Novedades & Claves en CÁNCER de PULMÓN 2025

Haga clic para modificar el estilo de texto del patrón

Conclusiones

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GECP lung cancer research

Biomarkers

Integrated prognostic model and artificial intelligence

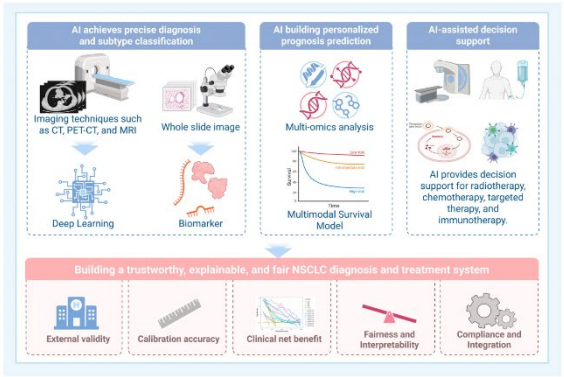


Figure 1 AI-enabled NSCLC pathway for precise diagnosis, personalized prognosis and clinical decision support

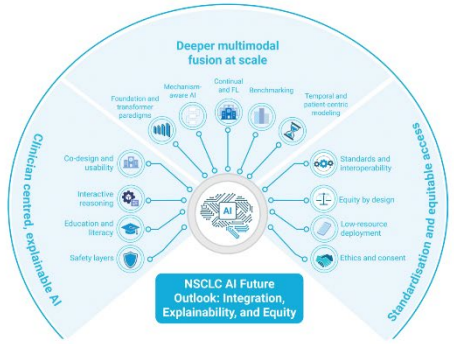
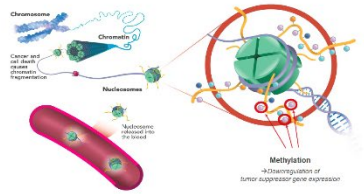


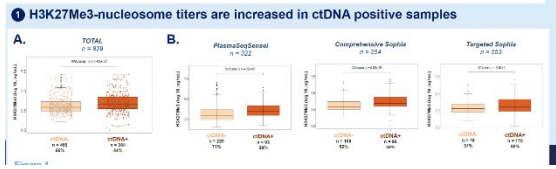
Figure 5 NSCLC AI Future Outlook: Integration, Explainability, and Equity

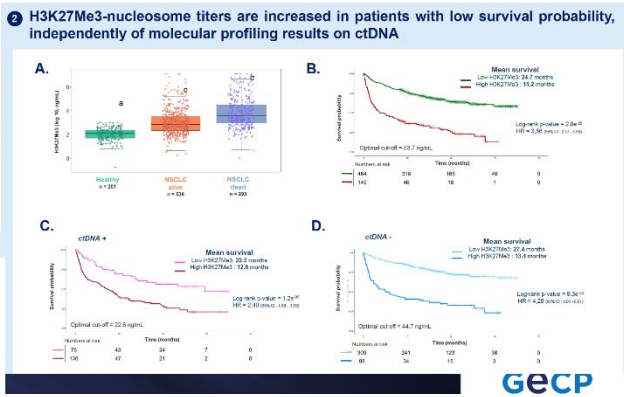
Host-immune based and genomic prognostic biomarkers

H3K27Me3-nucleosome is a strong prognostic biomarker in NSCLC: interim results from the analysis of up to 832 patients at baseline

- ✓ Epigenetic modifications of nucleosomes play a crucial role in gene expression and are commonly dysregulated in tumors (Scheme 1).Aberrant levels of methylated nucleosomes in plasma have already been reported in lung cancer (Grolleau et al., 2023)
- ✓ To evaluate the complementarity of ctDNA molecular profiling and H3K27Me3-nucleosome titers in the prediction of NSCLC patients' outcome at diagnosis.







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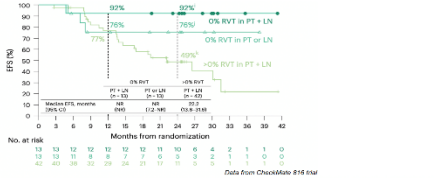
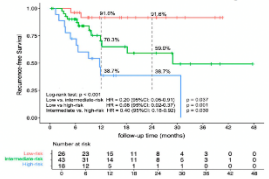
Clinical and pathological biomarkers

Prognostic value of residual viable tumor in lymph nodes of non-small cell lung cancer after neoadjuvant chemoimmunotherapy

- ✓ MPR definition differ among trials: CM-816 (≤ 10% residual tumor in primary tumor and lymph nodes) vs. AEGEAN (no nodal assessment.



- The **low-risk group** demonstrated significantly improved RFS than the **intermediate-risk group**, and the latter had better outcomes than the **high-risk group**.

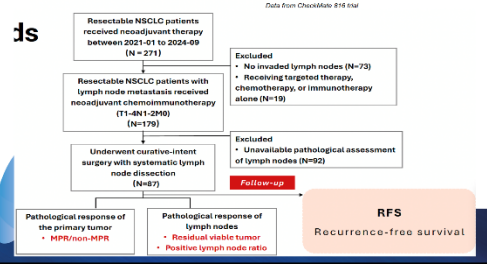


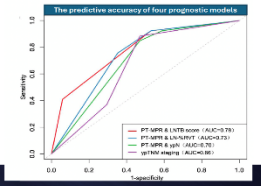
PT-MPR & LNTB-score

- Low-risk
- Intermediate-risk
- High-risk

pairwise log-rank p values

	Low-risk	Intermediate-risk
Intermediate-risk	0.024	-
High-risk	<0.001	0.024

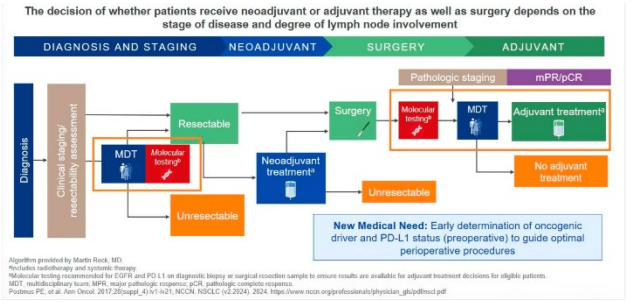




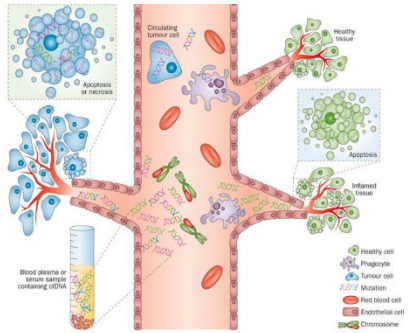
Han T et al WLCC 2025

GECP lung cancer research

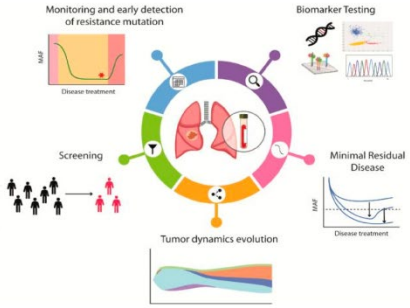
Key Trends in Lung Cancer Biomarkers for 2025



- ✓ Multi-omics Integration
  - ✓ Combining genomics + proteomics + transcriptomics + TME (microenvironment)
- ✓ Liquid Biopsies
  - ✓ Non-invasive diagnosis
  - ✓ Response monitoring
  - ✓ Early detection of therapeutic resistance
- ✓ Expanding Clinical Panels
  - ✓ RET, NTRK, BRAF, and MET
- ✓ AI Applied to Biomarkers
  - ✓ Validation and clinical deployment of complex biological signals
- ✓ From Diagnosis to Prognosis/Monitoring
  - ✓ Monitor tumor dynamics and predict disease progression



Crowley, E. et al. (2013) Nat. Rev. Clin. Oncol.



Romero, A et al. Curr Treat Options Oncol. 2021 Aug 23;22(10):86.

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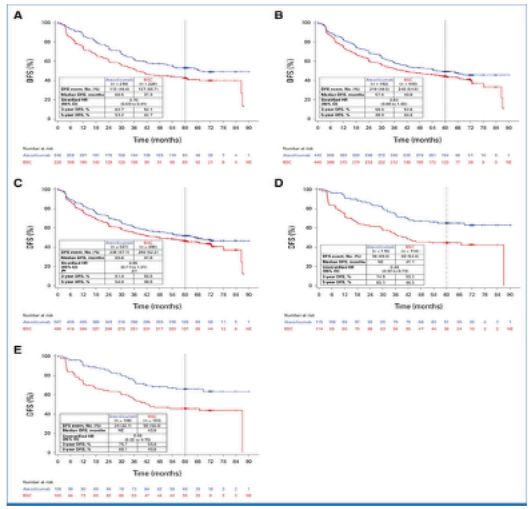
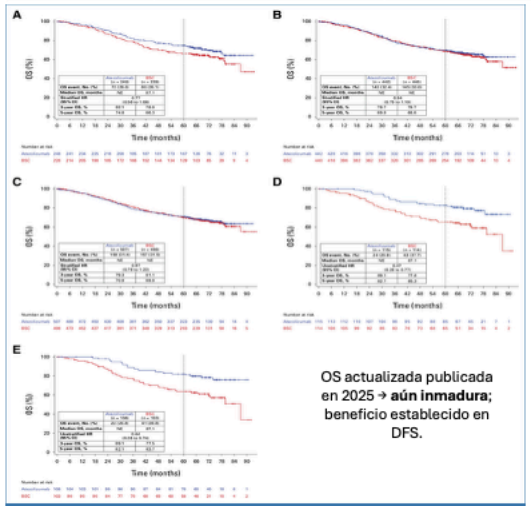
Adjuvant Treatment

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

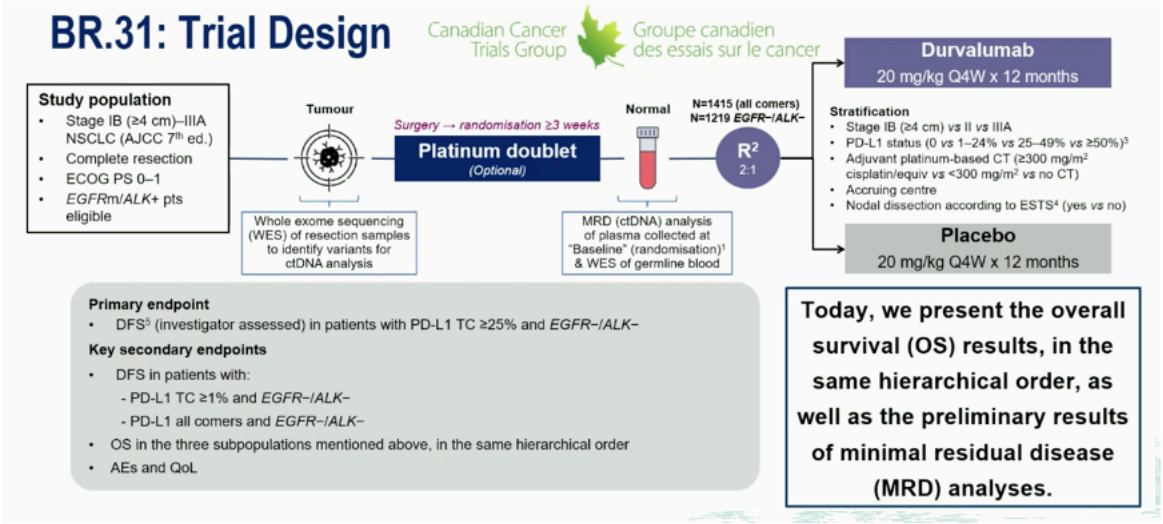


	SLE	SG
ITT	0.85 (95% CI, 0.71 to 1.01; *P* = .07)	0.97 (95% CI, 0.78 to 1.22)
Estadio II-III-A	HR: 0.83 (95% CI, 0.69 to 1.00)	0.94 (95% CI, 0.75 to 1.19)
Estadio II-III-A PD-L1 ≥ 1%	HR: 0.70 (95% CI, 0.55 to 0.91	0.77 (95% CI, 0.56 to 1.06)
Estadio II-III-A PD-L1 ≥ 50% (EGFR/ALK wt)	HR: 0.49 (95% CI,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



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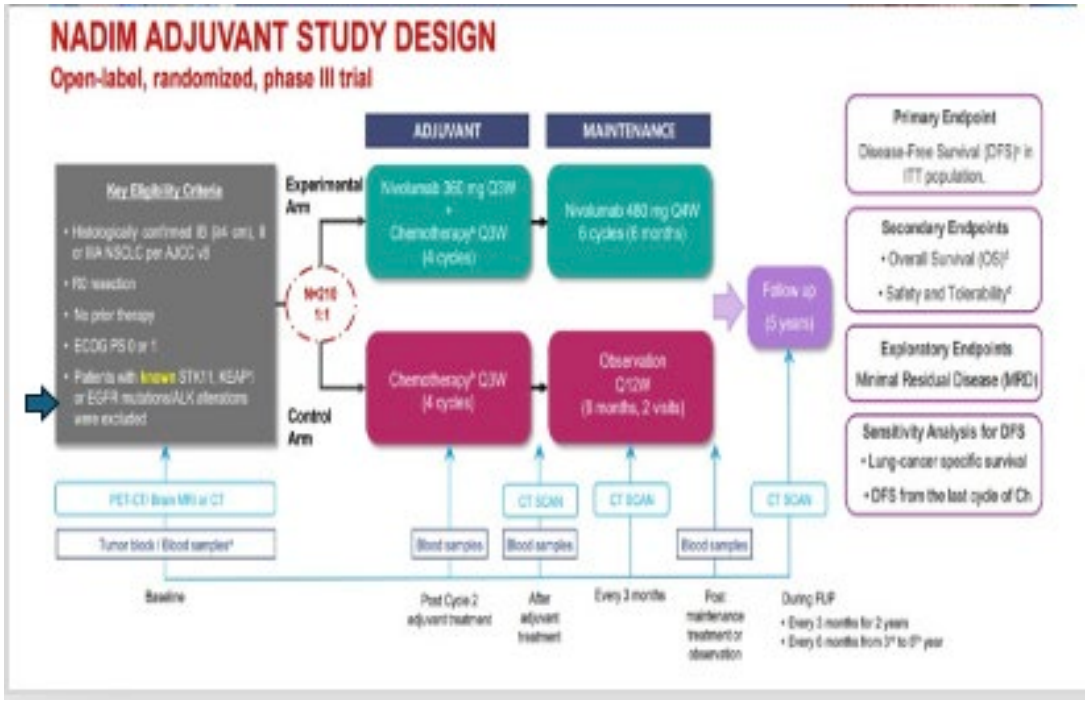
Adjuvant Treatment. NADIM Adjuvant



CONCLUSIONS

- **NADIM ADJUVANT is the first phase III trial** showing the impact of immediate post-surgical adjuvant chemo-immunotherapy in resected stage IB–IIIA NSCLC.
- At this interim analysis **DFS and OS data remain immature**, but a clinically **meaningful reduction** in relapse rates was observed:

  20.4% in the experimental arm **vs** 38.8% in the control arm.
- The inclusion of **all patients after surgery** provides a **real-world evidence perspective**, since postoperative mortality and/or toxicity during the adjuvant period can affect DFS.

  Sensitivity **analysis of cancer-specific DFS**: HR=0.54 (95% CI: 0.32–0.93; p = 0.025).

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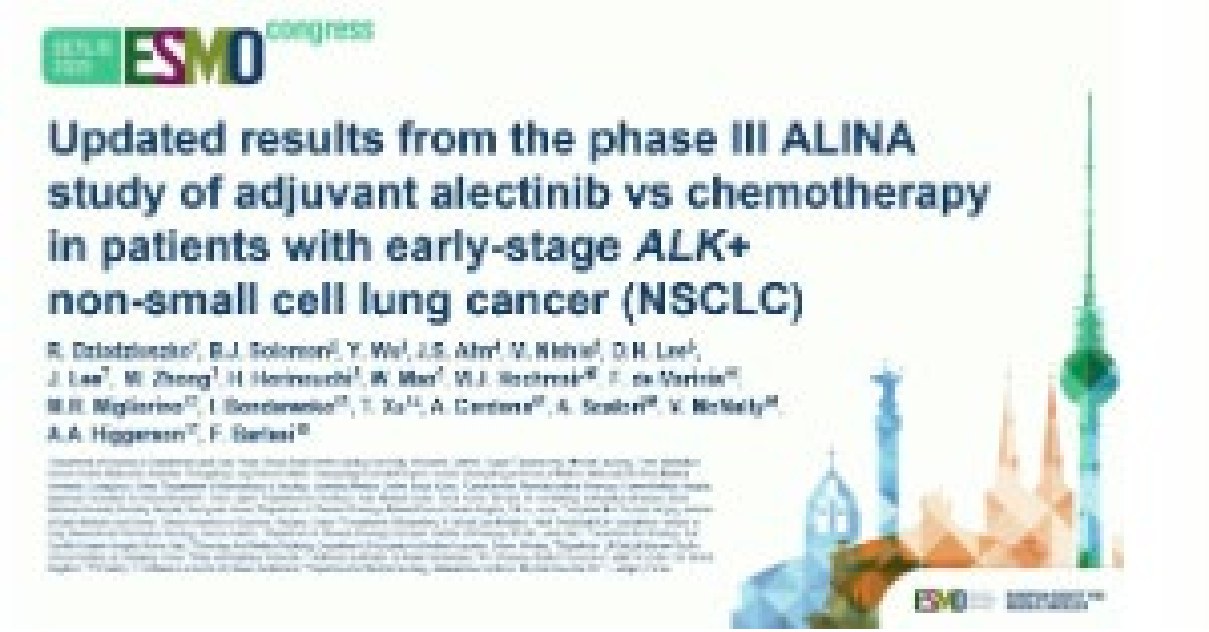
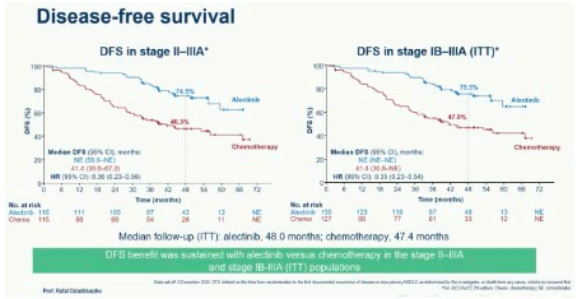
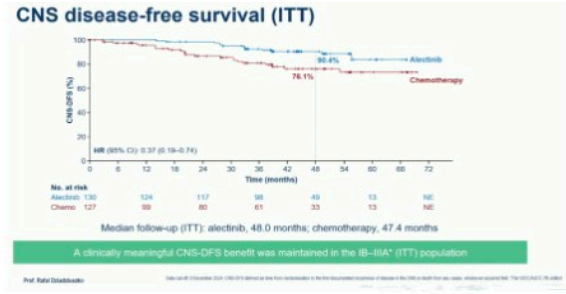
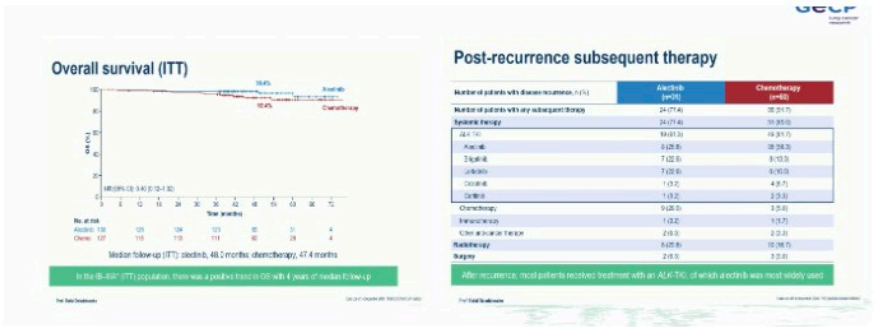
Adjuvant Treatment in NSCLC with Drivers

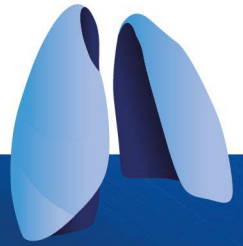
Something more than ADAURA....











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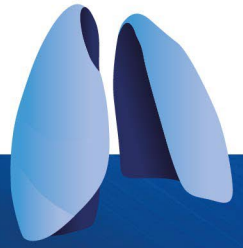
Key takeaways 2025 – Early NSCLC

- ✓ LDCT screening could increase detection at operable stages and improve survival
- ✓ Minimally invasive surgery remains central to stage IA-IIIA cancer
- ✓ The use of adjuvant immunotherapy is a reality
- ✓ Adjuvant targeted therapies (EGFR, ALK) are already part of recommendations for patients with specific biomarkers



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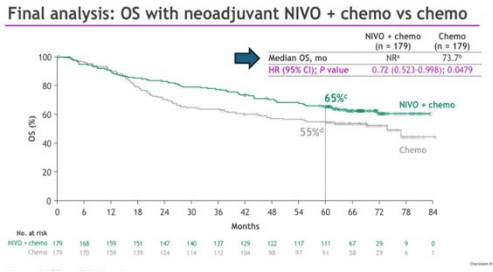
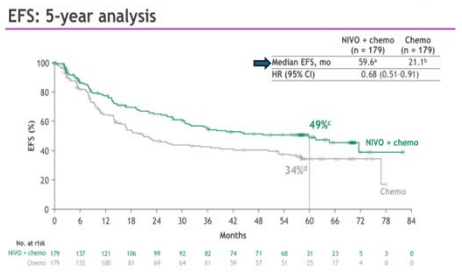
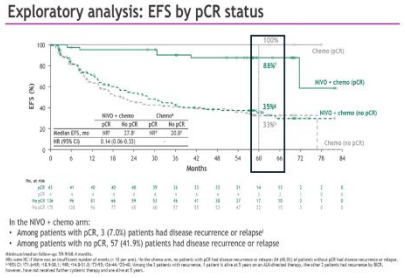
Neadjuvant Treatment





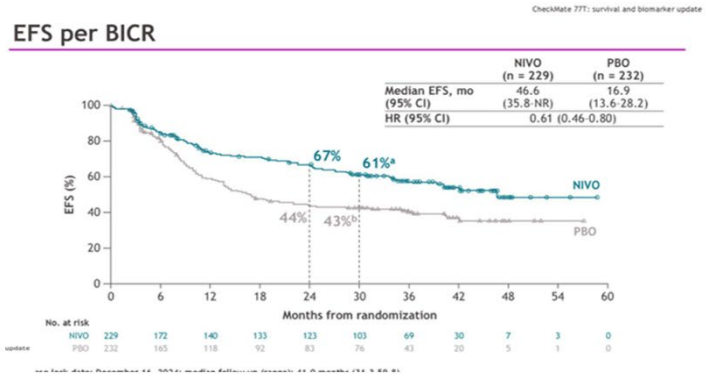


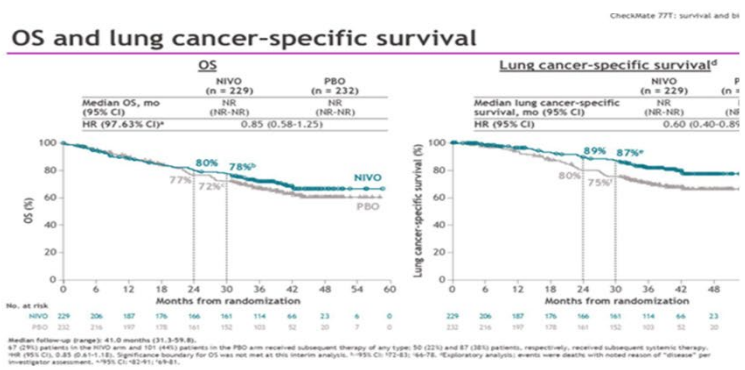
Análisis pronostico : según pCR (con independencia del PDL1)

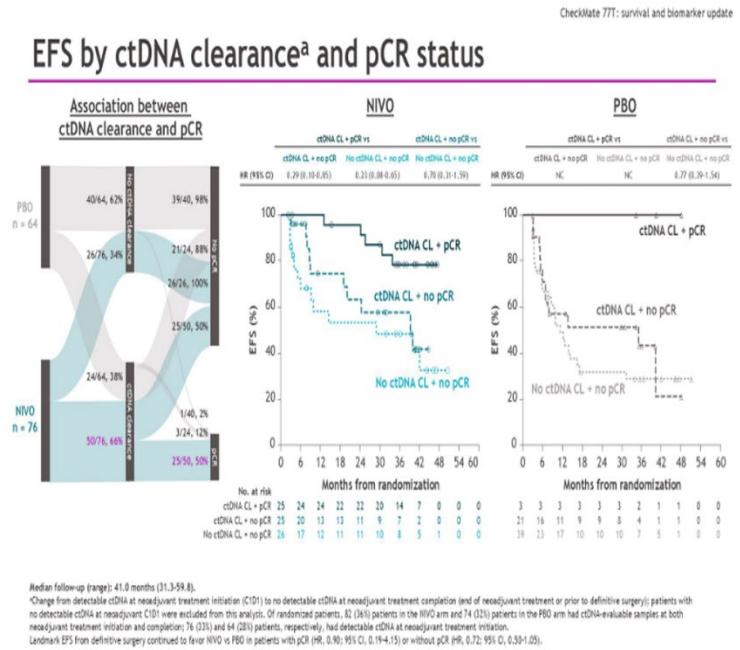
Esquema de uso aprobado PDL1 >1%

CHECKMATE 816

CHECKMATE-77T







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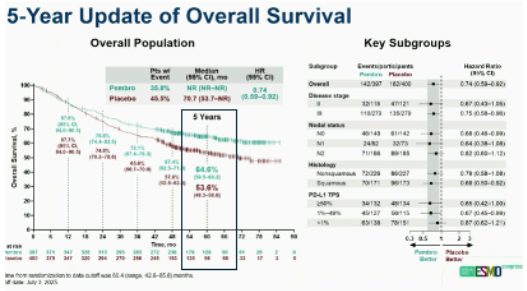
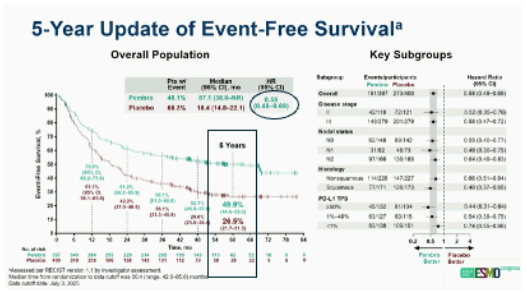
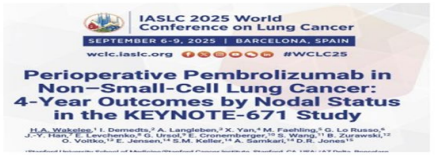
Neoadjuvant Treatment

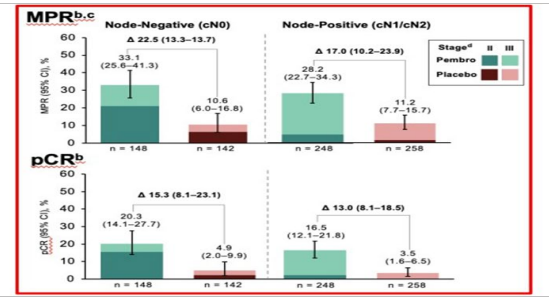
Datos a 5 años

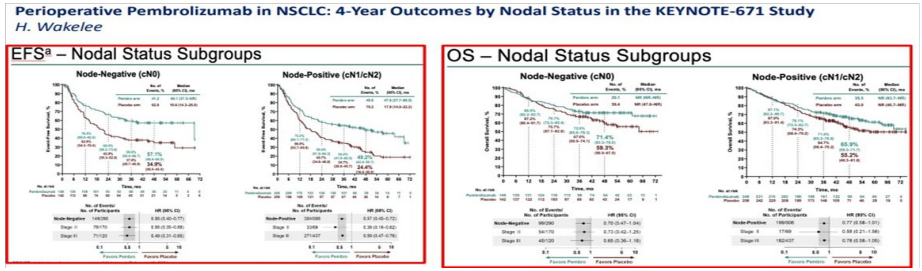




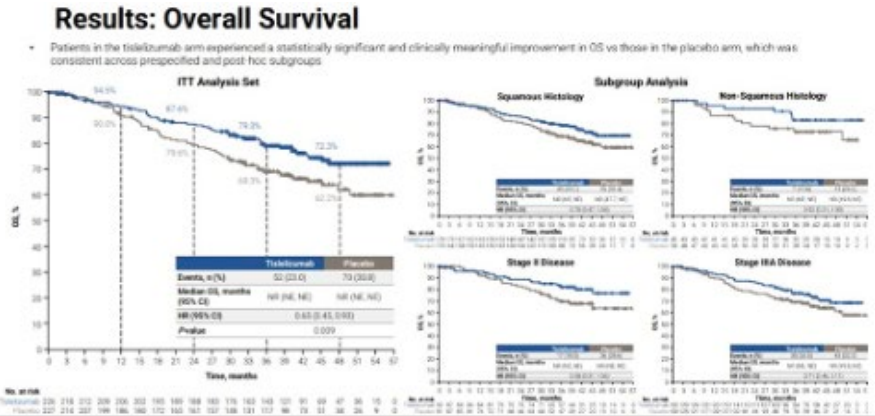
KEYNOTE-671

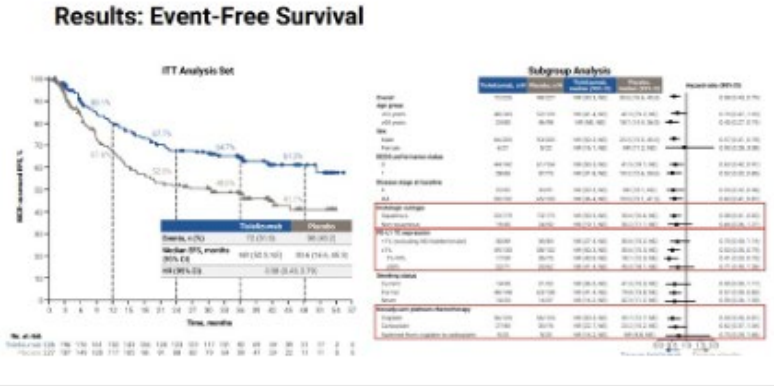






Perioperatorio con pembro **sostiene beneficio en OS** y prácticamente **duplica la proporción viva y libre de evento** respecto a QT sola.





RATIONALE 315

Neoadjuvant Treatment in NSCLC with drivers

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**

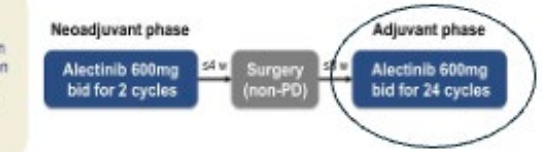
Lo que no resuelve todavía :
No es un ensayo diseñado para demostrar OS madura en 2025.
¿Necesitamos quimioterapia añadida al osimertinib neoadyuvante?

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

ALNEO

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

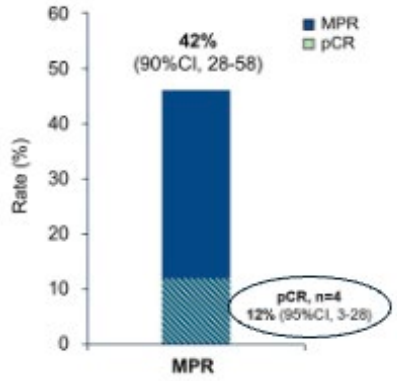


Primary Endpoint: MPR (≤10% viable tumor) by BICR
Secondary Endpoints: pCR by BICR, ORR, EFS, DFS, OS, AEs
Ancillary biological study*: correlation of tissue and cell-free biomarkers with MPR and DFS

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%

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

*5 patients did not undergo surgery, 1 patient underwent exploratory thoracotomy



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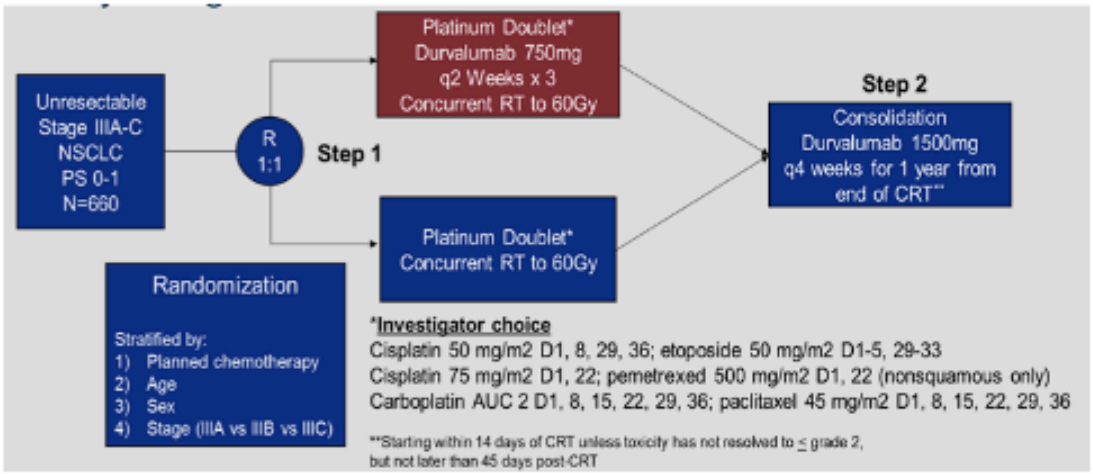
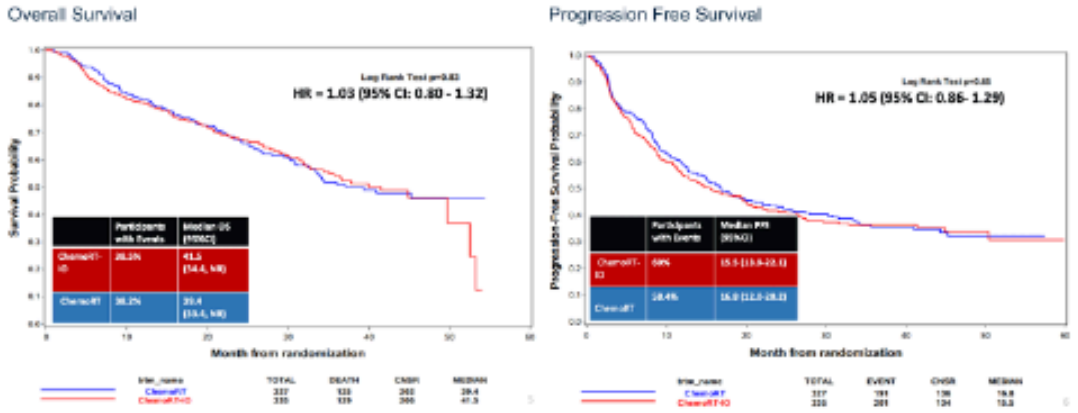
Is there anything beyond the Pacific….?

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

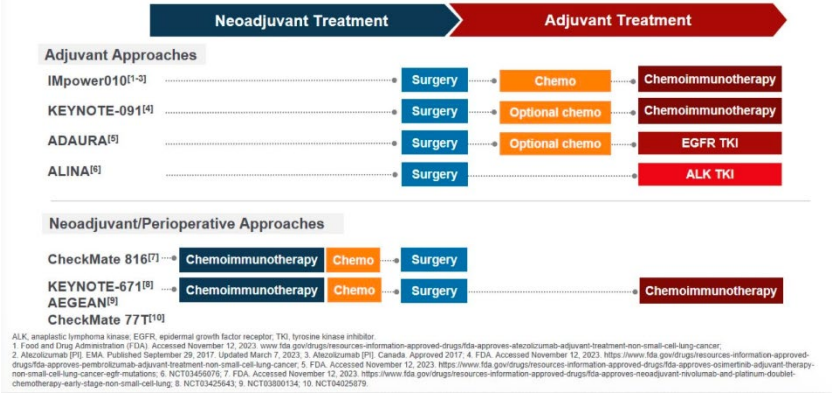


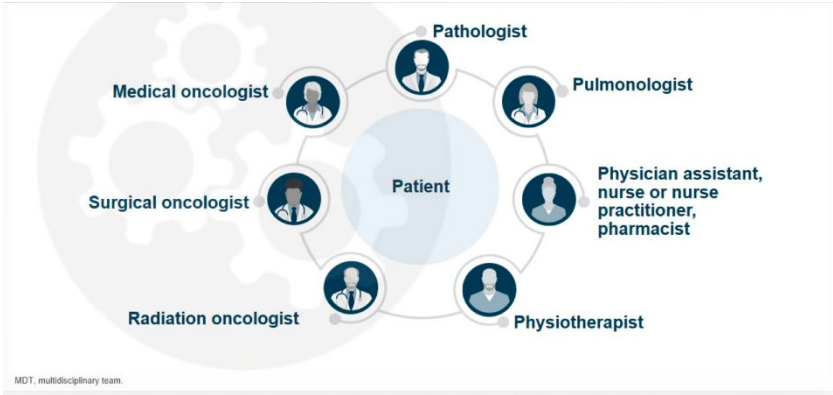


GeCP
lung cancer research

Key takeaways 2025 – Locally advanced NSCLC

- ✓ The use of periopertive immunotherapy (neoadjuvant/adjuvant) is a reality and is changing the standards
- ✓ In locally advanced cancer, chemoradiotherapy + immunotherapy/targeted therapy offers better results.
- ✓ Multidisciplinary management with precision medicine is essential for





GECP lung cancer research

Metastatic Disease

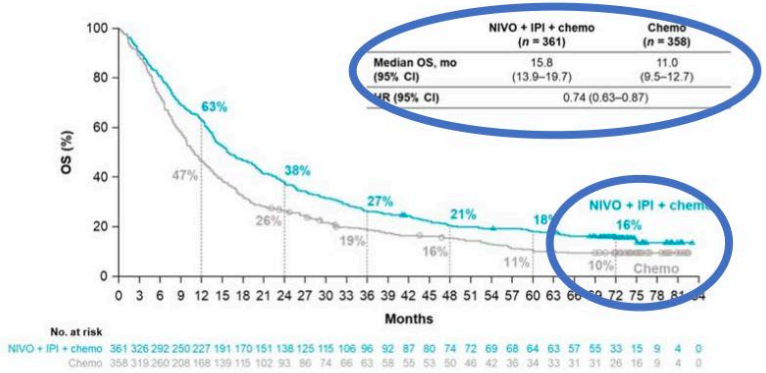
ARTICLE IN PRESS

ESMO OPEN

ORIGINAL ARTICLE

Nivolumab plus ipilimumab with chemotherapy as first-line treatment of patients with metastatic non-small-cell lung cancer: final, 6-year outcomes from CheckMate 9LA

OS in all randomized patients - Fig 1



Minimum/median follow-up for OS: 68.6/75.8 months.

2025 ASCO ANNUAL MEETING

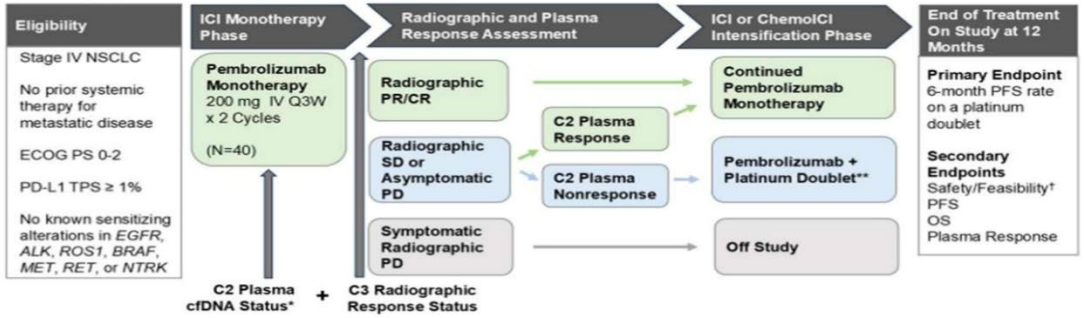
Plasma-guided adaptive first-line chemoimmunotherapy for non-small cell lung cancer (NSCLC)

Julia K. Rotow, Grace Heavey, Mizuki Nishino, Shail Maingi, Christopher S. Lathan, Umit Tapan, Alexandra S. Bailey, Zihan Wei, Emanuele Mazzola, Diandra Ocot, Geoffrey R. Oxnard, David A. Barbie, Pasi A. Jänne, Cloud P. Paweletz, Michael L. Cheng

Julia Rotow, MD
Clinical Director, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute
Assistant Professor, Harvard Medical School

2025 ASCO #ASCO25 ASCO

Plasma response-guided adaptive treatment of advanced NSCLC receiving first-line pembrolizumab



*Plasma Response defined as ≥50% reduction in plasma ctDNA max AF for patients with high shed [≥0.5% max AF] at baseline or continued low shed [<0.5% max AF] for patients with low shed at baseline, as measured by amplicon-based plasma NGS

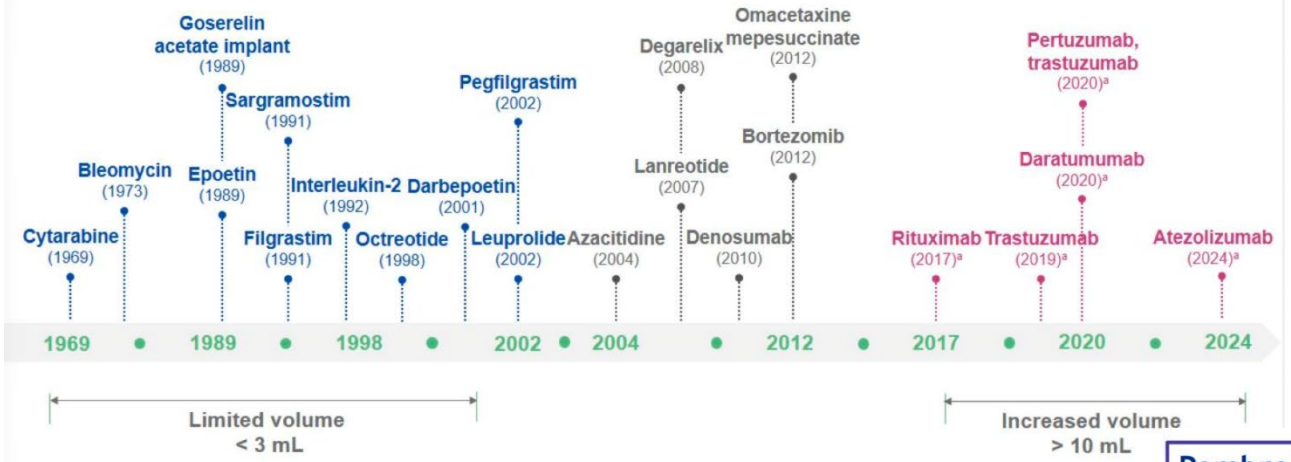
**NSQ: Carboplatin AUC 5 + Pemetrexed 500 mg/m2 Q3W x 4 cycles followed by Pemetrexed 500 mg/m2 Q3W; SQ: Carboplatin AUC 6 + Paclitaxel 200 mg/m2 Q3W x 4 cycles, with concurrent pembrolizumab 200 mg IV Q3W to end of study treatment

†Feasibility defined as completion of the integrated plasma response and C3 imaging assessment, with one-sided upper 90% binomial confidence interval >82.5%

GECP lung cancer research

Subcutaneous Therapies in Cancer

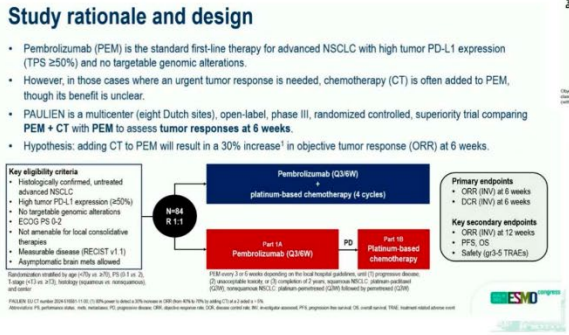
SC forms of administration have evolved over time to facilitate higher-volume medications

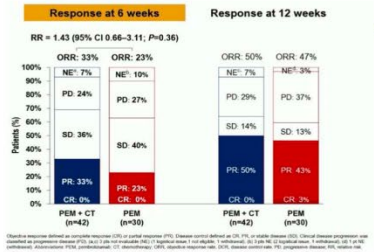


Pembrolizumab plus chemotherapy vs pembrolizumab as first-line therapy for advanced NSCLC with PDL1 (TPS) ≥ 50%: open-label, phase 3, randomized trial (PAULIEN)

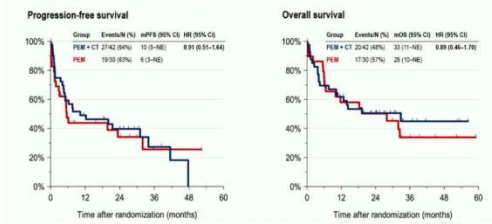
Study rationale and design

- Pembrolizumab (PEM) is the standard first-line therapy for advanced NSCLC with high tumor PD-L1 expression (TPS ≥50%) and no targetable genomic alterations.
- However, in those cases where an urgent tumor response is needed, chemotherapy (CT) is often added to PEM, though its benefit is unclear.
- PAULIEN is a multicenter (eight Dutch sites), open-label, phase III, randomized controlled, superiority trial comparing **PEM + CT** with **PEM** to assess **tumor responses at 6 weeks**.
- Hypothesis: adding CT to PEM will result in a 30% increase[1] in objective tumor response (ORR) at 6 weeks.





Progression-free survival and overall survival



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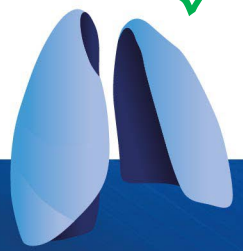
New approaches, drugs or combinations in Metastatic NSCLC

- ✓ Classical immunotherapy and something more
  - ✓ Relatlimab
  - ✓ Rilvesgotomig
  - ✓ Volrustomig
- ✓ Comparative studies against other combinations
- ✓ ADC
  - ✓ Anti-TROP2 (Datopotomab Deruxtecan) +/- QT
- ✓ Antiangiogenics + Immunotherapy



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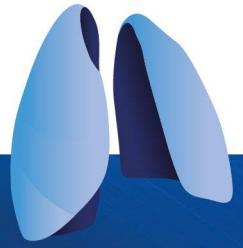
And, in metastatic NSCLC with driver genes

- ✓ FLAURA2 vs MARIPOSA Dilemma
- ✓ Second lines in EGFR+
- ✓ New drugs in ALK
- ✓ ROS1
- ✓ KRAS
- ✓ BRAF
- ✓ HER-2
- ✓ MET
- ✓ MTAP
- ✓ ……

GECP lung cancer research

Key takeaways for 2025 — Metastatic Disease NSCLC

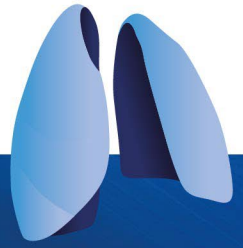
- ✓ Newly approved antibody-drugs conjugates (ADCs) offer targeted options with good tolerability profiles
- ✓ Innovative and next-generation therapies (ROS1 inhibitors, viral immunotherapy) aim to overcome therapeutic resistance
- ✓ Combination therapies and maintenance therapy enhance outcomes after initial response
- ✓ Molecular profiling and biomarkers guide precise treatment decisions
- ✓ Survival is gradually improving, although the challenge of metastatic disease remains enormous



GECP lung cancer research

SCLC 2025

- ✓ Maintenance treatment with Lubinectidine + Atezolizumab
- ✓ Tarlatamab
- ✓ ADC



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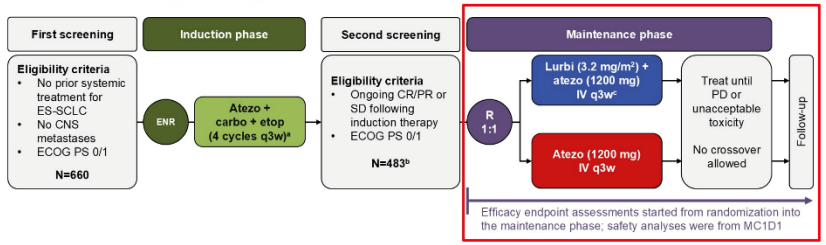
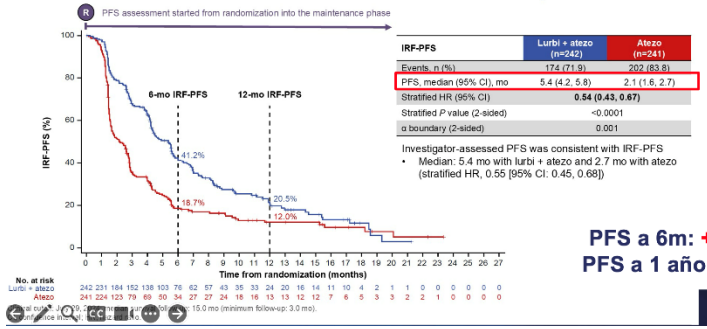
MANTENIMIENTO LURBINECTEDINA-ATEZOLIZUMAB – Ph3 IMforte





IRF-PFS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	174 (71.9)	202 (83.8)
PFS, median (95% CI), mo	5.4 (4.2, 5.8)	2.1 (1.6, 2.7)
Stratified HR (95% CI)	**0.54 (0.43, 0.67)**	
Stratified *P* value (2-sided)	<0.0001	
α boundary (2-sided)	0.001	

Investigator-assessed PFS was consistent with IRF-PFS
- Median: 5.4 mo with lurbi + atezo and 2.7 mo with atezo (stratified HR, 0.55 [95% CI: 0.45, 0.68])

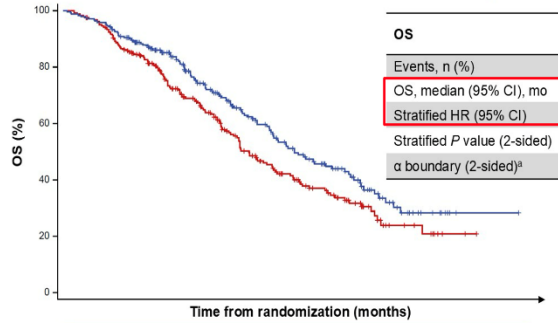
ORR: 19.4% vs. 10.4%
DoR: 9.0 m vs. 5.6m

PFS a 6m: +22.5%
PFS a 1 año: +8.5%

L.Paz-Ares, ASCO 2025
L.Paz-Ares, ASCO 2025

MANTENIMIENTO LURBINECTEDINA-ATEZOLIZUMAB – Ph3 IMforte

OS from randomization into maintenance phase



OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	113 (46.7)	136 (56.4)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	**0.73 (0.57, 0.95)**	
Stratified *P* value (2-sided)	0.0174	
α boundary (2-sided)[a]	0.0313	

Induction treatment
Atezo + carbo + etop
3.2 months[a]

R

Maintenance treatment
Lurbi + atezo
Median OS from randomization: 13.2 months

Maintenance treatment
Atezo
Median OS from randomization: 10.6 months

IMforte results do not include time on induction treatment

TARLATAMAB EN 2L - Ph3 DeLLphi-304

Key inclusion criteria
- Histologically or cytologically confirmed SCLC
- Progression after 1L platinum-based chemotherapy +/- anti-PD-(L)1
- ECOG PS 0 or 1
- Asymptomatic, treated or untreated brain metastases

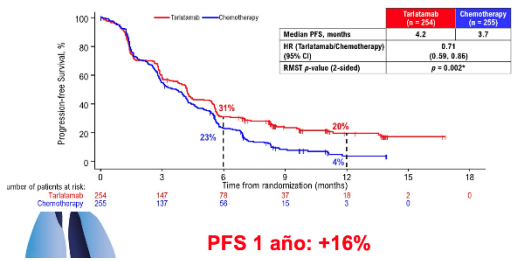
Randomization stratified by
- Prior anti-PD-(L)1 exposure (yes/no)
- Chemotherapy-free interval (< 90 days vs ≥ 90 to < 180 days vs ≥ 180 days)
- Presence of (previous/current) brain metastases (yes/no)
- Intended chemotherapy (topotecan/amrubicin vs lurbinectedin)

R 1:1 (N = 509)

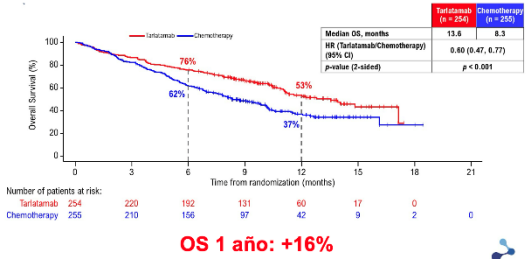
- Tarlatamab (n = 254)
- Chemotherapy* (n = 255)

Topotecan (n = 185); Lurbinectedin (n = 47); Amrubicin (n = 23)

CFI <90d: T 43%; CT 45%
Brain M1: T 44%; CT 45%



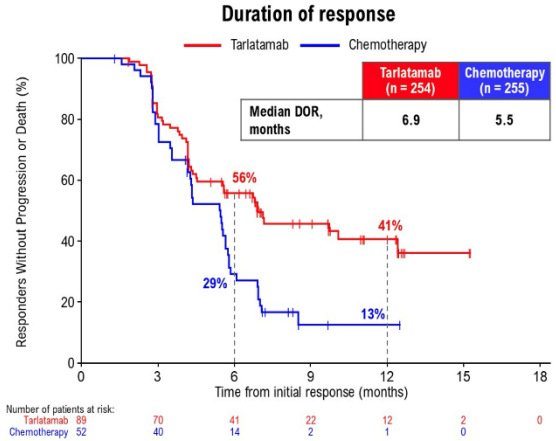
PFS 1 año: +16%



OS 1 año: +16%

TARLATAMAB EN 2L - Ph3 DeLLphi-304

	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Best overall response[*†], n (%)		
Complete response	3 (1)	0 (0)
Partial response	86 (34)	52 (20)
Stable disease	84 (33)	112 (44)
Progressive disease	56 (22)	50 (20)
Not evaluable/no post-baseline scan	25 (10)	41 (16)
Objective response rate[‡], % (95% CI)	35 (29–41)	20 (16–26)
Median duration of response, months	6.9	5.5
Median time to objective response, months	1.5	1.4
Ongoing response at data cutoff, n[§] (%)	42 (47)	8 (15)



TARLATAMAB EN 1L - Ph1b: DeLLphi-303

Cohortes 2,4,7

1L Chemo-IO: Platinum-etoposide + Anti-PD-L1[b]

Key Inclusion Criteria
- ✓ Adults with ES-SCLC who **received 1 cycle of chemo-IO** (Enrollment allowed regardless of response to 1 cycle of chemo-IO)
- ✓ Measurable disease by modified RECIST 1.1
- ✓ ECOG PS 0 or 1
- ✓ Patients with treated, asymptomatic brain metastases were allowed
- ✓ No active autoimmune disease or disease requiring immunosuppressive therapy[c]

1L Chemo-IO + Tarlatamab Cycles 1-3: Tarlatamab 20 mg IV Q3W[d] + Platinum-etoposide (Carboplatin to match AUC 5 IV on day 1 etoposide 100 mg/m² on days 1-3) + Anti-PD-L1[e] (Atezolizumab: 1200 mg IV Q3W OR Durvalumab: 1500 mg IV Q3W)

1L Maintenance Cycles 4+: Tarlatamab 20 mg IV Q3W + Anti-PD-L1 (Atezolizumab: 1200 mg IV Q3W OR Durvalumab: 1500 mg IV Q3W)

Treatment until progressive disease[f]

Cohortes 5,6,8

1L Chemo-IO: Platinum-etoposide + anti-PD-L1[c] (4-6 cycles)

Enrollment
Key Inclusion Criteria
- ✓ No disease progression following 4–6 cycles of 1L chemo-IO
- ✓ ECOG PS 0 or 1
- ✓ Patients with treated and asymptomatic brain metastases were permitted
- ✓ No active autoimmune disease or disease requiring immunosuppressive therapy[d]

Non randomized[a]

Switching to a different anti-PD-L1 than that received in 1L chemo-IO was permitted

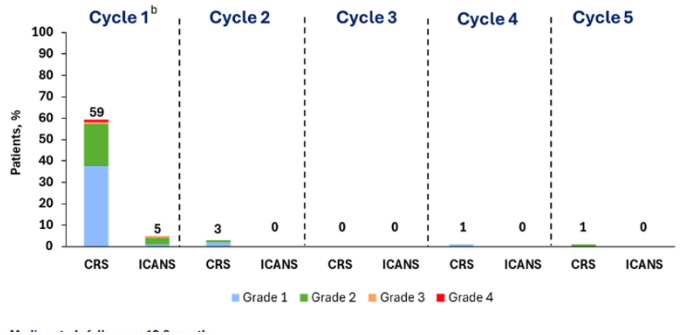
1L Maintenance[b]
- Tarlatamab (10 mg IV Q2W) + Atezolizumab (1680 mg IV Q4W) n = 48
- Tarlatamab (10 mg IV Q2W) + Durvalumab (1500 mg IV Q4W) n = 40

TARLATAMAB EN 1L - Ph1b: DeLLphi-303

DESDE INDUCCIÓN (Cohortes 2,4,7)

Treatment-emergent CRS and ICANS by cycle[a]

DeLLphi 303



- CRS and ICANS were associated with a low rate of
  - tarlatamab dose interruptions (CRS and ICANS: 1% each)
  - tarlatamab discontinuations (CRS and ICANS: 1% each)
- There were no fatalities related to CRS or ICANS
- The median time to onset of CRS from last prior dose of tarlatamab was 13.3 hours (IQR: 8.0–19.3)
- The median time to onset of ICANS from last prior dose of tarlatamab was 5 days (IQR: 3.0–5.0)

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ADCs EN CPCP

DLL3

Rova-T
SHR-4849 (IDE819)

SEZ-6

ABBV-706
ABBV-011

B7-H3

HMB088C
HS-20093 (GSK5764227)
I-DXd (DS7300)
YL201

TROP-2

SACI-GOVITECAN
SHR-A1921

ADCs EN CPCP PREVIAMENTE TRATADOS

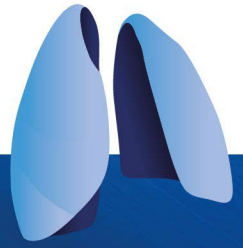
	ABBV-706 1.8mg/kg (N=41)	QLC5508 (MHB088C) 1.6-2.4mg/kg (N=103)	I-DXd 12mg/kg (N=137)	HS20093 (GSK5764227) 8mg/kg (N=31)[1]	YL201 1.6-2.8mg/kg (N=72)[2]	Sacituzumab Govitecan (N=43)[3]
Target	SEZ6	B7-H3	B7-H3	B7-H3	B7-H3	TROP2
Payload	Top1 inhibitor	Top1 inhibitor (SuperTopoi™)	Top1 inhibitor (DXd)	Top1 inhibitor (HS-9265)	Top1 inhibitor	Top1 inhibitor (SN-38)
DAR	6	4	4	4	8	7.6
Linker	Cleavable	Cleavable	Cleavable	Cleavable	Cleavable	Cleavable
ORR/DCR	56%	36.9/90.3%	48.2/87.6%	61.3/80.6%	63.9/91.7%	41.9/83.7%
mPFS/OS	6.8 months/ 60%(9month OS)	5.72/11.50 months	4.9/10.3 months	5.9/9.8 months	6.3/- months	4.4/13.6 months
Main AEs	Hematological toxicity	Hematological toxicity	Hematological toxicity/GI toxicity	Hematological toxicity	Hematological toxicity	Diarrhea/Hematological toxicity

1) WCLC 2024, 2) Ma Y, et al. Nat Med. 2025 Jun;31(6):1949-1957. 3) Dowlati A et al. J Thorac Oncol. 2025 Jun;20(6):799-808.

GECP lung cancer research

Key Takeaways 2025 — SCLC

- ✓ Combined maintenance therapy with lurbinectedin + atezolizumab changes the first-line paradigm in ES-SCLC
- ✓ ADCs targeting B7-H3 and other targets offer promising options in pretreated disease
- ✓ Tarlatamab is a bispecific agent with great therapeutic potential
- ✓ Immunotherapy remains central, with research into innovative combinations
- ✓ Survival and disease control are gradually improving, but there is still a need for more effective and longer-lasting therapies



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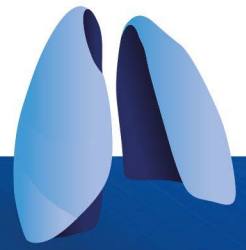
Other thoracic tumors

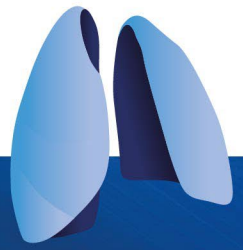
- ✓ Mesotheliomas
  - ✓ Combinations of Chemo + Immunotherapy
- ✓ Thymic Epithelial Tumors
  - ✓ Riboceranib



GECP lung cancer research

Key takeaways for 2025

- ✓ Lung cancer remains a priority in global cancer research
- ✓ AI and non-invasive tests are becoming more established for earlier diagnosis
- ✓ The use of immunotherapy and targeted therapies is moving towards earlier stages of treatment
- ✓ Ongoing trials with new anti-drug therapies (ADCs) could lead to new therapeutic standards in the coming years
- ✓ Promising new agents in SCLC
- ✓ Liquid biopsy is becoming increasingly useful not only for diagnosis but also for dynamic monitoring



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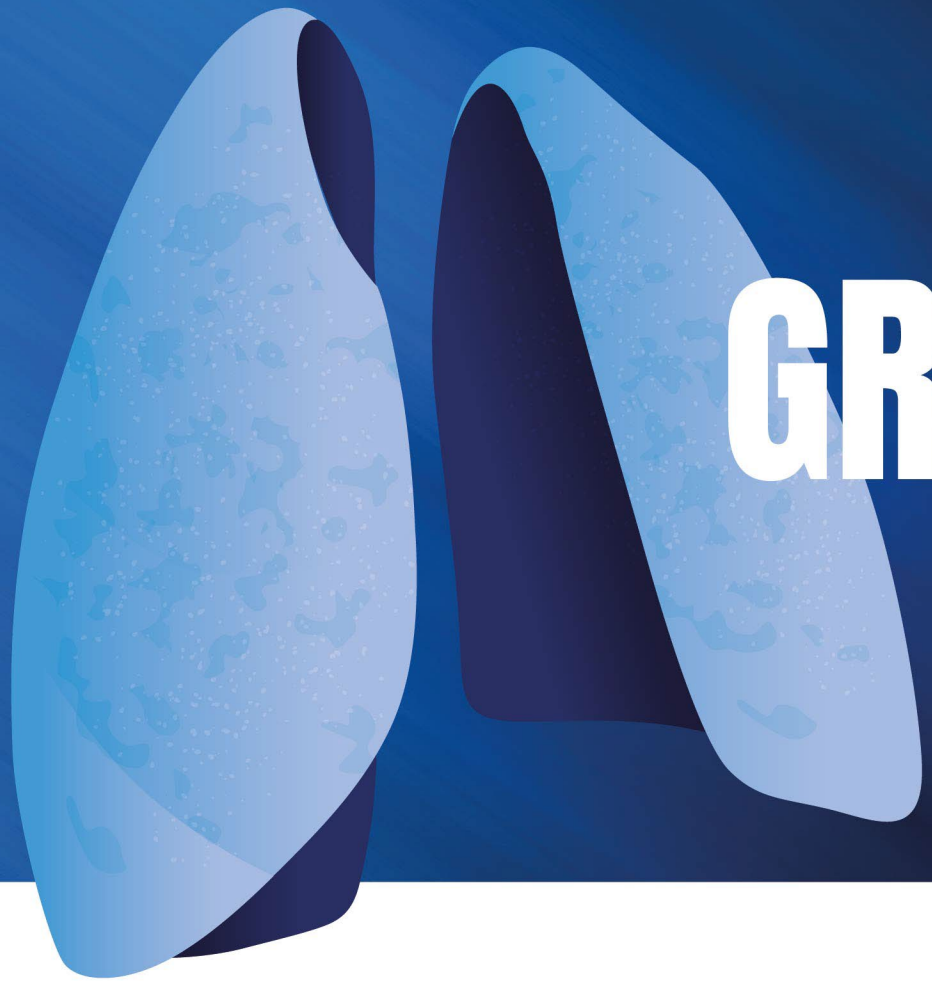
lung cancer research



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