.87 (0.56-1.37)	0.62 (0.46-0.85)
PEARLS/KEYNOTE-091	Adjuvant	Optional CT → Pembrolizumab vs. placebo	1.04 (0.75-1.45)	0.67 (0.54-0.83)
BR.31	Adjuvant	Optional CT → Durvalumab vs. placebo	0.92 (0.67-1.28)	0.80 (0.65-0.99)


Cancer Immunology, Immunotherapy (2024) 73:262
https://doi.org/10.1007/s00262-024-03844-w

REVIEW

Efficacy and safety of perioperative immunotherapy combinations for resectable non-small cell lung cancer: a systematic review and network meta-analysis

Yuelin Han[1] · Xiangtian Xiao[1] · Tingting Qin[2] · Shuxi Yao[1] · Xinyue Liu[1] · Yanqi Feng[1] · Zhou Li[1] · Yiming Li[1] · Shu Xia[1]

According to the EFS results, the sandwich mode was found to be effective specifically for squamous cell carcinoma.

However, for nonsquamous cell carcinoma, both models received positive feedback and Neo showed a tendency to provide greater benefits for patients compared to Neo-Adj

Han Cancer Immunology, Immunotherapy (2024

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Tailoring Treatment: Subgroup Analyses by PDL-1 Status

EFS and DFS by Patient PD-L1 Subgroup in Phase 3 Trials of ICI-CT in Early NSCLC

Study	Treatment Approach	Treatment Regimen	PD-L1 <1% HR (95% CI)	PD-L1 1%-49% HR (95% CI)	PD-L1 ≥50% HR (95% CI)
NEOADJUVANT					
CheckMate 816	Neoadjuvant	Nivolumab + CT (3 cycles)	0.85 (0.54-1.32)	0.58 (0.30-1.12)	0.24 (0.10-0.61)
PERIOPERATIVE					
AEGEAN	Perioperative	Durvalumab + CT (4 cycles)	0.76 (0.49-1.17)	0.70 (0.46-1.05)	0.60 (0.35-1.01)
KEYNOTE-671	Perioperative	Pembrolizumab + CT (4 cycles)	0.77 (0.55-1.07)	0.51 (0.34-0.75)	0.42 (0.28-0.65)
CheckMate 77T	Perioperative	Nivolumab + CT (4 cycles)	0.76 (0.46-1.25)	0.26 (0.12-0.55)	0.46 (0.30-0.72)
Neotorch	Perioperative	Toripalimab + CT (3 cycles)	0.65 (0.33-1.23)	0.31 (0.17-0.54)	0.31 (0.15-0.60)
RATIONALE-315	Perioperative	Tislelizumab + CT (3-4 cycles)	0.80 (0.47-1.38)	0.34 (0.17-0.66)	0.71 (0.38-1.34)
ADJUVANT					
IMpower010	Adjuvant	CT → Atezolizumab vs. BSC	NR	0.91 (0.65-1.27)	0.48 (0.32-0.72)
PEARLS/KEYNOTE-091	Adjuvant	Optional CT → Pembrolizumab vs. placebo	0.67 (0.48-0.92)	0.82 (0.57-1.18)	1.04 (0.75-1.45)
BR.31	Adjuvant	Optional CT → Durvalumab vs. placebo	0.81 (0.60-1.11)	NR	0.97 (0.68-1.41)

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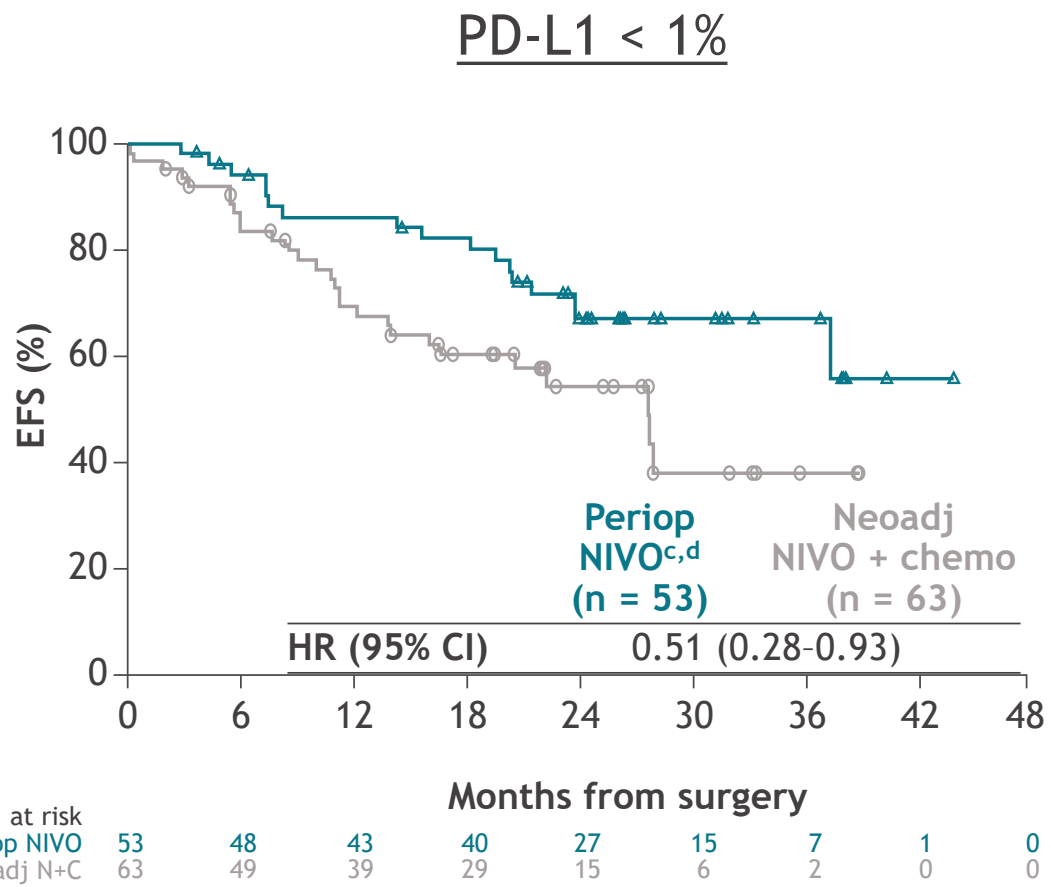
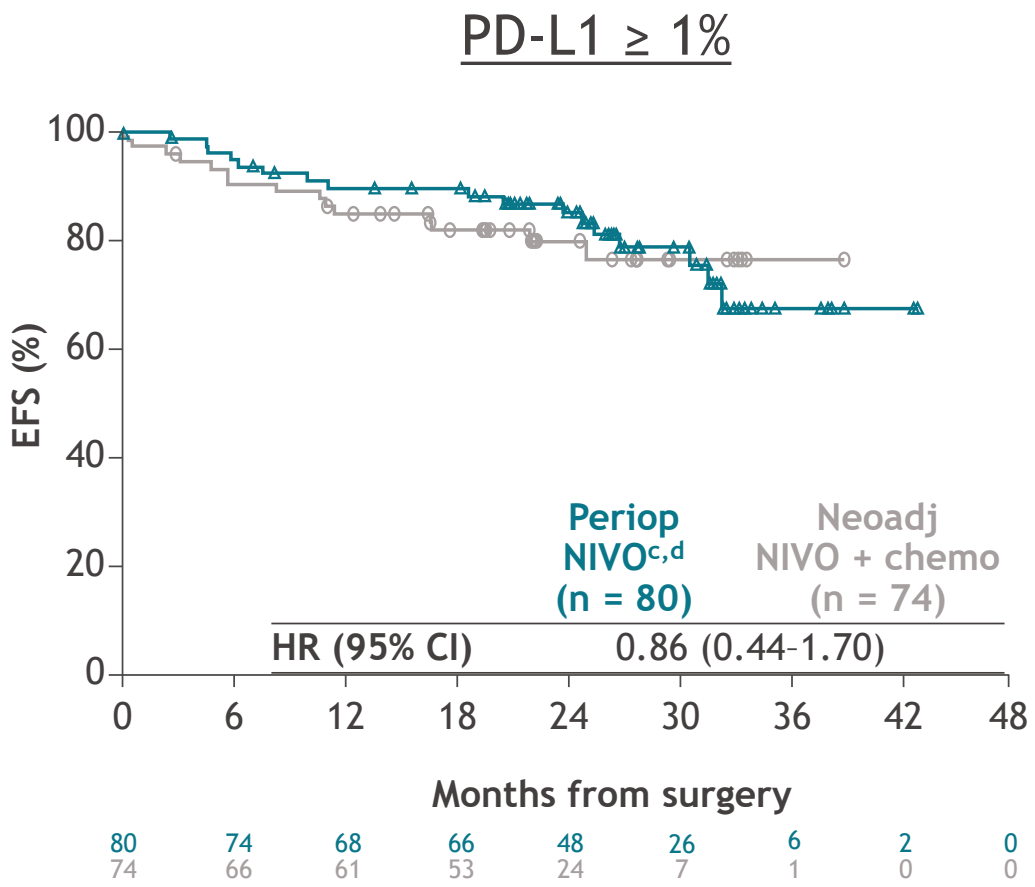
Individual Patient Level Analysis of CM816 and CM77T

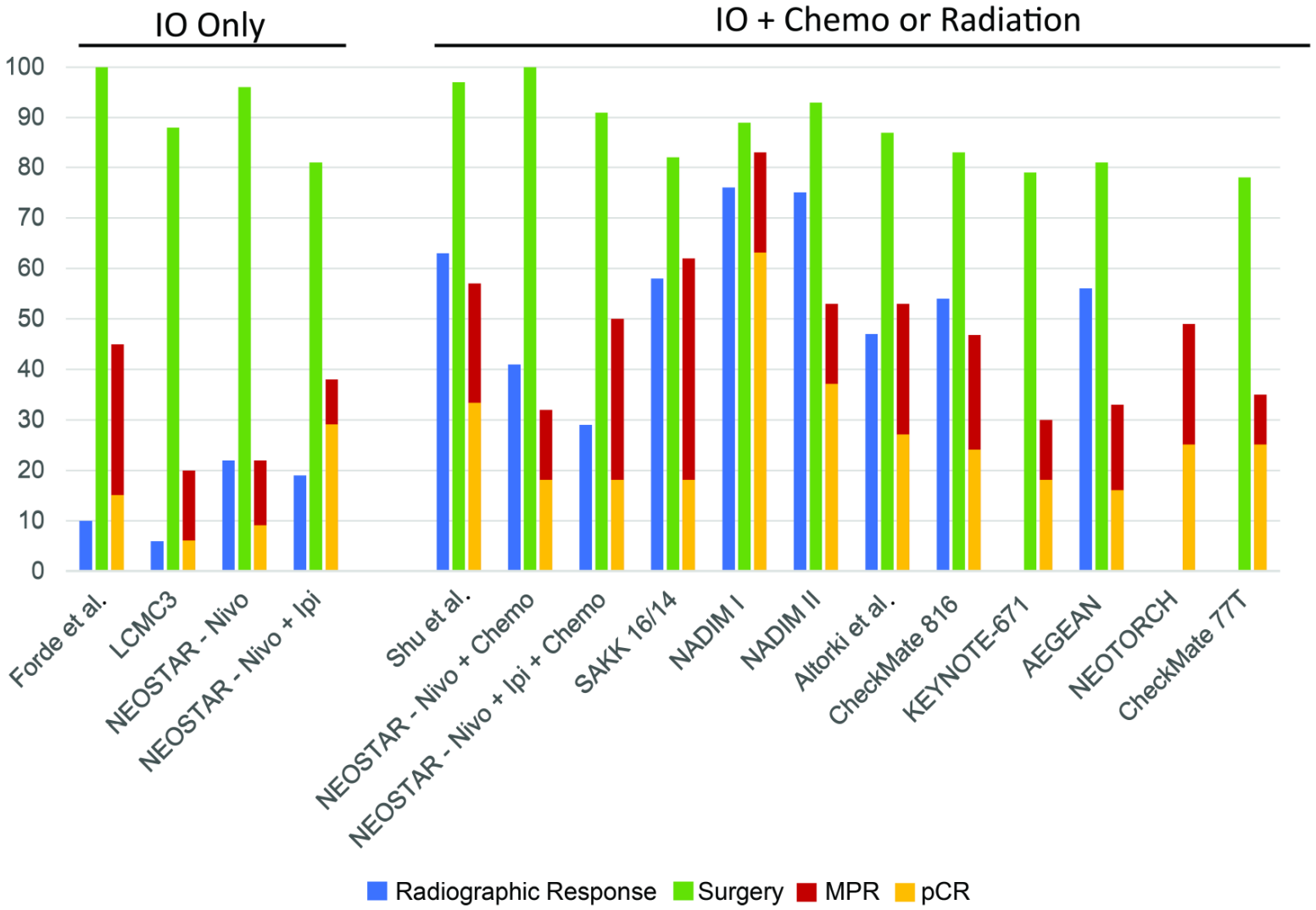




Forde PM WCLC 2024

Tailoring Treatment: Subgroup Analyses by pCR

Comparison of radiographic response, surgical resection, major pathologic response, and pathologic complete response rates between neoadjuvant and perioperative trials



- Neoadjuvant immunotherapy combined with chemotherapy significantly increases rates of major pathologic response (MPR) and pathologic complete response (pCR) compared with immunotherapy alone in resectable non–small cell lung cancer (NSCLC).

- Surgery rates remain high across all neoadjuvant approaches, indicating that combining immunotherapy with chemotherapy does not compromise resectability.

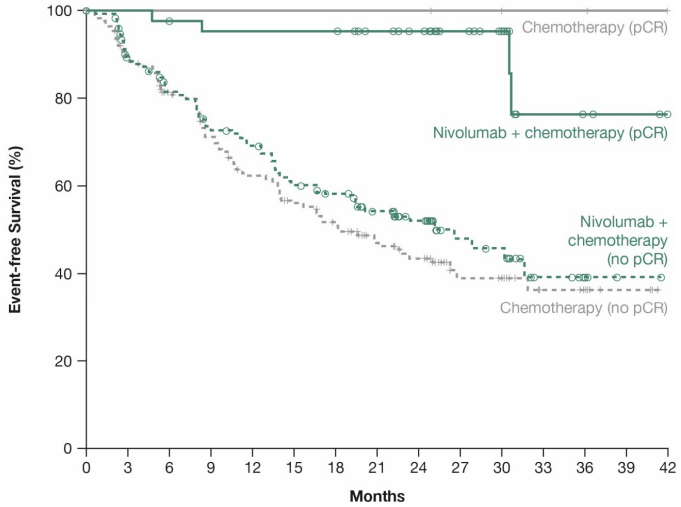
- Combination therapy leads to improved radiographic and pathological tumor regression, supporting its use as the new standard option for perioperative treatment in early-stage NSCLC.

Dunne Ann Thorac Surg 2025

Tailoring Treatment: Subgroup Analyses by pCR

EFS by pCR status

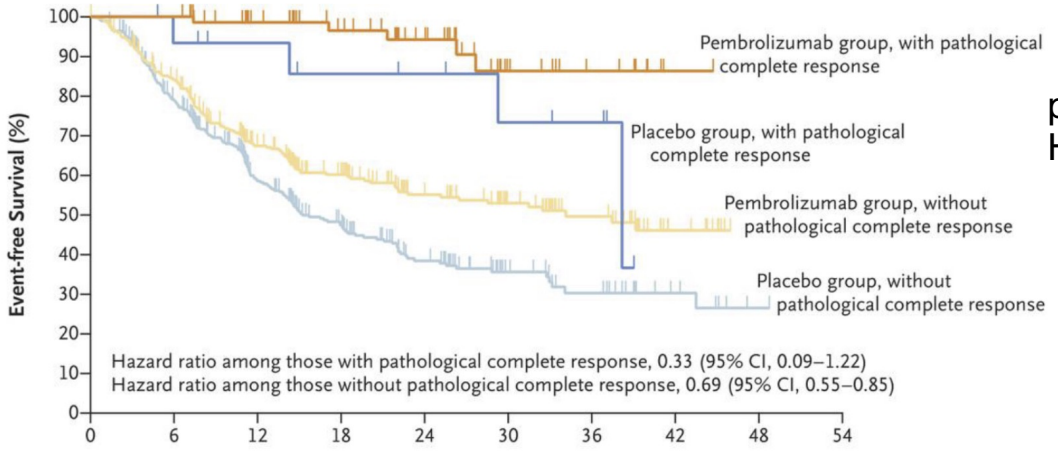
CheckMate 816 (neoadjuvant)



pCR:
HR not calculated

No pCR:
HR 0.84

KEYNOTE-671 (perioperative)

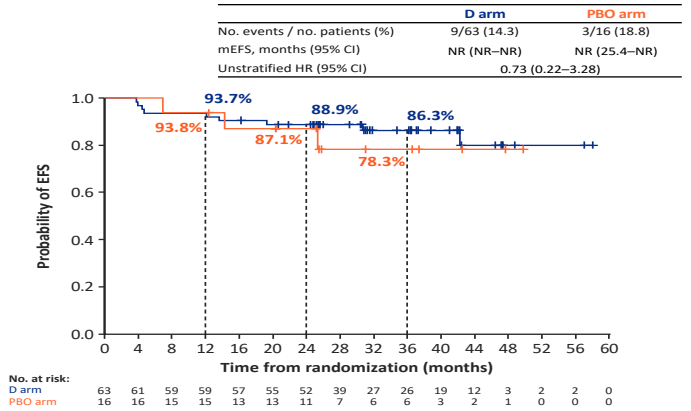


pCR:
HR 0. 33

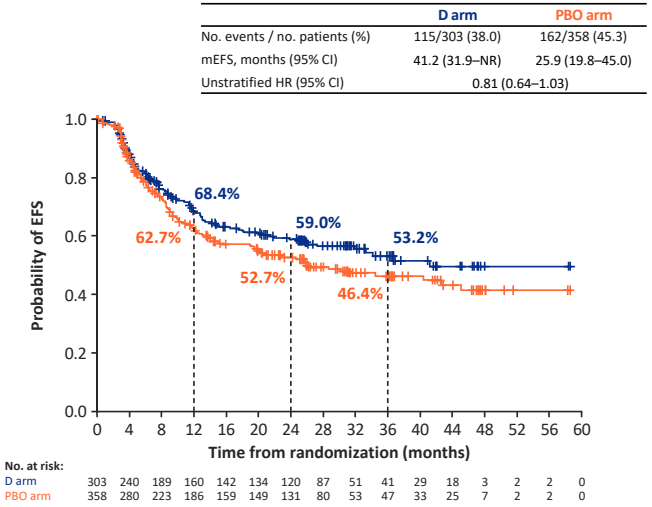
No pCR:
HR 0.69

AEGEAN (perioperative)

pCR



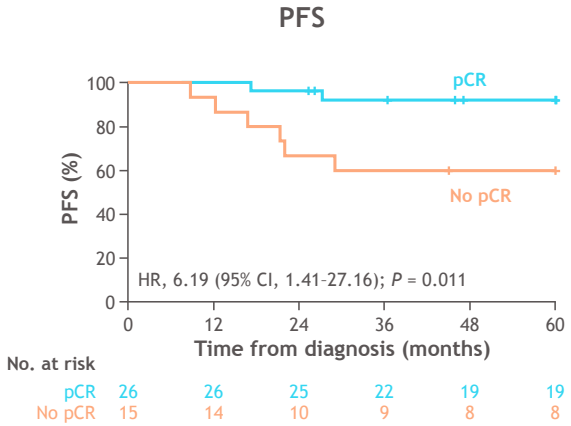
No pCR

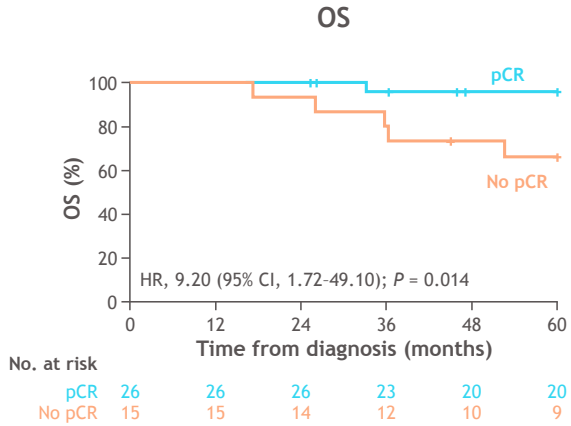


Wakelee et al NEJM 2023; Forde et al NJEM 2022 Heymach JV WCLC2024

Tailoring Treatment: Subgroup Analyses by pCR

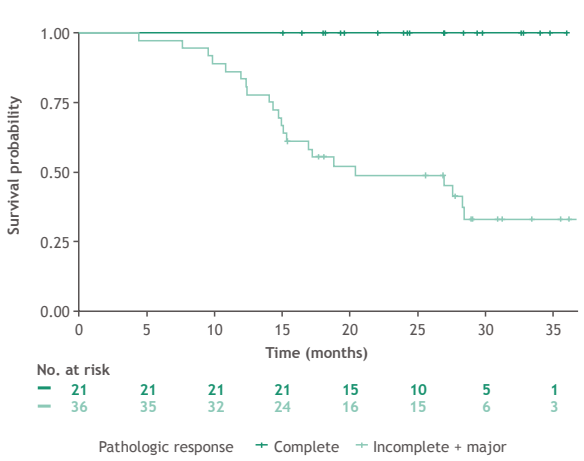
PFS and OS by pathologic response in resected patients NADIM II

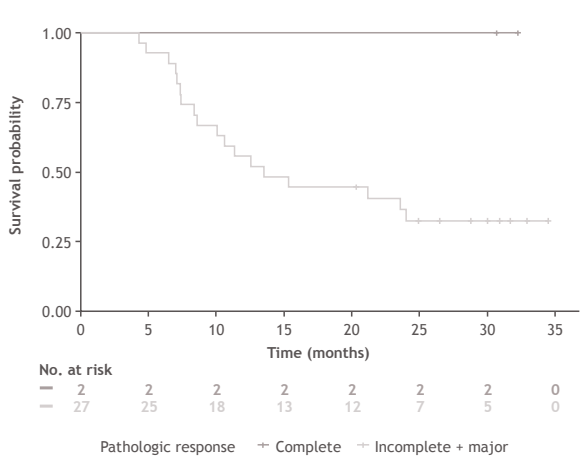




5-year PFS rates
- pCR: 92.0% (95% CI, 70.5-97.9)
- No pCR: 60.0% (95% CI, 31.8-79.7)

5-year OS rates
- pCR: 95.8% (95% CI, 73.9-99.4)
- No pCR: 66.0% (95% CI, 36.5-84.3)





Adapted with permission.

pCR is the most critical prognostic factor, with dramatic improvements in both PFS and OS.

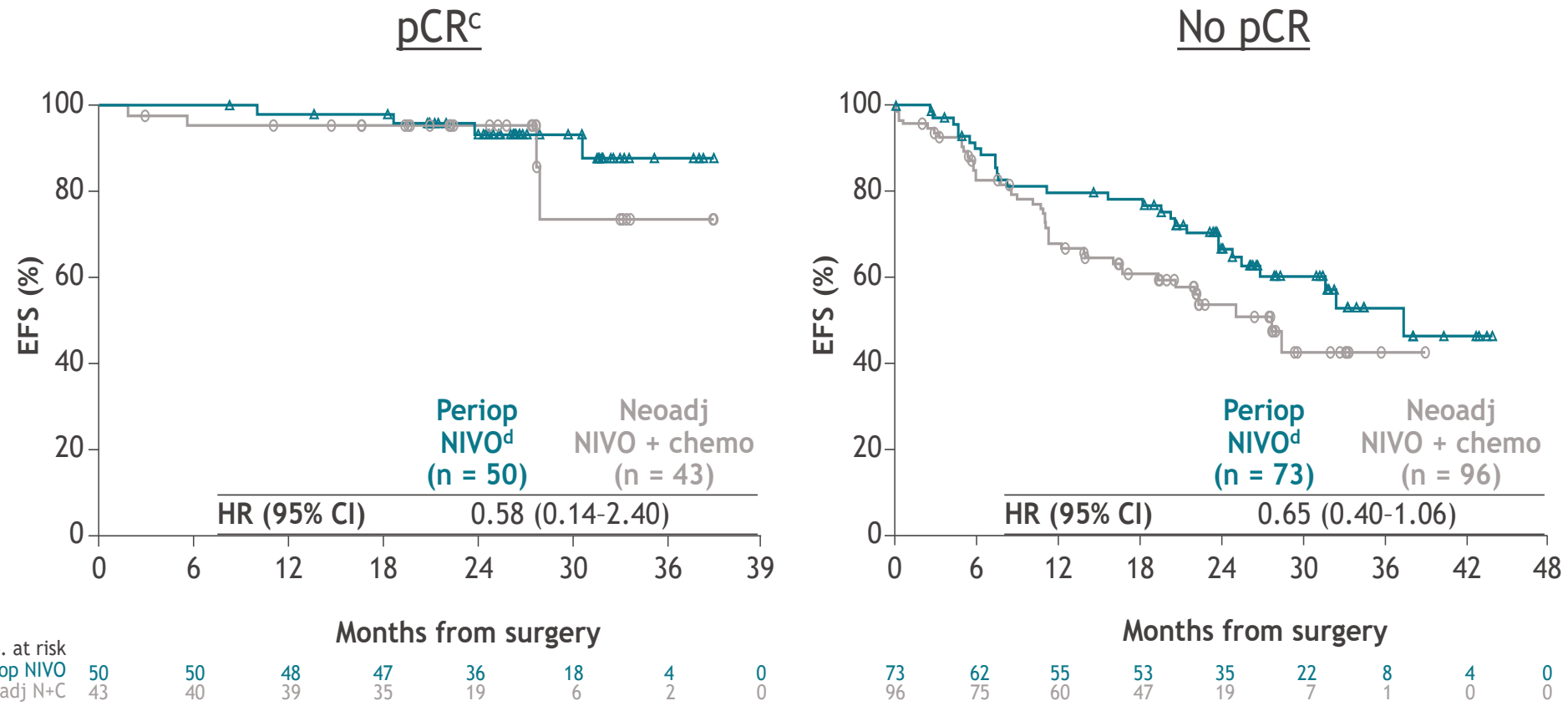
Achieving pathological complete response should be a primary treatment goal

The treatment comparison suggests modest differences between regimens, but pCR status appears more impactful than the specific treatment approach

These findings support pCR as a valid surrogate endpoint for long-term outcomes in neoadjuvant therapy

Tailoring Treatment: Subgroup Analyses by pCR

Individual Patient Level Analysis of CM816 and CM77T



Among patients without pathological complete response, we observe a decline in EFS over time in both arms.

EFS drops to approximately 40-45% by 48 months in both groups.

The hazard ratio is 0.65 (95% CI: 0.40-1.06), showing a trend favoring perioperative NIVO, though not statistically significant

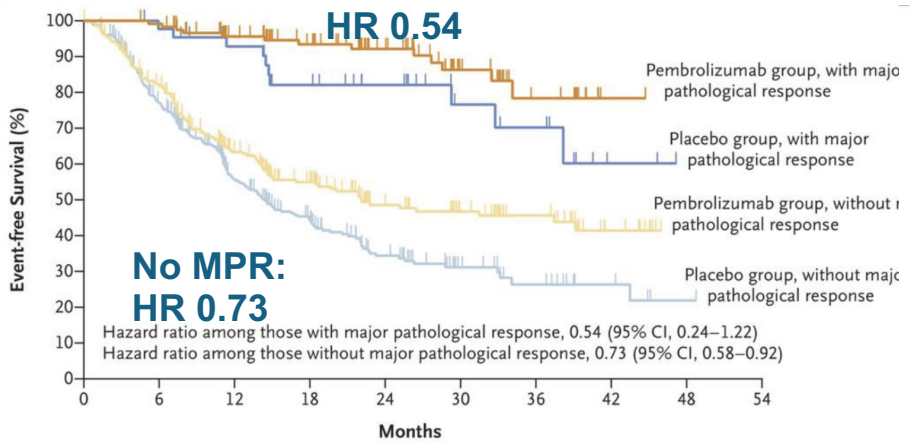
Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Patients with non-evaluable pCR status were excluded. [b]Unweighted analyses.
[c]pCR rates in this analysis population: perioperative NIVO, 40.7%; neoadjuvant NIVO + chemo, 30.5%. [d]Includes only patients who received ≥ 1 dose of adjuvant NIVO.

In patients achieving pathological complete response, both treatment arms show excellent outcomes with EFS remaining above 85% at 39 months.
The hazard ratio is 0.58 with a 95% confidence interval of 0.14 to 2.40, suggesting no significant difference between groups.
This demonstrates that regardless of treatment approach, achieving pCR is associated with favorable prognosis.

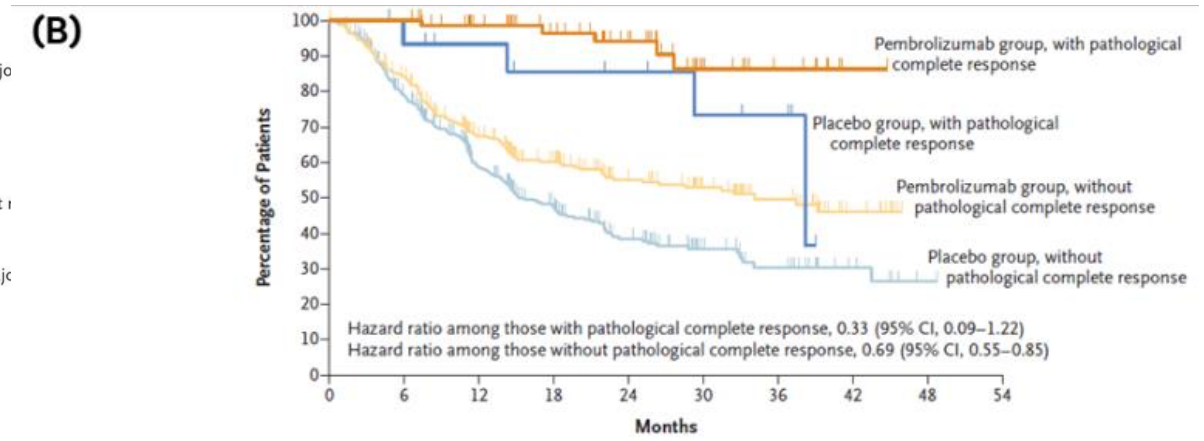
Forde PM WCLC 2024

Tailoring Treatment: Subgroup Analyses by MPR

KEYNOTE-671



No. at Risk										
With major pathological response										
Pembrolizumab group	120	117	99	79	60	30	15	1	0	0
Placebo group	44	42	36	28	22	12	10	2	0	0
Without major pathological response										
Pembrolizumab group	277	213	137	93	57	42	27	10	0	0
Placebo group	356	252	147	96	52	26	14	7	1	0



No. at Risk										
With pathological complete response										
Pembrolizumab group	72	72	59	46	33	15	8	1	0	0
Placebo group	16	14	12	10	9	5	4	0	0	0
Without major pathological response										
Pembrolizumab group	325	258	177	126	84	57	34	10	0	0
Placebo group	384	280	171	114	65	33	20	9	1	0

mPR was 30.2% (95% CI, 25.7-35.0) in the pembrolizumab group and 11.0% (95% CI, 8.1-14.5) in the placebo group (difference, 19.2; 95% CI, 13.9-24.7; P<0.0001).

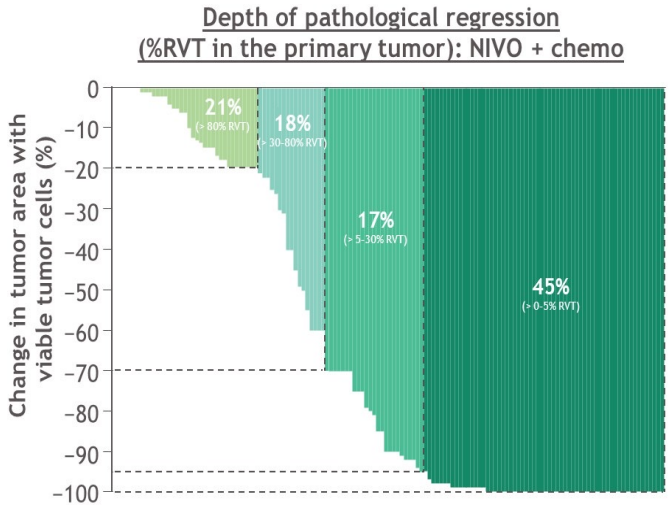
Pathological complete response occurred in 72 subjects (18.1%; 95% CI, 14.5-22.3) in the pembrolizumab group and in 16 subjects (4.0%; 95% CI, 2.3-6.4) in the placebo group (difference, 14.2; 95% CI, 10.1-18.7; P<0.001).

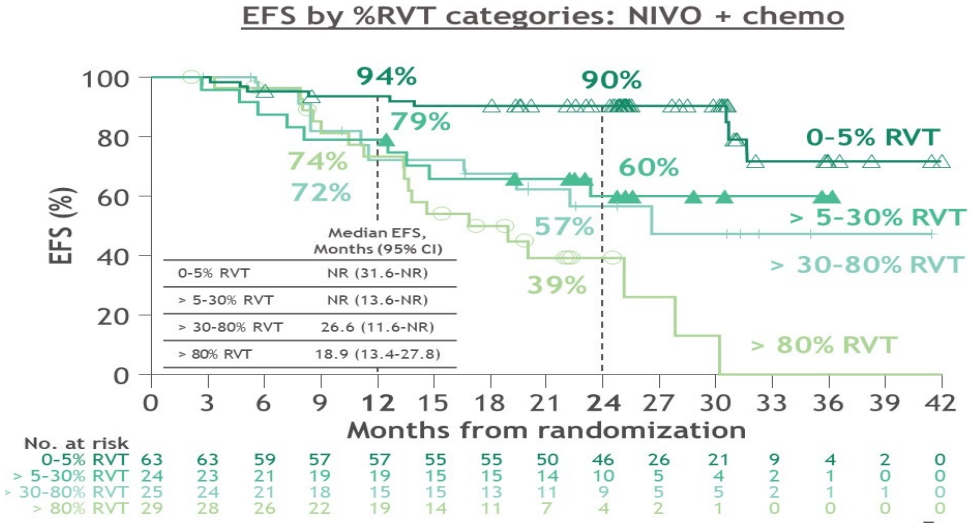
Spicer JD Lancet 2024

Tailoring Treatment: Subgroup Analyses by Residual Viable Tumor

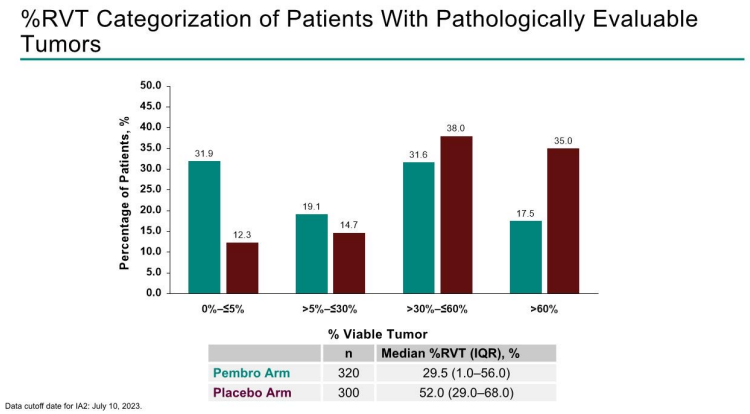
%RVT as a prognostic factor for EFS

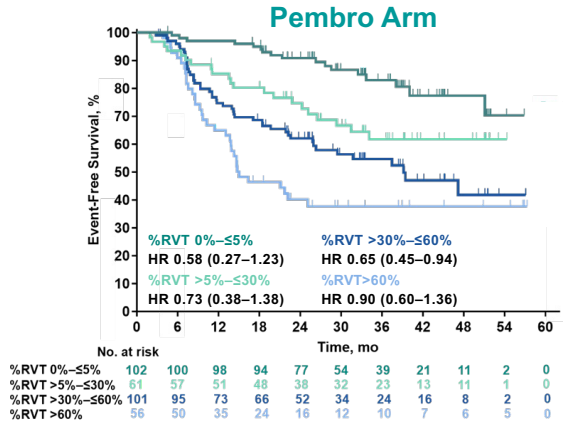
CM-816

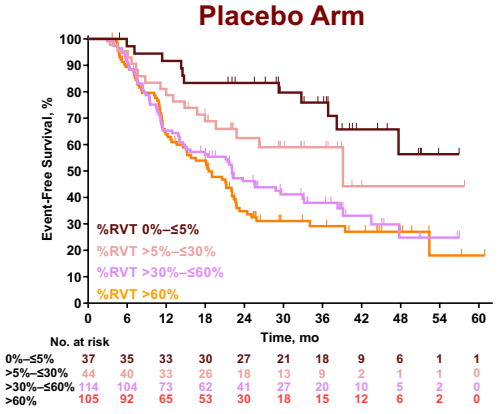




KN-617







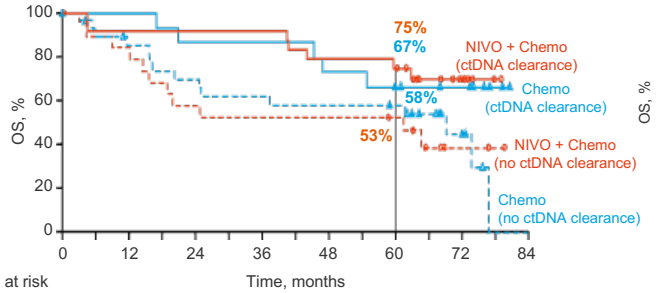
Deutsch, J Nat Med 2024; Jones, D. WCLC 2024

Tailoring Treatment: Analyses by ct DNA

CheckMate 816

OS by ctDNA clearance status

	Nivolumab + chemotherapy		Chemotherapy	
	ctDNA CL	No ctDNA CL	ctDNA CL	No ctDNA CL
Median OS, mo	NR	61.5	NR	69.2
HR (95%CI)	0.38 (0.15, 1.00)		0.39 (0.14, 1.11)	

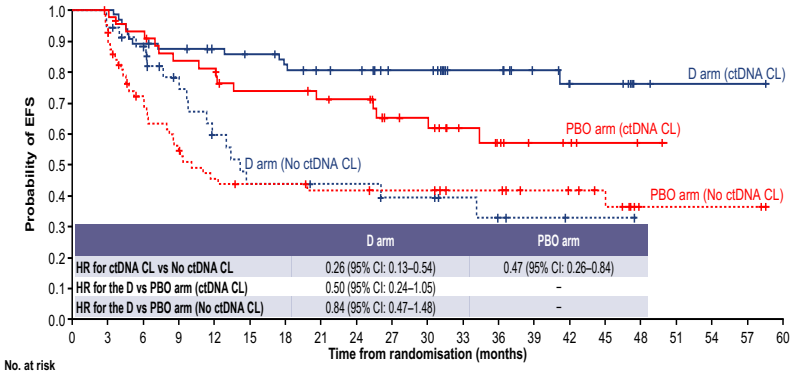


No. at risk

ctDNA clearance	24	22	22	22	22	22	20	19	19	18	11	6	1	0
ctDNA clearance	15	15	15	14	13	13	13	13	11	11	9	8	7	2	0
No ctDNA clearance	19	17	16	13	11	10	10	10	10	10	9	4	2	1	0
No ctDNA clearance	28	24	22	19	18	16	16	15	15	15	14	9	5	0	0

At 5 years, 75% of those with ctDNA clearance during neoadjuvant therapy were alive vs. 53% of those with ctDNA persistence

AEGEAN



	D arm	PBO arm
HR for ctDNA CL vs No ctDNA CL	0.26 (95% CI: 0.13–0.54)	0.47 (95% CI: 0.26–0.84)
HR for the D vs PBO arm (ctDNA CL)	0.50 (95% CI: 0.24–1.05)	-
HR for the D vs PBO arm (No ctDNA CL)	0.84 (95% CI: 0.47–1.48)	-

No. at risk

D arm (No ctDNA CL)	35	33	29	21	15	11	11	10	10	8	8	6	4	3	1	1	0	0	0	0	0
D arm (ctDNA CL)	65	65	57	55	52	50	47	44	43	35	35	24	24	19	14	12	2	1	1	1	0
PBO arm (No ctDNA CL)	63	60	41	31	25	23	23	21	21	17	17	14	14	11	10	7	2	2	2	2	0
PBO arm (ctDNA CL)	45	44	40	35	34	29	29	27	26	20	19	13	10	6	5	3	1	0	0	0	0

CheckMate 77T

EFS by ctDNA clearance and pCR status

Nivolumab	ctDNA CL + pCR vs ctDNA CL + no pCR	ctDNA CL + pCR vs No ctDNA CL + no pCR	ctDNA CL + no pCR vs No ctDNA CL + no pCR
HR (95%CI)	0.29 (0.10, 0.85)	0.23 (0.08, 0.65)	0.70 (0.31, 1.59)

Placebo	ctDNA CL + pCR vs ctDNA CL + no pCR	ctDNA CL + pCR vs No ctDNA CL + no pCR	ctDNA CL + no pCR vs No ctDNA CL + no pCR
HR (95%CI)	NC	NC	0.77 (0.39, 1.54)

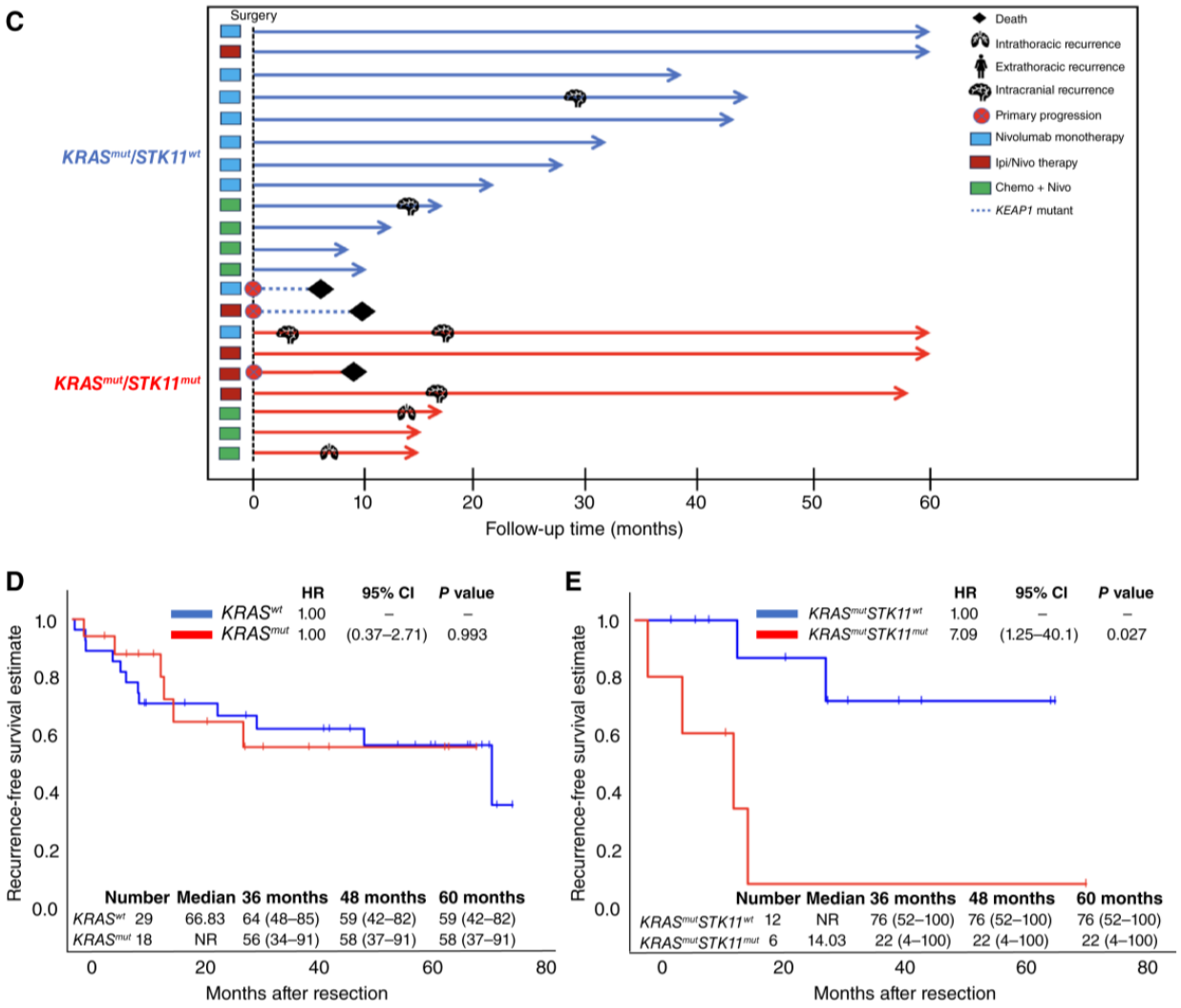
Associations of ctDNA clearance (CL) during neoadjuvant Tx with pathological response and event-free survival (EFS)

Group[a,b,c]		Median EFS, mo (95%CI)		
Durvalumab	Yes, n (%)	Yes	No	HR (95%CI)
Neoadj. C2D1 ctDNA CL (n=121)	41 (33.9)	NR (NR, NR)	41.2 (18.2, NR)	0.30 (0.12, 0.71)
Neoadj. C3D1 ctDNA CL (n=115)	62 (53.9)	NR (NR, NR)	21.8 (11.3, NR)	0.25 (0.13, 0.49)
Neoadj. C4D1 ctDNA CL (n=102)	63 (61.8)	NR (NR, NR)	14.2 (9.0, NR)	0.23 (0.11, 0.47)
ctDNA CL at pre-surgery (n=100)	65 (65.0)	NR (NR, NR)	14.2 (9.8, NR)	0.26 (0.13, 0.54)
Pre-surgery OR (n=142)	89 (62.7)	NR (NR, NR)	14.9 (9.7, NR)	0.38 (0.21, 0.68)
pCR (n=142)	32 (22.5)	NR (NR, NR)	41.2 (21.8, NR)	0.16 (0.05, 0.52)
MPR (n=142)	59 (41.5)	NR (NR, NR)	31.9 (14.2, NR)	0.26 (0.13, 0.52)
Adj. C1D1 ctDNA CL (n=76)	66 (86.8)	NR (NR, NR)	9.7 (4.0, 14.2)	0.04 (0.01, 0.13)
Placebo				
Neoadj. C2D1 ctDNA CL (n=119)	27 (22.7)	40.4 (25.4, NR)	11.7 (7.3, NR)	0.53 (0.27, 1.02)
Neoadj. C3D1 ctDNA CL (n=115)	50 (43.5)	45.0 (30.0, NR)	9.4 (6.1, NR)	0.47 (0.27, 0.82)
Neoadj. C4D1 ctDNA CL (n=104)	51 (49.0)	42.6 (25.7, NR)	8.6 (6.1, 45.0)	0.46 (0.26, 0.81)
ctDNA CL at pre-surgery (n=108)	45 (41.7)	NE (25.7, NR)	10.1 (6.4, NR)	0.47 (0.26, 0.84)
Pre-surgery OR (n=141)	65 (46.1)	42.6 (20.6, NR)	11.0 (5.6, 45.0)	0.53 (0.33, 0.87)
pCR (n=141)	6 (4.3)	NE (7.0, NR)	30.0 (11.7, 45.0)	0.45 (0.11, 1.85)
MPR (n=141)	20 (14.2)	NE (20.6, NR)	22.8 (9.4, 42.6)	0.40 (0.17, 0.92)
Adj. C1D1 ctDNA CL (n=71)	64 (90.1)	NE (42.6, NR)	9.0 (6.1, 12.2)	0.12 (0.04, 0.32)

Forde PM, ASCO 2025; Provencio M, ASCO 2025; Reck M,ESMO 2024; . Goos G, ESMO 2025

Tailoring Treatment: What are other possible metrics?

Certain molecular subgroups e.g. KRAS STK11 are likely at higher risk of recurrence however it is unclear if more PD-1 blockade helps



CheckMate 77T

EFS by tumor mutation status

	Nivolumab	Placebo
KRASm ± KEAP1m ±STK11m, n	33	34
Median EFS, mo (95%CI)	28.9 (13.2, NR)	10.5 (18.8, 31.4)
HR (95%CI)	0.63 (0.32, 1.23)	
KRASwt ± KEAP1wt ±STK11wt, n	65	58
Median EFS, mo (95%CI)	NR (29.0, NR)	17.0 (10.8, NR)
HR (95%CI)	0.65 (0.39, 1.10)	

	Nivolumab (n=229)	Placebo (n=232)
Median OS, mo (95%CI)	NR (NR, NR)	NR (NR, NR)
HR (97.6%CI)	0.85 (0.58, 1.25)	

Rosner. CCR 2025 Provencio M ASCO 2025

Key Concerns After Prior Neoadjuvant Therapy: Toxicity

Individual Patient Level Analysis of CM816 and CM77T

Safety summary: analysis populations

Patients, n (%)	Perioperative NIVO (n = 139)		Neoadjuvant NIVO + chemo (n = 147)	
	Any grade[b]	Grade 3-4[b]	Any grade[c]	Grade 3-4[c]
All AEs	137 (99)	64 (46)	138 (94)	63 (43)
TRAEs	130 (94)	38 (27)	125 (85)	52 (35)
All AEs leading to discontinuation	29 (21)	10 (7)	16 (11)	8 (5)
TRAEs leading to discontinuation	22 (16)	9 (6)	16 (11)	8 (5)
All SAEs	57 (41)	37 (27)	23 (16)	16 (11)
Treatment-related SAEs	23 (16)	14 (10)	17 (12)	13 (9)
Surgery-related AEs[d]	53 (38)	15 (11)	61 (42)	17 (12)
Treatment-related deaths[e]	0		0	

Forde PM WCLC 2024

Key Concerns After Prior Neoadjuvant Therapy: Finantial Toxicity and Patient Time

- Cost-effectiveness studies for neoadjuvant, adjuvant, and perioperative strategies have all shown the addition of IO to be cost-effective
- Total cost of neoadjuvant regimen is lower owing to less cycles of chemo-IO
- IF all have similar efficacy, the financial toxicity of adjuvant/perioperative regimens COULD be much higher

Table 1. ICER per QALY

Settings	ICER (cost) per QALY
Neoadjuvant	
CheckMate-816 (no PD-L1 selection)	$32,846
Perioperative	
KEYNOTE-671 (no PD-L1 selection)	$94,222
Adjuvant	
IMpower010 (PD-L1 50% cutoff for use)	$68,858

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality adjust life year.

Table: 1287P

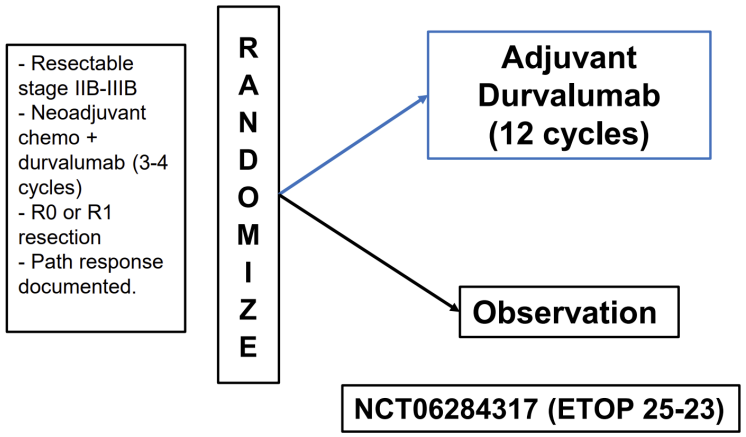
IO status at Recurrence	Neo Nivo		Adj Atezo	
	Stage IB-IIIA, any PD-L1	Stage IB-IIIA, PD-L1>1%	Stage II-IIIA, PD-L1>1%	Stage II-IIIA, PD-L1>50%
No IO	−$86,599	−$95,405	−$20,112	−$39,641
Ineffective IO	−$57,250	−$87,387	$34,051	−$24,670
Effective IO	−$103,924	−$100,339	−$58,101	−$42,318

- Difference in number of infusions for each strategy:
  - Neoadjuvant: 3
  - Adjuvant: 16-20
  - Perioperative: 16-17
- Potential substantial differences in costs for co-pays, parking, time off work, caregiver burden, and even direct financial costs to patients

Muthusamy Annals of Onc 2023; Tian Front. Immunol 2023

Key Concerns After Prior Neoadjuvant Therapy: Future Directions

ADOPT-LUNG



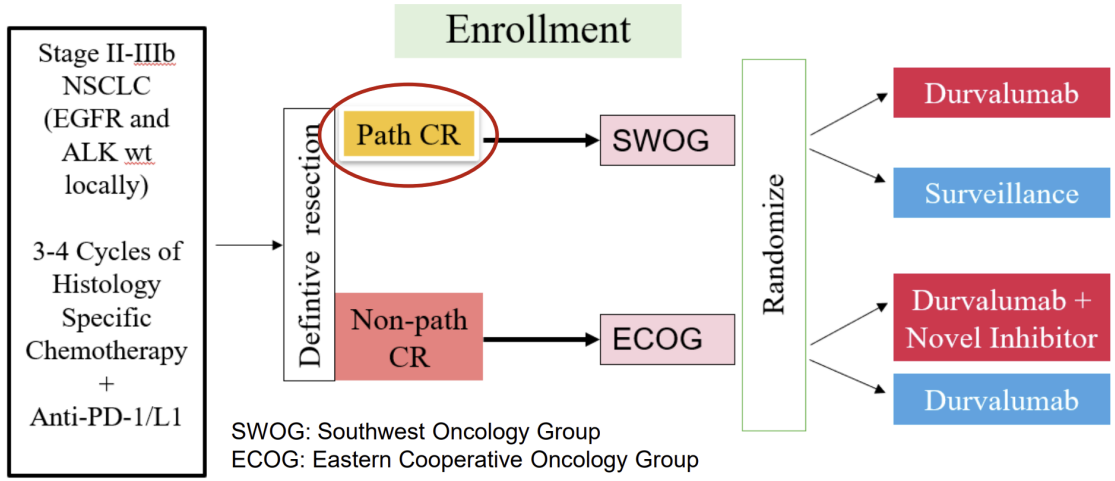
Primary Endpoint:
- DFS in non-PCR group

Sample Size:
- 290

Study Start:
- Oct 2024

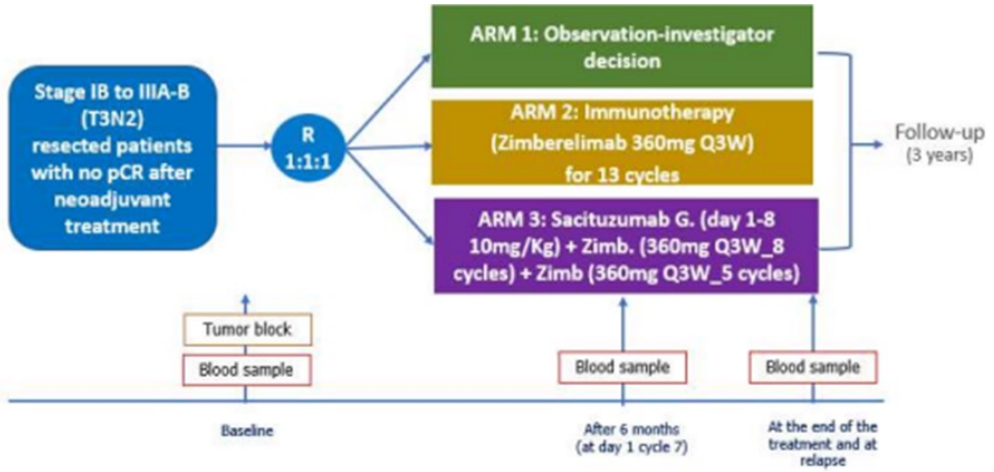
Study Completion:
- Mar 2030

CLEAR-INSIGHT



SWOG: Southwest Oncology Group
ECOG: Eastern Cooperative Oncology Group

ARIAN



To wrap up

1. There are no comparative studies determining whether the perioperative approach is more effective than neoadjuvant therapy in lung cancer.

2. Neither stage nor histology can guide the decision to give adjuvant therapy after neoadjuvant treatment. pCR, PD-L1 expression, and ctDNA may help guide this decision in the future.

3. The drawbacks of the perioperative approach must be considered, including financial toxicity and the impact on the lives of patients who undergo surgery for potentially curable lung cancer.

4. If neoadjuvant chemo-immunotherapy has not eradicated the tumor, will continuing the same treatment eradicate the residual disease, or should we change the therapeutic strategy?

Muchas Gracias !!!

ecarcereny@iconcologia.net
@ECarcereny

16th CONGRESS Lung ON CANCER

BARCELONA 27 / 28 NOVEMBER 2025

THANK YOU

GECP lung cancer research