Estadios iniciales y enfermedad localmente avanzada

Patricia Cruz Castellanos

Hospital General Universitario Ciudad Real

GECP
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CONFLICTO DE INTERESES

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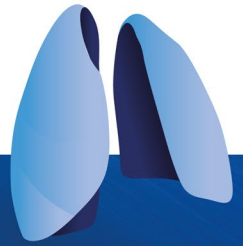

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La estrategia perioperatoria es el futuro

La NA con IO es una realidad

La determinación molecular es fundamental en cualquier estadio

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¿ Que novedades tenemos ?

Estrategia NA y perioperatoria :

- **Checkmate 816**
- **Checkmate 77T**
- **Keynote 671**
- **Rationale 315**

Adyuvancia

- **Nadim adyuvant**
- **Impower 010**

Que es un cambio de estándar ???

Que es lo próximo que esta por llegar???

ONCOGENE-ADDICTED TEMPRANO: ALK y EGFR (resecable y estadio III)

ESTADIO III IRRESECABLE ---Pacific y Apollo

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NA y estrategia perioperatoria

2025 es el año de la perioperatoria

CHECKMATE 816

CHECKMATE-77T

KEYNOTE-671

RATIONALE 315

Checkmate 816

2025 ASCO ANNUAL MEETING

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Overall Survival with Neoadjuvant Nivolumab plus Chemotherapy in Lung Cancer

Patrick M. Forde, M.B., B.Ch., Ph.D.,[1] Jonathan D. Spicer, M.D., Ph.D.,[2] Mariano Provencio, M.D., Ph.D.,[3] Tetsuya Mitsudomi, M.D., Ph.D.,[4] Mark M. Awad, M.D., Ph.D.,[5] Changli Wang, M.D.,[6] Shun Lu, M.D., Ph.D.,[7] Enriqueta Felip, M.D., Ph.D.,[8] Scott J. Swanson, M.D.,[9] Julie R. Brahmer, M.D.,[10] Keith Kerr, M.B., Ch.B.,[11] Janis M. Taube, M.D.,[12] Tudor-Eliade Ciuleanu, M.D., Ph.D.,[13] Fumihiro Tanaka, M.D., Ph.D.,[14] Gene B. Saylors, M.D.,[15] Ke-Neng Chen, M.D., Ph.D.,[16] Hiroyuki Ito, M.D., Ph.D.,[17] Moishe Liberman, M.D., Ph.D.,[18] Claudio Martin, M.D.,[19] Stephen Broderick, M.D.,[10] Lily Wang, M.D.,[20] Junliang Cai, M.D.,[20] Quyen Duong, Ph.D.,[20] Stephanie Meadows-Shropshire, Ph.D.,[20] Joseph Fiore, Pharm.D.,[20] Sumeena Bhatia, Ph.D.,[20] and Nicolas Girard, M.D., Ph.D.,[21] for the CheckMate 816 Investigators*

Actualización de OS a 5 años

CheckMate 816: 5-y OS final analysis

CheckMate 816 study design[a]

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

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

N = 358 → R 1:1

Primary analysis population (Concurrently randomized)
- NIVO 360 mg Q3W + chemo[d] Q3W (3 cycles)
- Chemo[e] Q3W (3 cycles)

→ Radiologic restaging → Surgery (within 6 weeks post-treatment) → Optional adjuvant chemo and/or RT → Follow-up

Minimum/median follow-up: 59.9/68.4 months

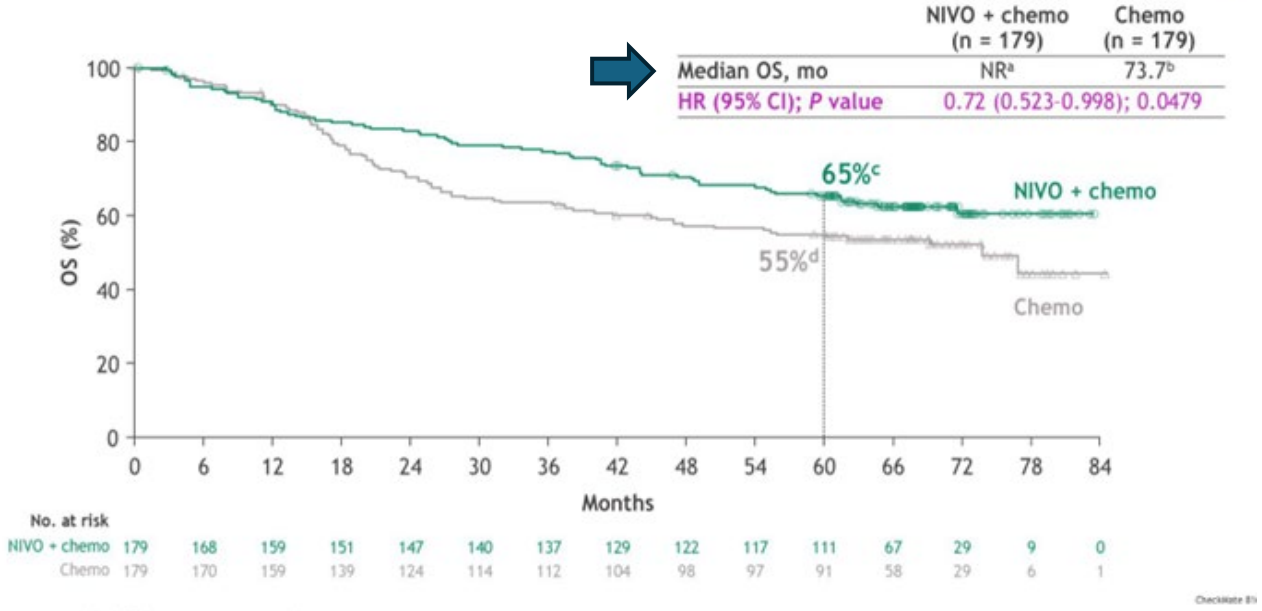
Primary endpoints	Key secondary endpoints	Exploratory analyses
• pCR by BIPR	• OS	• OS by pCR, ctDNA clearance
• EFS by BICR	• MPR by BIPR	• Lung cancer-specific survival
	• TTDM	

Database lock: January 23, 2025. From *The New England Journal of Medicine*, Forde PM, et al., Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer, 2022;386:1973-1985. Copyright © 2022 Massachusetts Medical Society. Adapted with permission from Massachusetts Medical Society. [a]NCT02998528. [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako). [c]Included patients with PD-L1 expression status not evaluable and indeterminate. [d]Nonsquamous: pemetrexed + cisplatin or paclitaxel + carboplatin; squamous: gemcitabine + cisplatin or paclitaxel + carboplatin. [e]Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (squamous only), pemetrexed + cisplatin (nonsquamous only), or paclitaxel + carboplatin.

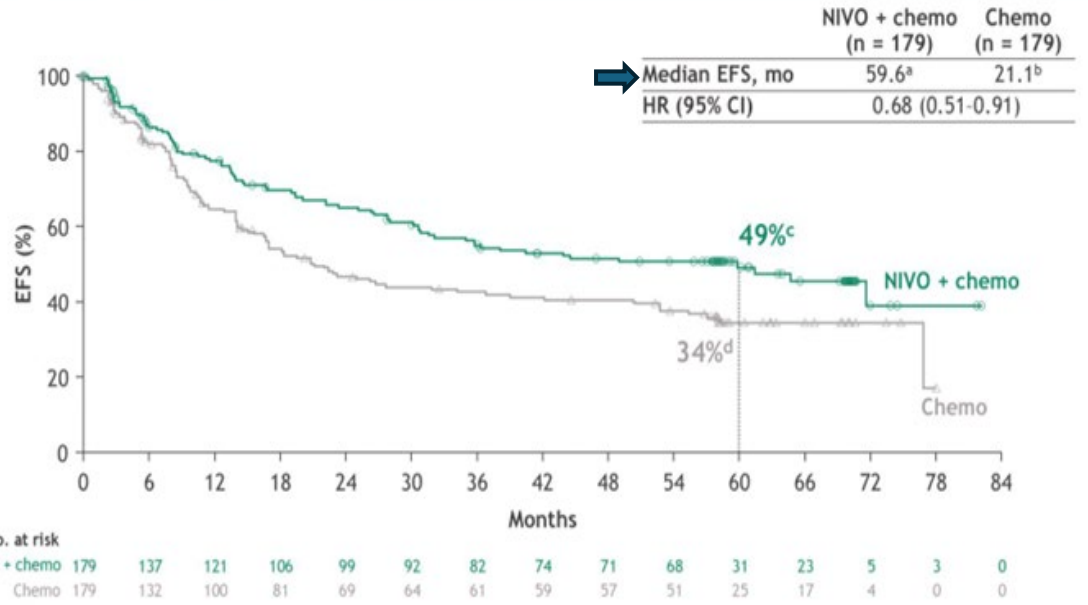
Overall survival with neoadjuvant nivolumab plus chemotherapy in resectable NSCLC: CheckMate-816. *ASCO Annual Meeting 2025.*

ecp lung cancer research

Final analysis: OS with neoadjuvant NIVO + chemo vs chemo

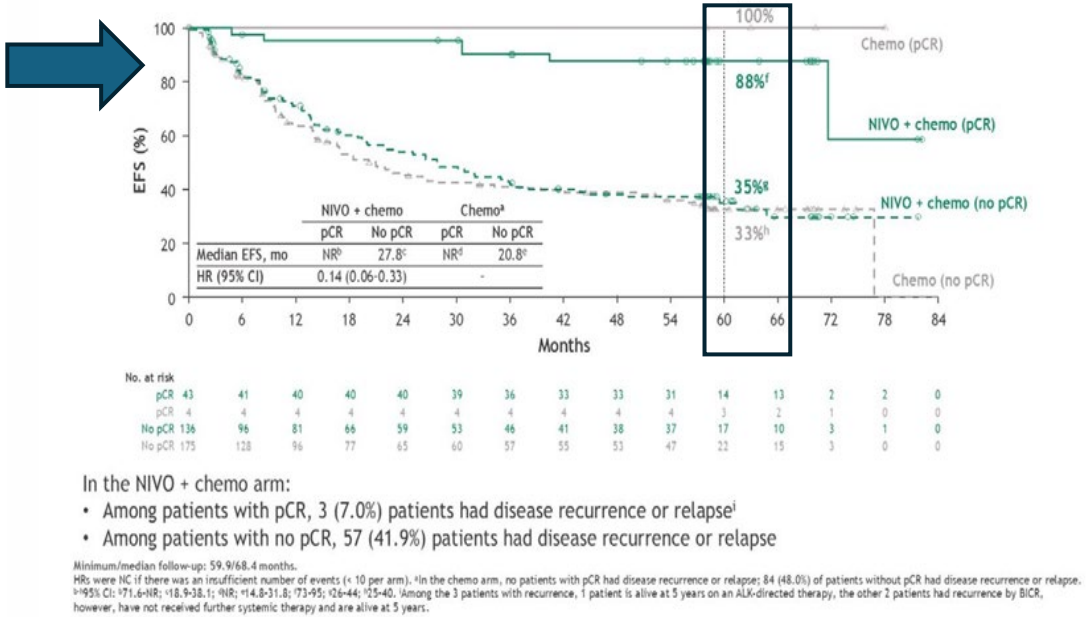


EFS: 5-year analysis



Exploratory analysis: EFS by pCR status

Separación precoz tras la cx



In the NIVO + chemo arm:

- Among patients with pCR, 3 (7.0%) patients had disease recurrence or relapse[i]
- Among patients with no pCR, 57 (41.9%) patients had disease recurrence or relapse

Minimum/median follow-up: 59.9/68.4 months.
HRs were NC if there was an insufficient number of events (< 10 per arm). [a]In the chemo arm, no patients with pCR had disease recurrence or relapse; 84 (48.0%) of patients without pCR had disease recurrence or relapse. [b-h]95% CI: [b]71.6-NR; [c]18.9-38.1; [d]NR; [e]14.8-31.8; [f]73-95; [g]26-44; [h]25-40. [i]Among the 3 patients with recurrence, 1 patient is alive at 5 years on an ALK-directed therapy, the other 2 patients had recurrence by BICR, however, have not received further systemic therapy and are alive at 5 years.

Análisis pronostico : según pCR (con independencia del PDL1)

Esquema de uso aprobado PDL1 >1%

¿ Que pasaría si continuásemos con IO adyuvante ?

2025 ASCO ANNUAL MEETING

Perioperative nivolumab vs placebo in patients with resectable NSCLC: updated survival and biomarker analyses from CheckMate 77T

Tina Cascone,[1] Mark M. Awad,[2] Jonathan D. Spicer,[3] Jie He,[4] Shun Lu,[5] Fumihiro Tanaka,[6] Robin Cornelissen,[7] Lubos B. Petruzelka,[8] Hiroyuki Ito,[9] Ludmila de Oliveira Muniz Koch,[10] Lin Wu,[11] Sabine Bohnet,[12] Cinthya Coronado Erdmann,[13] Stephanie Meadows-Shropshire,[14] Jaclyn Neely,[14] Yu-Han Hung,[14] Padma Sathyanarayana,[14] Sumeena Bhatia,[14] Mariano Provencio[15]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]McGill University Health Centre, Montreal, Quebec, Canada; [4]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [5]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [6]University of Occupational and Environmental Health, Kitakyushu, Japan; [7]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [8]Charles University, Prague, Czech Republic; [9]Kanagawa Cancer Center, Yokohama, Japan; [10]Hospital Israelita Albert Einstein, Sao Paulo, Brazil; [11]Hunan Cancer Hospital, Changsha, China; [12]University Medical Center Schleswig-Holstein, Lubeck, Germany; [13]Bristol Myers Squibb, Boudry, Switzerland; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]Hospital Universitario Puerta de Hierro, Madrid, Spain

CheckMate 77T[a] study design

Key eligibility criteria

- Resectable, stage IIA (> 4 cm)-IIIB (N2) NSCLC (per AJCC 8th edition)
- No prior systemic anti-cancer treatment
- ECOG PS 0-1
- No *EGFR* mutation/known *ALK* alterations[b]

Stratified by histology (NSQ vs SQ) disease stage (II vs III), and tumor PD-L1[c] (≥ 1% vs < 1% vs not evaluable/indeterminate)

N = 461 → R 1:1

- NIVO 360 mg Q3W + chemo[d] Q3W (4 cycles) → Radiologic restaging → Surgery (within 6 weeks post-neoadjuvant treatment) → NIVO 480 mg Q4W (1 year) → Follow-up
- PBO Q3W + chemo[d] Q3W (4 cycles) → Radiologic restaging → Surgery (within 6 weeks post-neoadjuvant treatment) → PBO Q4W (1 year) → Follow-up

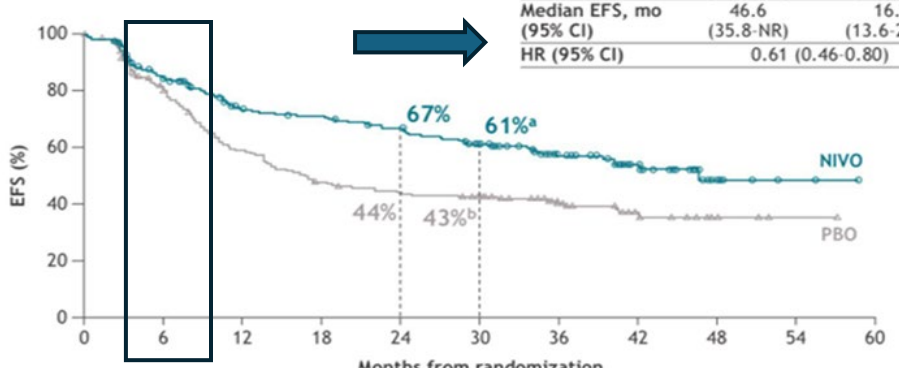
Follow-up, median (range): 25.4 (15.7-44.2) months

Primary endpoint	Secondary endpoints	Exploratory analyses
• EFS by BICR	• pCR[e] by BIPR • MPR[e] by BIPR • OS • Safety	• EFS by pCR/MPR • EFS by adjuvant treatment

CheckMate 77T: survival and biomarker update

EFS per BICR

	NIVO (n = 229)	PBO (n = 232)
Median EFS, mo (95% CI)	46.6 (35.8-NR)	16.9 (13.6-28.2)
HR (95% CI)	0.61 (0.46-0.80)	



Separación de las curvas desde los 6 ms , y mantenida en el tiempo

CheckMate 77T: survival and bi

OS and lung cancer-specific survival

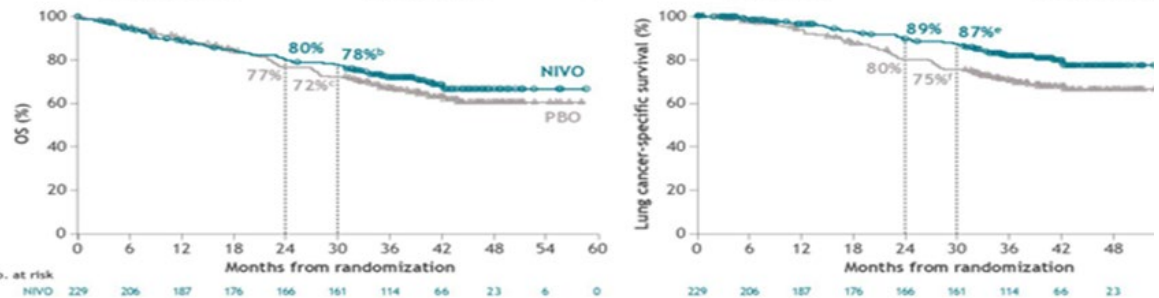
No OS madura

OS

	NIVO (n = 229)	PBO (n = 232)
Median OS, mo (95% CI)	NR (NR-NR)	NR (NR-NR)
HR (97.63% CI)[a]	0.85 (0.58-1.25)	

Lung cancer-specific survival[d]

	NIVO (n = 229)	P (n =
Median lung cancer-specific survival, mo (95% CI)	NR (NR-NR)	(NR
HR (95% CI)	0.60 (0.40-0.8	

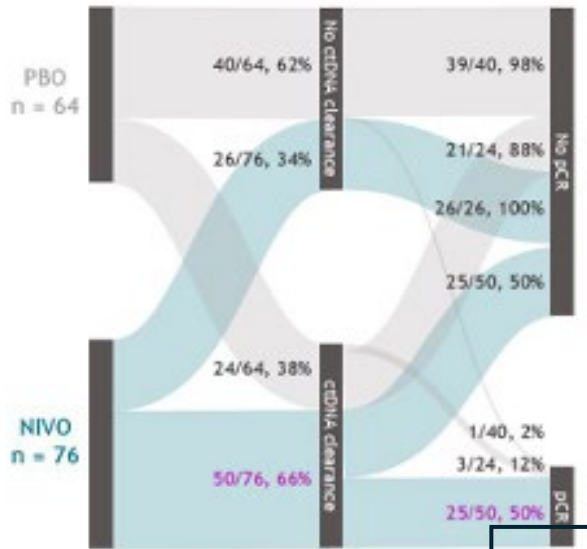


Median follow-up (range): 41.0 months (31.3-59.8).
67 (29%) patients in the NIVO arm and 101 (44%) patients in the PBO arm received subsequent therapy of any type; 50 (22%) and 87 (38%) patients, respectively, received subsequent systemic therapy.
[a]HR (95% CI), 0.85 (0.61-1.18). Significance boundary for OS was not met at this interim analysis. [b]95% CI: [c]72-83; [d]66-78. [e]Exploratory analysis; events were deaths with noted reason of "disease" per investigator assessment. [f]95% CI: [g]82-91; [h]69-81.

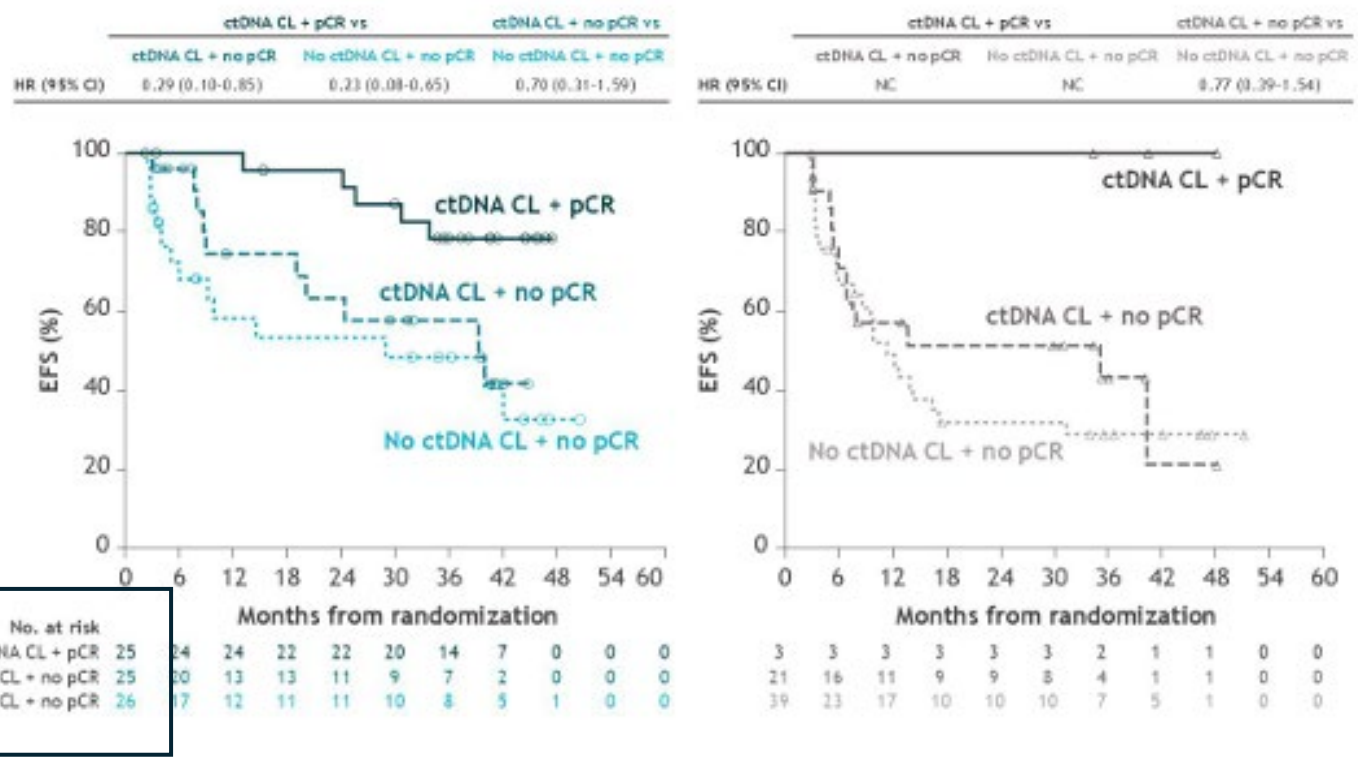
Spicer J, Provencio M, Nadal E, *et al.* **Updated event-free survival and overall survival outcomes from the CheckMate 77T trial of perioperative nivolumab plus chemotherapy in resectable NSCLC.** *ASCO Annual Meeting 2025.*

EFS by ctDNA clearance[a] and pCR status

Association between ctDNA clearance and pCR



NIVO



PBO

Muy pocos eventos

Median follow-up (range): 41.0 months (31.3-59.8).
[a]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); patients with no detectable ctDNA at neoadjuvant C1D1 were excluded from this analysis. Of randomized patients, 82 (36%) patients in the NIVO arm and 74 (32%) patients in the PBO arm had ctDNA-evaluable samples at both neoadjuvant treatment initiation and completion; 76 (33%) and 64 (28%) patients, respectively, had detectable ctDNA at neoadjuvant treatment initiation.
Landmark EFS from definitive surgery continued to favor NIVO vs PBO in patients with pCR (HR, 0.90; 95% CI, 0.19-4.15) or without pCR (HR, 0.72; 95% CI, 0.50-1.05).

Las dos ramas se benefician del uso perioperatorio

BERLIN 2025 ESMO congress

Consolidación de la estrategia perioperatoria con datos a 5 años de OS

KEYNOTE-671 Study Design
Randomized, Double-Blind, Phase 3 Trial

Key Eligibility Criteria
- Pathologically confirmed, resectable stage II, IIIA, or IIIB (N2) NSCLC per AJCC v8
- No prior therapy
- Able to undergo surgery
- Provision of tumor sample for PD-L1 evaluation[a]
- ECOG PS 0 or 1

~786 R 1:1

Pembrolizumab 200 mg IV Q3W + Cisplatin and Gemcitabine[b] or Cisplatin and Pemetrexed[c] for up to 4 cycles → Surgery[d] → Pembrolizumab 200 mg IV Q3W for up to 13 cycles

Placebo IV Q3W + Cisplatin and Gemcitabine[b] or Cisplatin and Pemetrexed[c] for up to 4 cycles → Surgery[d] → Placebo IV Q3W for up to 13 cycles

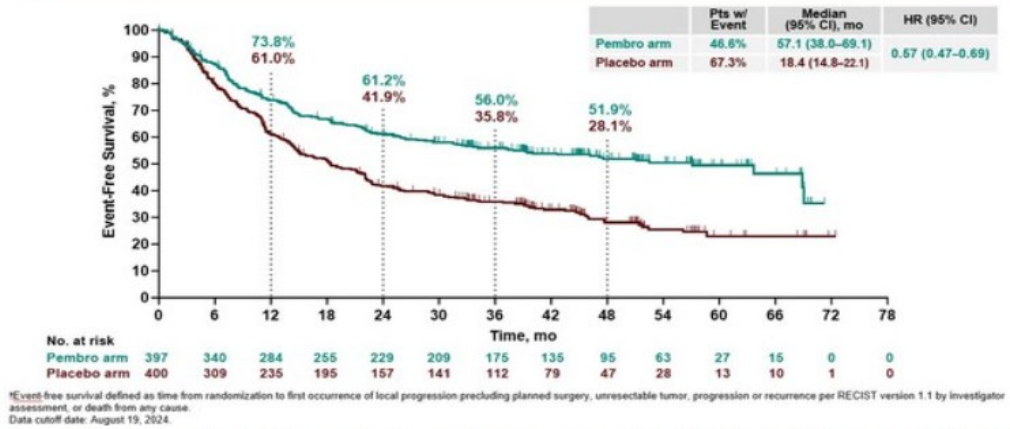
Stratification Factors
- Disease stage (II vs III)
- PD-L1 TPS[a] (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (east Asia vs not east Asia)

Dual primary end points: EFS per investigator review and OS

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

[a] Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. [b] Cisplatin 75 mg/m² IV Q3W + gemcitabine 1000 mg/m² IV on days 1 and 8 Q3W was permitted for squamous histology only. [c] Cisplatin 75 mg/m² IV Q3W + pemetrexed 500 mg/m² IV Q3W was permitted for nonsquamous histology only. [d] Radiotherapy was to be administered to participants with microscopic positive margins, gross residual disease, or extracapsular nodal extension following surgery and to participants who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.

Event-Free Survival[a]
Median Follow-Up: 41.1 (range, 0.4–75.3) months



[a] Event-free survival defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST version 1.1 by investigator assessment, or death from any cause.
Data cutoff date: August 19, 2024.

Figure. Event-free survival data reported in the 4-year update of the KEYNOTE-671 study (LBA3, ESMO Immuno-Oncology Congress 2024)

Demographics and Baseline Clinical Characteristics

	Pembro Arm (n = 397)	Placebo Arm (n = 400)
Age, median (range), y	63.0 (26–83)	64.0 (35–81)
Male	279 (70.3)	284 (71.0)
Race		
Asian	124 (31.2)	125 (31.3)
Black or African American	6 (1.5)	10 (2.5)
White	250 (63.0)	239 (59.8)
Missing	13 (3.3)	16 (4.0)
Other	4 (1.0)	10 (2.5)
Geographic region		
East Asia	123 (31.0)	121 (30.3)
Not east Asia	274 (69.0)	279 (69.8)
ECOG PS 1	144 (36.3)	154 (38.5)
Current/former smoker	343 (86.4)	353 (88.3)
Nonsquamous histology	226 (56.9)	227 (56.8)

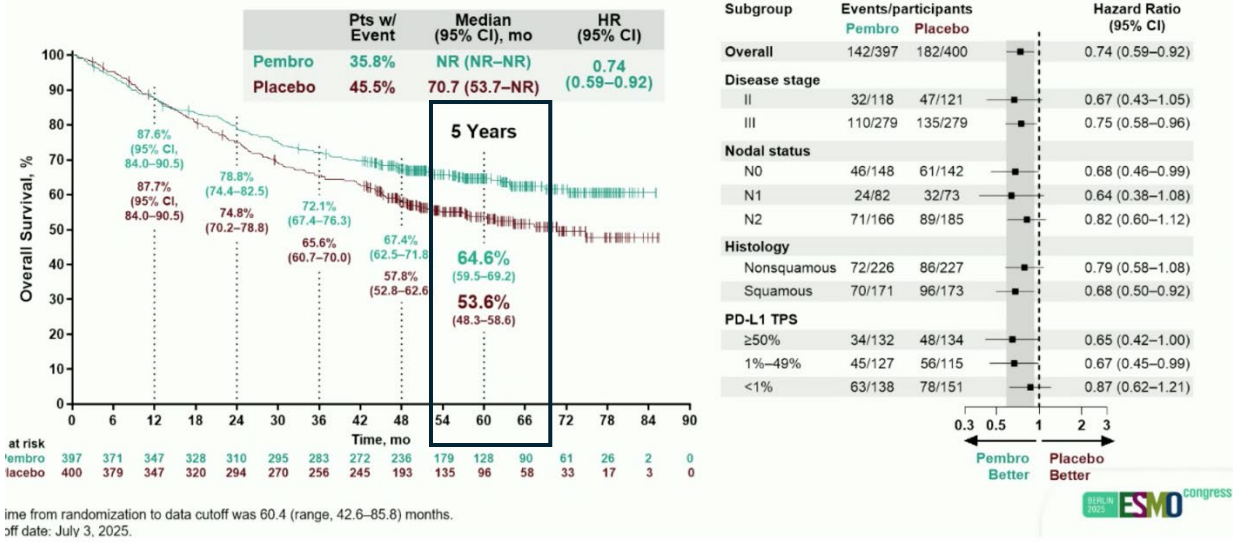
	Pembro Arm (n = 397)	Placebo Arm (n = 400)
Clinical disease stage		
II	118 (29.7)	121 (30.3)
III	279 (70.3)	279 (69.8)
Clinical node stage		
N0	148 (37.3)	142 (35.5)
N1	82 (20.7)	73 (18.3)
N2	166 (41.8)	185 (46.3)
NX	1 (0.3)	0
PD-L1 TPS		
≥50%	132 (33.2)	134 (33.5)
1%–49%	127 (32.0)	115 (28.8)
<1%	138 (34.8)	151 (37.8)
Known *EGFR* mutation[a]	14 (3.5)	19 (4.8)
Known *ALK* translocation[b]	12 (3.0)	9 (2.3)

Wakelee H, Provencio M, Felip E, *et al.* **Overall survival with perioperative pembrolizumab plus chemotherapy in resectable non–small-cell lung cancer (KEYNOTE-671).** *ASCO Annual Meeting 2025*.

Datos a 5 años

5-Year Update of Overall Survival

Overall Population

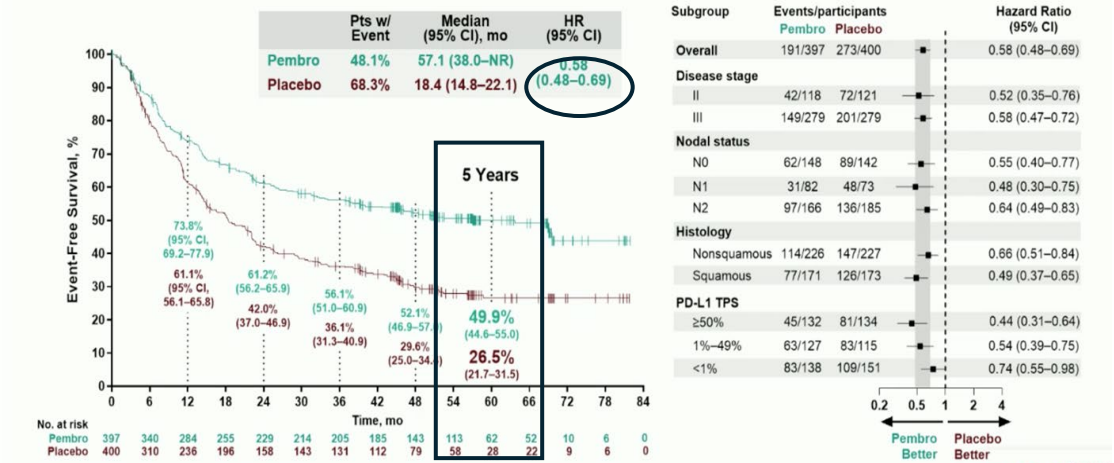


ime from randomization to data cutoff was 60.4 (range, 42.6–85.8) months.
off date: July 3, 2025.

Key Subgroups

5-Year Update of Event-Free Survival[a]

Overall Population



[a]Assessed per RECIST version 1.1 by investigator assessment.
Median time from randomization to data cutoff was 60.4 (range, 42.6–85.8) months.
Data cutoff date: July 3, 2025.

Key Subgroups

Perioperatorio con pembro **sostiene beneficio en OS** y prácticamente **duplica la población viva y libre de evento** respecto a QT sola.

	Checkmate 77T	Keynote 816
Población incluida	CPCNP resecable **estadios II–IIIB (**	CPCNP resecable **estadios II–IIIB**
Enfermedad N2	**Sí, incluida (N2 resecable)**	**Sí, incluida (N2 resecable)**
Tamaño muestral	~460 pacientes	~800 pacientes
Endpoint primario	**EFS**	**EFS y OS**
EFS (resultado principal)	Mediana **46.6 vs 16.9 meses**; HR ≈ **0.58**	**EFS a 5 años 49.9% vs 26.5%**; HR ≈ **0.58**
OS – estado 2025	**Señal favorable**, aún **inmadura**	**OS madura positiva**
OS – datos clave	Curvas empiezan a separarse; mediana **no alcanzada**	**OS a 5 años 64.6% vs 53.6%**; HR ≈ **0.74**
Mediana de seguimiento (OS)	**~38–40 meses** (≈3,2 años)	**~60 meses (5 años)**
Respuesta patológica (pCR)	Incremento significativo vs QT	Incremento significativo vs QT
Relación pCR–beneficio	Beneficio de EFS **también en pacientes sin pCR** (papel de la adyuvancia)	pCR marcador pronóstico; beneficio poblacional sostenido
Biomarcadores exploratorios	pCR + **ctDNA/MRD** asociados a mejor EFS	Subgrupos consistentes; MRD no integrada prospectivamente
Calidad de vida (PROs)	**No empeora HRQoL**, retrasa deterioro	PROs consistentes con QT + IO
Mensaje clave 2025	La **adyuvancia nivolumab mantiene el beneficio** en pacientes sin pCR	Primer perioperatorio con **beneficio en OS a 5 años**

CAMBIO DE PARADIGMA

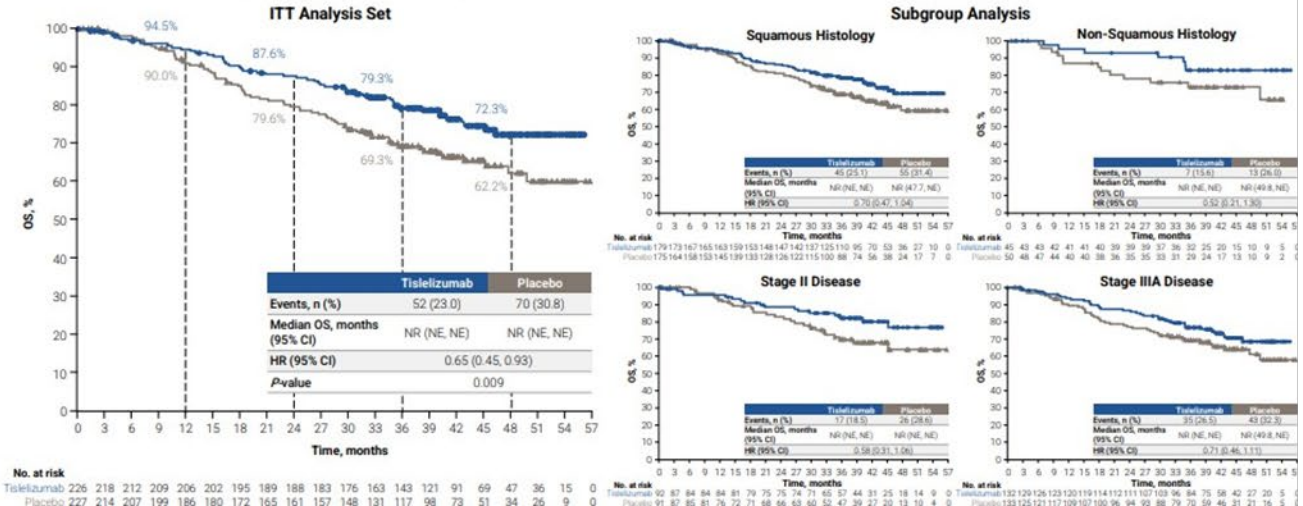
PERIOPERATIVE TISLELIZUMAB FOR RESECTABLE NON-SMALL CELL LUNG CANCER: FINAL ANALYSIS OF RATIONALE-315

Conclusions

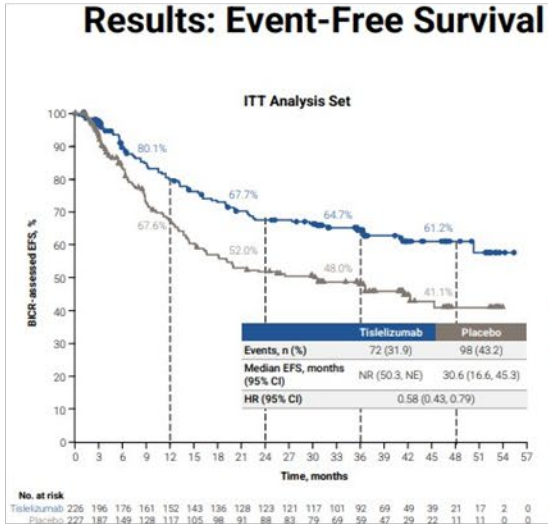
- A statistically significant and clinically meaningful benefit in OS was observed with perioperative tislelizumab plus PtDb chemotherapy vs placebo plus PtDb chemotherapy (HR=0.65 [95% CI: 0.45, 0.93]; one-sided *P*-value=0.009)
  - This benefit was consistent across prespecified and post-hoc subgroups
- There were clinically meaningful improvements in EFS, consistent with results from the prespecified and post-hoc subgroups in this analysis and the primary EFS analysis
- Perioperative tislelizumab plus PtDb chemotherapy was well tolerated, and the safety profile was consistent with the known risks of the individual therapies and the profile reported previously
- These final results of RATIONALE-315 further support perioperative tislelizumab plus neoadjuvant PtDb chemotherapy as an efficacious and well-tolerated treatment in patients with resectable NSCLC

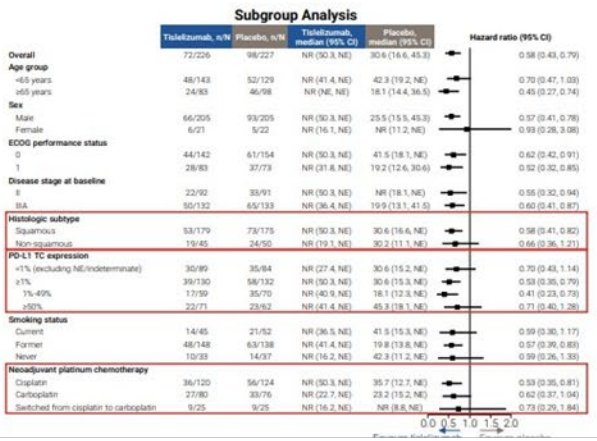
Results: Overall Survival

- Patients in the tislelizumab arm experienced a statistically significant and clinically meaningful improvement in OS vs those in the placebo arm, which was consistent across prespecified and post-hoc subgroups



Results: Event-Free Survival





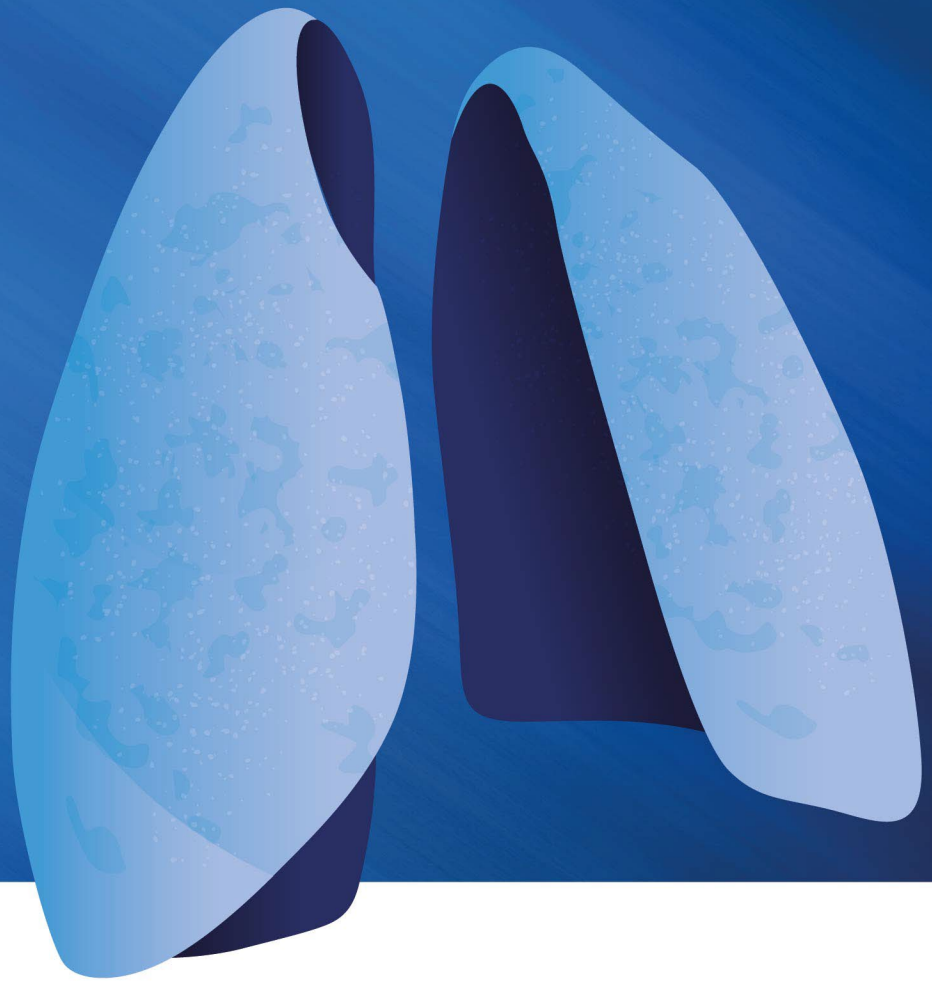
El perioperatorio es ya una estrategia con impacto en supervivencia→ KEYNOTE-671 confirma **beneficio en OS a 5 años.**

La adyuvancia marca la diferencia en pacientes sin pCR
→ CheckMate-77T y KEYNOTE-671 muestran que **mantener IO tras la cirugía prolonga EFS**, incluso sin pCR

CAMBIO DE PARADIGMA

Las distintas estrategias no son equivalentes
→ Neoadyuvancia-only (816): opción válida y financiada en España en **PD-L1 ≥1%**
→ Perioperatorio completo (77T, 671, RATIONALE-315): mayor control de enfermedad residual y enfoque preferente en **alto riesgo / N+**

Novedades en adyuvancia

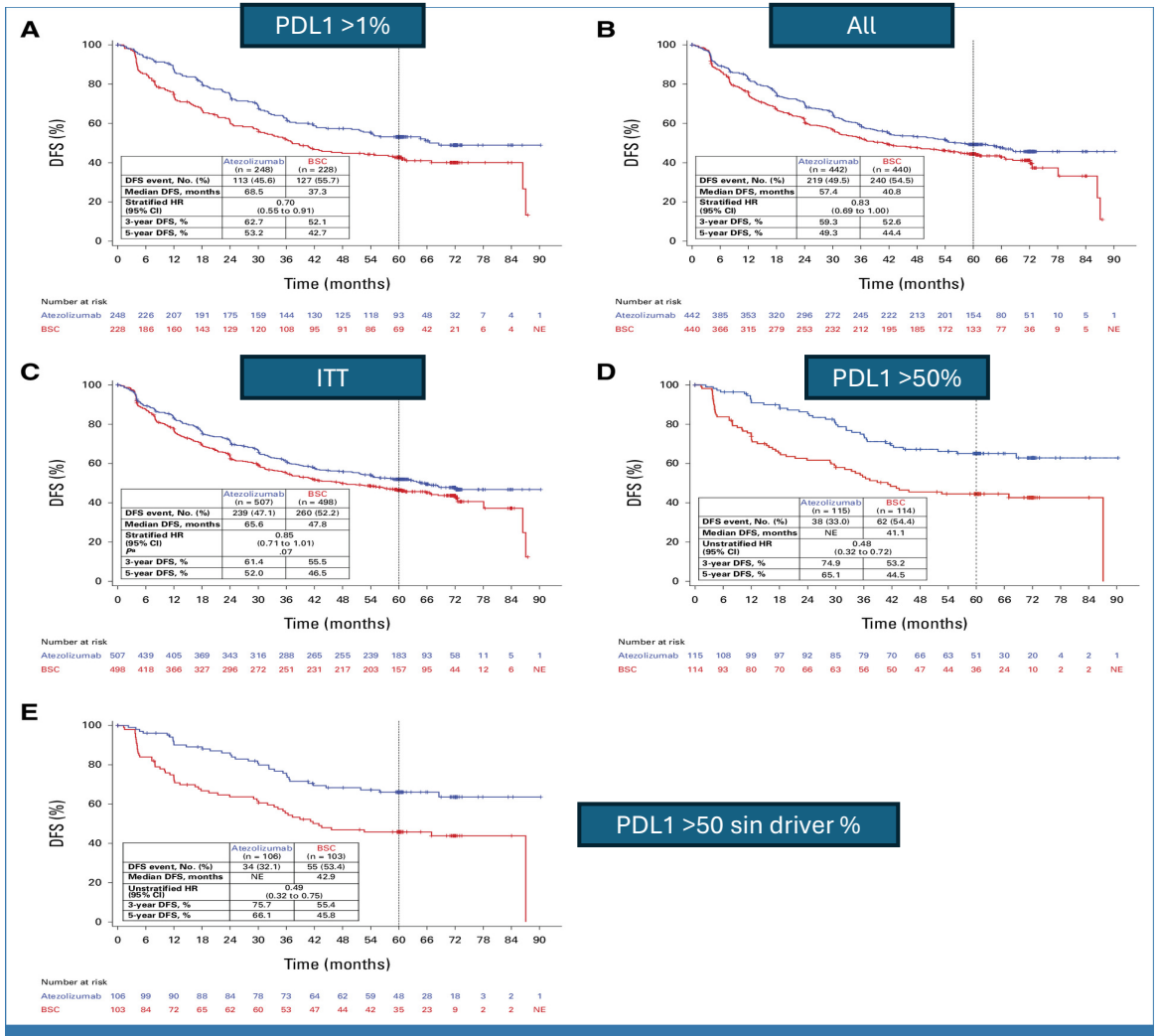


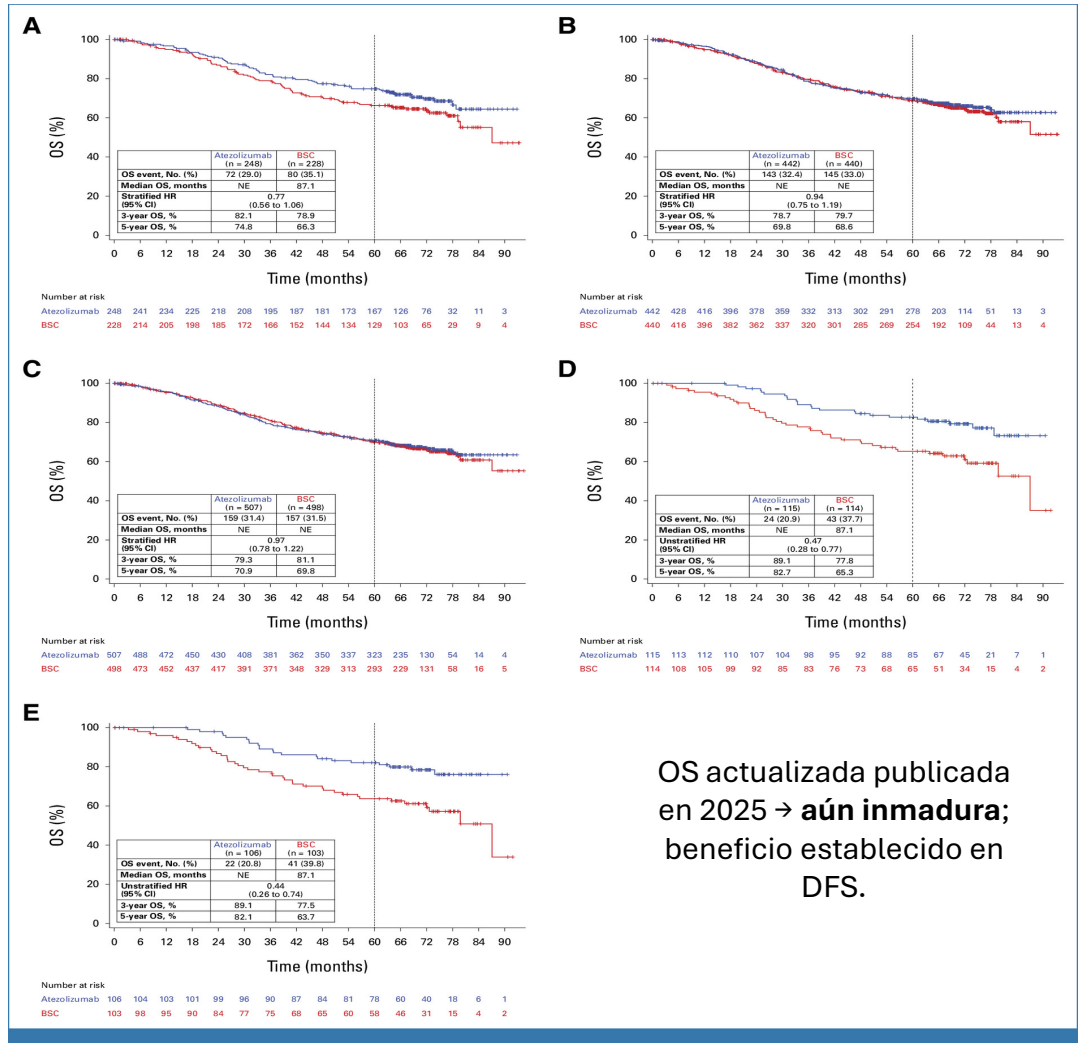
IMpower010

NADIM ADJUVANT

Five-Year Survival Outcomes With Atezolizumab After Chemotherapy in Resected Stage IB-IIIA Non–Small Cell Lung Cancer (IMpower010): An Open-Label, Randomized, Phase III Trial

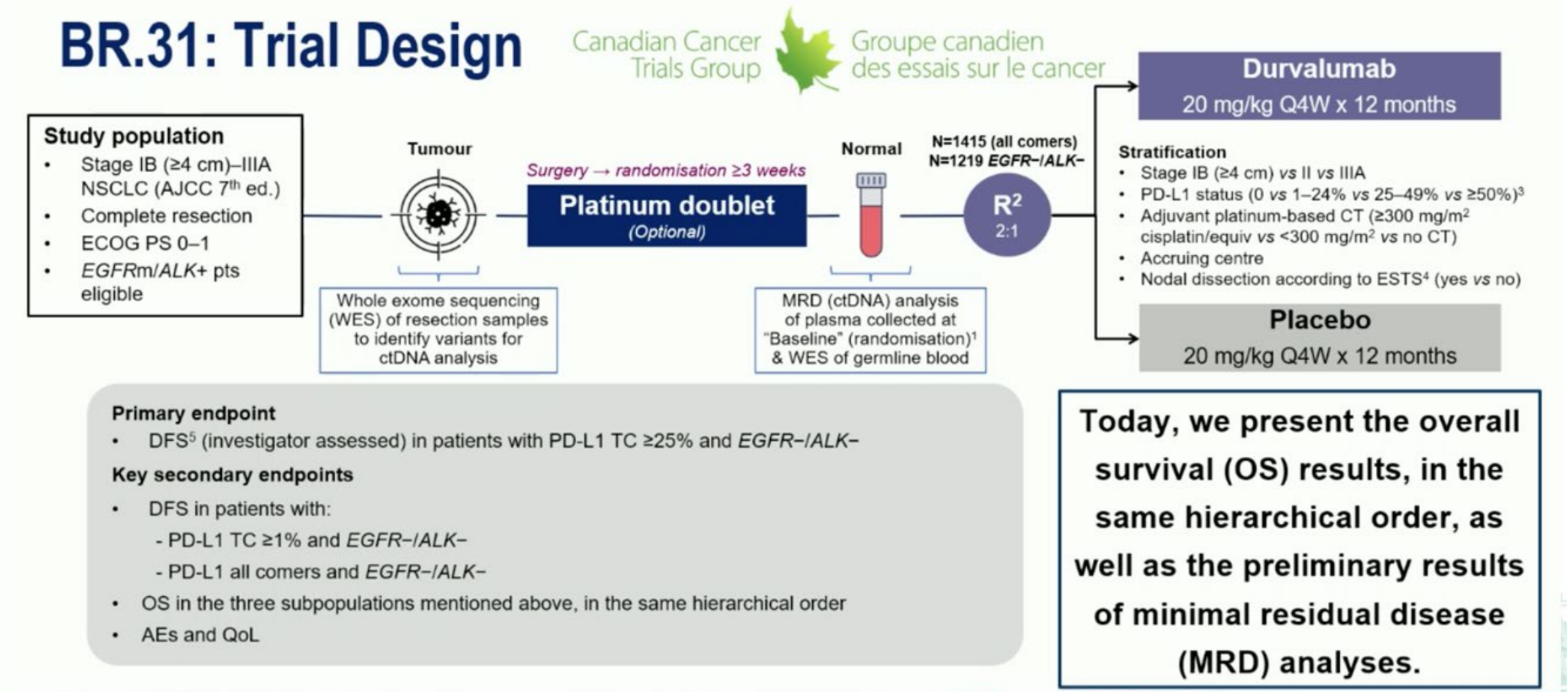
	SLE	SG
ITT	0.85 (95% CI, 0.71 to 1.01; *P* = .07)	0.97 (95% CI, 0.78 to 1.22)
Estadio II-III-A	HR: 0.83 (95% CI, 0.69 to 1.00)	0.94 (95% CI, 0.75 to 1.19)
Estadio II-III-A PD-L1 ≥ 1%	HR: 0.70 (95% CI, 0.55 to 0.91	0.77 (95% CI, 0.56 to 1.06)
Estadio II-III-A PD-L1 ≥ 50% (EGFR/ALK wt)	HR: 0.49 (95% CI, 0.32 to 0.75)	HR: 0.44 (95% CI, 0.26 to 0.74).





OS actualizada publicada en 2025 → **aún inmadura**; beneficio establecido en DFS.

Ensayo negativo…

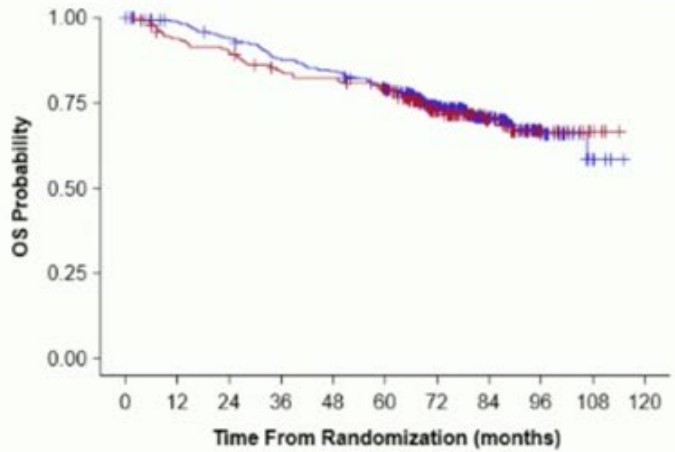


BR.31: Final OS by Subpopulation

- Adjuvant durvalumab did not improve OS in the primary population of PD-L1 TC ≥25% *EGFR−/ALK−* patients, or in key secondary subpopulations of PD-L1 TC ≥1% *EGFR−/ALK−* or PD-L1 all comers *EGFR−/ALK−* patients.
- Updated DFS results did not change substantively since previous presentation of data.

PD-L1 ≥ 25% and *EGFR−/ALK−*

	D arm n=316	PBO arm n=161
No. of events (%)	88 (27.8)	45 (28.0)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	0.98 (0.69–1.42)	
P-value (2-sided)	0.93	

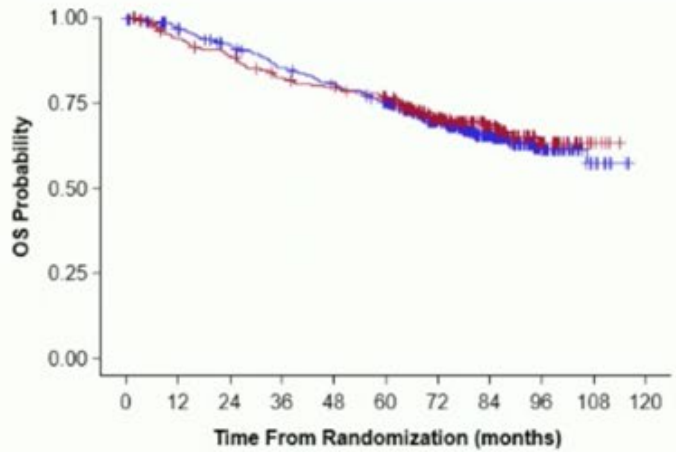


No. at risk:

D arm	316	301	286	266	256	237	172	100	40	6	0
PBO arm	161	147	140	129	126	121	84	44	20	4	0

PD-L1 ≥ 1% and *EGFR−/ALK−*

	D arm n=469	PBO arm n=240
No. of events (%)	149 (31.8)	72 (30.0)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	1.10 (0.83–1.47)	
P-value (2-sided)	0.52	

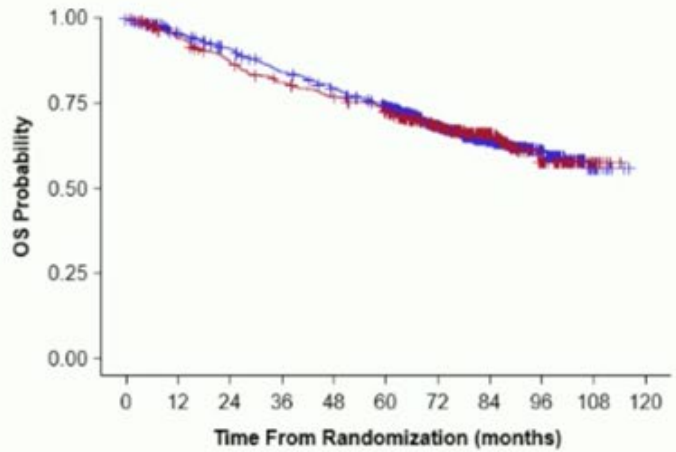


No. at risk:

D arm	469	439	409	378	356	326	236	133	58	10	0
PBO arm	240	219	205	188	181	173	123	66	30	5	0

PD-L1 All Comers and *EGFR−/ALK−*

	D arm n=815	PBO arm n=404
No. of events (%)	266 (32.6)	135 (33.4)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	1.00 (0.81–1.23)	
P-value (2-sided)	0.96	



No. at risk:

D arm	815	748	699	643	604	556	390	229	103	14	0
PBO arm	404	371	337	313	296	278	201	111	49	8	0

NR = not reached.

Panorama de adyuvancia actual

	Ensayo	IMpower010	BR.31
	Fármaco	Atezolizumab (anti–PD-L1)	Durvalumab (anti–PD-L1)
	Estadios incluidos	II–IIIA (IB ≥4 cm incluido inicialmente)	IB (≥4 cm)–IIIA
1	**Quimioterapia adyuvante**	**Obligatoria** en II–IIIA	**Opcional**
	Selección PD-L1	Análisis jerárquico (≥1%, mayor efecto ≥50%)	PD-L1 positivo (endpoint primario)
2	**DFS (resultado)**	**Positiva** \nHR ≈ **0.66** (PD-L1 ≥1%)	**Negativa** \nHR ≈ **1.0**
	OS (estado 2025)	**Inmadura** \nSin beneficio estadísticamente significativo	**Negativa / sin señal**
	Contexto biológico	Tumor “primado” tras QT obligatoria	Contexto heterogéneo
3	**Riesgo basal de recaída**	Alto (predominio II–IIIA)	Más bajo y heterogéneo
	Mensaje clave	IO adyuvante **puede funcionar** con buena selección	IO adyuvante **no aporta beneficio**

¿ La qt es necesaria ?

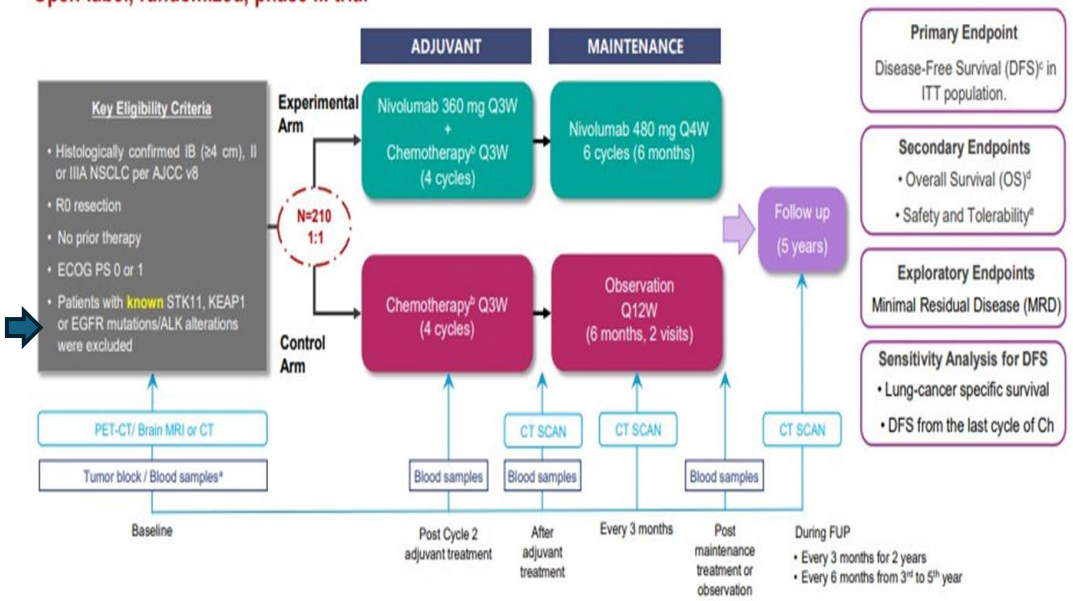
¿ Que pasaría si se iniciase la IO de forma precoz con la qt ?

Tto estándar en PDL1 >50% , en pacientes resecados

Primer Ec que evalua la QT mas lo en adyuvancia

NADIM ADJUVANT STUDY DESIGN

Open-label, randomized, phase III trial

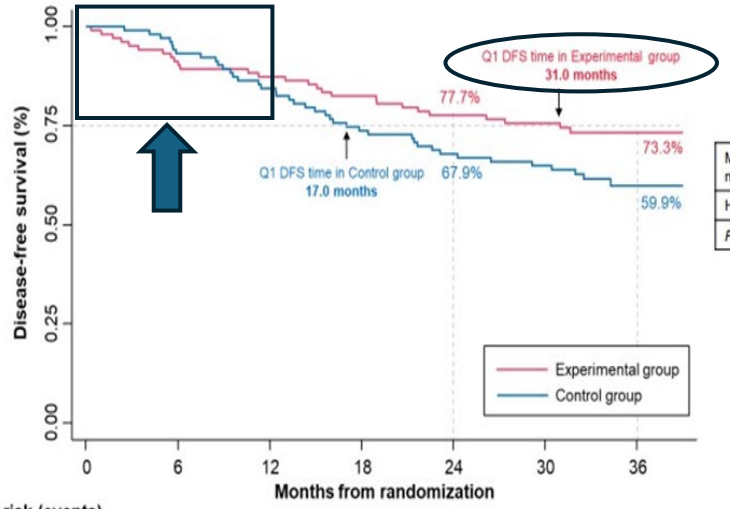


	Experimental arm N = 103	Control arm N = 103
Sex, male, n (%)	77 (74.8)	79 (76.7)
Age, mean (SD)	65.2 (8.9)	65.7 (7.6)
65 to 74 years, n (%)	42 (40.8)	50 (48.5)
≥ 75 years, n (%)	16 (15.5)	12 (11.7)
Min., max.,	40.0, 82.0	46.0, 83.0
Race, Caucasian, n (%)	102 (99)	99 (96.1)
ECOG Performance Status, n (%)		
0	53 (51.5)	58 (56.3)
Tobacco use history, n (%)		
Current/Former smoker	97 (94.2)	97 (94.2)
Any comorbidity, n (%)	99 (96.1)	95 (92.2)
Hypertension	52 (50.5)	39 (37.9)
Dyslipidemia	43 (41.7)	39 (37.9)
Mellitus Diabetes	17 (16.5)	27 (26.2)
COPD	31 (30.1)	25 (24.3)
PDL1, n (%)		
Done	80 (77.6)	89 (86.4)
Positive	51 (63.7)	50 (56.2)
1% – 49%	31 (60.8)	28 (56.0)
≥ 50%	20 (39.2)	22 (44.0)

	Experimental arm N = 103	Control arm N = 103
EGFR, n (%)		
Done	77 (74.8)	76 (73.8)
ALK, n (%)		
Done	55 (53.4)	62 (60.2)
KEAP1 and STK11, n (%)		
Done	2 (1.9)	8 (7.8)
Histology, n (%)		
Adenocarcinoma	65 (63.1)	67 (65)
Squamous	36 (35)	34 (33)
Pathological Stage, n (%)		
IB	3 (2.9)	3 (2.9)
IIA	15 (14.6)	6 (5.8)
IIB	47 (45.6)	53 (51.5)
IIIA	38 (36.9)	40 (38.8)
IIIB	0	1 (1)
Inclusion N Clinical Stage, n (%)		
N0	51 (49.5)	54 (52.4)
N1	35 (34.0)	32 (31.1)
N2	17 (16.5)	17 (16.5)
Type of surgery		
Lobectomy, n (%)	82 (79.6)	82 (79.6)
Pneumonectomy, n (%)	10 (9.7)	12 (11.7)

Provencio M, *et al. Nadim Adyuvant first interim analysis. IASCL 2025*

PRIMARY ENDPOINT: DISEASE-FREE SURVIVAL (DFS)



	Experimental (n=103)	Control (n=103)
Median DFS (95% CI), months	Not reached	Not reached
HR_{3years} (95% CI)	0.65 (0.40-1.07)	
P value	0.085[a]	

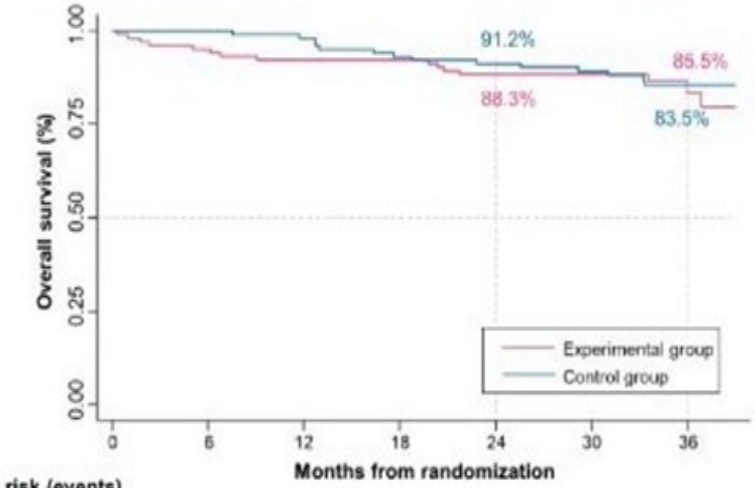
Median follow-up: 34.0 mo (IQR: 32.6-36.6)

Maturity data: 57%

Number at risk (events)

Experimental group	103	(9)	94	(4)	90	(5)	85	(5)	80	(2)	67	(2)	21
Control group	103	(7)	96	(9)	87	(11)	76	(6)	70	(3)	63	(4)	18

SECONDARY ENDPOINT: OVERALL SURVIVAL (OS)



	Experimental (n=103)	Control (n=103)
Median OS (95% CI), mo	Not reached	Not reached
HR_{3years} (95% CI)	0.99 (0.49-2.01)	
P value	0.981[a]	

Median follow-up: 34.0 mo (IQR: 32.6-36.6)

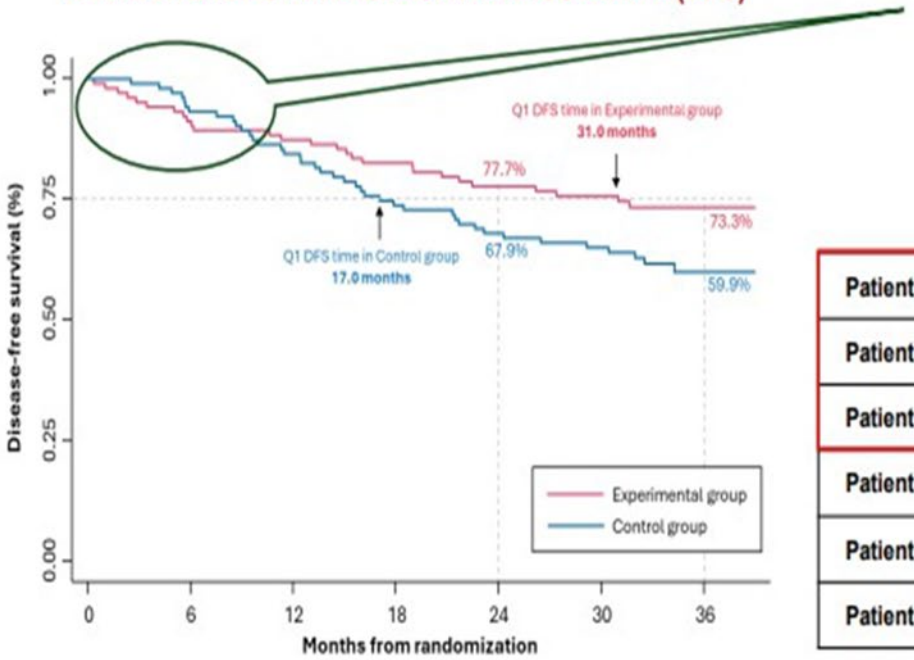
Maturity data: 57%

Number at risk (events)

Experimental group	103	(5)	98	(3)	95	(0)	95	(4)	91	(0)	78	(2)	26
Control group	103	(0)	102	(2)	100	(5)	95	(2)	93	(2)	87	(3)	29

Datos inmaduros

PRIMARY ENDPOINT: DISEASE-FREE SURVIVAL (DFS)



EARLY DEATHS IN EXPERIMENTAL ARM

	Experimental arm				
	Treatment related	Age (years)	OS (months)	Type of surgery	Cause of death
Patient #1	No	77	1.5	Minor resection	Acute coronary syndrome
Patient #2	No	74	2.5	Pneumonectomy Left	Myocardial infarction
Patient #3	No	69	2.5	Lobectomy	Cardiac arrest
Patient #4	No	63	5.4	Pneumonectomy Left	Pneumococcal sepsis
Patient #5	Yes	82	0.4	Lobectomy	Colitis complications
Patient #6	Yes	71	7	Lobectomy	Pneumonitis

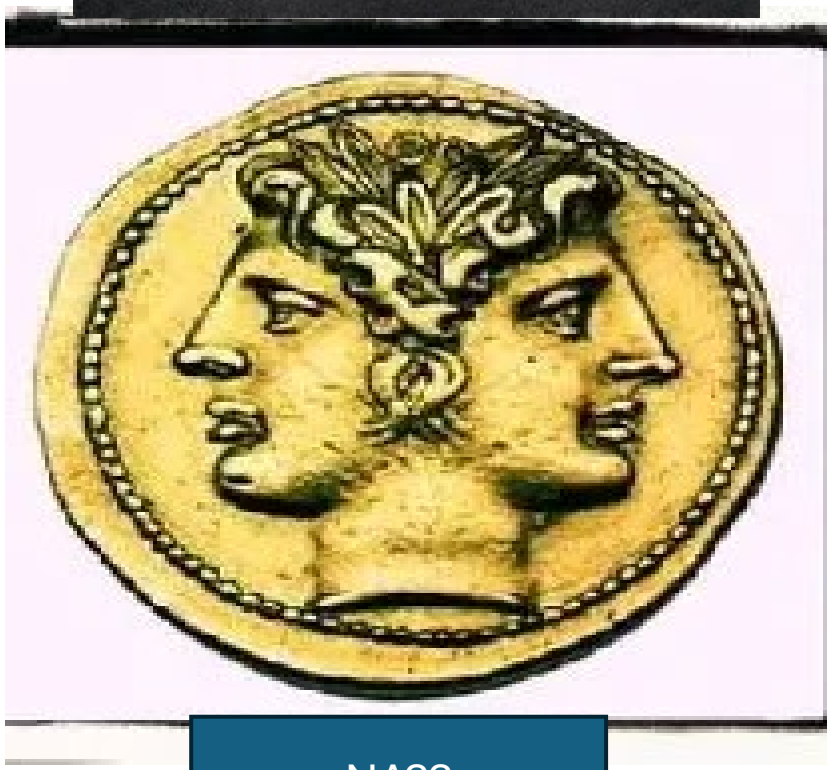
No datos de OS aun

ATEZO pdl1 >50%

¿Mayor control de recaída a costa de **toxicidad precoz?**

¿Y si la rama control fuese QT---IO (IMPOWER 010) ?

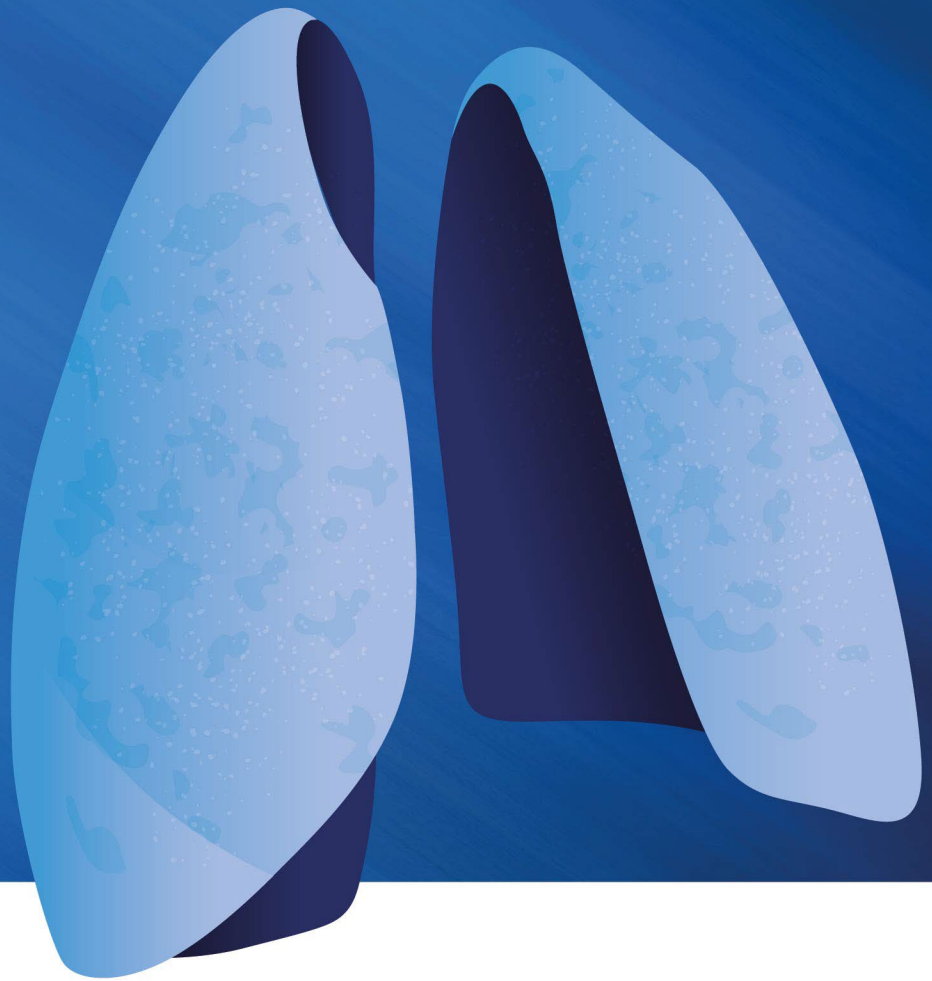
Perioperatorio ???



NA??

Adyuvancia ???

Y que pasa en este escenario con los drivers ???



NA : Neo Adaura /Alneo

Adyuvancia : ALINA

GECP lung cancer research

Enfermedad EGFR

2025 ASCO ANNUAL MEETING

Neoadjuvant osimertinib ± chemotherapy vs chemotherapy alone in resectable epidermal growth factor receptor-mutated (EGFRm) NSCLC: NeoADAURA

Jamie E. Chaft[1], Walter Weder, Jianxing He, Ke-Neng Chen, Maximilian J. Hochmair, Jin-Yuan Shih, Sung Yong Lee, Kang-Yun Lee, Nguyen Viet Nhung, Somcharoen Saeteng, Carlos H.A. Teixeira, Carles Escriu, Alex Martinez-Marti, Collin M. Blakely, Yasushi Yatabe, Sanja Dacic, Xiangning Huang, Yuri Rukazenkov, Anupriya Dayal, Masahiro Tsuboi

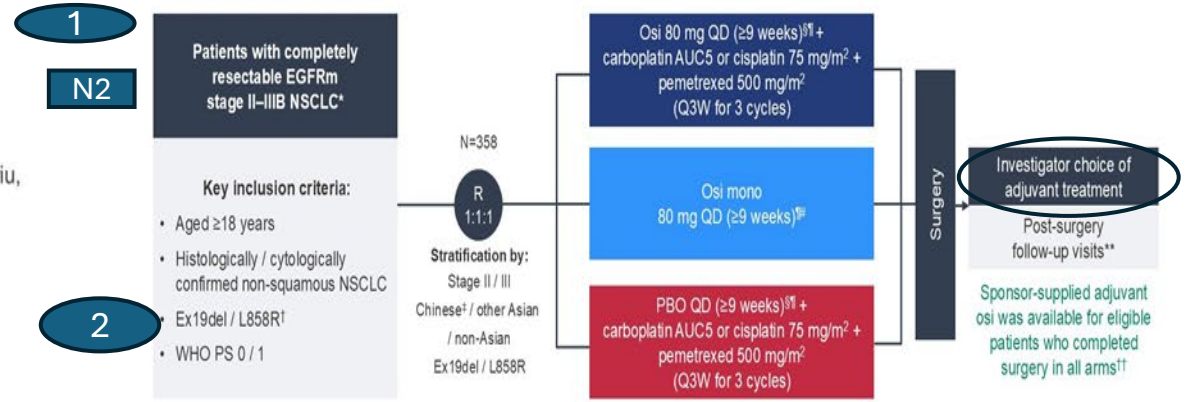
[1]Thoracic Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; Department of Medicine, Weill Cornell Medical College, New York, NY, USA

1 N2

2

3 ¿ Cuantos recibieron Osi adyuvante ?

NeoADAURA: global, randomized, Phase 3 controlled study



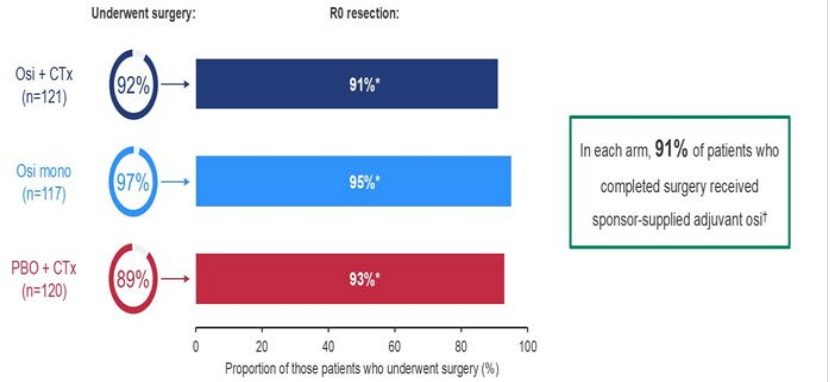
Endpoints:
- **Primary: major pathological response (MPR; by blinded central pathology review)**
- Secondary: event-free survival, pathological complete response, nodal downstaging and safety

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.

Chaft JE / He J et al. **NeoADAURA**. ASCO Annual Meeting 2025 (oral abstract).

Surgery summary

Misma tasa de cx en ambas ramas

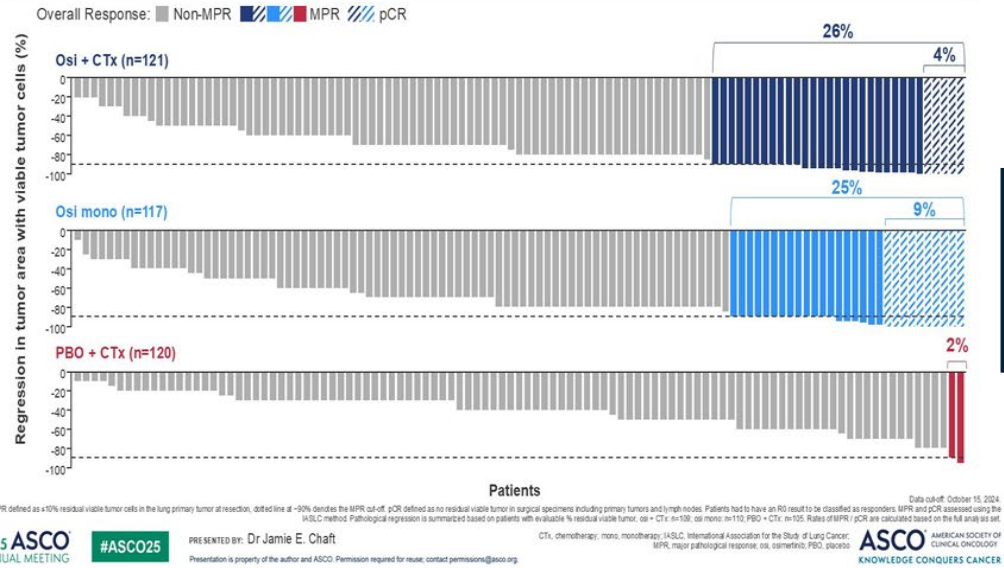


In each arm, **91%** of patients who completed surgery received sponsor-supplied adjuvant osi†

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

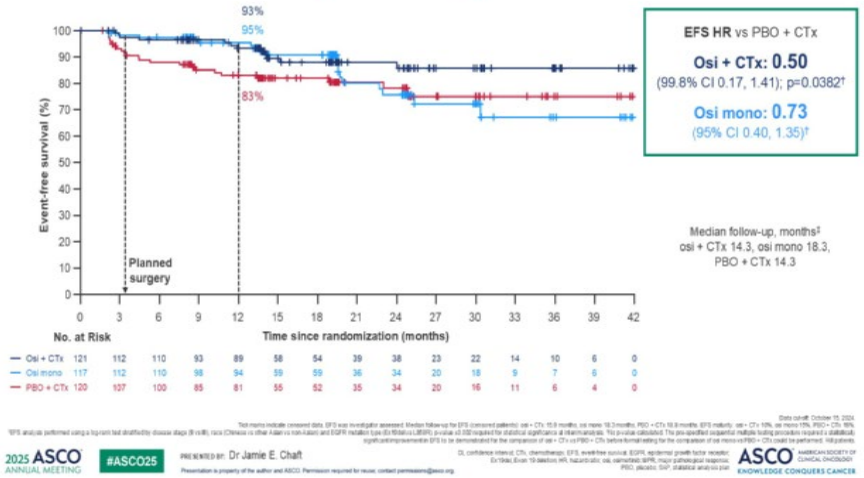
Depth of pathological response

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



MPR similar en ambas ramas de Osimertinib

Interim EFS analysis (15% maturity)



Conclusions

- Neoadjuvant osi, with or without CTx, demonstrated statistically significant improvement in MPR rates vs CTx alone (26% or 25% vs 2%) in resectable EGFRm stage II–IIIB NSCLC
- Interim EFS trends favored the osi-containing arms (osi + CTx HR 0.50; 99.8% CI 0.17, 1.41; osi mono HR 0.73; 95% CI 0.40, 1.35)
- Fewer patients with an MPR had an EFS event vs patients without an MPR (2% vs 18%)
- Over 50% of patients with baseline N2 disease were down-staged at surgery with osi-containing arms vs 21% with CTx alone
- Safety findings were consistent with the known profiles of the individual agents

Neoadjuvant osi, with or without CTx, should be considered when planning treatment for patients with resectable EGFRm stage II–IIIB NSCLC

Valor de combinación con QT ?

¿ Cambio de estándar ?

Chaft JE / He J et al. **NeoADAURA**. ASCO Annual Meeting 2025 (oral abstract).

Que nos aporta el Neoadaura …

Lo que sí aporta:
Confirma que, en EGFR resecable, una estrategia con **TKI neoadyuvante** puede generar **respuesta patológica relevante** y es **quirúrgicamente viable**

Lo que no resuelve todavía :
No es un ensayo diseñado para demostrar OS
¿Necesitamos quimioterapia añadida al osimertinib neoadyuvante?

¿ Cómo se integra con **adyuvancia osimertinib (ADAURA)**, porque en la vida real muchos pacientes recibirán adyuvancia?

Enfermedad ALK

2025 ASCO ANNUAL MEETING

GOIRC GRUPPO ONCOLOGICO ITALIANO DI RICERCA CLINICA

Alectinib as Neoadjuvant Treatment in Potentially Resectable Stage III ALK-positive NSCLC: Final Analysis of ALNEO Phase II Trial (GOIRC-01-2020-ML42316)

Alessandro Leonetti[1], Luca Boni[2], Letizia Gnetti[3], Diego Luigi Cortinovis[4], Giulia Pasello[5], Francesca Mazzoni[6], Alessandra Bearz[7], Francesco Gelsomino[8], Francesco Passiglia[9], Sara Pilotto[10], Giulio Metro[11], Angelo Delmonte[12], Fabiana Letizia Cecere[13], Federica Bertolini[14], Luca Toschi[15], Hector Soto Parra[16], Serena Ricciardi[17], Emilio Bria[18], Michele Tognetto[19], Marcello Tiseo[20]

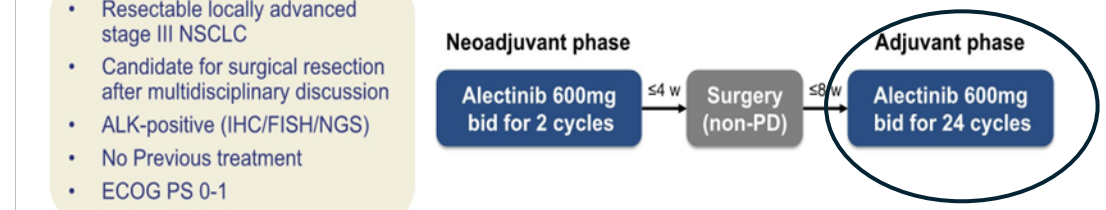
[1]Medical Oncology Unit, University Hospital of Parma, Parma, Italy; [2]Epidemiology Unit, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [3]Pathology Unit, University Hospital of Parma, Parma, Italy; [4]SC Oncologia medica Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy; Università degli Studi Milano-Bicocca, Milan, Italy; [5]Department of Surgery, Oncology and Gastroenterology, University of Padova Medical School; Medical Oncology 2, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy; [6]Medical Oncology Unit, Careggi University Hospital, Florence, Italy; [7]Department of Medical Oncology, CRO-IRCCS National Cancer Institute Aviano, Aviano, Italy; [8]Medical Oncology, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [9]Department of Oncology, University of Turin, San Luigi Hospital, Orbassano, Italy; [10]Section of Oncology, Department of Engineering for Innovative Medicine, University of Verona, Verona, Italy; [11]Division of Medical Oncology, Azienda Ospedaliera di Perugia, Santa Maria della Misericordia Hospital, Perugia, Italy; [12]Thoracic Oncology Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" (IRST), Meldola, Italy; [13]Medical Oncology 2, IRCCS Regina Elena National Cancer Institute Rome, Italy; [14]Oncology, Modena University Hospital, Modena, Italy; [15]Medical Oncology, IRCCS Humanitas Research Hospital, Rozzano, Italy; [16]Medical Oncology, Policlinico Vittorio Emanuele, Catania, Italy; [17]Pneumo-Oncology Unit, San Camillo-Forlanini Hospital, Rome, Italy; [18]UOSD Oncologia Toraco-Polmonare, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli IRCCS; Medical Oncology, Department of Translational Medicine and Surgery, Università Cattolica del Sacro Cuore, Rome, Italy; [19]Gruppo Oncologico Italiano di Ricerca Clinica, GOIRC, Parma, Italy; [20]Department of Medicine and Surgery, University of Parma; Medical Oncology Unit, University Hospital of Parma; Gruppo Oncologico Italiano di Ricerca Clinica, GOIRC, Parma, Italy.

2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Marcello Tiseo, MD, PhD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Study Design

- 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 (≤10% viable tumor) by BICR

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

Ancillary biological study[a]: correlation of tissue and cell-free biomarkers with MPR and DFS

According to the Simon's two-stage mini-max design, the null hypothesis that the MPR is ≤20% will be tested and will be rejected if 11 or more MPR are observed in 33 patients at the final analysis. This design yields a one-sided 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; MPR, Major Pathologic Response; ORR, Objective Response Rate; OS, Overall Survival; pCR, Pathologic Complete Response; PD, Progressive Disease

[a]tissue collection at diagnosis and surgery; plasma collection at baseline, after 4 and 8 weeks of neoadjuvant therapy, within 2 weeks of surgery, and at the time of recurrence

2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Marcello Tiseo, MD, PhD

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ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

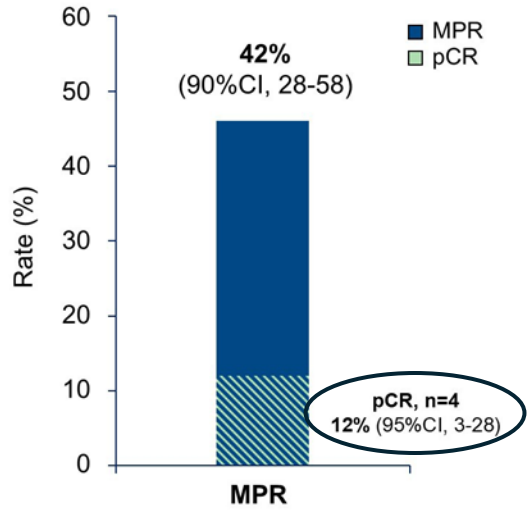
EC Fase II académico (no aleatorizado)

Final analysis of the ALNEO trial: neoadjuvant alectinib in resectable ALK-positive NSCLC. *ASCO Annual Meeting* ***2025***.

Results – Primary Endpoint: MPR by BICR

Pathologic Response	N=33
MPR (≤10% viable tumor), n (%)	14 (42)
Non-MPR (>10% viable tumor), n (%)	13 (40)
Not assessed, n (%)	6 (18)[a]

[a]5 patients did not undergo surgery, 1 patient underwent explorative thoracotomy



Abbreviations: CI, Confidence Interval; MPR, Major Pathologic Response; pCR, Pathologic Complete Response

Más del 90% llegan a cx

MPR solo en el 42%
pCR 12%

Prueba de concepto

No cambio de estándar

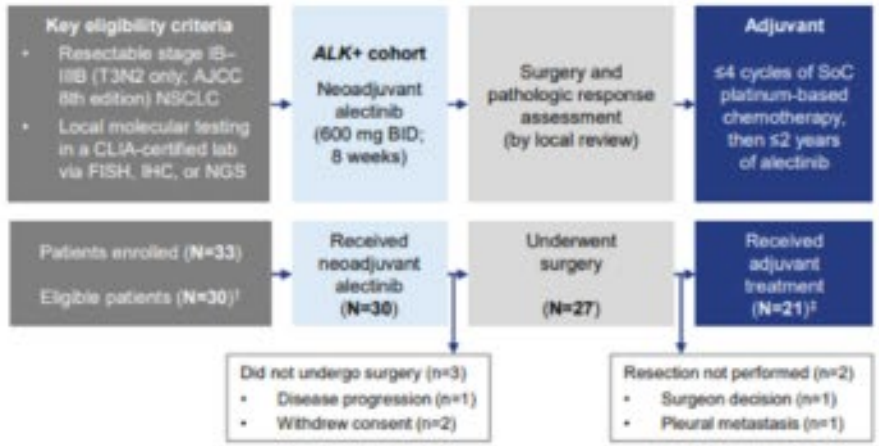
Conclusions

- ALNEO phase II trial met its primary endpoint with neoadjuvant alectinib in potentially resectable stage III ALK-positive NSCLC patients
  - **MPR 42%** (90%CI, 28-58); pCR 12% (95%CI, 3-28)
- The treatment was well-tolerated and the safety profile was consistent with previous alectinib studies
- With the limitation of a small phase II non-randomized trial, ALNEO study suggests alectinib as an active and feasible peri-operative option in resectable stage III ALK-positive NSCLC patients
- Molecular sub-study on tissue and liquid biopsies is ongoing

Selección molecualr en enf precoz

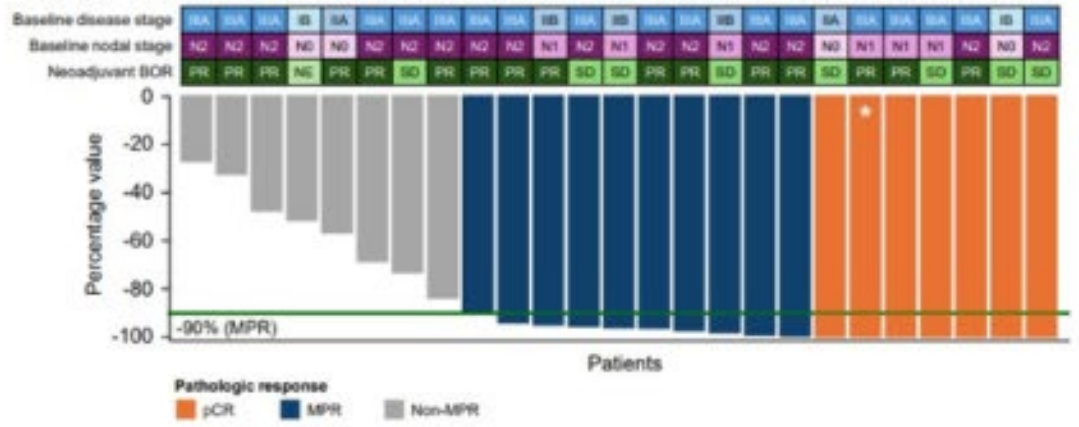
NAUTIKA1: Clinical Outcomes and Pathologic Regression with Neoadjuvant Alectinib in Resectable Stage IB–IIIB *ALK*+ NSCLC

- **NAUTIKA1** (NCT04302025) is a phase II umbrella study investigating targeted neoadjuvant treatments in patients with early-stage NSCLC harboring study-eligible oncogenic drivers[1]
- We present clinical and surgical outcomes for the ***ALK*+ cohort***



Pathologic and radiographic response

Weighted % viable tumor regression in the pathologic response analysis population (n=25)



n (%)	*ALK*+ cohort
Pathologic response (N=28)†	
MPR	17 (**60.7**)
pCR‡	7 (**25.0**)
Radiographic response§ (N=30)¶	
ORR	19 (**63.3**)
PR	19 (**63.3**)
SD	9 (**30.0**)
PD	1 (**3.3**)
NE	1 (**3.3**)

Conclusions

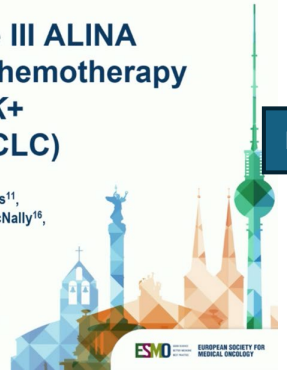
- Alectinib is globally approved in the adjuvant setting for patients with resected *ALK*+ NSCLC, based on results from the phase III ALINA study (NCT03456076)[1]
- The results presented here from the NAUTIKA1 study suggest there is a potential role for neoadjuvant alectinib alongside the ALINA regimen[1], as a promising perioperative approach for patients with resectable, stage IB–IIIB *ALK*+ NSCLC

BERLIN 2025 ESMO congress

Updated results from the phase III ALINA study of adjuvant alectinib vs chemotherapy in patients with early-stage *ALK*+ non-small cell lung cancer (NSCLC)

R. Dziadziuszko[1], B.J. Solomon[2], Y. Wu[3], J.S. Ahn[4], M. Nishio[5], D.H. Lee[6], J. Lee[7], W. Zhong[3], H. Horinouchi[8], W. Mao[9], M.J. Hochmair[10], F. de Marinis[11], M.R. Migliorino[12], I. Bondarenko[13], T. Xu[14], A. Cardona[15], A. Scalori[16], V. McNally[16], A.A. Higgerson[17], F. Barlesi[18]

[1]Department of Oncology & Radiotherapy and Early Phase Clinical Trials Centre, Medical University of Gdańsk, Gdańsk, Poland [2]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; [3]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China; [4]Department of Haematology & Oncology, Samsung Medical Centre, Seoul, Korea; [5]Department of Thoracic Medical Oncology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; [6]Department of Oncology, Asan Medical Centre, Seoul, Korea; [7]Division of Haematology and Medical Oncology, Seoul National University Bundang Hospital, Seongnam, Korea; [8]Department of Thoracic Oncology, National Cancer Centre Hospital, Tokyo, Japan; [9]Department of Thoracic surgery, Institute of Basic Medicine and Cancer, Chinese Academy of Sciences, Zhejiang, China; [10]Department of Respiratory & Critical Care Medicine, Klinik Floridsdorf, Karl-Landsteiner-Institute for Lung Research and Pulmonary Oncology, Vienna, Austria; [11]Department of Thoracic Oncology, European Institute of Oncology (IRCSS), Milan, Italy; [12]Department of Oncology, San Camillo Forlanini Hospital, Rome, Italy; [13]Oncology And Medical Radiology Department, Dnipropetrovsk Medical Academy, Dnipro, Ukraine; [14]Department of Clinical Science, Roche (China) Holding Ltd, Shanghai, China; [15]Data and Statistical Sciences, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]PD Oncology, Roche Products Ltd, Welwyn Garden City, United Kingdom; [17]PD Safety, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [18]Department of Medical Oncology, International Centre for Thoracic Cancers (CICT), Villejuif, France



No N2

Key eligibility criteria:
- Resected stage IB (≥4cm)–IIIA *ALK*+ NSCLC per UICC/AJCC 7th edition
- ECOG PS 0–1
- No prior systemic cancer therapy

R 1:1

N=257

Alectinib 600 mg BID 2 years → Recurrence

Platinum-based chemotherapy* Q3W; 4 cycles → Recurrence

Further treatments at investigator's choice and survival follow-up

Stratification factors:
- Stage: IB (≥ 4cm) vs II vs IIIA
- Race: Asian vs non-Asian†

Primary endpoint
- DFS per investigator tested hierarchically: Stage II–IIIA → stage IB–IIIA (ITT)

Other endpoints
- CNS-DFS, OS, safety

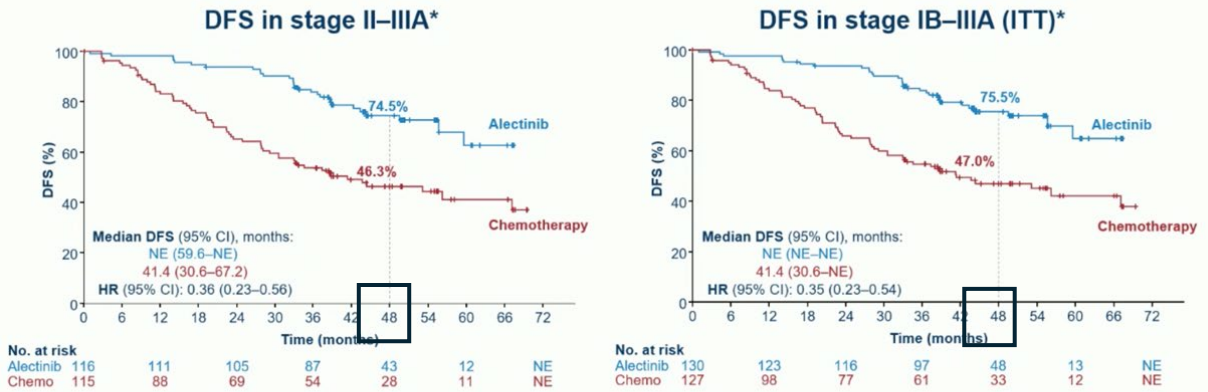
Here, we present updated data from the ALINA study with a median follow-up of 4 years
All patients in the alectinib arm had completed 2 years of treatment with ≥1 year of follow-up

CAMBIO DE ESTÁNDAR

Patient demographics and baseline characteristics (ITT)

Characteristic[1,2]	Alectinib (n=130)	Chemotherapy (n=127)
Median age <65 / ≥65 years, %	54 years 79 / 21	57 years 73 / 27
Sex: female / male, %	58 / 42	46 / 54
Smoking status: never / former / current, %	65 / 32 / 4	55 / 43 / 2
Race: Asian / non-Asian, %	55 / 45	56 / 44
ECOG PS: 0 / 1, %	55 / 45	51 / 49
Stage at diagnosis per AJCC 7th edition: IB / II / IIIA, %	11 / 36 / 53	9 / 35 / 55
Stage at diagnosis per AJCC 8th edition: IB* / IIA / IIB / IIIA / IIIB, %	5 / 8 / 31 / 51 / 5	4 / 3 / 35 / 54 / 5
Nodal status: N0 / N1 / N2, %	16 / 35 / 49	14 / 34 / 52
Histology: squamous / non-squamous, %	5 / 95	2 / 98
Surgical procedure: Lobectomy / other†, %	97 / 3	92 / 8

Disease-free survival



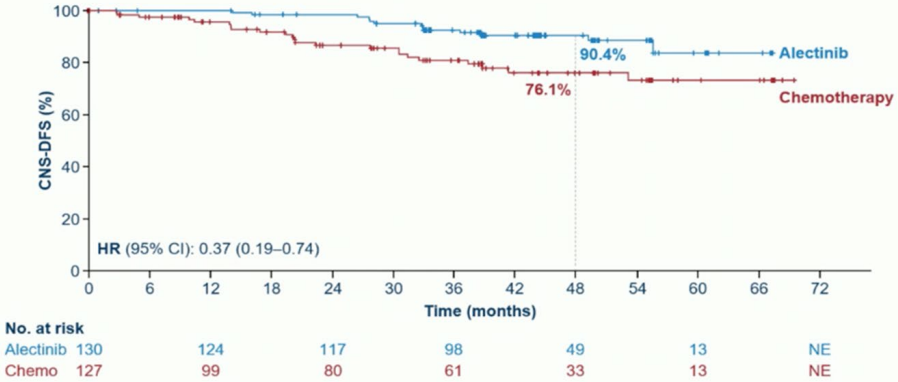
Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

DFS benefit was sustained with alectinib versus chemotherapy in the stage II–IIIA and stage IB-IIIA (ITT) populations

Data cut-off: 8 December 2024. DFS defined as the time from randomisation to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurred first. *Per UICC/AJCC 7th edition. Chemo, chemotherapy; NE, not estimable

Prof. Rafal Dziadziuszko

CNS disease-free survival (ITT)



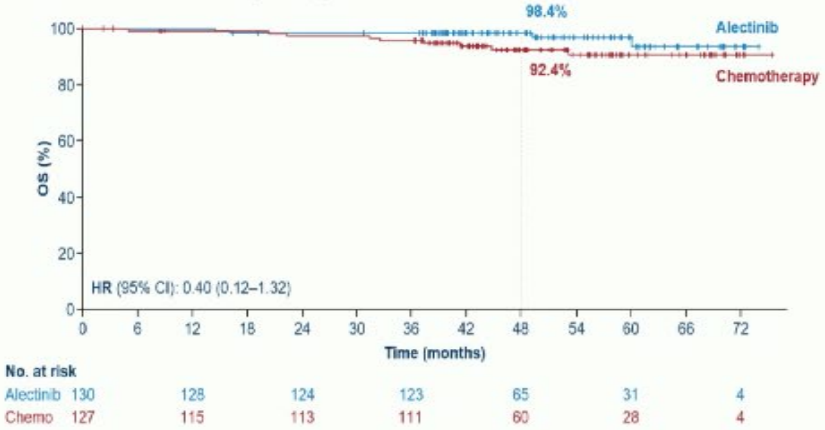
Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

A clinically meaningful CNS-DFS benefit was maintained in the IB–IIIA* (ITT) population

Prof. Rafal Dziadziuszko

Data cut-off: 8 December 2024. CNS-DFS defined as time from randomisation to the first documented recurrence of disease in the CNS or death from any cause, whichever occurred first. *Per UICC/AJCC 7th edition

Overall survival (ITT)



Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

In the IB–IIIA* (ITT) population, there was a positive trend in OS with 4 years of median follow-up

Prof. Rafal Dziadziuszko

Data cut-off: 8 December 2024. *Per UICC/AJCC 7th edition

Post-recurrence subsequent therapy

Number of patients with disease recurrence, n (%)	Alectinib (n=31)	Chemotherapy (n=60)
Number of patients with any subsequent therapy	24 (77.4)	55 (91.7)
Systemic therapy	24 (77.4)	51 (85.0)
ALK TKI	19 (61.3)	49 (81.7)
Alectinib	8 (25.8)	35 (58.3)
Brigatinib	7 (22.6)	8 (13.3)
Lorlatinib	7 (22.6)	6 (10.0)
Crizotinib	1 (3.2)	4 (6.7)
Ceritinib	1 (3.2)	2 (3.3)
Chemotherapy	9 (29.0)	3 (5.0)
Immunotherapy	1 (3.2)	1 (1.7)
Other anti-cancer therapy	2 (6.5)	2 (3.3)
Radiotherapy	8 (25.8)	10 (16.7)
Surgery	2 (6.5)	3 (5.0)

After recurrence, most patients received treatment with an *ALK*-TKI, of which alectinib was most widely used

Prof. Rafal Dziadziuszko

Data cut-off: 8 December 2024. TKI, tyrosine kinase inhibitor

BERLIN 2025 ESMO congress

Ensartinib as adjuvant therapy in patients with stage IB–IIIB ALK-positive (ALK+) non-small cell lung cancer (NSCLC) after complete tumor resection: the phase III randomized ELEVATE trial

Dongsheng Yue[1], Meijuan Huang[2], Pingping Song[3], Yuejun Chen[4], Bin Li[5], Junke Fu[6], Jianji Guo[7], Chao Cheng[8], Qixun Chen[9], Shidong Xu[10], Hongxu Liu[11], Fang Lv[12], Jian Hu[13], Ke Jiang[14], Weimin Mao[15], Feng Ye[16], Bo Shen[17], Lieming Ding[18], You Lu[2], Changli Wang[1]

[1]Tianjin Medical University Institute & Hospital, Tianjin, China; [2]West China Hospital, Sichuan University, Chengdu, China; [3]Shandong Cancer Hospital and Institute, Jinan, China; [4]Hunan Cancer Hospital, Changsha, China; [5]The Second Hospital & Clinical Medical School, Lanzhou University, Lanzhou, China; [6]The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China; [7]The First Affiliated Hospital of Guangxi Medical University, Nanning, China; [8]The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [9]Zhejiang Cancer Hospital, Hangzhou, China; [10]Harbin Medical University Cancer Hospital, Harbin, China; [11]Liaoning Cancer Hospital & Institute, Dalian, China; [12]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [13]The First Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China; [14]Union Hospital Tongji Medical College Huazhong University of Science and Technology, Wuhan, China; [15]Jiangxi Cancer Hospital, Nanchang, China; [16]The First Affiliated Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China; [17]Jiangsu Cancer Hospital, Nanjing, China; [18]Betta pharmaceuticals Co., Ltd., Hangzhou, China

Study design

Randomized, double-blind phase III trial (data cutoff for interim analysis: 6/26/2025)

Key Inclusion Criteria:
- Age ≥18 years
- Completely resected (R0), histologically confirmed stage IB, II, IIIA or IIIB (T3N2M0) NSCLC per the 8th edition of AJCC/UICC
- Adjuvant chemotherapy permitted
- ECOG PS 0-1
- Confirmed positive ALK

Stratification by
- **Histological stage** (IB vs. II vs. III)
- **Prior adjuvant chemotherapy** (yes vs. no)

Ensartinib 225 mg once daily

Randomization (1:1) N=270

Placebo once daily

Preplanned treatment duration: 2 years

Treatment until:
- Disease recurrence
- Treatment completed
- Met the discontinuation criteria

Follow-up:
Baseline and every 12 weeks for the first 2 years, and then every 24 weeks annually until the occurrence of disease recurrence

Primary endpoint: Investigator-assessed DFS* in patients with stage II to IIIB disease

Secondary endpoints: Investigator-assessed DFS in patients with stage IB-IIIB disease (ITT), 3/5-year DFS rate, OS, safety

Statistical analysis:
- This preplanned interim analysis was performed when 70% of events (57 events) were observed in patients with stage II-IIIB disease.

*Defined as the time from randomization to disease recurrence or death from any cause.
AJCC: American Joint Committee on Cancer; DFS, disease-free survival; ECOG PS: Eastern Cooperative Oncology Group performance-status; ITT: Intention-to-Treat Population; UICC: Union for International Cancer Control

Dr. Dongsheng Yue

Baseline characteristics (ITT)

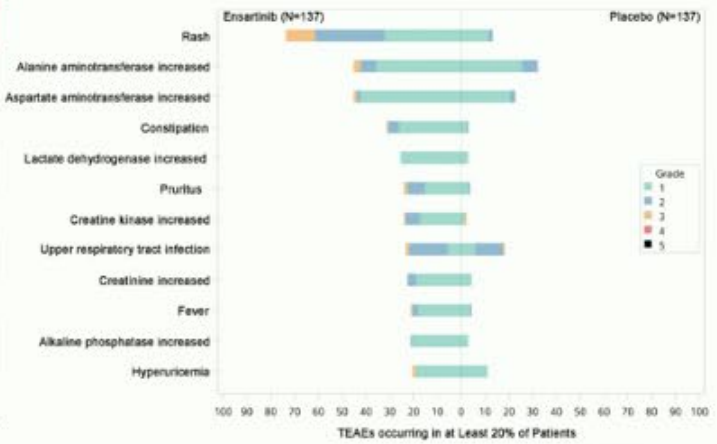
Characteristics	Ensartinib (n=137)	Placebo (n=137)
Median age	55 years	54 years
<65/≥65 years, %	84.7/15.3	86.9/13.1
Sex: female/male, %	66.4/33.6	61.3/38.7
ECOG PS: 0/1, %	54.7/45.3	62.8/37.2
Smoking status: never/former/current,%	83.9/15.3/0.7	79.6/19.7/0.7
Stage*: IB/II/III[&], %	24.8/34.3/40.9	25.5/33.6/40.9
Prior chemotherapy: yes/no, %	68.6/31.4	70.8/29.2

*The histological stage was classified according to the 8th edition of the Cancer Staging Manual of the AJCC/UICC.
[&]The stage III included IIIA and IIIB.

Safety summary

- At least one treatment-emergent adverse event (TEAE) was reported by 98.5% in the ensartinib arm and 92.0% in the placebo arm.
- The majority were grade 1 or 2 events.
- One grade 5 (fatal) TEAE (cerebral hemorrhage) was reported in the ensartinib arm but was not ensartinib-related.

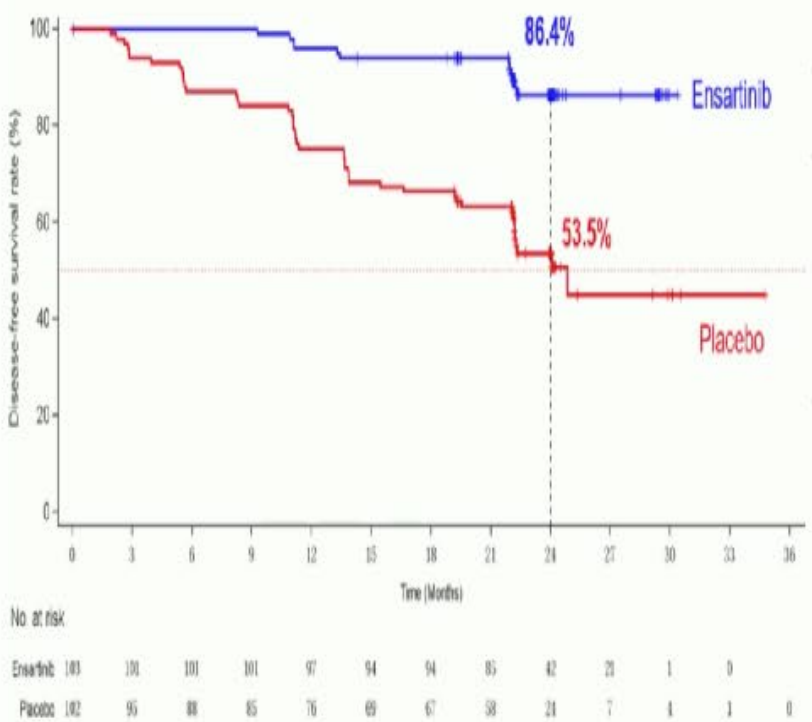
	Ensartinib (n=137)	Placebo (n=137)
Median duration of treatment	22.1 months	17.1 months
Any TEAEs, %	135 (98.5)	126 (92.0)
Grade 3-4	48 (35.0)	23 (16.8)
Grade 5	1 (0.7)	2 (1.5)
SAEs, %	25 (18.2)	14 (10.2)
TEAE leading to dose reduction, n (%)	41 (29.9)	2 (1.5)
TEAE leading to dose interruption, n (%)	48 (35.0)	20 (14.6)
TEAE leading to dose discontinuation, n (%)	3 (2.2)	2 (1.5)



Dr. Dongsheng Yue

Ensartinib showed an improved DFS in patients with II-IIIB disease

Investigator-assessed DFS

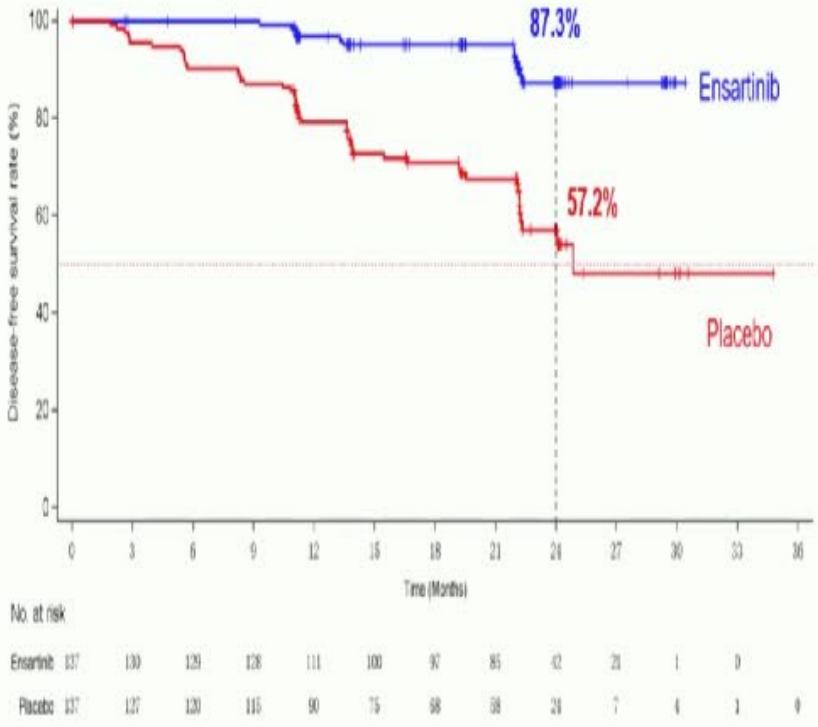


	Ensartinib (n=103)	Placebo (n=102)
Median follow-up	24.0 months	24.0 months
Events	12 (11.7%)	46 (45.1%)
Median DFS, months (95% CI)	NE (NE, NE)	24.8 (22.2, NE)
DFS HR (95% CI)	0.20 (0.11, 0.38), p<0.0001	

Datos prometedores pero inmaduros

Ensartinib showed an improved DFS in patients with IB-IIIB disease

Investigator-assessed DFS



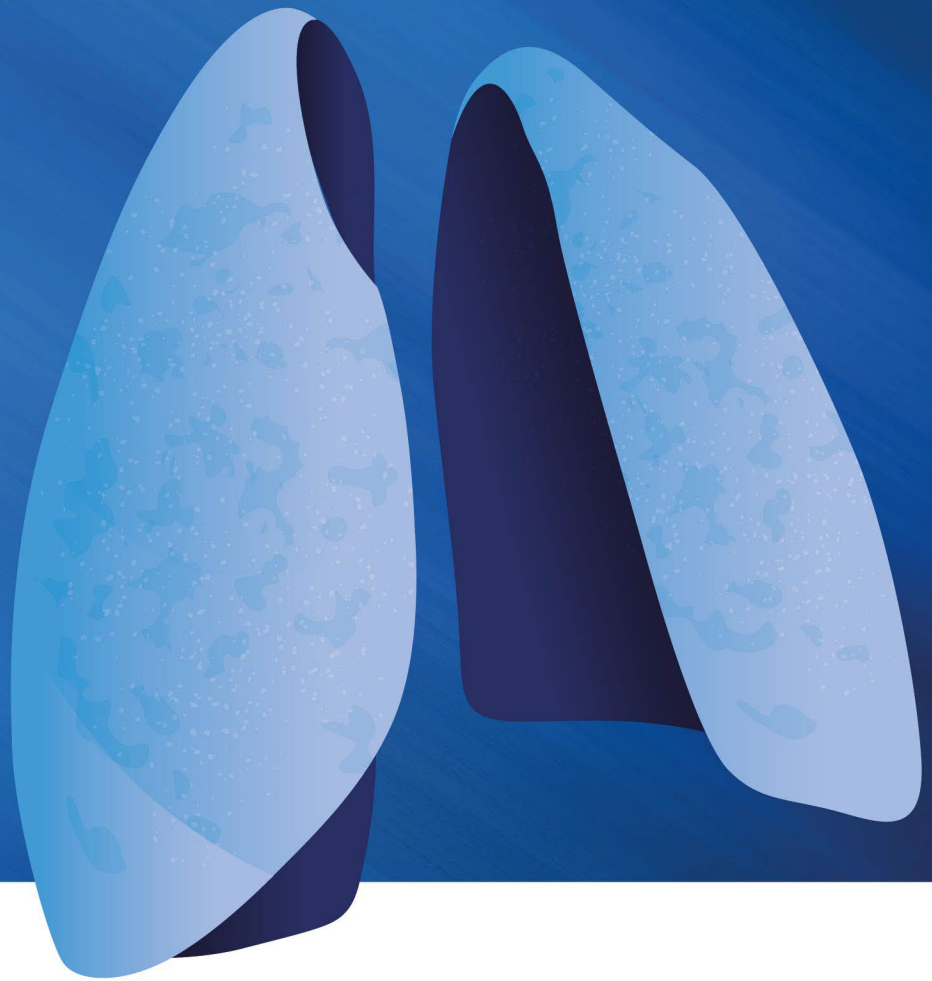
	Ensartinib (n=137)	Placebo (n=137)
Median follow-up	22.2 months	22.1 months
Events	12 (8.8%)	48 (35.0%)
Median DFS, months (95% CI)	NE (NE, NE)	24.8 (22.2, NE)
DFS HR (95% CI)	0.20 (0.10, 0.37), p<0.0001	

¿Añadimos en este escenario la QT ?
Ya tenemos un estudio positivo sin QT

Como esta el panorama

EC ALINA Adyuvancia con ALK

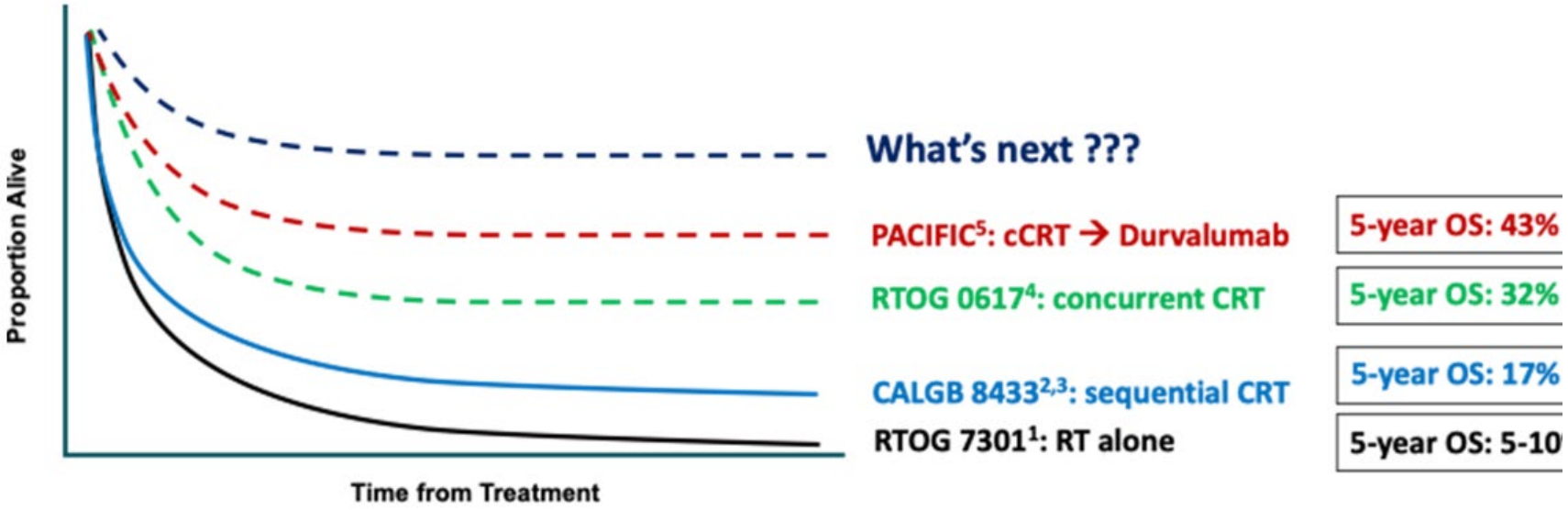
NeoADUARA ni ALNEO



ESTADIO III IRRESECABLE

GeCP
lung cancer research

¿ Que hay mas allá del PACIFIC ?

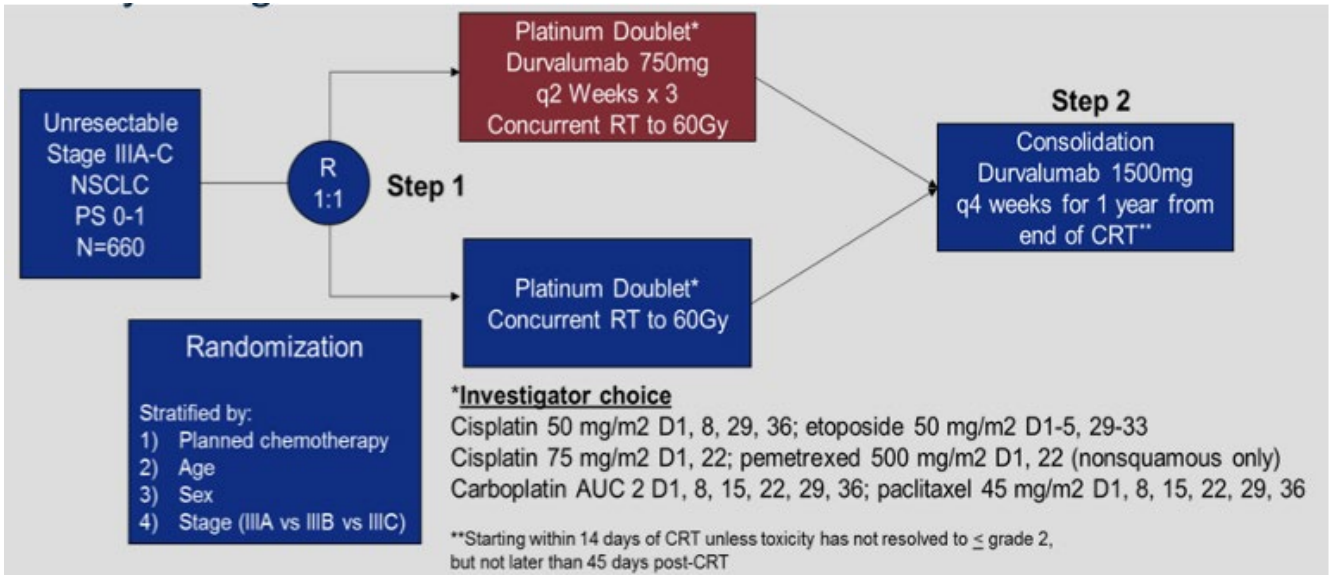


Nuevas estrategias exploradas

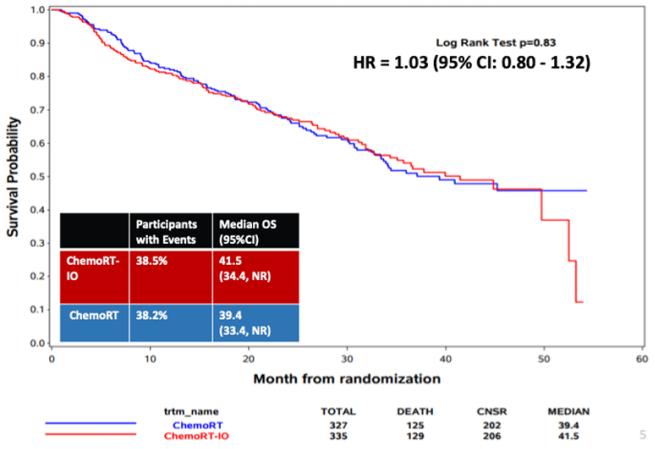
, Cancer 1982; 2. Dilman, NEJM 1990; 3. Dilman, JNCI 1996; 4. Bradley, JCO 2021; 5. Spigel, JCO 2022

ECOG-ACRIN EA5181: Phase 3 Trial of Concurrent and Consolidative Durvalumab vs Consolidation Durvalumab Alone for Unresectable Stage III NSCLC

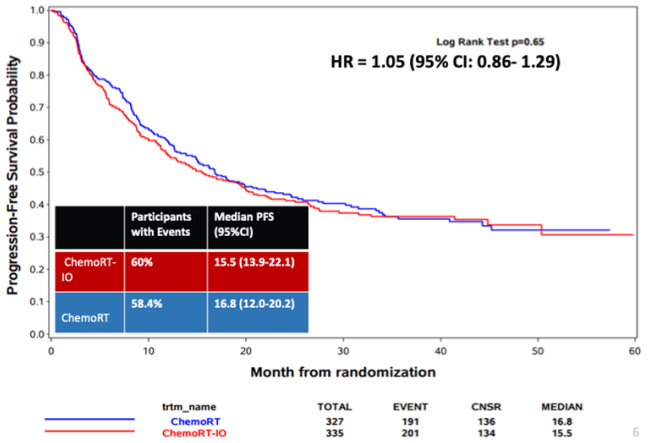
EC negativo , consolida la estrategia PACIFIC



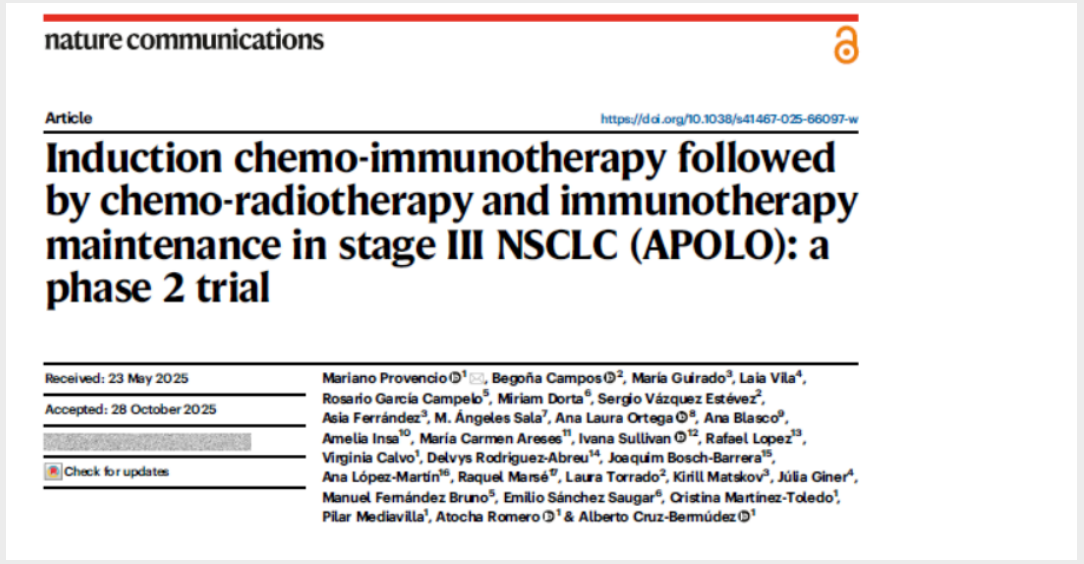
Overall Survival



Progression Free Survival



Fundación GECP lung cancer research



nature communications

Article

https://doi.org/10.1038/s41467-025-66097-w

Induction chemo-immunotherapy followed by chemo-radiotherapy and immunotherapy maintenance in stage III NSCLC (APOLO): a phase 2 trial

Received: 23 May 2025

Accepted: 28 October 2025

Check for updates

Mariano Provencio[1], Begoña Campos[2], María Guirado[3], Laia Vila[4], Rosario García Campelo[5], Miriam Dorta[6], Sergio Vázquez Estévez[2], Asia Ferrández[3], M. Ángeles Sala[7], Ana Laura Ortega[8], Ana Blasco[9], Amelia Insa[10], María Carmen Areses[11], Ivana Sullivan[12], Rafael Lopez[13], Virginia Calvo[1], Delvys Rodriguez-Abreu[14], Joaquim Bosch-Barrera[15], Ana López-Martín[16], Raquel Marsé[17], Laura Torrado[2], Kirill Matskov[3], Júlia Giner[4], Manuel Fernández Bruno[5], Emilio Sánchez Saugar[6], Cristina Martínez-Toledo[1], Pilar Mediavilla[1], Atocha Romero[1] & Alberto Cruz-Bermúdez[1]

¿ Nueva estrategia ?

CONCLUSIONES

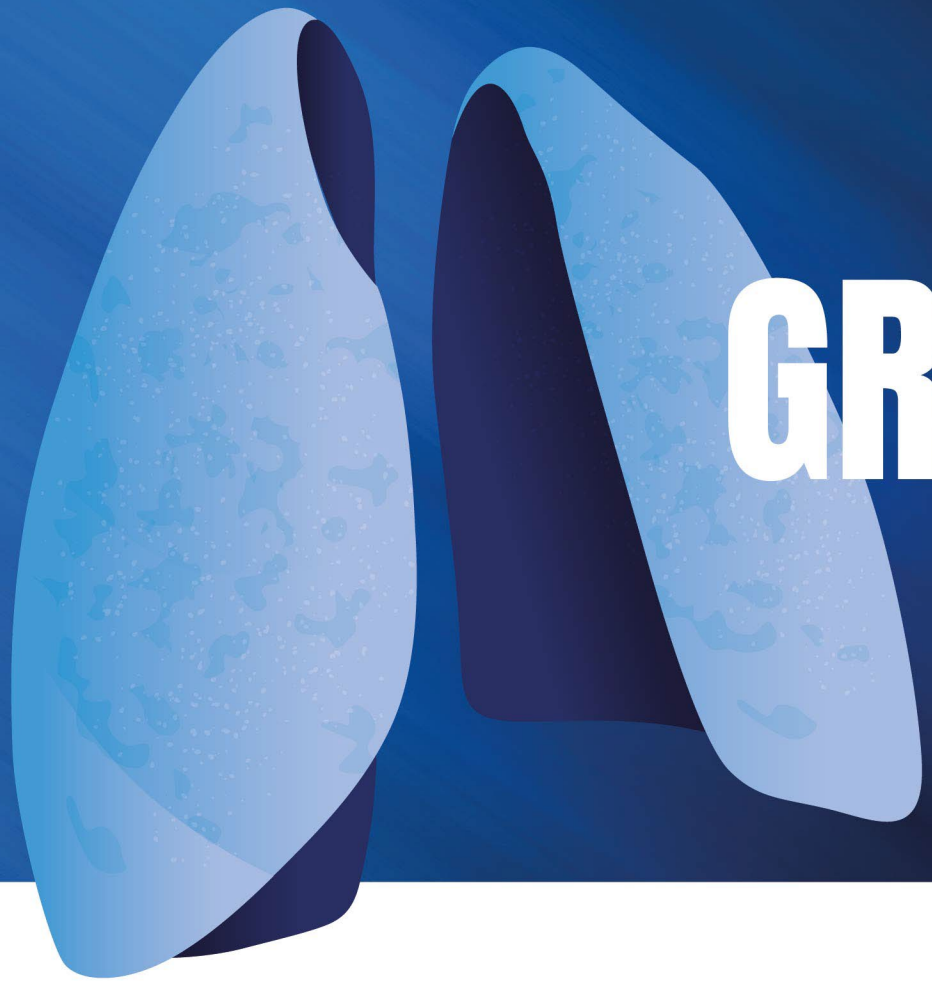
NA con IO es un hecho

En la enf localizada hay que buscar driver

Periadyuvancia es el futuro

Estrategia de intensifiacion de PACIFIC ha fracaso

Propósito de año nuevo



GRACIAS

GeCP
lung cancer
research