Lung Cancer UPDATES
IASLC HIGHLIGHTS
San Diego, USA
ESMO HIGHLIGHTS
Barcelona, Spain

Iniciativa científica de:
GECP
lung cancer research

Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

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Disclosures

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- **Advisory / Consultancy :** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Roche, Takeda
- **Speaker Bureau / Expert testimony:** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Pfizer, Roche, Takeda
- **Travel / Accommodation / Expenses** :Bristol-Myers Squibb, Pfizer, Roche, Takeda, Astra Zeneca

TAKE AWAY ...

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1. **Pembrolizumab + Chemo**: Greater pathologic regression (%RVT 29.5% vs 52%) vs placebo. Higher %RVT linked to poorer EFS.
2. **AEGEAN Trial**: Durvalumab shows consistent EFS benefit (HR 0.69), enhanced in adjuvant-treated patients, regardless of pCR.
3. **Alectinib**: Effective (MPR 39%, pCR 17%) and well-tolerated in stage III ALK+ NSCLC.
4. **NADIM I**: Chemo-immunotherapy shows 5-year benefit, especially in patients with CPR. ctDNA clearance predicts better PFS/OS.
5. **Surgery vs Chemoradiation**: Surgery improved OS in cT4N2M0 NSCLC patients compared to chemoradiation plus IO.
6. **pCR/MPR**: Significant EFS improvement (>90% at 24 months). Similar EFS between neoadjuvant and perioperative regimens.
7. **NIVO + Chemo**: 40% reduction in recurrence/death with adjuvant NIVO. Greater benefit in PD-L1 < 1% patients.
8. **Novel Combinations**: Oleclumab, Monalizumab, and Dato-DXd combos show promising pCR and mPR rates vs historical benchmarks.
9. **BR.31 Trial**: Adjuvant durvalumab didn't improve DFS in PD-L1 ≥25% patients (EGFR−/ALK−).
10. **CheckMate 77T**: NIVO improves EFS (HR 0.59). Neoadjuvant NIVO + chemo enhances ctDNA clearance, linked to pCR and EFS benefits

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AGENDA

- Association of Pathologic Regression With Event-Free Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC WCLC2024
- Perioperative Durvalumab for Resectable NSCLC Updated Outcomes from the Phase 3 AEGEAN Trial WCLC2024
- Neoadjuvant Alectinib in Potentially Resectable Stage III ALK-positive NSCLC: Interim Analysis of ALNEO-GOIRC-01-2020 Phase II Trial WCLC2024
- 5-Year Clinical Outcomes of Perioperative Nivolumab and Chemotherapy in Stage III NSCLC (NADIM trial) Definitive Chemoradiation Followed by Immunotherapy vs. Surgery for cT4N2M0 NSCLC : A Contemporary Nationwide Analysis. WCLC2024
- Survival outcomes and pathologic response after chemoimmunotherapy in resectable NSCLC: an individual patient data meta-análisis WCLC2024
- NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC WCLC2024
- Perioperative vs neoadjuvant nivolumab for resectable NSCLC: patient-level data analysis of CheckMate 77T vs CheckMate 816 WCLC2024
- Perioperative nivolumab vs placebo in patients with resectable NSCLC: clinical update from the phase 3 CheckMate 77T study ESMO2024
- CCTG BR.31: A double-blind placebo- controlled randomized phase 3 trial of adjuvant durvalumab in completely resected non-small-cell lung cancer ESMO2024

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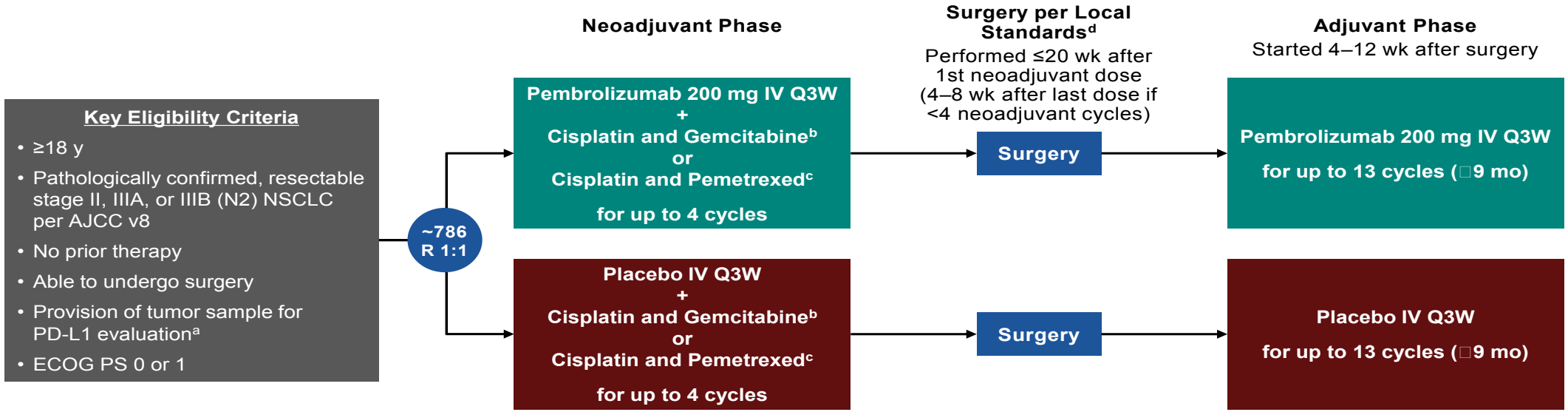
Association of Pathologic Regression With Event-Free Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC

KEYNOTE-671 Study Design

Randomized, Double-Blind, Phase 3 Trial



Stratification Factors
- Disease stage (II vs III)
- PD-L1 TPS[a] (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (East Asia vs not East Asia)

Dual primary end points: EFS per investigator review and OS

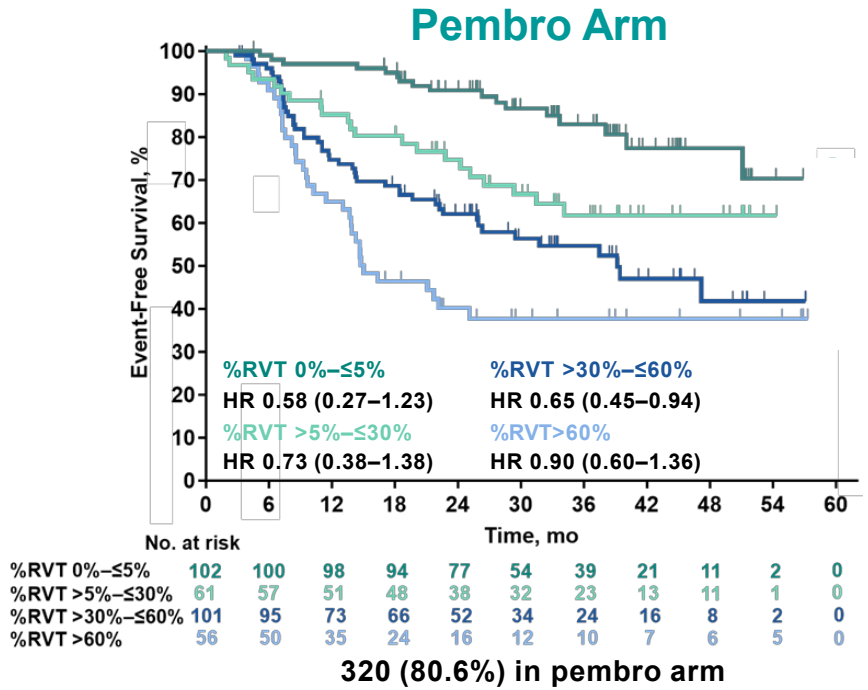
Key secondary end points: mPR and pCR per blinded, independent pathology review and safety

Pathologic regression categorization: Patients who underwent surgery and had tissue evaluable for blinded independent pathology review were categorized by %RVT in the primary lung tumor and sampled lymph nodes

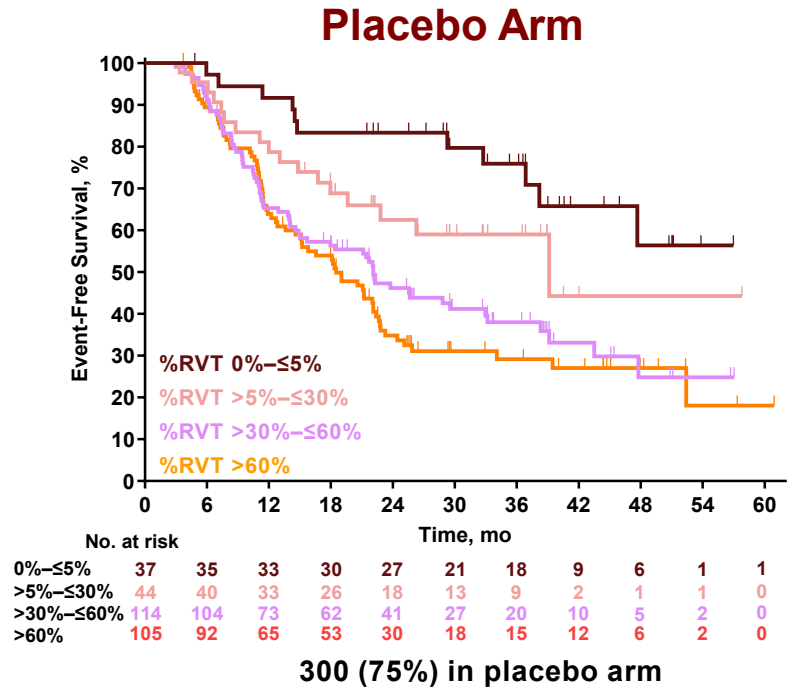
[a]Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. [b]Cisplatin 75 mg/m^2 IV Q3W + gemcitabine 1000 mg/m^2 IV on days 1 and 8 Q3W (squamous histology only). [c]Cisplatin 75 mg/m^2 IV Q3W + pemetrexed 500 mg/m^2 IV Q3W (nonsquamous histology only). [d]Radiotherapy was to be administered to patients with microscopic positive margins, gross residual disease, or extracapsular nodal extension after surgery and to patients who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.

Association of Pathologic Regression With Event-Free Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC

KEYNOTE-671 EFS Analysis by RVT: Key Results



320 (80.6%) in pembro arm



300 (75%) in placebo arm

- %RVT was associated with poorer EFS from randomization
- Irrespective of treatment arm
- EFS benefit with perioperative pembro extended to pts with RVT after neoadjuvant phase, <u>but up to RVT 60% cutpoint</u>

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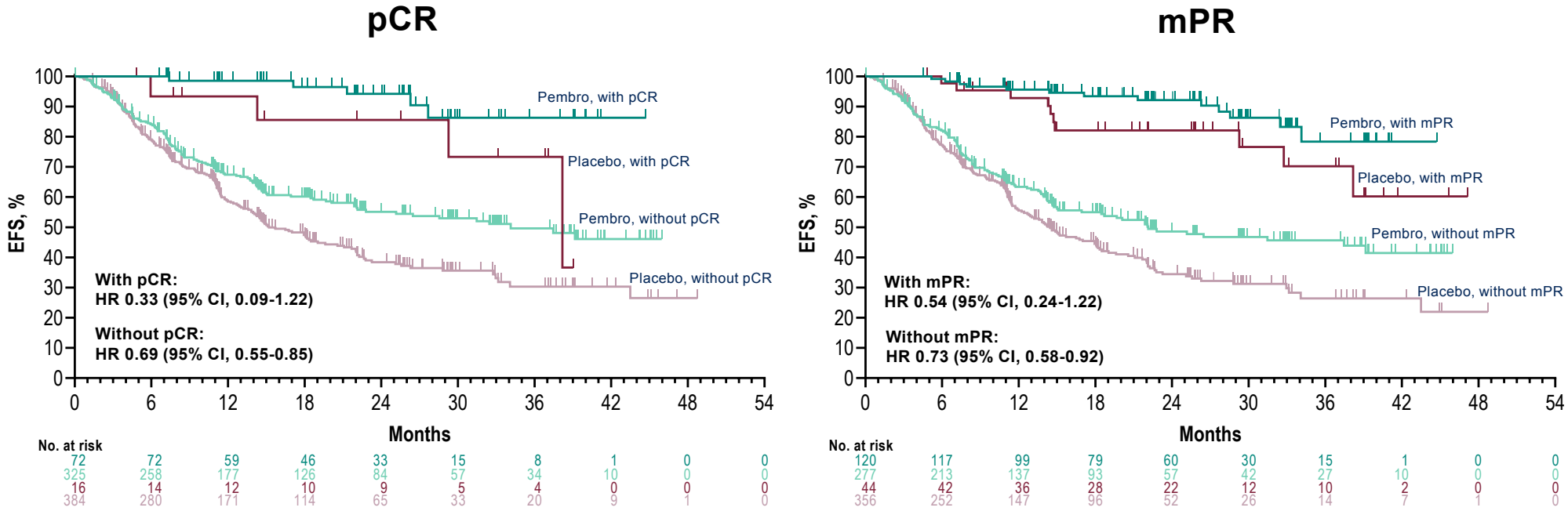
Association of Pathologic Regression With Event-Free Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC

Event-Free Survival Among Patients With pCR or mPR[a,1]



Objective of this analysis was to evaluate efficacy of perioperative pembrolizumab across different RVT cutpoints, beyond pCR and mPR

[1]Wakelee H et al. *N Engl J Med* 2023;389:491–503.
[a]Exploratory analysis. pCR defined as absence of residual invasive cancer in resected primary tumor and lymph nodes (ypT0/Tis ypN0). [b]mPR defined as ≤10% viable tumor cells in resected primary tumor and lymph nodes. EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause. Data cutoff date for IA1: July 29, 2022.

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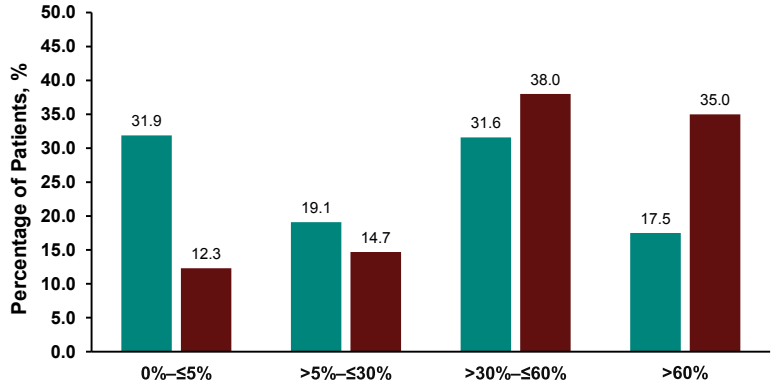
Association of Pathologic Regression With Event-Free Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC

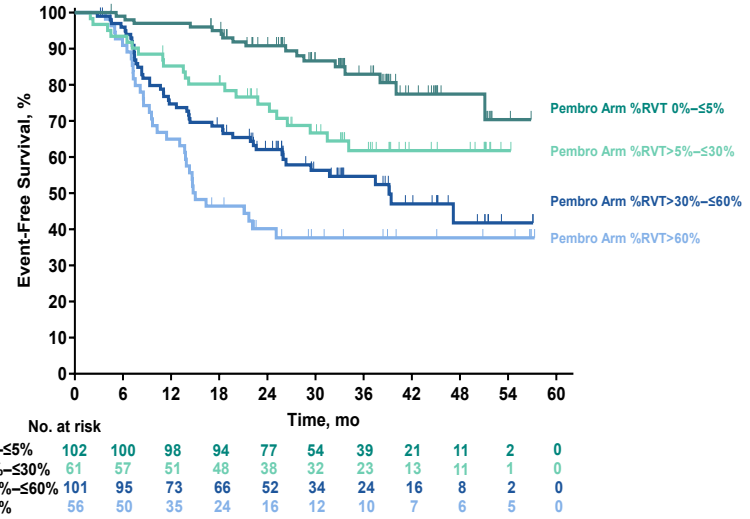
%RVT Categorization of Patients With Pathologically Evaluable Tumors



	n	Median %RVT (IQR), %
Pembro Arm	320	29.5 (1.0–56.0)
Placebo Arm	300	52.0 (29.0–68.0)

Data cutoff date for IA2: July 10, 2023.

Event-Free Survival
According to %RVT Categorization in the Pembrolizumab Arm



Data cutoff date: July 10, 2023.

Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Perioperative Durvalumab for Resectable NSCLC Updated Outcomes from the Phase 3 AEGEAN Trial

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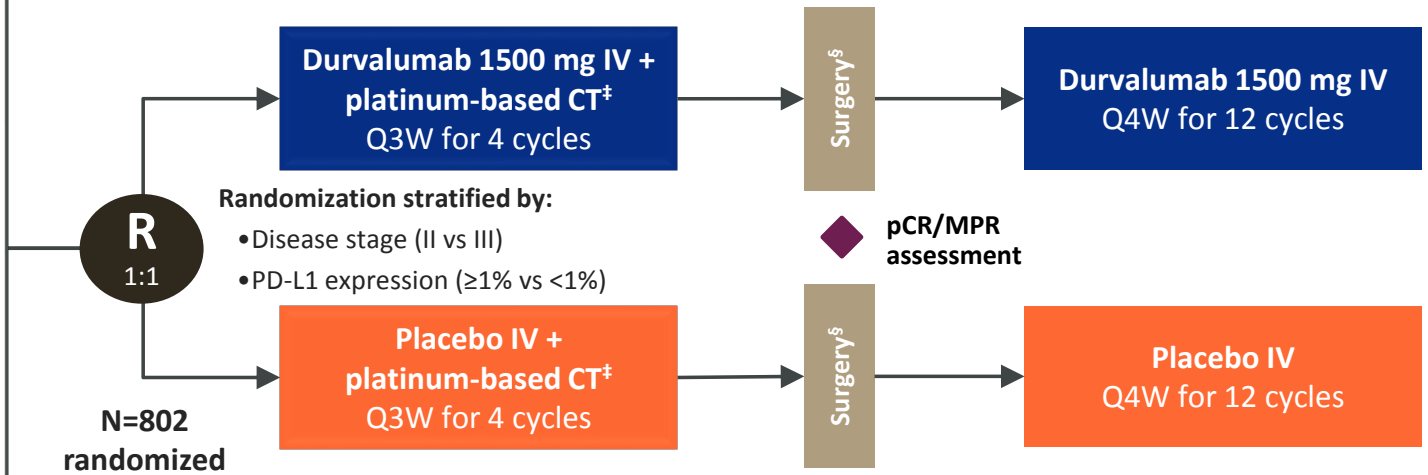
AEGEAN study design

Study population

- Resectable NSCLC* (stage IIA–IIIB[N2]; AJCC 8th ed)
- Treatment-naïve
- ECOG PS 0 or 1
- Lobectomy, sleeve resection, or bilobectomy as planned surgery*
- Confirmed PD-L1 status†
- No documented *EGFR/ALK* aberrations*



Efficacy analyses were performed in the mITT population (or its resected subpopulation), which excluded patients with documented EGFR/ALK *aberrations*¶

Primary endpoints: pCR, evaluated centrally (IASLC 2020[1]), and EFS per BICR (RECIST v1.1)

Key secondary endpoints: MPR, evaluated centrally (IASLC 2020[1]), DFS per BICR (RECIST v1.1) in the resected subpopulation, and OS

	EFS interim analysis #1	EFS interim analysis #2 (reported here)
Data cutoff	November 10, 2022	May 10, 2024
Median EFS follow-up	11.7 months (censored patients)	25.9 months (censored patients)
Data maturity	31.9%	39.1%

[1]Travis WD, et al. *J Thorac Oncol* 2020;15:709–40.

*The protocol was amended while enrollment was ongoing to exclude (1) patients with tumors classified as T4 for any reason other than size; (2) patients with planned pneumonectomies; and (3) patients with documented *EGFR/ALK* aberrations. †Ventana PD-L1 (SP263) immunohistochemistry assay. ‡Choice of CT regimen determined by histology and at the investigator's discretion. For non-squamous: cisplatin + pemetrexed or carboplatin + pemetrexed. For squamous: carboplatin + paclitaxel or cisplatin + gemcitabine (or carboplatin + gemcitabine for patients who had comorbidities or who were unable to tolerate cisplatin per the investigator's judgment). §Post-operative radiotherapy (PORT) was permitted where indicated per local guidance. ¶The mITT population included 740 patients and its resected subpopulation included 473 patients. AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; IASLC, International Association for the Study of Lung Cancer; IV, intravenous; mITT, modified intent-to-treat; MPR, major pathologic response; PD-L1, programmed cell death-ligand 1; QXW, every X weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1.

Perioperative Durvalumab for Resectable NSCLC Updated Outcomes from the Phase 3 AEGEAN Trial

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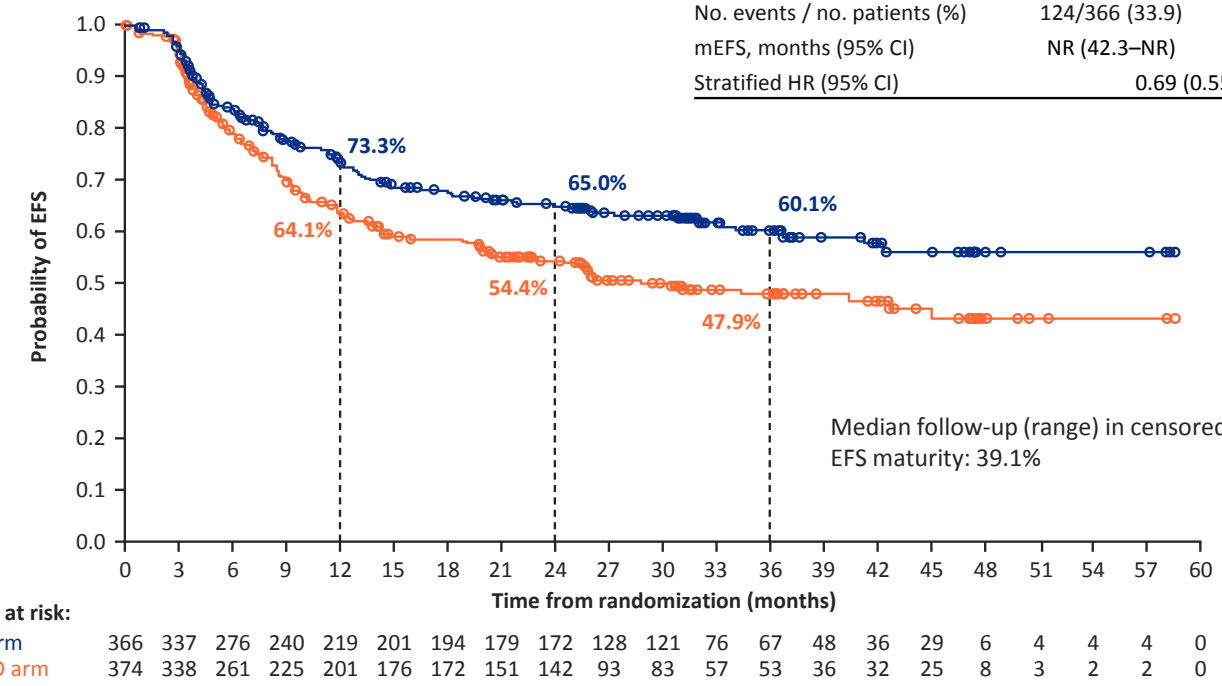
Updated EFS (second planned interim analysis; mITT)

- EFS benefit favoring the durvalumab arm was maintained and consistent with that reported previously[1]

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



Median follow-up (range) in censored patients: 25.9 (0.0–58.6) months
EFS maturity: 39.1%

[1]Heymach JV, et al. *N Engl J Med* 2023;389:1672–84.

DCO = May 10, 2024. mEFS, median EFS; NR, not reached.

Perioperative Durvalumab for Resectable NSCLC Updated Outcomes from the Phase 3 AEGEAN Trial

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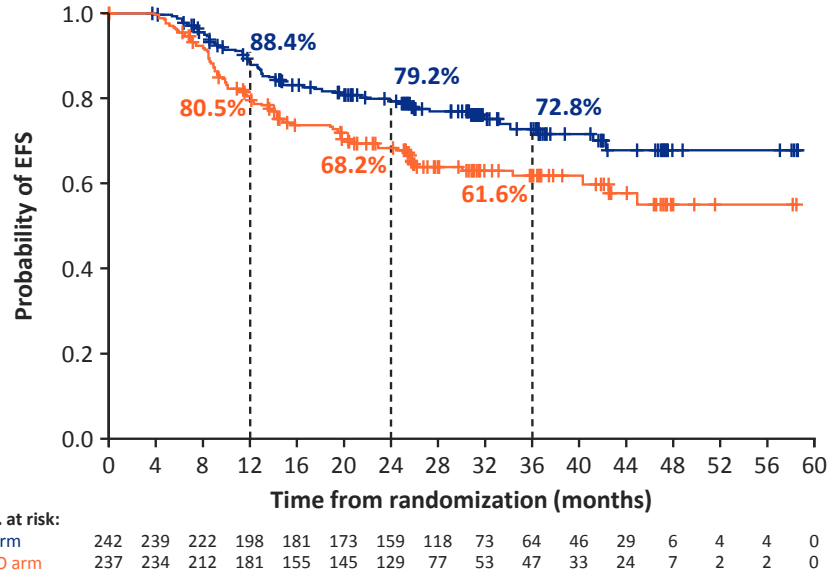
EFS by adjuvant treatment status (exploratory analysis, mITT)

- EFS benefit in the durvalumab arm was more pronounced in patients who received adjuvant treatment

Received adjuvant treatment

	D arm	PBO arm
No. events / no. patients (%)	58/242 (24.0)	83/237 (35.0)
mEFS, months (95% CI)	NR (NR–NR)	NR (42.6–NR)
Unstratified HR (95% CI)	0.62 (0.44–0.86)	

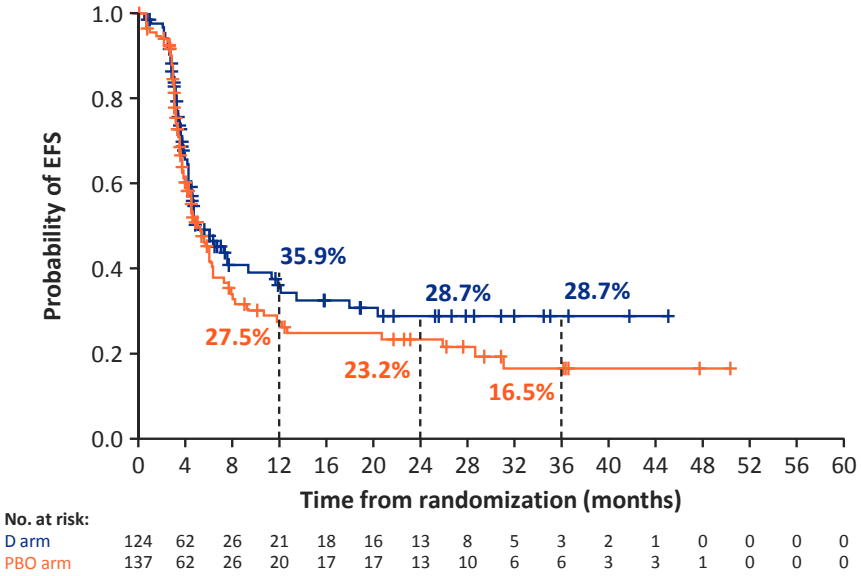


No. at risk:

D arm	242	239	222	198	181	173	159	118	73	64	46	29	6	4	4	0
PBO arm	237	234	212	181	155	145	129	77	53	47	33	24	7	2	2	0

Did not receive adjuvant treatment

	D arm	PBO arm
No. events / no. patients (%)	66/124 (53.2)	82/137 (59.9)
mEFS, months (95% CI)	5.1 (4.5–9.3)	5.2 (4.1–6.3)
Unstratified HR (95% CI)	0.83 (0.60–1.14)	



No. at risk:

D arm	124	62	26	21	18	16	13	8	5	3	2	1	0	0	0	0
PBO arm	137	62	26	20	17	17	13	10	6	6	3	3	1	0	0	0

DCO = May 10, 2024. Received adjuvant treatment subset includes all mITT patients who received adjuvant treatment regardless of whether they are included in the modified resected subpopulation.

Perioperative Durvalumab for Resectable NSCLC Updated Outcomes from the Phase 3 AEGEAN Trial

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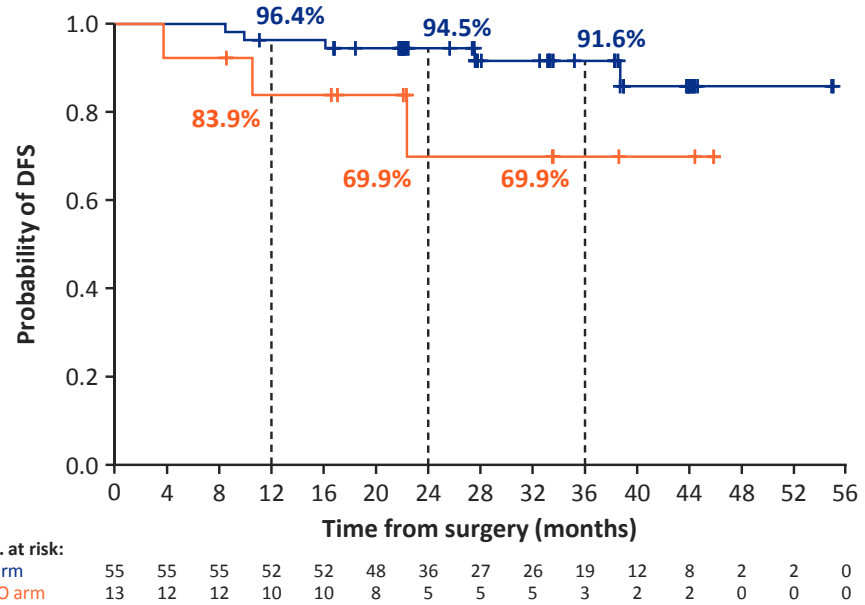
DFS by pCR status (exploratory analysis; modified resected subpopulation)

- Larger magnitude of DFS benefit with durvalumab was observed in patients with pCR

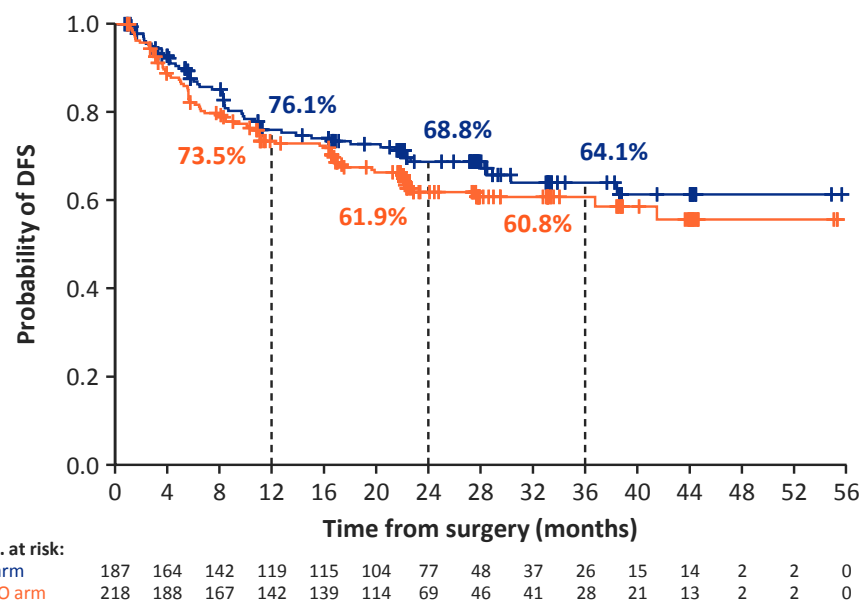
Patients with pCR

	D arm	PBO arm
No. events / no. patients (%)	5/55 (9.1)	3/13 (23.1)
mDFS, months (95% CI)	NR (NR–NR)	NR (10.5–NR)
Unstratified HR (95% CI)	0.31 (0.07–1.51)	



Patients without pCR

	D arm	PBO arm
No. events / no. patients (%)	55/187 (29.4)	78/218 (35.8)
mDFS, months (95% CI)	NR (NR–NR)	NR (41.5–NR)
Unstratified HR (95% CI)	0.82 (0.58–1.15)	



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Perioperative Durvalumab for Resectable NSCLC Updated Outcomes from the Phase 3 AEGEAN Trial

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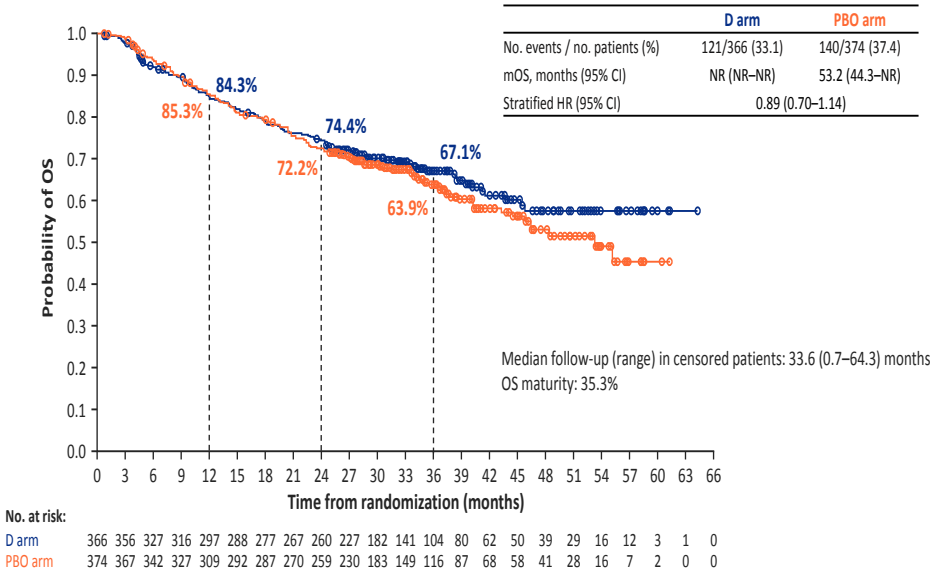
OS (mITT)

- Based on 35% maturity, an OS trend favoring the durvalumab arm was observed



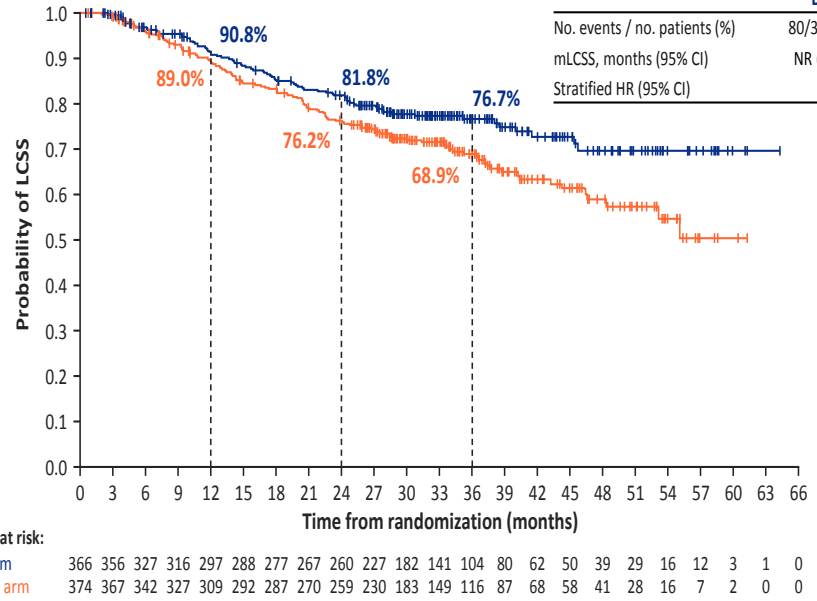
	D arm	PBO arm
No. events / no. patients (%)	121/366 (33.1)	140/374 (37.4)
mOS, months (95% CI)	NR (NR–NR)	53.2 (44.3–NR)
Stratified HR (95% CI)	0.89 (0.70–1.14)	

Median follow-up (range) in censored patients: 33.6 (0.7–64.3) months
OS maturity: 35.3%

- Preplanned analysis censoring patients with cause of death due to COVID-19: OS HR = 0.84 (95% CI: 0.66–1.08)

Lung cancer-specific survival (exploratory analysis; mITT)

- Improvement in lung cancer-specific survival also favored the durvalumab arm



	D arm	PBO arm
No. events / no. patients (%)	80/366 (21.9)	117/374 (31.3)
mLCSS, months (95% CI)	NR (NR–NR)	NR (48.3–NR)
Stratified HR (95% CI)	0.70 (0.52–0.93)	

Neoadjuvant Alectinib in Potentially Resectable Stage III ALK-positive NSCLC: Interim Analysis of ALNEO-GOIRC-01-2020 Phase II Trial

ALNEO Study Design

20 Italian Centers

- Resectable locally advanced stage III NSCLC
- Candidate for surgical resection after multidisciplinary discussion
- ALK positive (IHC/FISH/NGS)
- No Previous treatment
- ECOG PS 0-1

Primary Endpoint: MPR by BICR

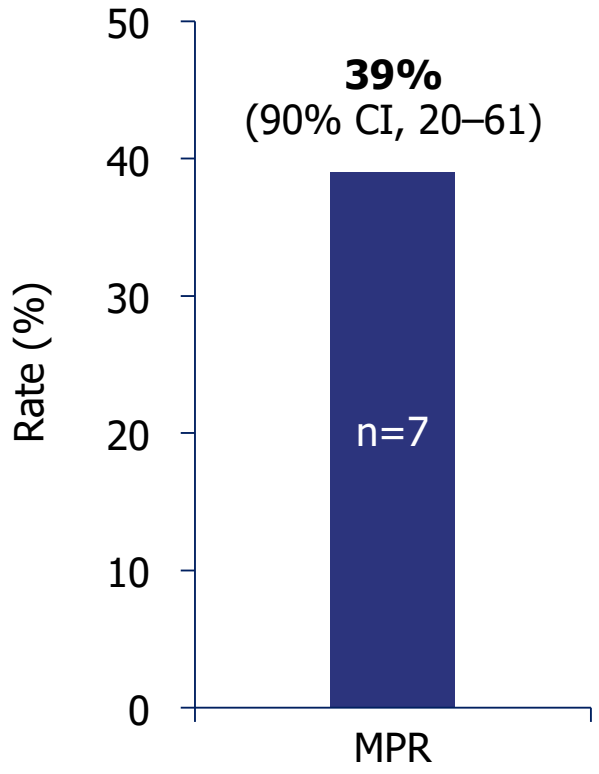
Secondary Endpoints: pCR by BICR, OR, EFS, DFS, OS, AEs

According to the Simon's two-stage mini-max design, the null hypothesis that the MPR is ≤20% will be tested against a one-sided alternative. In the first stage, 18 patients will be accrued. If there are 4 or fewer MPR in these 18 patients, the study will be stopped early for futility. Otherwise, 15 additional patients will be accrued for a total of 33. The null hypothesis will be rejected if 11 or more MPR are observed in 33 patients. This design yields a type I error rate of 0.05 and power of 0.80 when the true MPR is 40%.

Abbreviations: AEs, adverse events; BICR, blinded independent central review; DFS, disease-free survival; EFS, event-free survival; OS, overall survival; pCR, pathologic complete response; MPR, major pathologic response; OR, objective response.

Neoadjuvant Alectinib in Potentially Resectable Stage III ALK-positive NSCLC: Interim Analysis of ALNEO-GOIRC-01-2020 Phase II Trial

Results – Primary Endpoint



Pathologic Response	n=18
MPR, n (%)	7 (39)
pCR, n (%)	3 (17)
No MPR, n (%)	6 (33)
Not Assessed, n (%)	5 (28)[a]

Objective Response[b]	n=25
CR, n (%)	1 (4)
PR, n (%)	19 (76)
SD, n (%)	4 (16)
PD, n (%)	1 (4)
ORR, (%)	20 (80)

	n=25
Underwent Surgery, n (%)	21 (84)
R0, n (% of surgery)	18 (86)
Type of surgery, n (%)	
Lobectomy	17 (81)
Pneumonectomy	2 (9.5)
Other Surgery	2 (9.5)
Received adjuvant alectinib, n (% of surgery)	20 (95)[c]
Median interval from surgery, weeks (IQR)	4.5 (2.7–6.0)
Median n of cycles, n (IQR)	6 (1–20)

[a]4 patients did not undergo surgery, 1 patient underwent explorative thoracotomy; [b]at pre-surgical evaluation; [c]2 patients received adjuvant alectinib even though surgery was not radical.

- Neoadjuvant treatment was well tolerated. G1-2 TEAEs were reported in 14 (56%) cases. No Grade ≥3 treatment-related AEs were observed;
- After a median follow-up of 10.8 months (IQR: 4.9–22.5), a total of 159 adjuvant courses were administered and the treatment appeared to be well tolerated.

Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

5-Year Clinical Outcomes of Perioperative Nivolumab and Chemotherapy in Stage III NSCLC (NADIM trial)

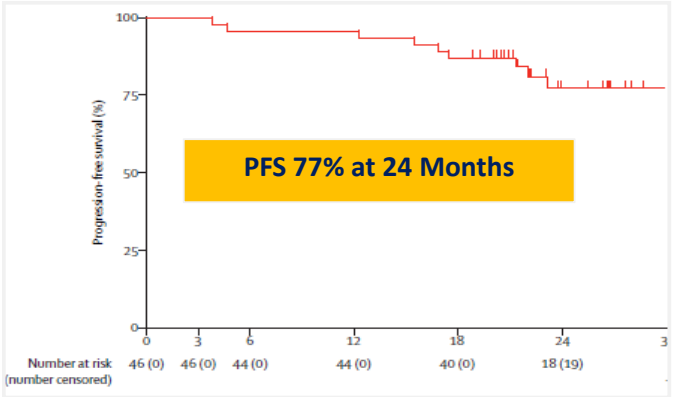
Iniciativa científica de: GECP lung cancer research

5-y NADIM

INTRODUCTION

- Neoadjuvant chemoimmunotherapy has been shown to be highly effective in resectable stage IIIA NSCLC.
- The significance of established immunotherapy biomarkers (PD-L1 TPS, TMB, ctDNA…) remains uncertain.
- We present the 5-year survival outcomes of the NADIM I study.

NADIM Patient baseline characteristics	N=46 (ITT)
Age (median, range)	63(41-77)
Co-morbidities, N (%)	43 (93,5)
N2	**33 (89.2)**
Multiple station	**25 (75.8)**



Provencio M. et al. **Lancet Oncol 2020; 21:1413-22**

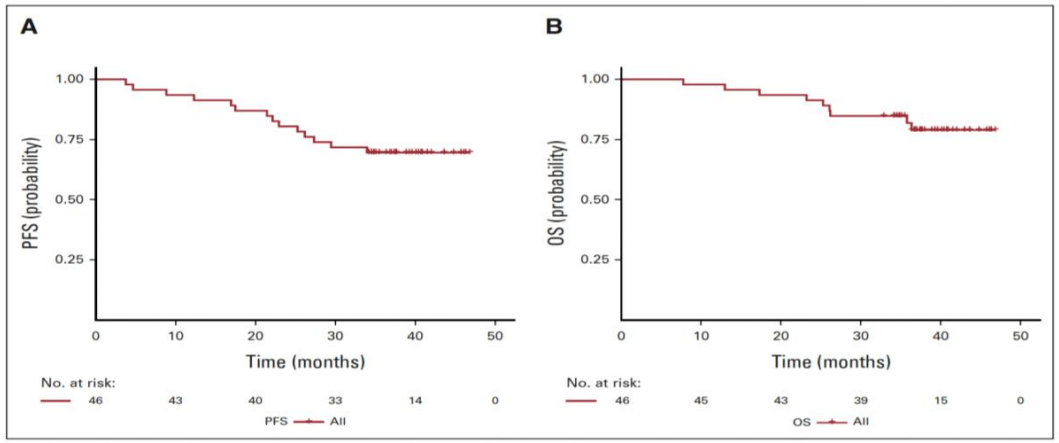


FIG 1. Kaplan-Meier curves for (A) PFS and (B) OS in the ITT population (N = 46). ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival.

OS at 36 months was 81.9% (95% CI, 66.8 to 90.6) in the intention-to-treat population, rising to 91.0% (95% CI, 74.2 to 97.0) in the per-protocol population

Provencio M. et al. **J Clin Oncol. 2022**

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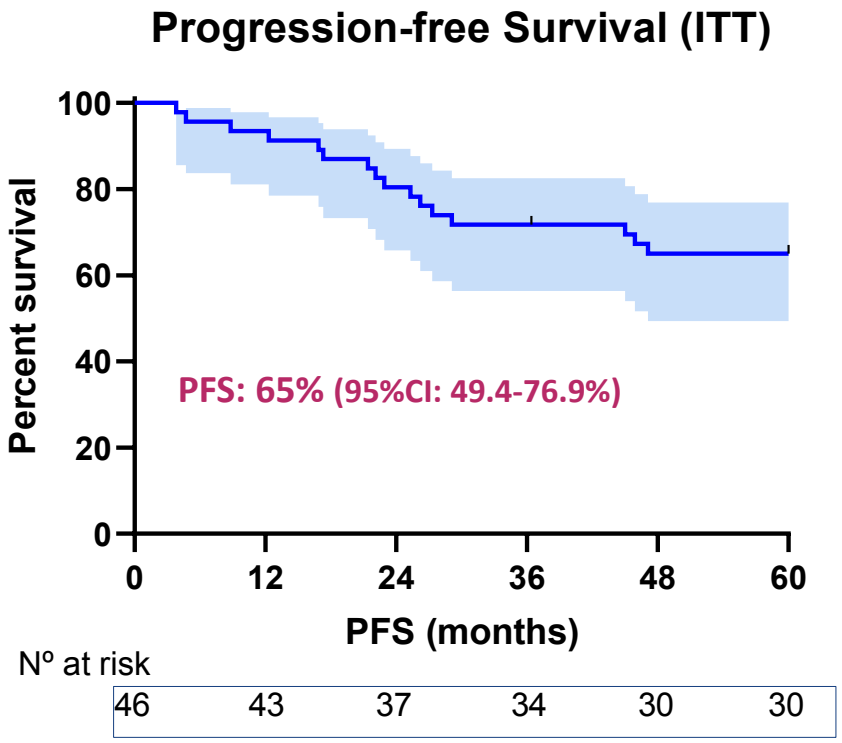
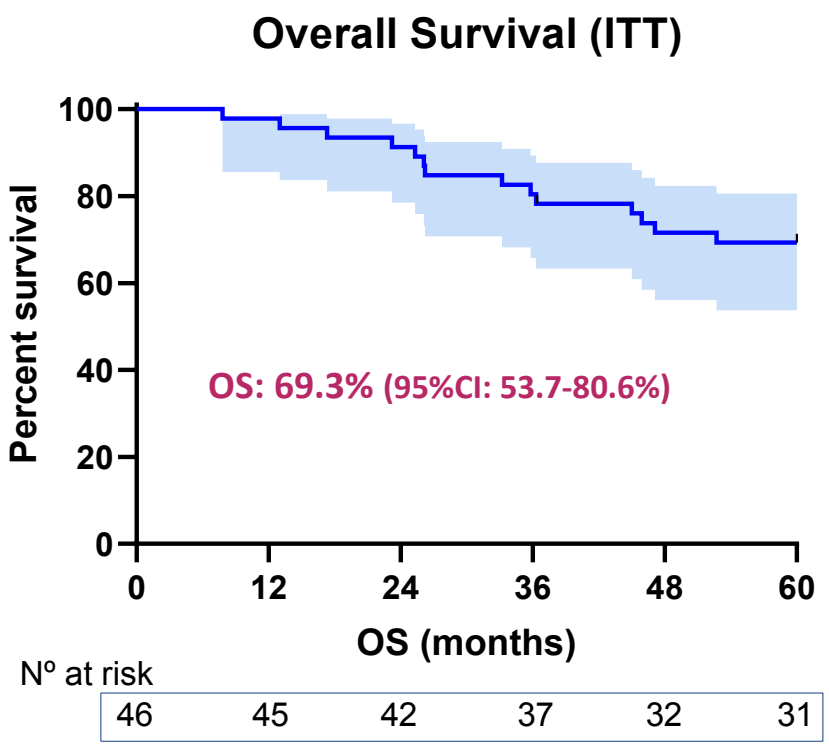
5-y NADIM

PFS and OS at 5-y in ITT population (n= 46)





97.8% maturity at 60 months

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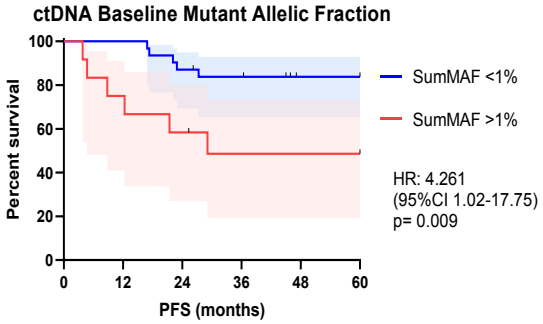
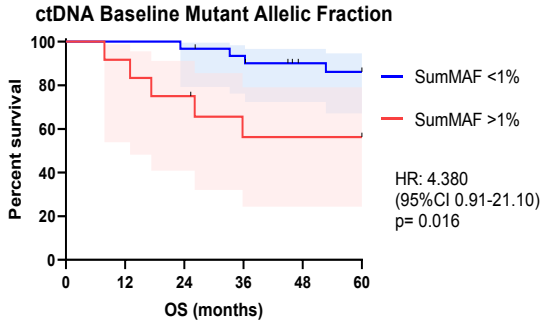
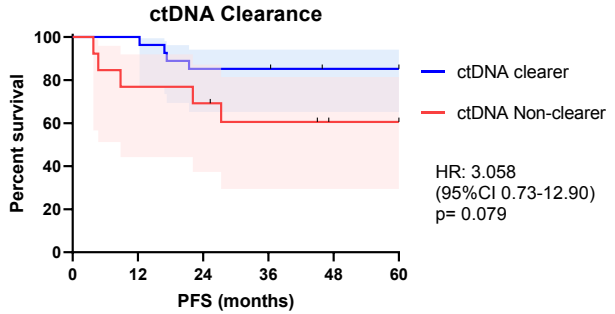
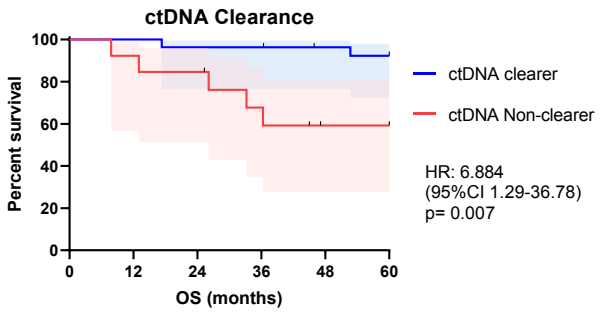
5-Year Clinical Outcomes of Perioperative Nivolumab and Chemotherapy in Stage III NSCLC (NADIM trial)

5-y NADIM PREDICTIVE BIOMARKERS (II)









PFS SumMAF ≥1%: 48.6% (95%CI: 19.2-73%)

PFS SumMAF <1%: 83.7% (95%CI: 63-92.9%)

OS SumMAF ≥1%: 56.3% (95%CI: 24.4-79.1%)

OS SumMAF <1%: 86.2% (95%CI: 67.1-94.6%)

PFS Non-ctDNA clearer: 60.6% (95%CI: 29.4-81.4%)

PFS ctDNA clearer: 85.2% (95%CI: 65.2-94.2%)

OS Non-ctDNA clearer: 59.2% (95%CI: 27.9-80.7%)

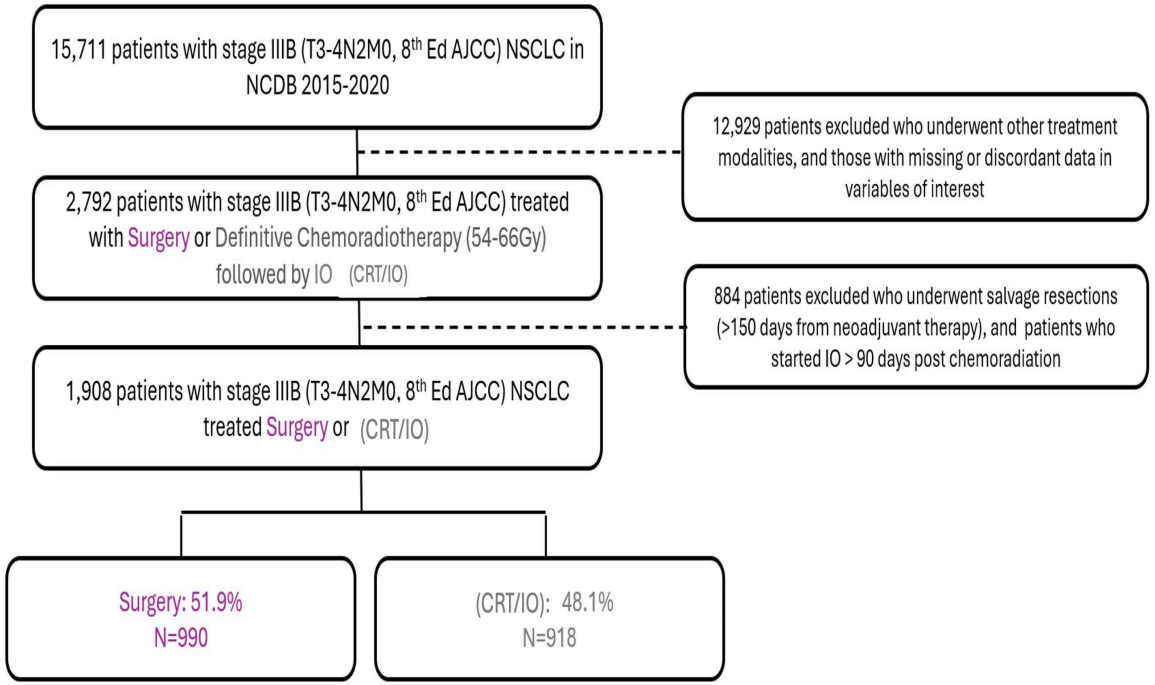
OS ctDNA clearer: 92.3% (95%CI: 72.5-98%)

- **ctDNA clearance** after neoadjuvant treatment showed a **good prediction of PFS and OS** (especially valuable in patients with a worse prognosis).
- **Neither PD-L1 tumor proportion score nor TMB are markers of PFS or OS**

Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Iniciativa científica de: GECP lung cancer research

Definitive Chemoradiation Followed by Immunotherapy vs. Surgery for cT4N2M0 NSCLC : A Contemporary Nationwide Analysis.



Demographics of the study cohort and multivariable analysis for factors associated with surgical resection.

	Surgery (N=990, 51.9%)	CRT/IO (N=918, 48.1%)	P-value	Adjusted Odds Ratio (95%CI)
Age (Median, IQR)	65 (58 -71)	66 (60-72)	<0.001	0.98 (0.97 to 0.99)
Race, N (%)				
White	846 (85.5%)	747 (81.4%)	0.013	Ref.
Black	86 (8.7%)	118 (12.9%)		0.59 (0.42 to 0.82)
Other	58 (5.9%)	53 (5.8%)		0.78 (0.51 to 1.20)
Charlson-Deyo Index, N (%)				
0	646 (65.3%)	519 (56.5%)	<0.001	Ref.
1	232 (23.4%)	254 (27.7%)		0.80 (0.63 to 1.00)
2	75 (7.6%)	76 (8.3%)		0.96 (0.66 to 1.40)
3 or >	37 (3.7%)	69 (7.5%)		0.60 (0.38 to 0.94)
Type of Facility, N (%)				
Community	60 (6.1%)	77 (8.4%)	<0.001	Ref.
Comprehensive Community	294 (29.7%)	365 (39.8%)		0.98 (0.66 to 1.46)
Academic Program	434 (43.8%)	284 (30.9%)		1.59 (1.06 to 2.40)
Integrated Network Program	202 (20.4%)	192 (20.9%)		1.29 (0.85 to 1.96)
Histology, N (%)				
Adenocarcinoma	488 (49.3%)	351 (38.2%)	<0.001	Ref.
Squamous	419 (42.3%)	535 (58.3%)		0.60 (0.49 to 0.74)
Other	83 (8.4%)	32 (3.5%)		2.05 (1.27 to 3.29)
Tumor location, N (%)				
Central	32 (3.2%)	64 (7.0%)	<0.001	Ref.
Right	561 (56.7%)	557 (60.7%)		3.17 (1.52 to 6.60)
Left	396 (40.0%)	293 (31.9%)		4.45 (2.10 to 9.40)

* Selected variables in the model are presented based on clinical relevance.

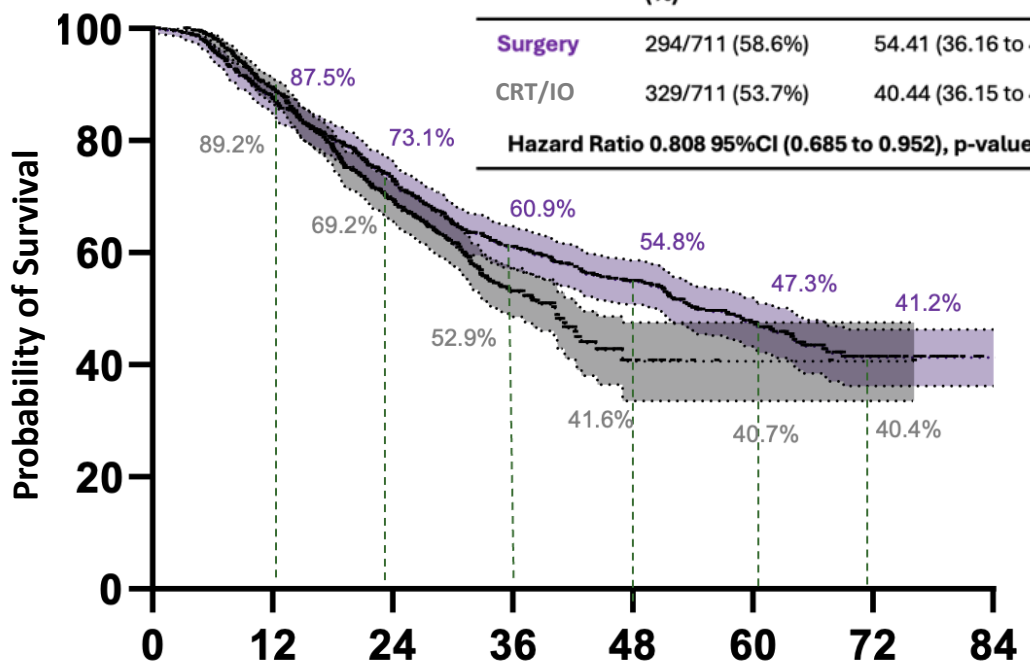
Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Iniciativa científica de: GECP lung cancer research

Definitive Chemoradiation Followed by Immunotherapy vs. Surgery for cT4N2M0 NSCLC : A Contemporary Nationwide Analysis.

Survival analysis: Surgery vs. CRT/IO in propensity-matched cohorts:

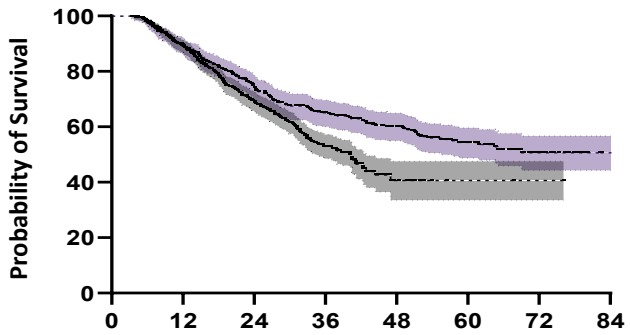
	No. of Events/Total N (%)	Median OS (95%CI), Months
Surgery	294/711 (58.6%)	54.41 (36.16 to 44.72)
CRT/IO	329/711 (53.7%)	40.44 (36.15 to 44.72)
Hazard Ratio 0.808 95%CI (0.685 to 0.952), p-value 0.011		



No at. Risk								
Surgery	711	612	471	342	243	127	40	4
CRT/IO	711	622	406	139	13	3	2	1

Subgroup Analysis

Neoadjuvant/Perioperative vs. CRT/IO



	No. of Events/Total N (%)	Median OS (95%CI), Months
Neoadjuvant	167/409 (40.8%)	Not-reached
Hazard Ratio 0.70 95%CI (0.58 to 0.85), p-value <0.001		

Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Iniciativa científica de: GECP lung cancer research

Survival outcomes and pathologic response after chemoimmunotherapy in resectable NSCLC: an individual patient data meta-analysis

Inclusion criteria: prospective trials (both single-arm and RCTs) of neoadjuvant/perioperative anti-PD-(L)1 in combination with platinum-based chemotherapy in patients with resectable NSCLC.

Data extraction: IPD was extracted from Kaplan-Meier curves of the included studies with the *IPDfromKM* method, only for the experimental arm. Display of Kaplan-Meier curves for pCR and/or MPR was required for IPD data extraction.

Literature search: MEDLINE/EMBASE/CENTRAL, Nov. 2023.

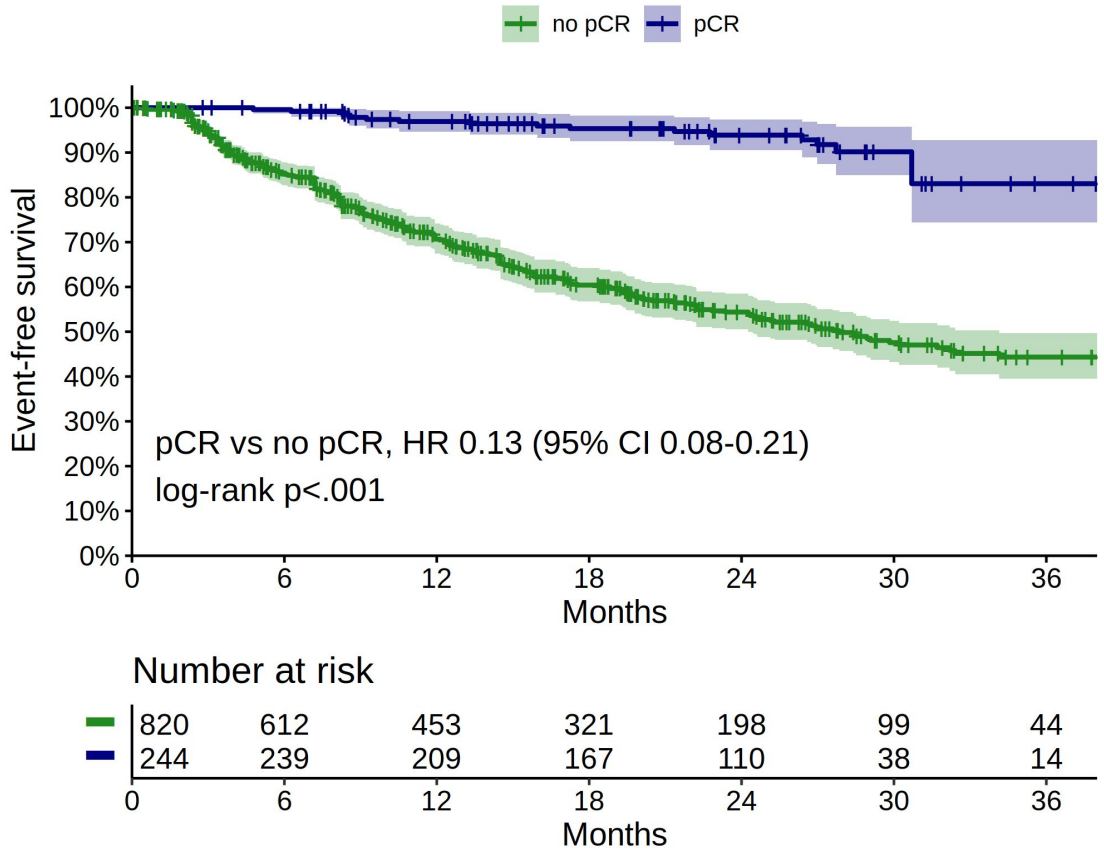
Endpoints: EFS from the start of neoadjuvant treatment in patients with or without pCR/MPR in the ITT population.

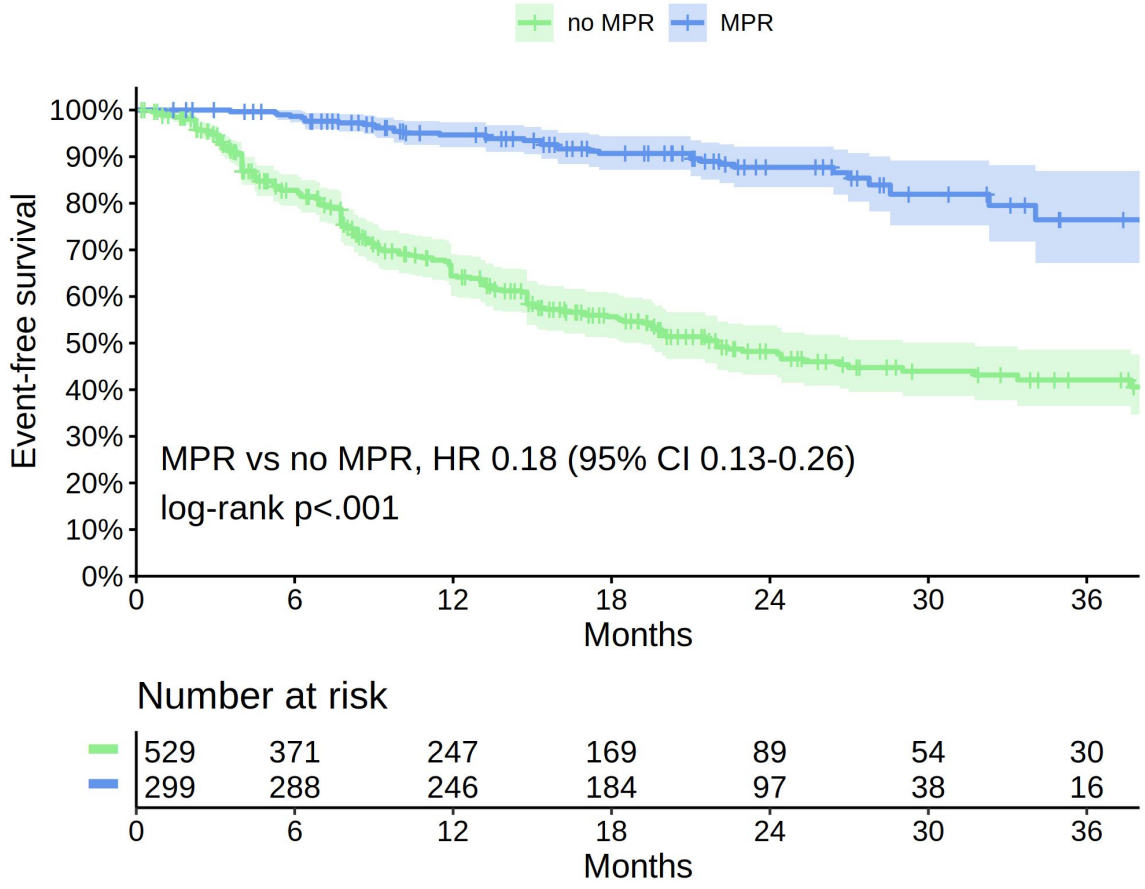
Included studies: CheckMate-77T, CheckMate-816, KEYNOTE-671, NADIM, NADIM-II, NEOSTAR, NeoTORCH.

Iniciativa científica de: GECP lung cancer research

Survival outcomes and pathologic response after chemoimmunotherapy in resectable NSCLC: an individual patient data meta-analysis

pCR and MPR are associated with longer EFS

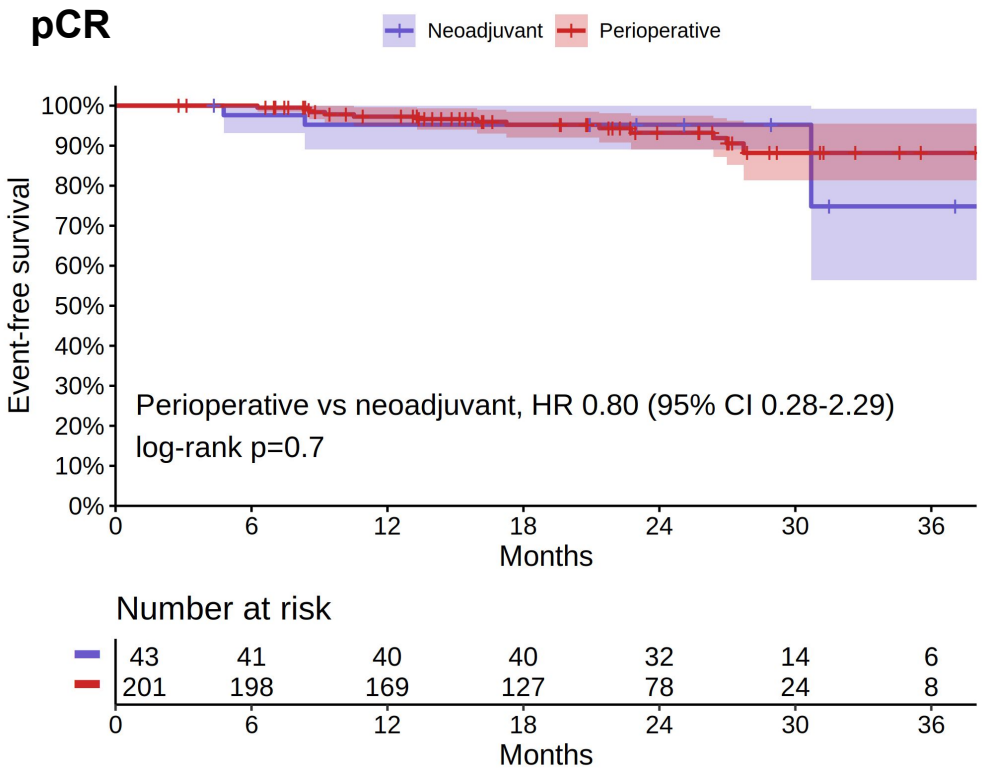


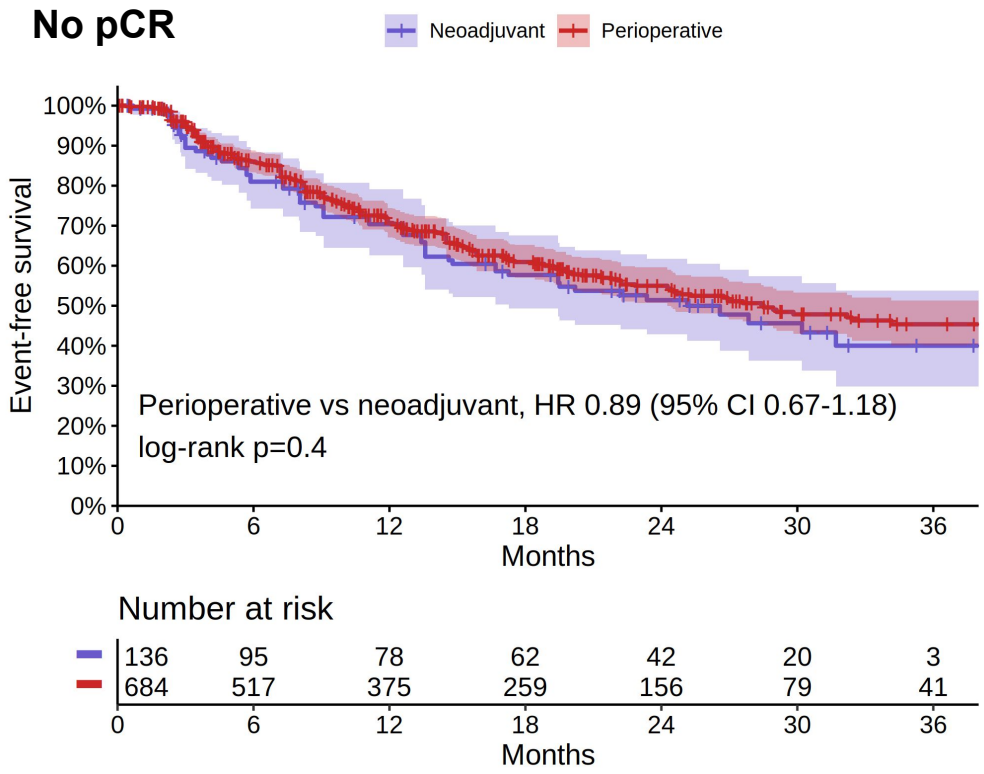


Iniciativa científica de: GECP lung cancer research

Survival outcomes and pathologic response after chemoimmunotherapy in resectable NSCLC: an individual patient data meta-analysis

Neoadjuvant/perioperative have similar EFS, regardless of pCR status



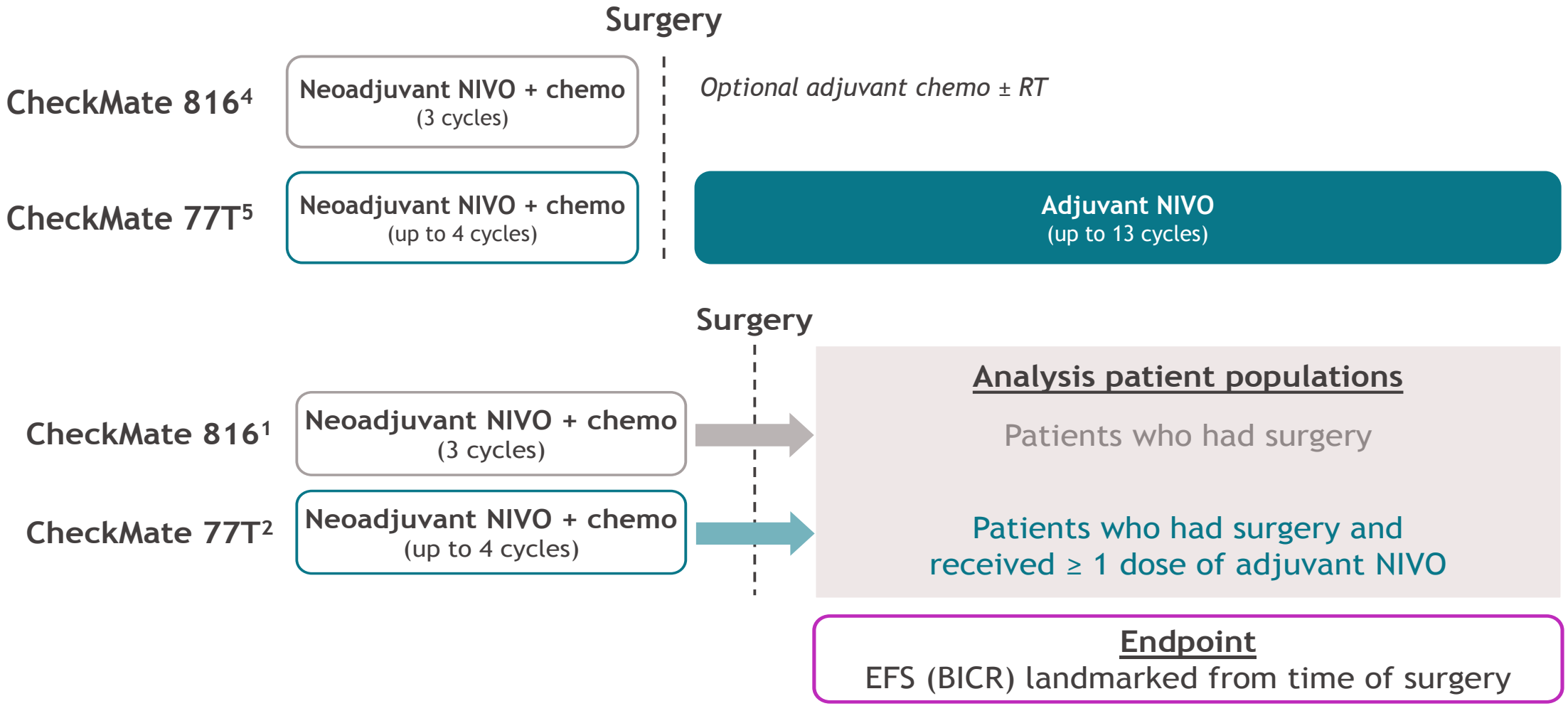


Neoadjuvant: CheckMate-816; perioperative: CheckMate-77T, KEYNOTE-671, NeoTORCH, NADIM-II.

The results remained consistent after the exclusion of NeoTORCH and NADIM-II, thereby only comparing phase III trials enrolling patients with stage II-III NSCLC (CheckMate-816, CheckMate-77T, KEYNOTE-671).

Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Perioperative vs neoadjuvant nivolumab for resectable NSCLC: patient-level data analysis of CheckMate 77T vs CheckMate 816



Iniciativa científica de: GECP lung cancer research

Perioperative vs neoadjuvant nivolumab for resectable NSCLC: patient-level data analysis of CheckMate 77T vs CheckMate 816

Baseline characteristics: analysis populations[a]

	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

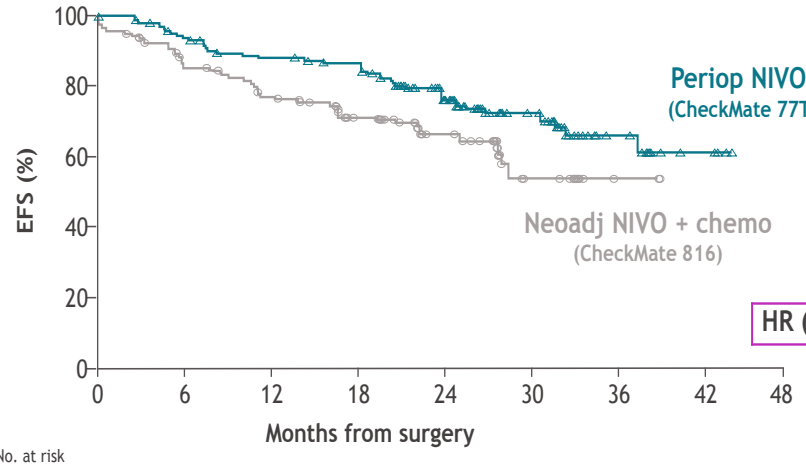
- Baseline characteristics between patients who received perioperative NIVO or neoadjuvant NIVO + chemo were generally balanced after propensity score weighting (ATT and ATE)[c]

Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Perioperative vs neoadjuvant nivolumab for resectable NSCLC: patient-level data analysis of CheckMate 77T vs CheckMate 816

Iniciativa científica de: GECP lung cancer research

Landmark 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)	

No. at risk

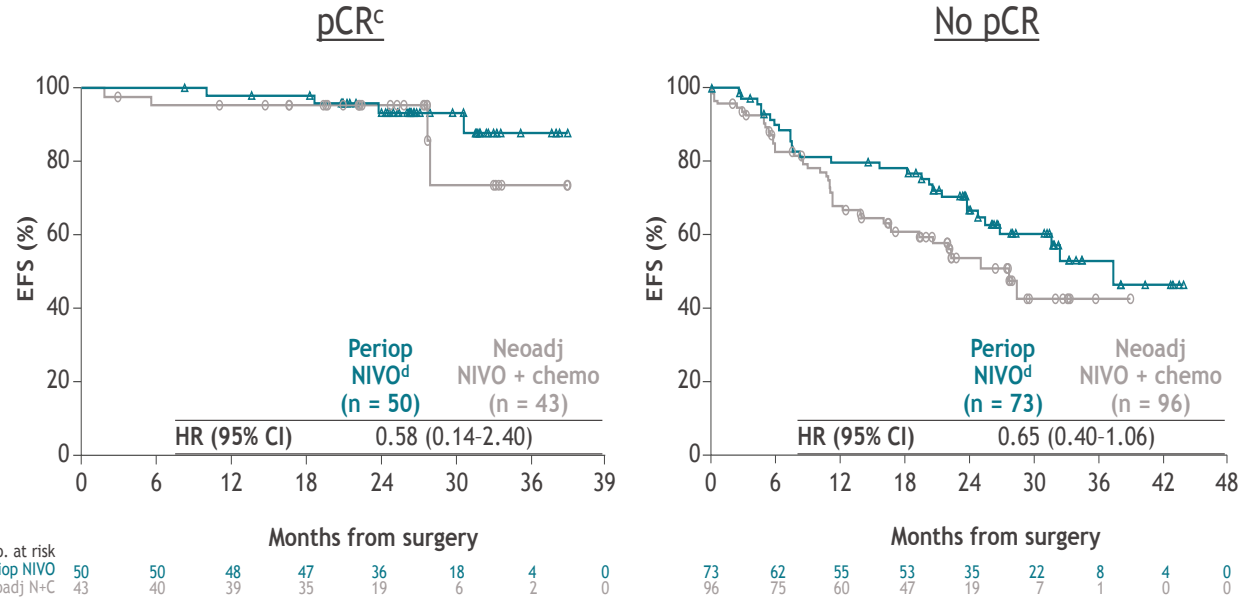
Periop NIVO	139.4	128.0	118.1	112.9	79.7	42.5	13.0	3.1	0
Neoadj N+C	147.5	121.0	106.2	84.2	39.1	12.1	2.2	0	0

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

Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Includes only patients who received ≥ 1 dose of adjuvant NIVO. [b]ATE: varying weights were applied to all patients in both neoadjuvant NIVO + chemo arm (CheckMate 816) and perioperative NIVO (CheckMate 77T) to make them comparable to one another. [c]N values fractional due to weighting. [d]ATT: varying weights were applied to patients in the neoadjuvant NIVO + chemo arm (CheckMate 816) to make them comparable to those in the perioperative NIVO arm (CheckMate 77T).

In the unweighted analysis population, 89 patients (64%) completed adjuvant therapy, and median number of doses (range) was 13.0 (1-13). Unweighted landmark EFS from surgery among all patients who had surgery (regardless of whether they received adjuvant NIVO in CheckMate 77T) for periop NIVO vs neoadj NIVO + chemo: HR = 0.82 (95% CI, 0.55-1.21).

Landmark EFS[a] (analysis population) by pCR status[a,b]



No. at risk

Periop NIVO	50	50	48	47	36	18	4	0	
Neoadj N+C	43	40	39	35	19	6	2	0	
Periop NIVO	73	62	55	53	35	22	8	4	0
Neoadj N+C	96	75	60	47	19	7	1	0	0

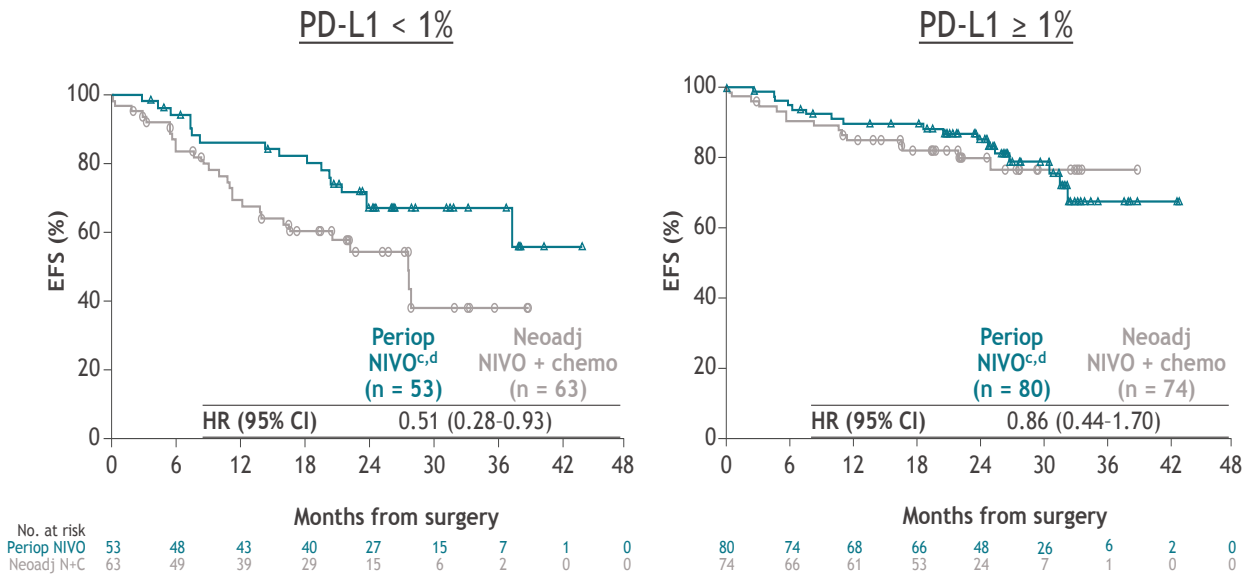
Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Patients with non-evaluable pCR status were excluded. [b]Unweighted analyses. [c]pCR rates in this analysis population: perioperative NIVO, 40.7%; neoadjuvant NIVO + chemo, 30.5%. [d]Includes only patients who received ≥ 1 dose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

Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Iniciativa científica de: GECP lung cancer research

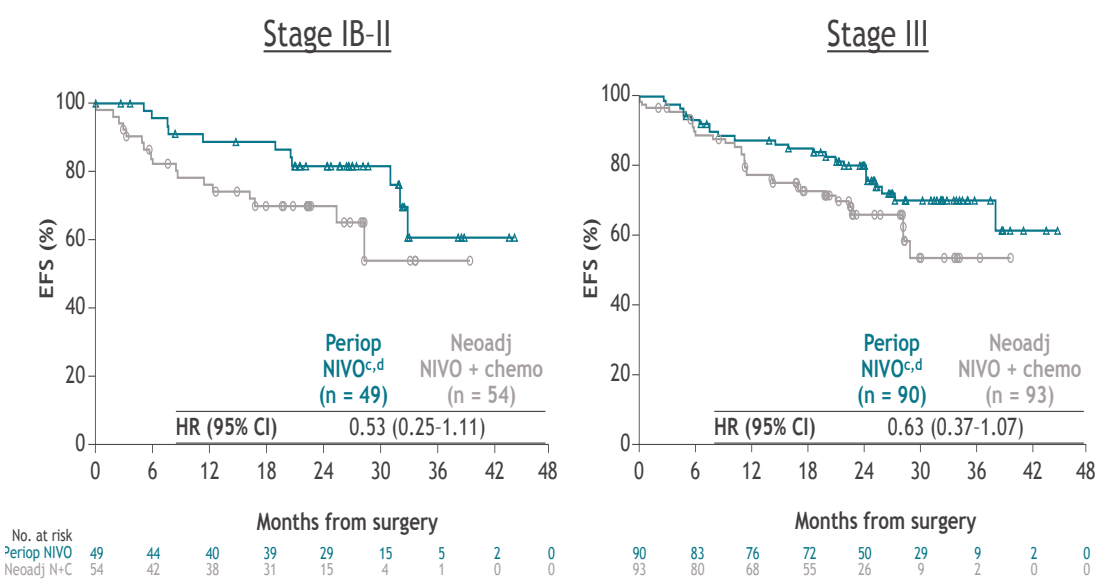
Perioperative vs neoadjuvant nivolumab for resectable NSCLC: patient-level data analysis of CheckMate 77T vs CheckMate 816

Landmark EFS (analysis population) by tumor PD-L1 expression[a,b]



Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Patients with non-evaluable PD-L1 expression were excluded. [b]Unweighted analyses. [c]Includes only patients who received ≥ 1 dose of adjuvant NIVO. [d]Completed adjuvant treatment: < 1%, 33 patients (62%) and ≥ 1%, 51 patients (64%). Median number of doses (range): < 1%, 13 (1-13) and ≥ 1%, 13 (1-13).

Landmark EFS (analysis population) by clinical stage[a,b]

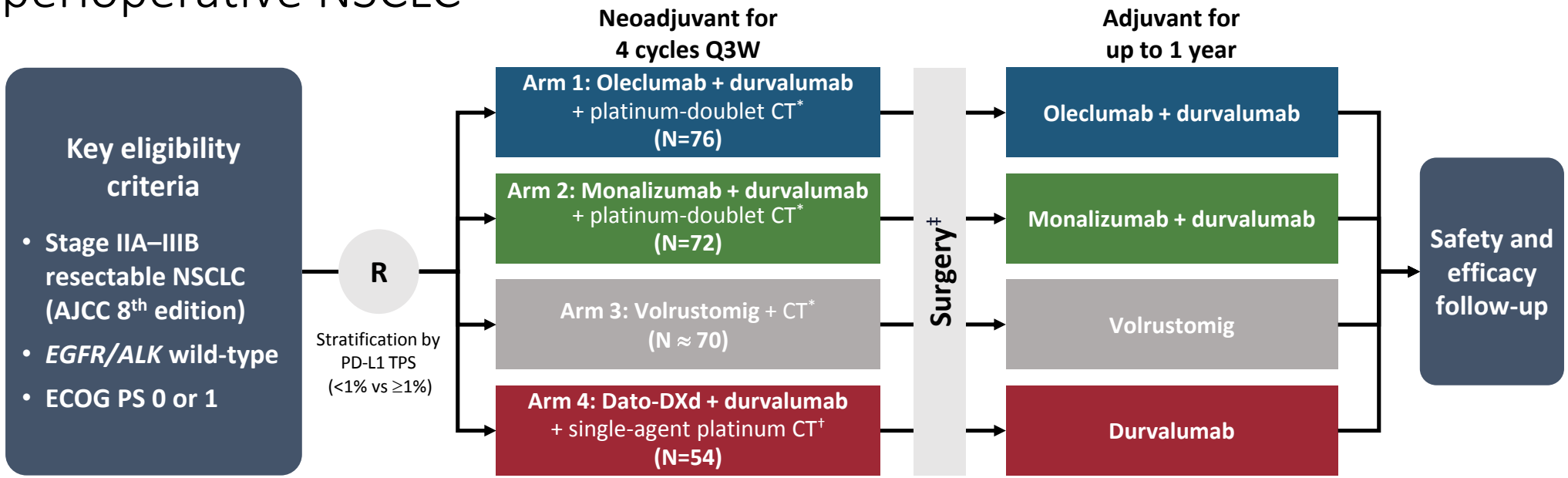


Median follow-up: CheckMate 816, 29.5 months; CheckMate 77T, 33.3 months. [a]Patients with disease stage other than IB, II, III were excluded. [b]Unweighted analyses. [c]Includes only patients who received ≥ 1 dose of adjuvant NIVO. [d]Completed adjuvant treatment: stage IB-II, 35 patients (71%) and stage III, 54 patients (60%). Median number of doses (range): stage IB-II, 13 (1-13) and stage III, 13 (1-13).

Iniciativa científica de: GECP lung cancer research

NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC

NeoCOAST-2: Open-label, multi-arm platform study in perioperative NSCLC



Primary endpoints
- pCR rate§
- Safety and tolerability

Key secondary endpoints
- mPR rate§ and EFS
- Feasibility of surgery

Statistical considerations
- This study was not powered to make direct statistical comparisons between arms.
- Descriptive statistics are summarised and presented.
- The primary intent was to look for preliminary efficacy signals by calculating pCR rates.

*Carboplatin + paclitaxel for squamous tumour histology, pemetrexed + cisplatin or carboplatin for non-squamous tumour histology. †Physician's choice of carboplatin or cisplatin. ‡Within 40 days of the last dose of neoadjuvant treatment. §Proportion of patients with no viable tumour cells and ≤10% residual viable tumour cells, respectively, in resected tumour specimen and sampled nodes at surgery. CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; EFS, event-free survival; mPR, major pathological response; NSCLC, non-small-cell lung cancer; pCR, pathological complete response; PD-L1, programmed cell death ligand-1; Q3W, every 3 weeks; R, randomised; TPS, tumour proportion score.

Iniciativa científica de: GECP lung cancer research

NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC

Baseline patient characteristics were well balanced across arms

	Arm 1 Oleclumab + durvalumab + CT N=76	Arm 2 Monalizumab + durvalumab + CT N=72	Arm 4 Dato-DXd + durvalumab + CT N=54
Median age, years (range)	66.5 (30–79)	66.0 (48–83)	65.0 (38–81)
Female/Male, n (%)	29 (38.2)/47 (61.8)	29 (40.3)/43 (59.7)	22 (40.7)/32 (59.3)
Race, n (%)			
Asian	7 (9.2)	5 (6.9)	5 (9.3)
Black or African American	1 (1.3)	0	0
White	48 (63.2)	43 (59.7)	37 (68.5)
Not reported	20 (26.3)	24 (33.3)	12 (22.2)
ECOG PS 0/1, n (%)	45 (61.6)/28 (38.4)*	49 (69.0)/22 (31.0)†	36 (66.7)/18 (33.3)
PD-L1 <1%/PD-L1 ≥1% TPS, n (%)	24 (31.6)/52 (68.4)	24 (33.3)/48 (66.7)	13 (24.1)/41 (75.9)
Stage, n (%)‡			
IIA	7 (9.2)	7 (9.7)	2 (3.8)
IIB	16 (21.1)	19 (26.4)	13 (24.5)
IIIA	40 (52.6)	33 (45.8)	27 (50.9)
IIIB	13 (17.1)	13 (18.1)	11 (20.8)
Histology, n (%)			
Adenocarcinoma	50 (65.8)	46 (63.9)	33 (61.1)
Squamous cell carcinoma	24 (31.6)	20 (27.8)	17 (31.5)
Other	2 (2.6)	6 (8.3)	4 (7.4)

- Consistent with real-world practice, the majority of patients received carboplatin compared with cisplatin: 72%, 77%, and 87% of patients received carboplatin vs cisplatin in Arms 1, 2, and 4, respectively.

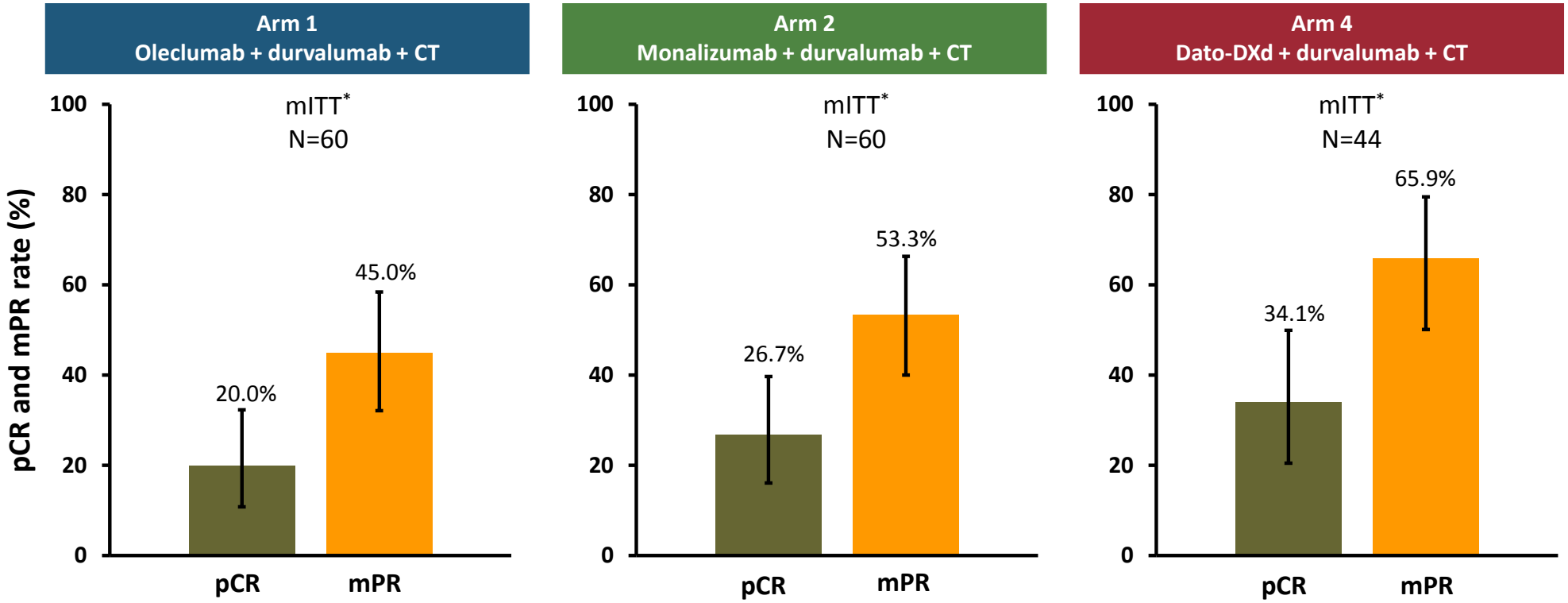
Cascone T| NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC

Data cut-off: 17 June 2024. *Data missing for 3 patients; †Data missing for 1 patient; ‡Data missing for 1 patient in Arm 4. CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed cell death ligand 1; TPS, tumour proportion score.

Iniciativa científica de: GECP lung cancer research

NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC

NeoCOAST-2: pCR and mPR rates across treatment arms



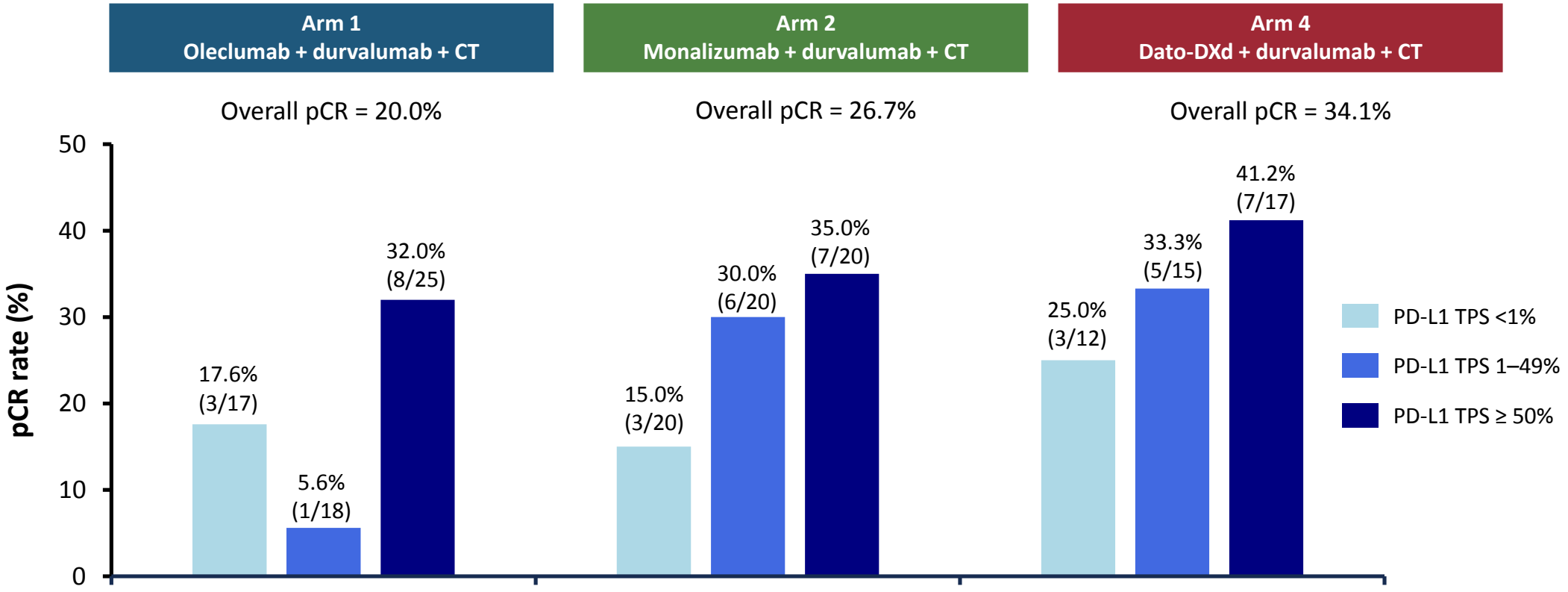
Pathological assessment performed locally or centrally†

Data cut-off: 17 June 2024. Error bars represent 95% confidence intervals.
*The mITT population includes all randomised patients with confirmed NSCLC histology who received at least 1 dose of study treatment and had central or local data available at the data cut-off, including those who were unable to receive or complete surgery. Some patients who underwent surgery did not have pathology results available at data cut-off. †Blind independent pathological review was used where available; proportion of local results were Arm 1: 9/55 (16.3%); Arm 2: 6/55 (11%); Arm 4: 16/41 (39%). Denominator includes only those patients who had surgery. CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; mITT, modified intention-to-treat population; mPR, major pathological response; NSCLC, non-small-cell lung cancer; pCR, pathological complete response.

Cascone T| NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC

NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC

pCR rates across baseline PD-L1 expression subgroups



Data cut-off: 17 June 2024. Based on the modified intention-to-treat population which includes all randomised patients with confirmed NSCLC histology who received at least 1 dose of study treatment and had data available at data cut-off, including those who were unable to receive or complete surgery. Baseline PD-L1 status is assessed using central (Ventana SP263) or local testing (Ventana SP263, pharmDx 28-8, or pharmDx 22C3). Proportion of central results were Arm 1: 12/60 (20%); Arm 2: 18/60 (30%); Arm 4: 13/44 (30%). Local results are reported for all other patients. CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; NSCLC, non-small-cell lung cancer; pCR, pathological complete response; PD-L1, programmed cell death ligand 1; TPS, tumour proportion score.

ascone T| NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + ovel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC

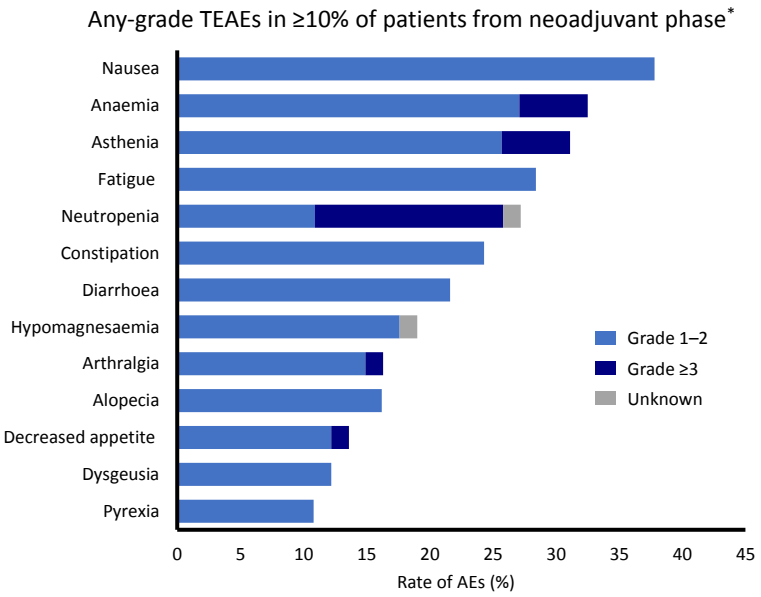
Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Iniciativa científica de: GECP lung cancer research

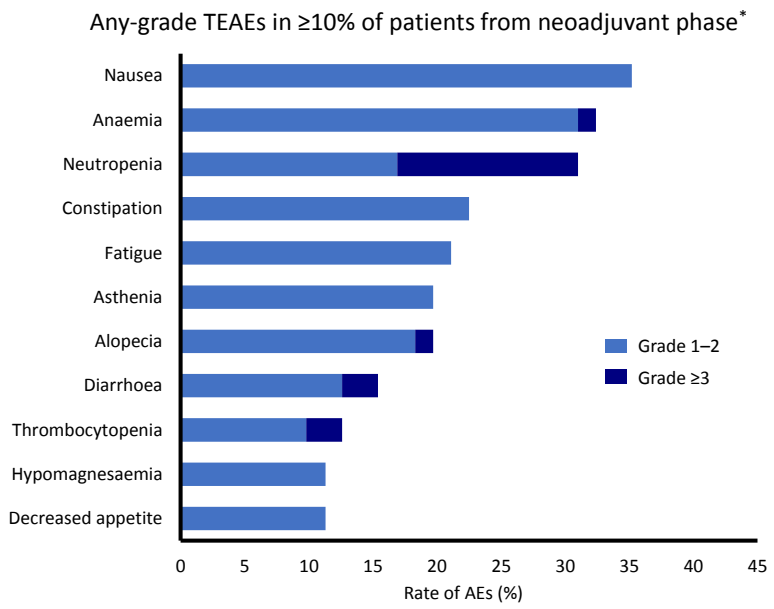
NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC

Safety profile

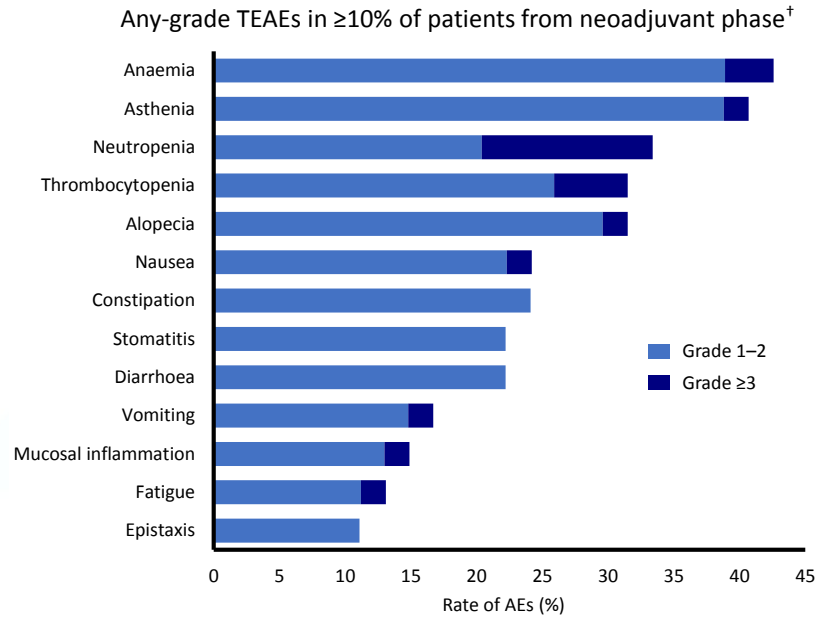
Oleclumab + durvalumab + CT



Monalizumab + durvalumab + CT.



Dato-DXd + durvalumab + CT

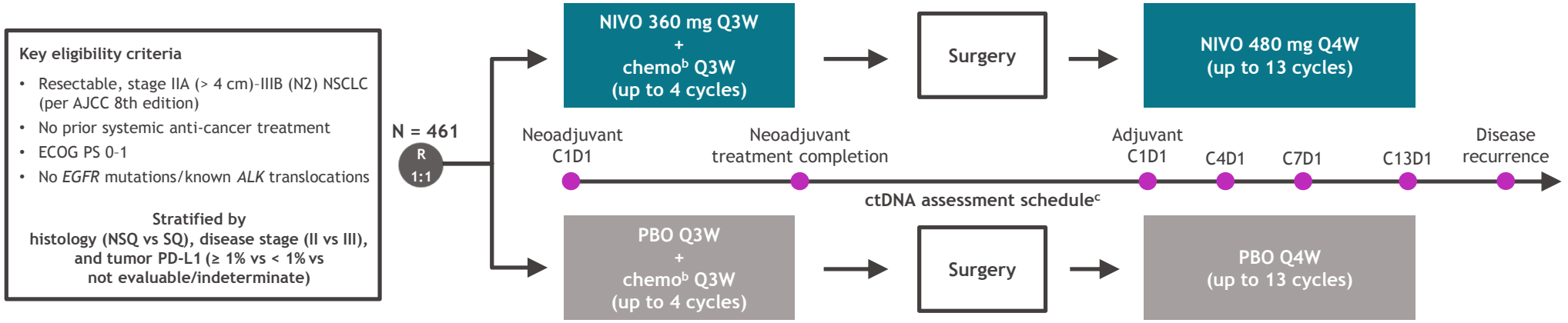


Cáncer de Pulmón de Célula No Pequeña: Enfermedad Localizada

Iniciativa científica de: GECP lung cancer research

Perioperative nivolumab vs placebo in patients with resectable NSCLC: clinical update from the phase 3 CheckMate 77T study

- In the phase 3 CheckMate 77T[a] study, perioperative NIVO demonstrated statistically significant and clinically meaningful EFS benefit vs PBO in patients with resectable NSCLC (HR, 0.58; 97.36% CI, 0.42–0.81; *P* < 0.001); pCR was also improved[1]
- **Here we report updated clinical outcomes from CheckMate 77T with a median follow-up of 33.3 months, exploratory outcomes by pCR status, and ctDNA analyses**



Primary endpoint
- EFS[d] by BICR

Secondary endpoints
- pCR[e] by BIPR
- MPR by BIPR
- OS
- Safety

Exploratory analyses
- Outcomes by pCR status
- ctDNA clearance[f] and recurrence[g]

Database lock date: April 26, 2024; median follow-up (range): 33.3 months (23.6–52.1).

[a]NCT04025879. [b]NSQ: cisplatin + pemetrexed, carboplatin + pemetrexed, or carboplatin + paclitaxel; SQ: cisplatin + docetaxel or carboplatin + paclitaxel. [c]ctDNA was measured using the Invitae Personalized Cancer Monitoring (tumor-informed) assay. [d]Time from randomization to any disease progression precluding surgery, abandoned surgery due to unresectability or disease progression, disease progression/recurrence after surgery, progression in patients without surgery, or death due to any cause. [e]0% residual viable tumor cells post-surgery in both primary tumor (lung) and sampled lymph nodes. [f]Change from detectable ctDNA at neoadjuvant treatment initiation (C1D1) to no detectable ctDNA at neoadjuvant treatment completion (end of neoadjuvant treatment or prior to definitive surgery). [g]Change from no detectable ctDNA at adjuvant treatment initiation (C1D1) to detectable ctDNA during the post-operative period (adjuvant C4D1, C7D1, or C13D1; disease recurrence). 1. Cascone T, et al. *N Engl J Med* 2024;390:1756–1769.

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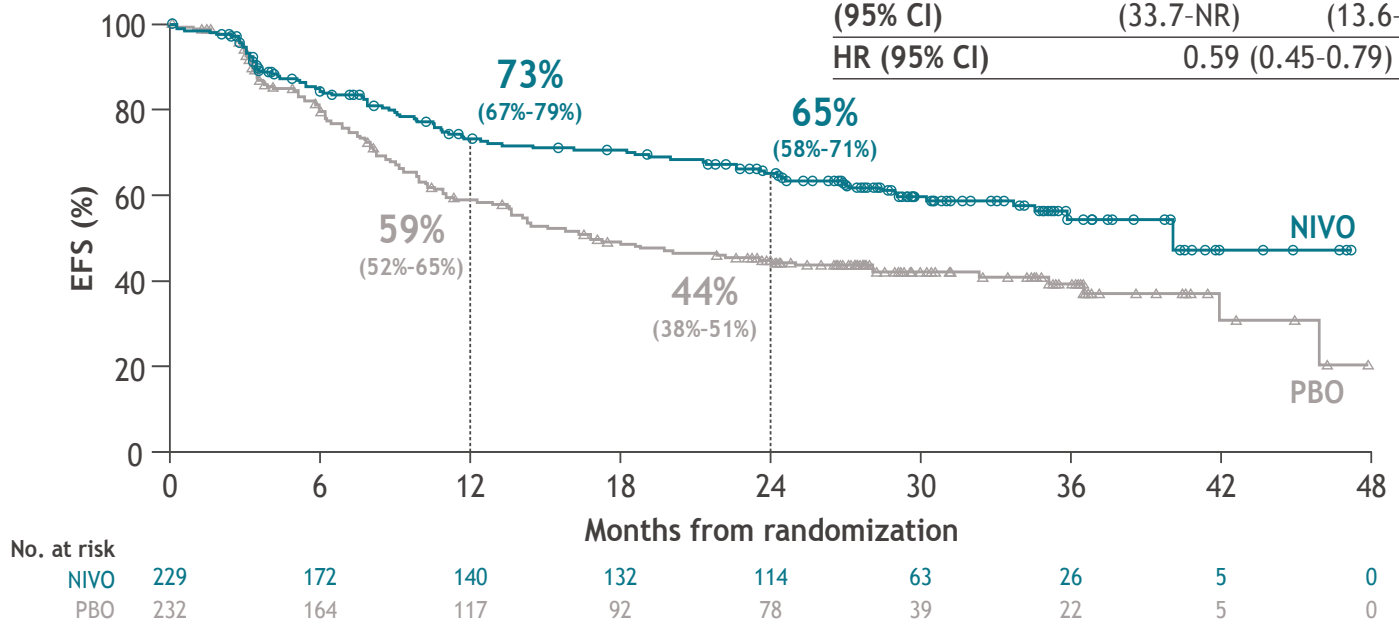
EFS per BICR

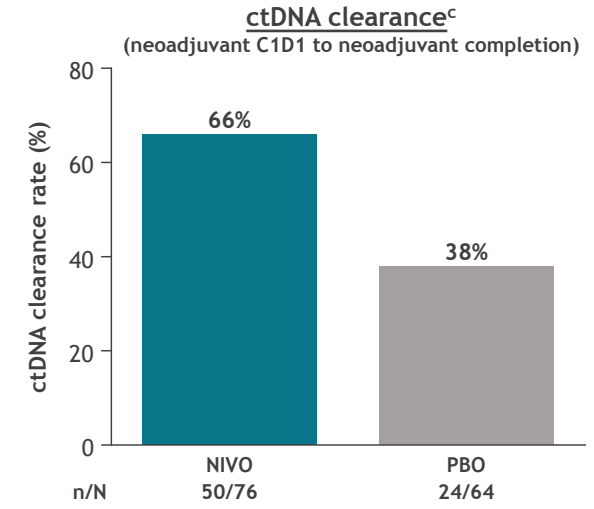
	NIVO (n = 229)	PBO (n = 232)
Median EFS, mo (95% CI)	40.1 (33.7-NR)	17.0 (13.6-28.1)
HR (95% CI)	0.59 (0.45-0.79)	



- Landmark EFS from definitive surgery among patients who had definitive surgery for NIVO (n = 178) vs PBO (n = 178): HR = 0.52 (95% CI, 0.37-0.73)

Median follow-up (range): 33.3 months (23.6-52.1).
95% CIs for EFS rates are designated in the parentheses.

- In an exploratory ctDNA analysis,
- —Neoadjuvant treatment with NIVO + chemo showed greater ctDNA clearance vs PBO + chemo, which was associated with pCR and EFS benefit
- —ctDNA recurrence appeared to be less frequent in patients who received adjuvant NIVO vs PBO, suggesting a potential benefit of adjuvant NIVO



Iniciativa científica de: GECP lung cancer research

CCTG BR.31: A double-blind placebo- controlled randomized phase 3 trial of adjuvant durvalumab in completely resected non-small-cell lung cancer

CCTG BR.31 Trial Design

Study population:
- Stage IB (≥4 cm)–IIIA NSCLC (AJCC 7th ed.)
- Complete resection
- ECOG PS 0–1
- EGFRm/ALK+ pts eligible

Surgery → randomization ≥3 weeks

Platinum doublet
(Chemo ineligible, chemo intolerant, patients who refuse chemo may also be included)

N=1415 (all comers)
N=1219 EGFR−/ALK−

R[1] 2:1

Durvalumab
20 mg/kg Q4W x 12 months

Stratification
- Stage IB (≥4 cm) *vs* II *vs* IIIA
- PD-L1 status (0 *vs* 1–24% *vs* 25–49% *vs* ≥50%)[2]
- Adjuvant platinum-based chemotherapy (≥300 mg/m^2 cisplatin/equiv *vs* <300 mg/m^2 vs no chemotherapy)
- Accruing center
- Nodal dissection according to ESTS[3] (yes *vs* no)

Placebo
20 mg/kg Q4W x 12 months

Primary endpoint
- DFS[4] (Investigator Assessed) in patients with PD-L1 TC ≥25% and EGFR−/ALK−

Key secondary endpoints
- DFS in patients with:
  - PD-L1 TC ≥1% and EGFR−/ALK−
  - All PD-L1 TC ≥25%
  - All randomized patients
  - PD-L1 all comers and EGFR−/ALK−
  - All PD-L1 TC ≥1%
- OS (six patient subpopulations)
- AEs
- QoL

Today, we will present the final DFS analysis from three EGFR−/ALK− populations

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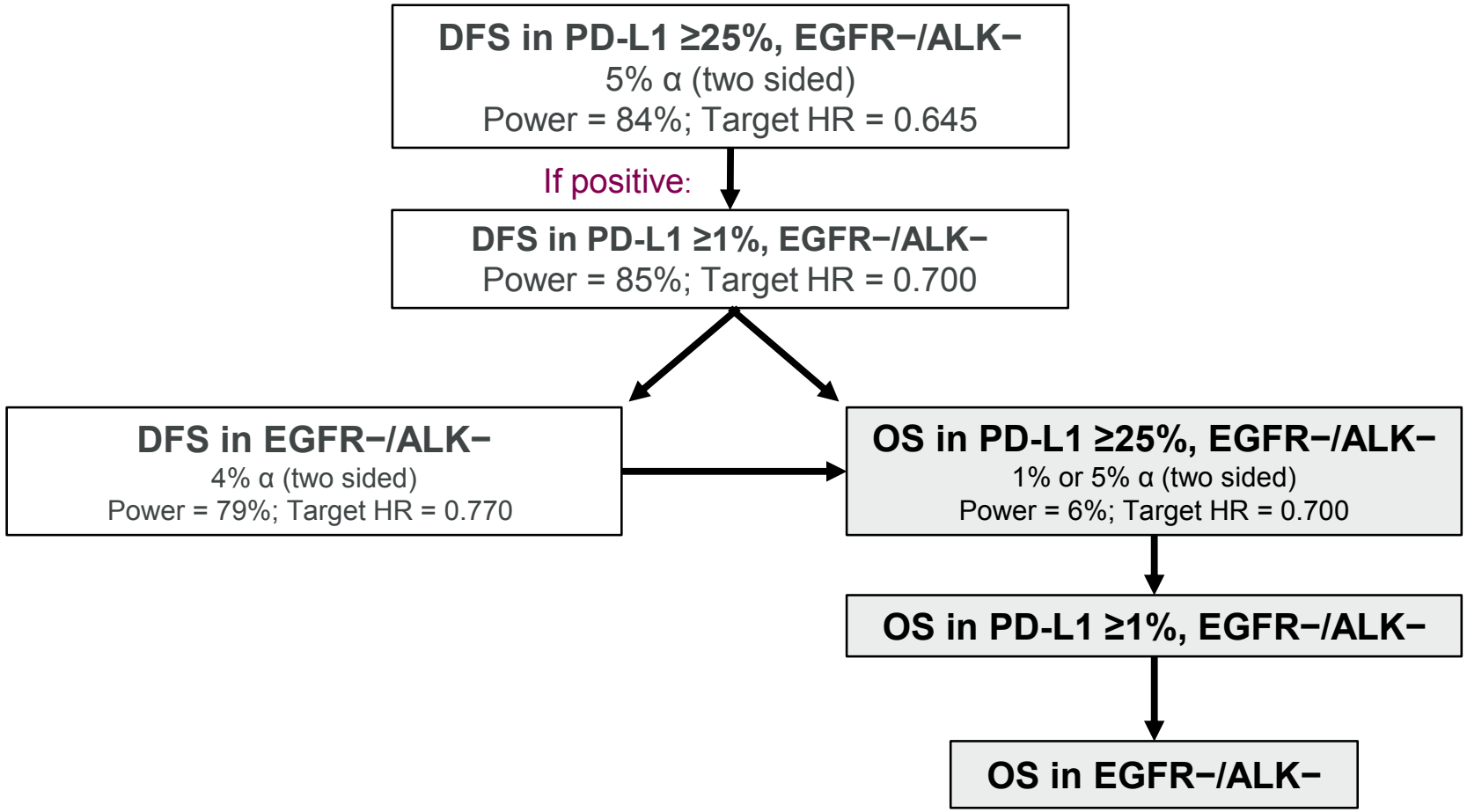
Multiple Hierarchical Testing Procedure[1]



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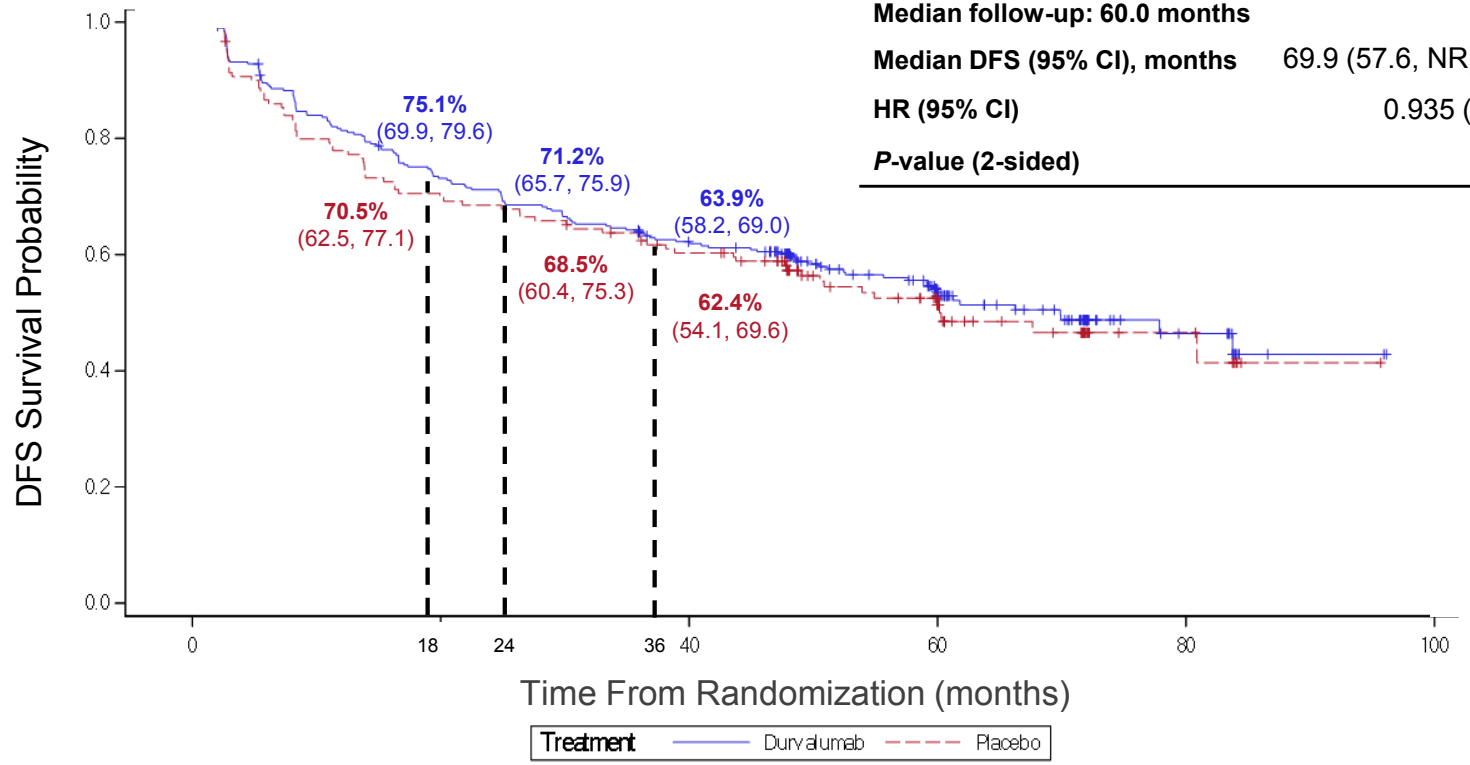
CCTG BR.31 Primary Endpoint

DFS in PD-L1≥25% EGFR−/ALK−

	D arm n=316	PBO arm n=161
Median follow-up: 60.0 months		
Median DFS (95% CI), months	69.9 (57.6, NR)	60.2 (47.7, NR)
HR (95% CI)	0.935 (0.706, 1.247)	
***P*-value (2-sided)**	0.642	



TAKE AWAY ...

Iniciativa científica de: GECP lung cancer research

1. **Pembrolizumab + Chemo**: Greater pathologic regression (%RVT 29.5% vs 52%) vs placebo. Higher %RVT linked to poorer EFS.
2. **AEGEAN Trial**: Durvalumab shows consistent EFS benefit (HR 0.69), enhanced in adjuvant-treated patients, regardless of pCR.
3. **Alectinib**: Effective (MPR 39%, pCR 17%) and well-tolerated in stage III ALK+ NSCLC.
4. **NADIM I**: Chemo-immunotherapy shows 5-year benefit, especially in patients with CPR. ctDNA clearance predicts better PFS/OS.
5. **Surgery vs Chemoradiation**: Surgery improved OS in cT4N2M0 NSCLC patients compared to chemoradiation plus IO.
6. **pCR/MPR**: Significant EFS improvement (>90% at 24 months). Similar EFS between neoadjuvant and perioperative regimens.
7. **NIVO + Chemo**: 40% reduction in recurrence/death with adjuvant NIVO. Greater benefit in PD-L1 < 1% patients.
8. **Novel Combinations**: Oleclumab, Monalizumab, and Dato-DXd combos show promising pCR and mPR rates vs historical benchmarks.
9. **BR.31 Trial**: Adjuvant durvalumab didn't improve DFS in PD-L1 ≥25% patients (EGFR−/ALK−).
10. **CheckMate 77T**: NIVO improves EFS (HR 0.59). Neoadjuvant NIVO + chemo enhances ctDNA clearance, linked to pCR and EFS benefits