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Biomarcadores pronósticos

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Hospital General Universitario de Valencia

GECP
lung cancer research

CONFLICTO DE INTERESES

- Consultation/Advisory boards: BMS, MSD, Johnson and Johnson
- Talks in public events: Roche, Pfizer, BMS, MSD, Regenneron, Johnson and Johnson, Astrazeneca
- Travel acommodation congress: Pfizer, Roche, Johnson and Johnson, MSD, Astrazeneca

AGENDA

1.- Dynamic based prognostic biomarkers (liquid biopsy)

2.- Integrated prognostic models and Artificial intelligence

3.- Host-immune based and genomic prognostic biomarkers

4.- Clinical and pathological biomarkers

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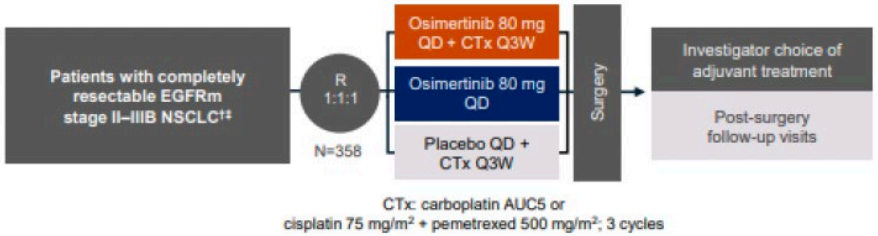
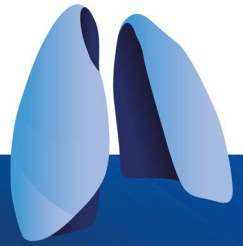
MRD analysis from NEOADAURA (OA02.02 ELCC 2025)



Primary endpoint: MPR (by blinded central pathology review)§
Secondary endpoints: EFS, pCR, nodal downstaging, safety, DFS and OS



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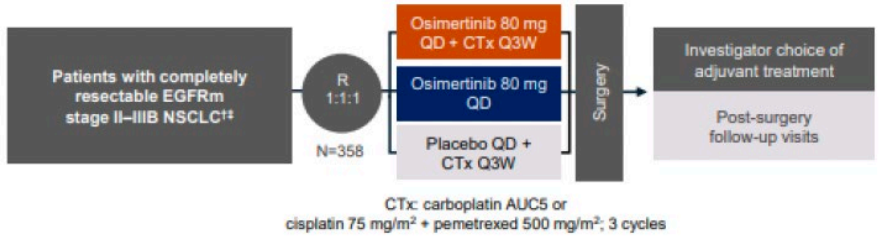

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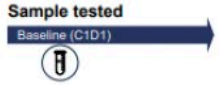

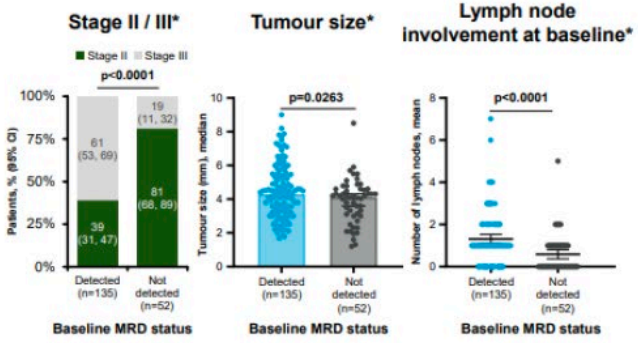

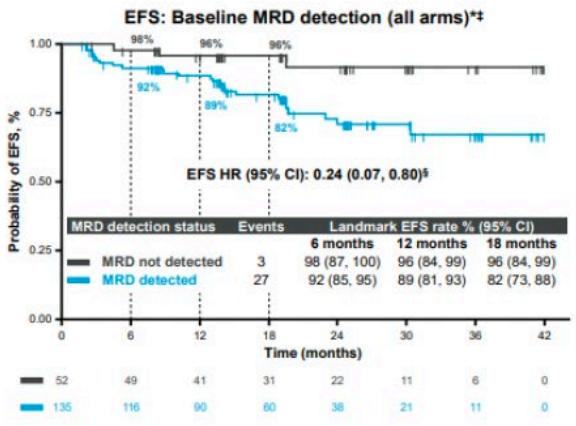

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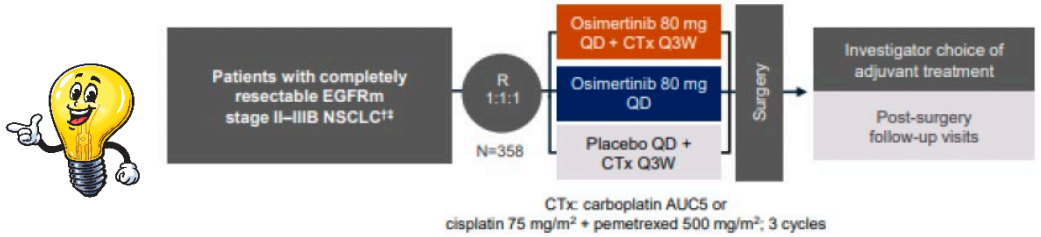

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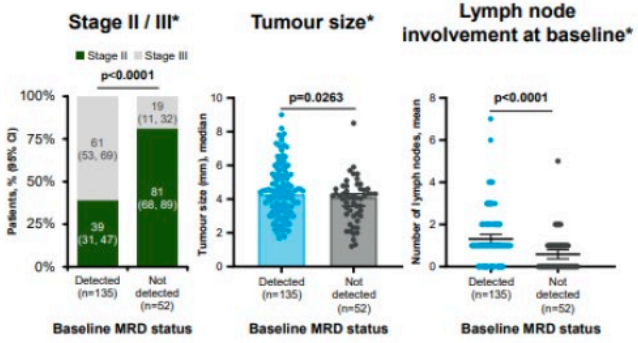

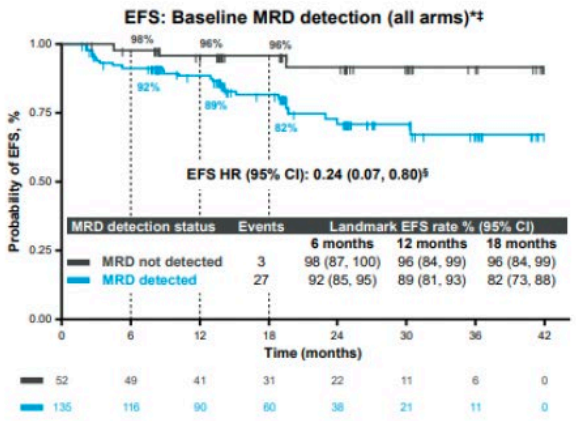

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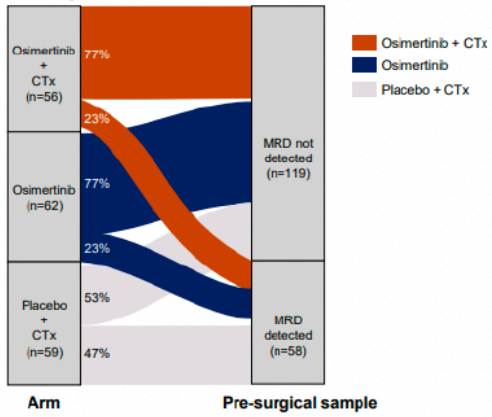
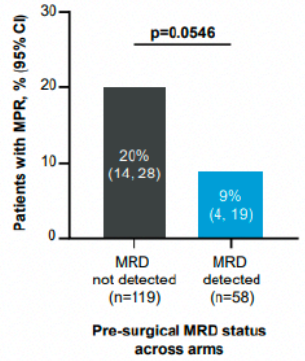
Pre-surgical MRD *not detected* rate was higher in osimertinib-containing regimens and in patients with MPR

Samples tested: Baseline (C1D1) Pre-surgical

Treatment with osimertinib-containing regimens led to higher rates of MRD not detected* vs placebo + CTx



MRD not detected was associated with MPR† across arms



Pre-surgical MRD *clearance* was enriched with osimertinib-containing regimens and in patients with MPR

Samples tested: Baseline (C1D1)‡ Pre-surgical

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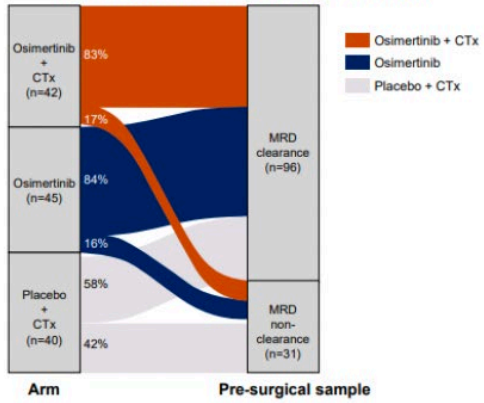
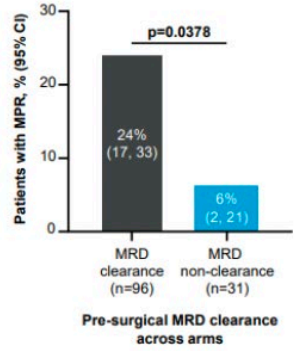


MRD clearance was associated with MPR§ across arms



MRD clearance: 10-fold decrease in ctDNA or MRD not detected in the presurgical sample after baseline MRD detected

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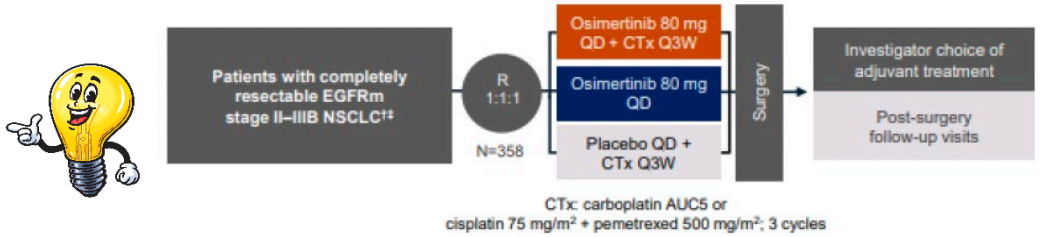

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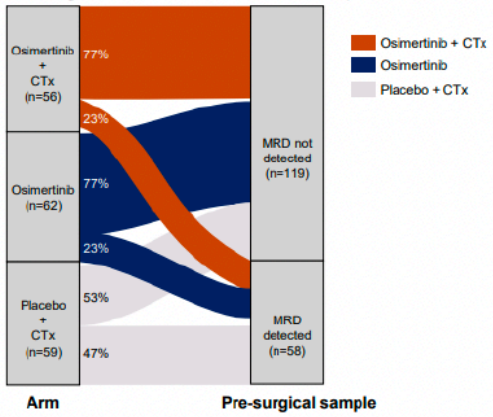

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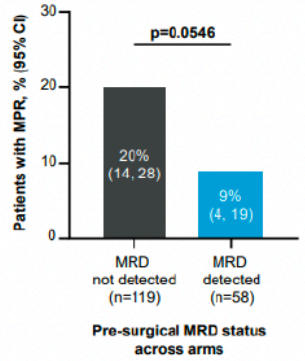

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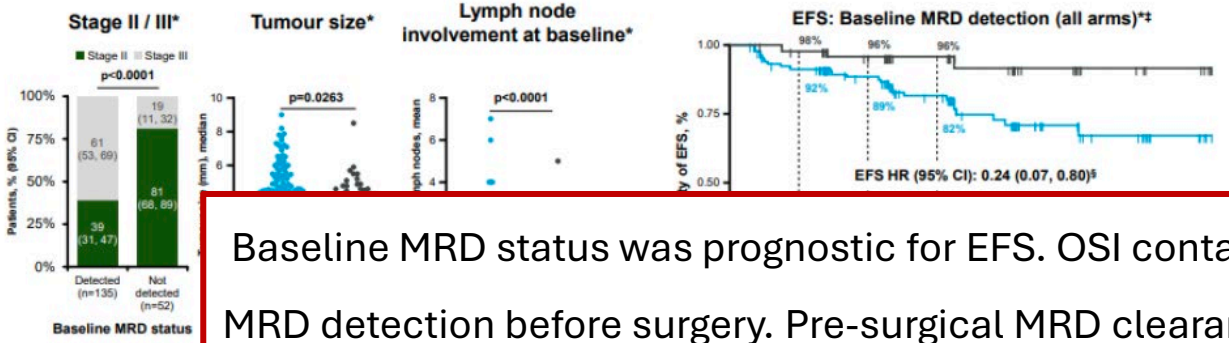

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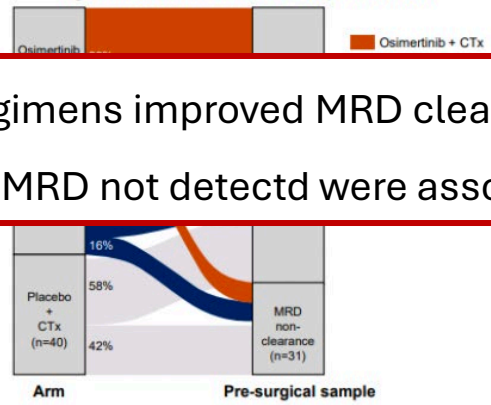

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MRD clearance: 10-fold decrease in ctDNA or MRD not detected in the presurgical sample after baseline MRD detected

Baseline MRD status was prognostic for EFS. OSI containing regimens improved MRD clearance and reducesd MRD detection before surgery. Pre-surgical MRD clearance and MRD not detectd were associated with MPR

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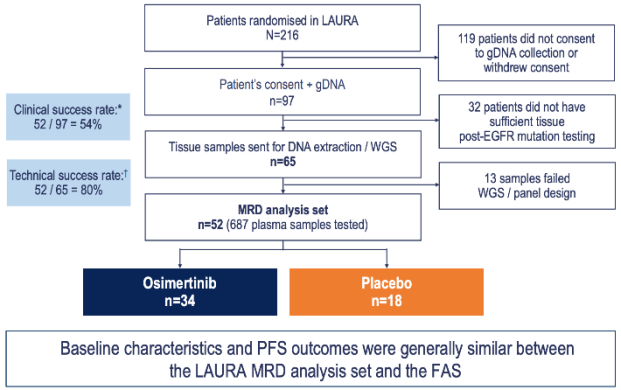
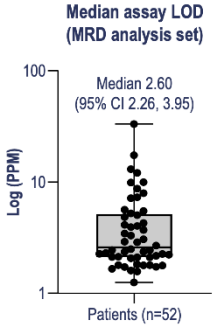
MRD analysis from the LAURA study of osimertinib in unresectable stage III EGFR-mutated NSCLC (ESMO 1817MO)

- ✓ Osimertinib demonstrated significant clinical Benefit vs placebo in patients with unresectable stage III EGFRm NSCLC without progession during/after CRT
- ✓ Irrespective of post-CRT MRD status, patients benefited from osimertinib treatment vs pbo.

MRD panel build had a technical success rate of 80%; median LOD 2.6 PPM





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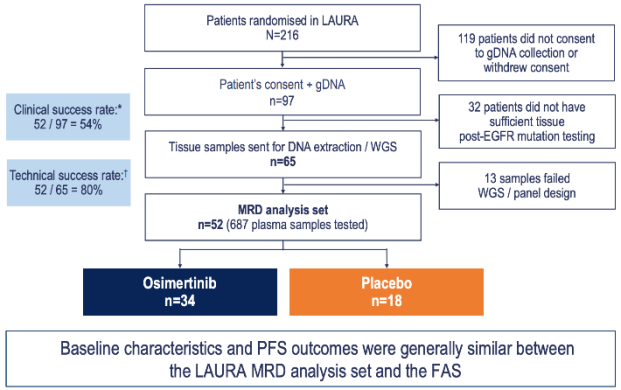
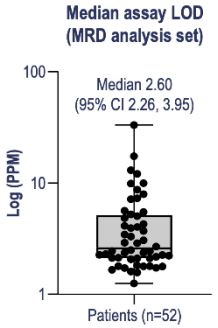
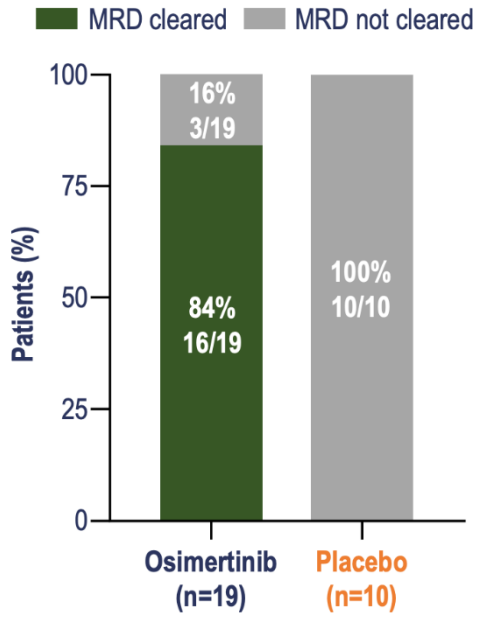




Clearance of post-CRT (randomisation) MRD



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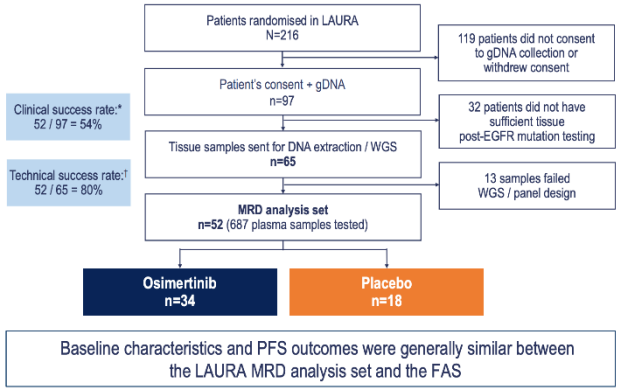

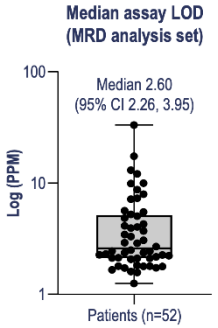

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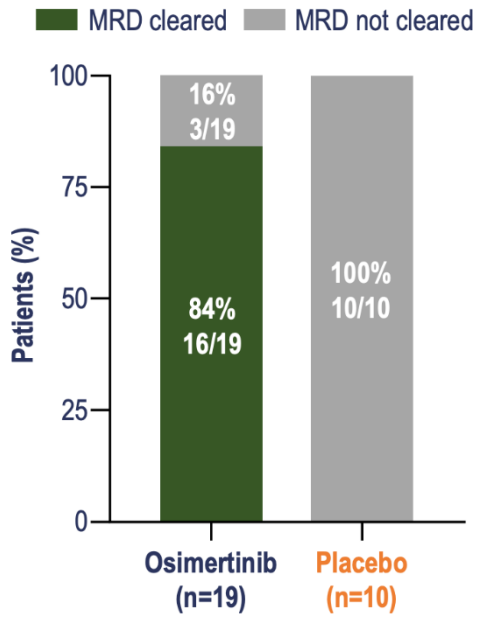
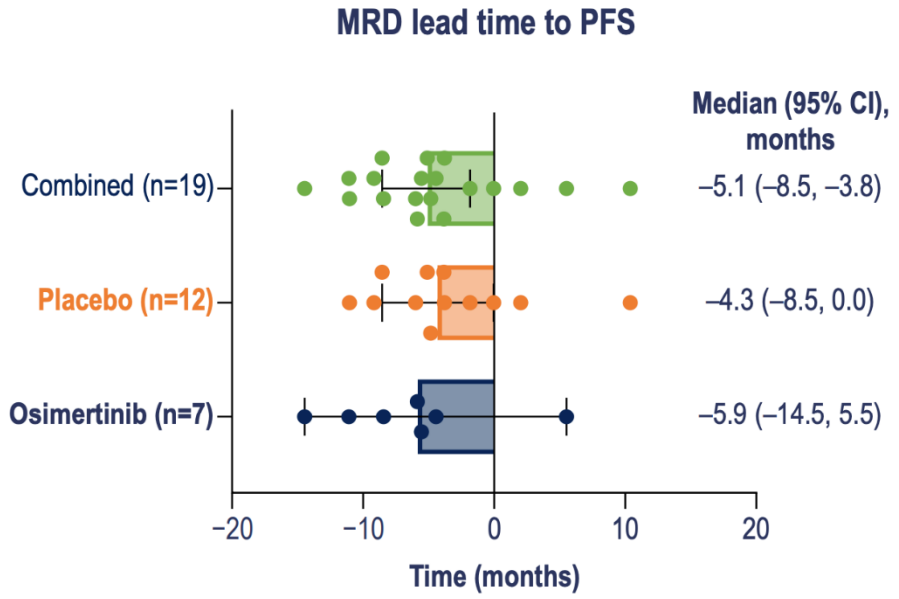
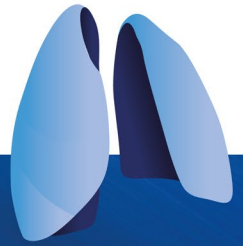


MRD lead time to PFS





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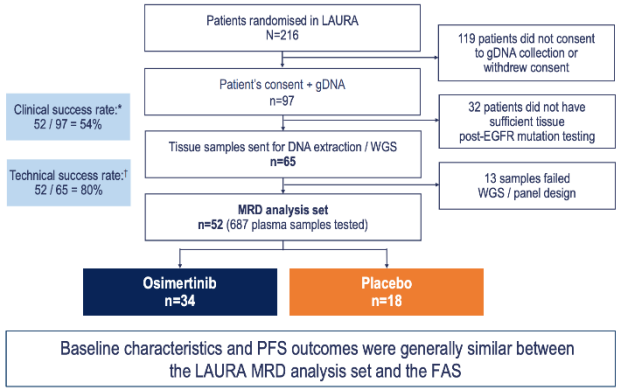

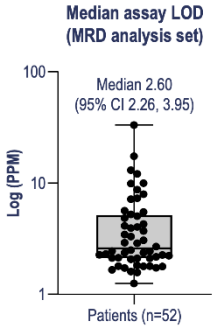

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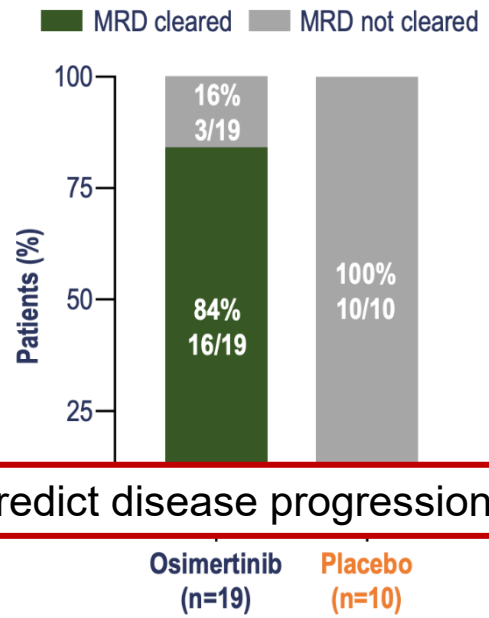

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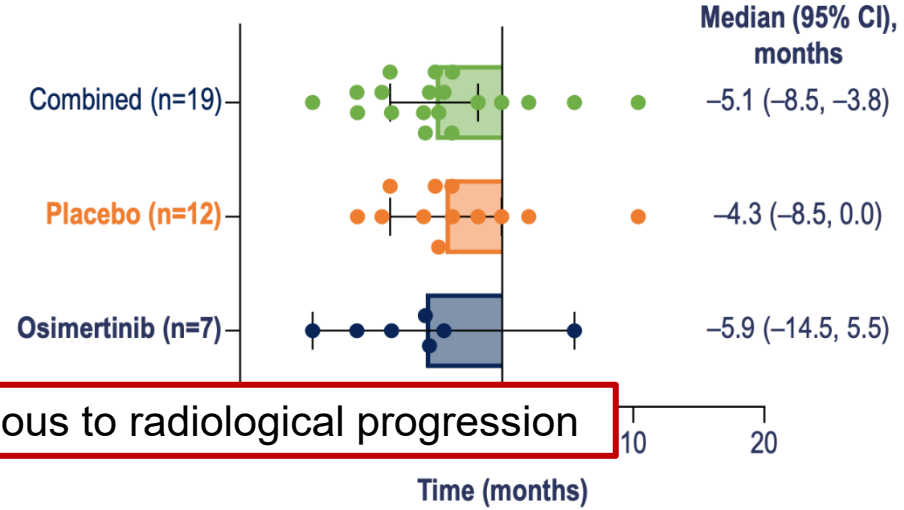
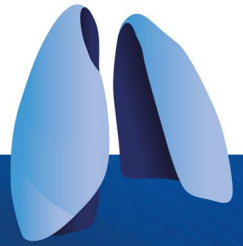


MRD monitoring was able to predict disease progression previous to radiological progression



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Day-7 ctDNA response as a prognostic marker in EGFRm NSCLC under osimertinib: The french study MELROSE (ESMO 1957P)

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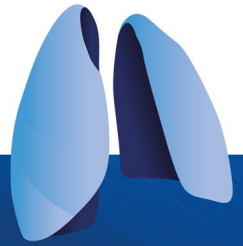

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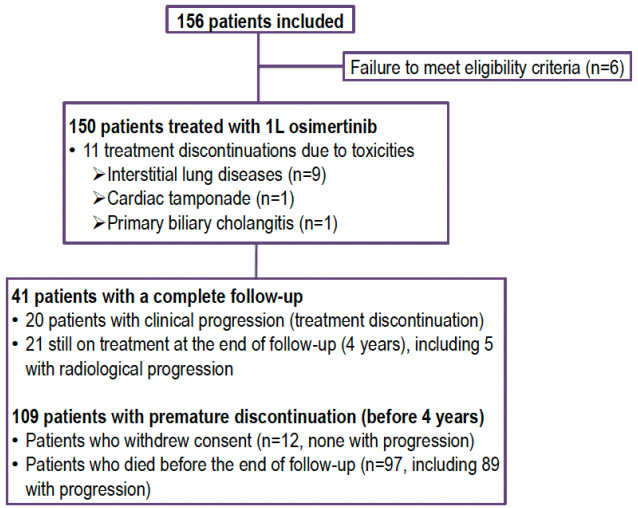
Main inclusion criteria and flow-chart

- Male or female, aged at least 18 years
- Pathologically confirmed untreated advanced carcinoma of the lung, harboring a common EGFR mutation (Ex19 deletions, L858R)
- Eastern Cooperative Oncology Group performance status of 0 to 1



Factors Associated With Overall Survival (univariate analysis)

	N	OS median [25-75th percentile]	HR	IC 95%	p-value
Performance status					
• 0	65	42.6 [24.7 ; NA]			
• 1	85	29.2 [14.2 ; 39.4]	1.93	(1.26 - 2.94)	0.002
EGFR mutation					
• Exon19 del	87	33.5 [21.1 ; NA]			
• L858R	63	26.4 [15.2 ; 47.5]	1.29	(0.87 - 1.94)	0.21
CNS metastases at inclusion					
• No	113	33.5 [17.0 ; NA]			
• Yes	37	30.3 [15.6 ; 47.5]	1.37	(0.88 - 2.14)	0.16
ctDNA at inclusion					
• Negative	48	35.6 [20.1 ; NA]			
• Positive	100	30.3 [16.3 ; 47.5]	1.50	(0.96 – 2.36)	0.07
ctDNA at day 7					
• Negative	88	35.4 [20.3 ; NA]			
• Positive	51	22.4 [12.4 ; 37.0]	2.06	(1.37 – 3.11)	0.001
ctDNA at month 1					
• Negative	40	32.0 [17.0 ; 47.5]			
• Positive	16	11.4 [5.0 ; 22.3]	2.77	(1.46 – 5.26)	<.0001
ctDNA evolution between baseline and day 7					
• Negative – negative	44	33.8 [20.1 ; NA]			
• Positive – negative	44	35.4 [23.8 ; NA]	0.97	(0.55 - 1.70)	0.92
• Positive – positive	50	22.8 [12.6 ; 41.8]	1.99	(1.21 – 3.27)	0.01

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156 patients included

Failure to meet eligibility criteria (n=6)

150 patients treated with 1L osimertinib
- 11 treatment discontinuations due to toxicities
  - ➢Interstitial lung diseases (n=9)
  - ➢Cardiac tamponade (n=1)
  - ➢Primary biliary cholangitis (n=1)

41 patients with a complete follow-up
- 20 patients with clinical progression (treatment discontinuation)
- 21 still on treatment at the end of follow-up (4 years), including 5 with radiological progression

109 patients with premature discontinuation (before 4 years)
- Patients who withdrew consent (n=12, none with progression)
- Patients who died before the end of follow-up (n=97, including 89 with progression)

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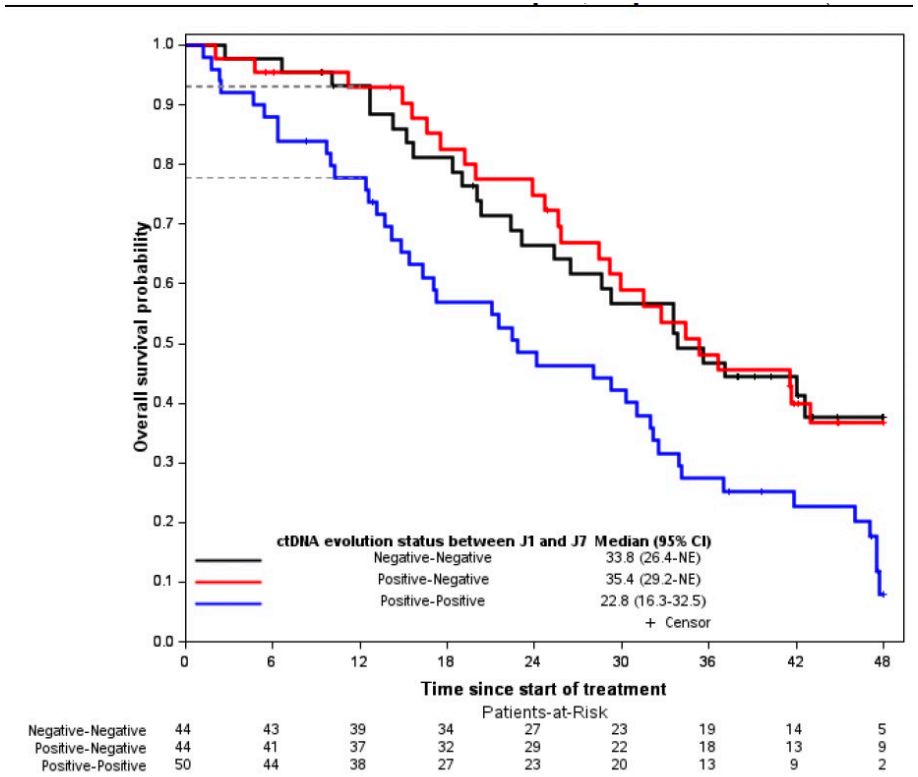
ctDNA at day 7					
• Negative	88	35.4 [20.3 ; NA]			
• Positive	51	22.4 [12.4 ; 37.0]	2.06	(1.37 – 3.11)	0.001
ctDNA at month 1					
• Negative	40	32.0 [17.0 ; 47.5]			
• Positive	16	11.4 [5.0 ; 22.3]	2.77	(1.46 – 5.26)	<.0001
ctDNA evolution between baseline and day 7					
• Negative – negative	44	33.8 [20.1 ; NA]			
• Positive – negative	44	35.4 [23.8 ; NA]	0.97	(0.55 - 1.70)	0.92
• Positive – positive	50	22.8 [12.6 ; 41.8]	1.99	(1.21 – 3.27)	0.01



Day-7 ctDNA response as a prognostic marker in EGFRm NSCLC under osimertinib: The french study MELROSE (ESMO 1957P)

✓ French multicentric pase II trial designed to assess the evolution of genomic tumor profile under 1st line OSI with serial plasama sampling (0,7,28 and monthly) and tumor biopsies performed at baseline and at disease progression

Main inclusion criteria and flow-chart

- Male or female, aged at least 18 years
- Pathologically confirmed untreated advanced carcinoma of the lung, harboring a common EGFR mutation (Ex19 deletions, L858R)
- Eastern Cooperative Oncology Group performance status of 0 to 1

156 patients included

Failure to meet eligibility criteria (n=6)

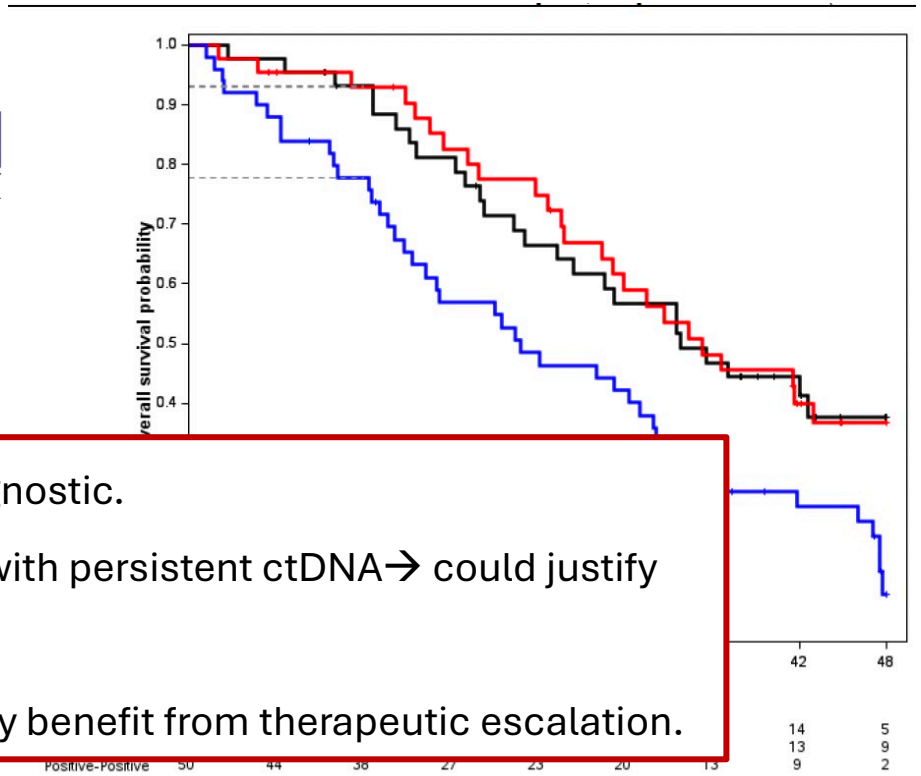
150 patients treated with 1L osimertinib
- 11 treatment discontinuations due to toxicities
  - ➢Interstiti
  - ➢Cardiac
  - ➢Primary

41 patients with a c
- 20 patients with clin
- 21 still on treatmen with radiological pr

109 patients with pr
- Patients who withd
- Patients who died with progression)

Factors Associated With Overall Survival (univariate analysis)

	N	OS median [25-75th percentile]	HR	IC 95%	p-value
Performance status					
• 0	65	42.6 [24.7 ; NA]			
• 1	85	29.2 [14.2 ; 39.4]	1.93	(1.26 - 2.94)	0.002
EGFR mutation					
• Exon19 del	87	33.5 [21.1 ; NA]			
• L858R	63	26.4 [15.2 ; 47.5]	1.29	(0.87 - 1.94)	0.21
CNS metastases at inclusion					
• No	113	33.5 [17.0 ; NA]			
• Yes	37	30.3 [15.6 ; 47.5]	1.37	(0.88 - 2.14)	0.16
ctDNA at inclusion					
• Negative	48	35.6 [20.1 ; NA]			
• Positive	100	30.3 [16.3 ; 47.5]	1.50	(0.96 - 2.36)	0.07



Day 7 ctDNA clearance was strongly prognostic.

Complete clearance at D7 significantly longer OS compared to those with persistent ctDNA→ could justify future de-escalation approaches.

Persistence or increase at D7 or M1 identifies high-risk patients who may benefit from therapeutic escalation.

nature medicine

Brief Communication https://doi.org/10.1038/s41591-024-03216-y

Ultrasensitive ctDNA detection for preoperative disease stratification in early-stage lung adenocarcinoma

NeXT Personal, a tumor-informed, whole-genome–based assay capable of detecting ctDNA at extremely low levels (1–3 parts per million) with **99.9% specificity**.

171 patients from the TRACERx study.

Preoperative ctDNA was detected in **81% of patients with LUAD,** including **57% of stage I cases**,

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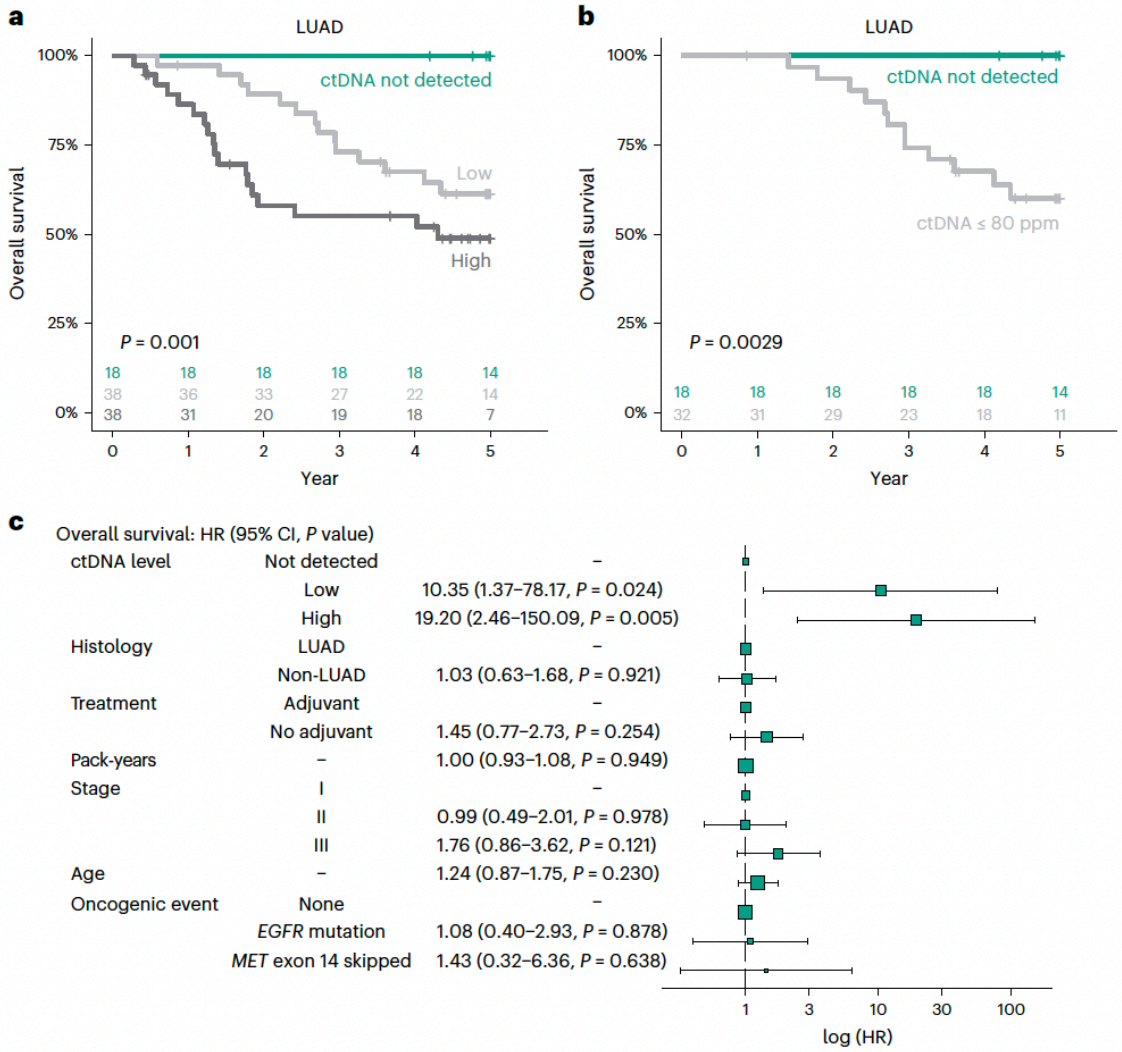
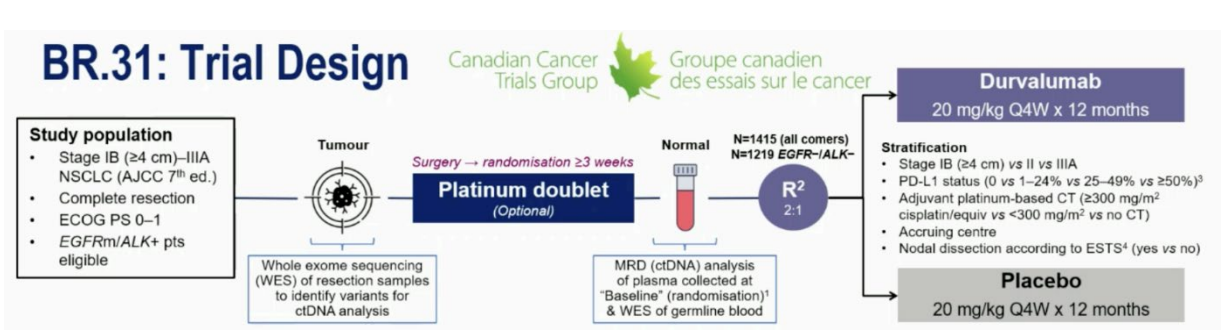


CCTG BR.31: Adjuvant durvalumab (D) in resected NSCLC : Final OS and MRD analyses (LBA68 ESMO 2025)



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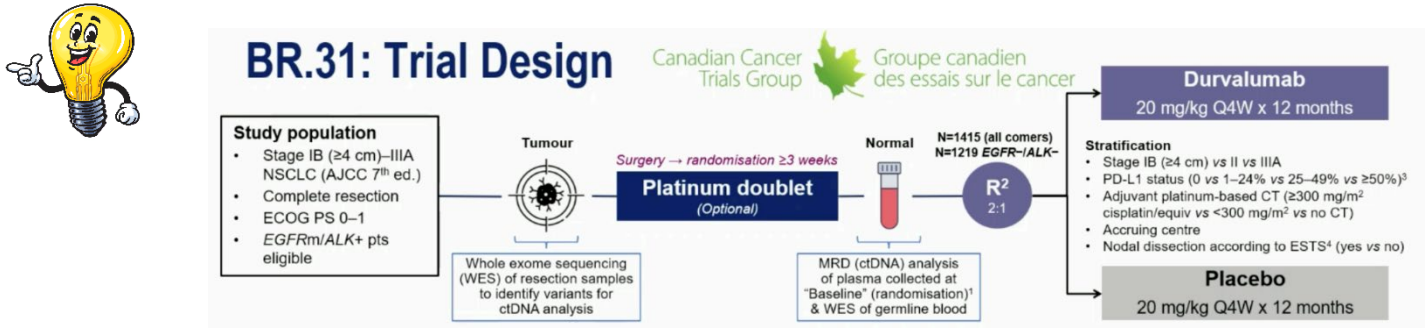

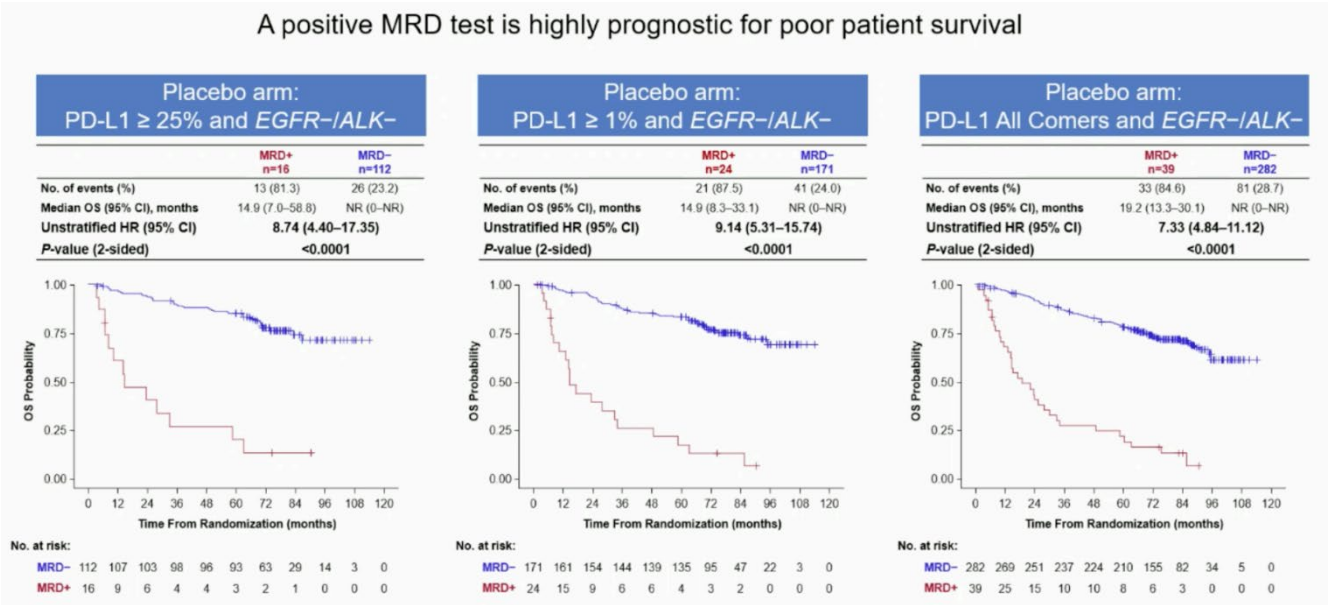

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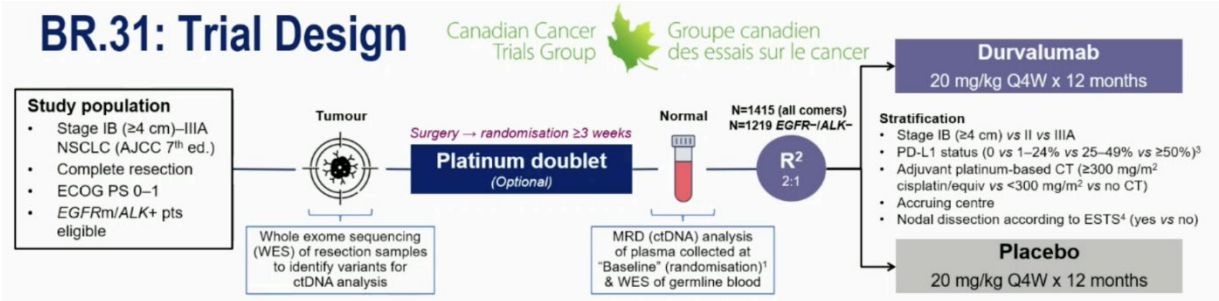

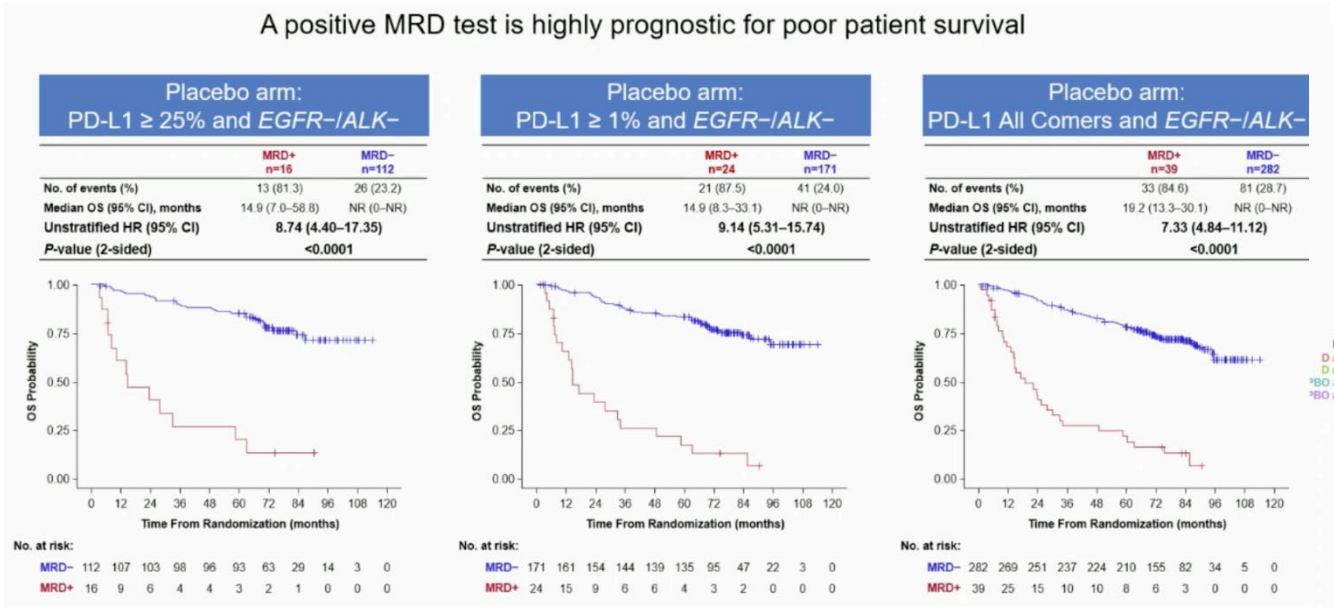

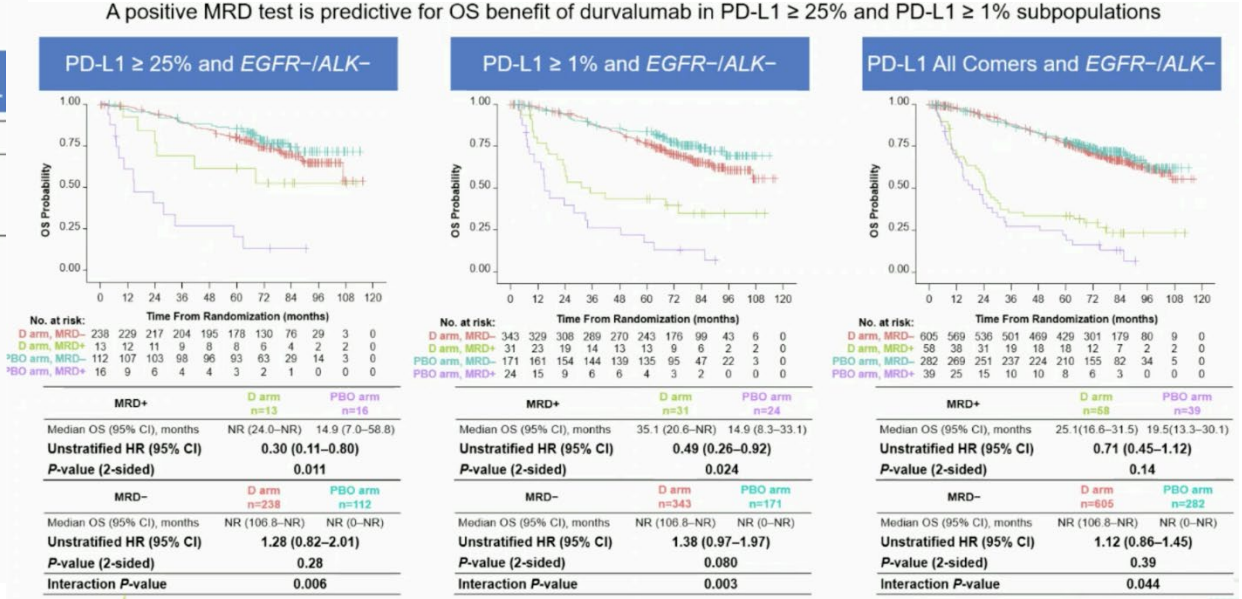

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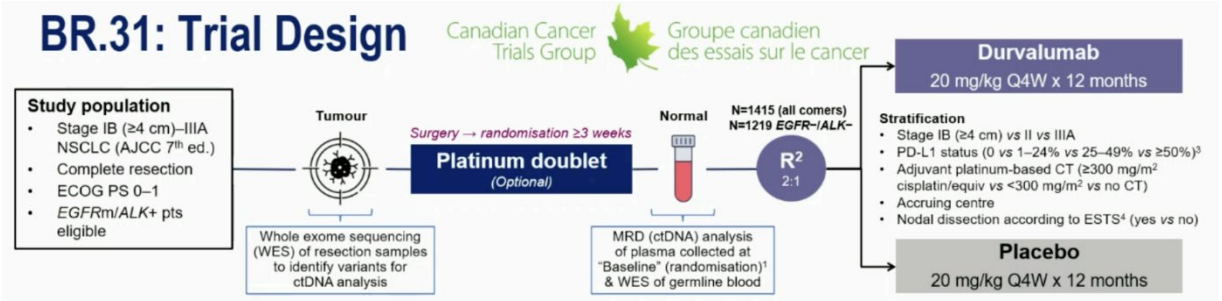

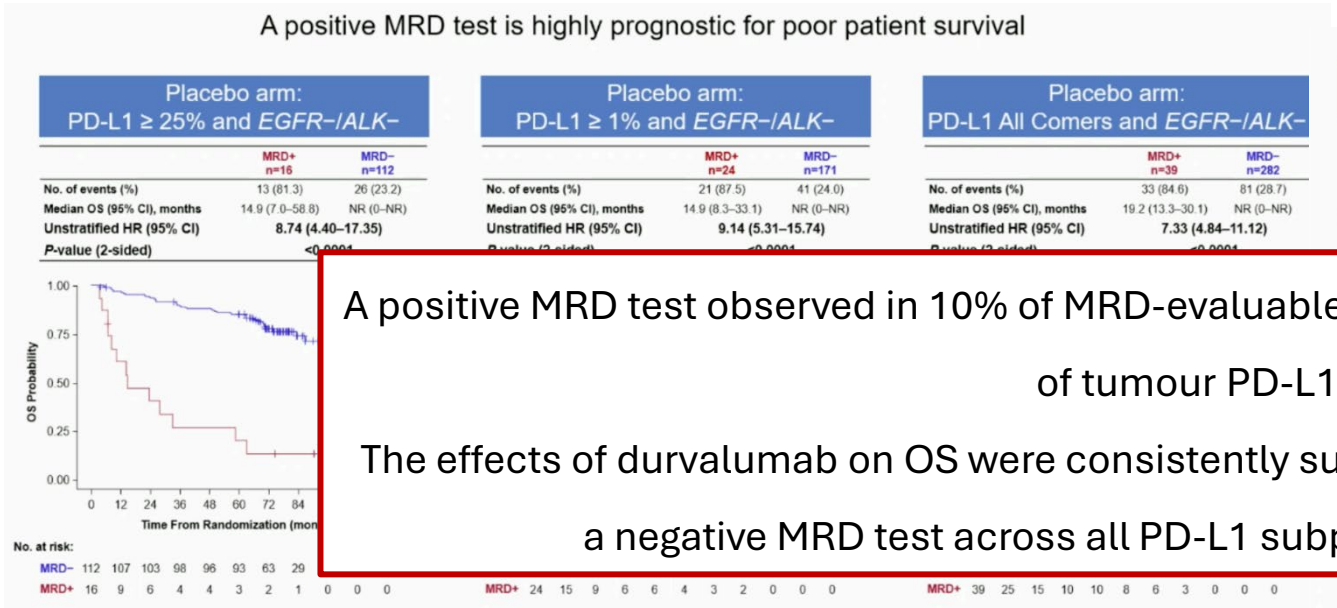

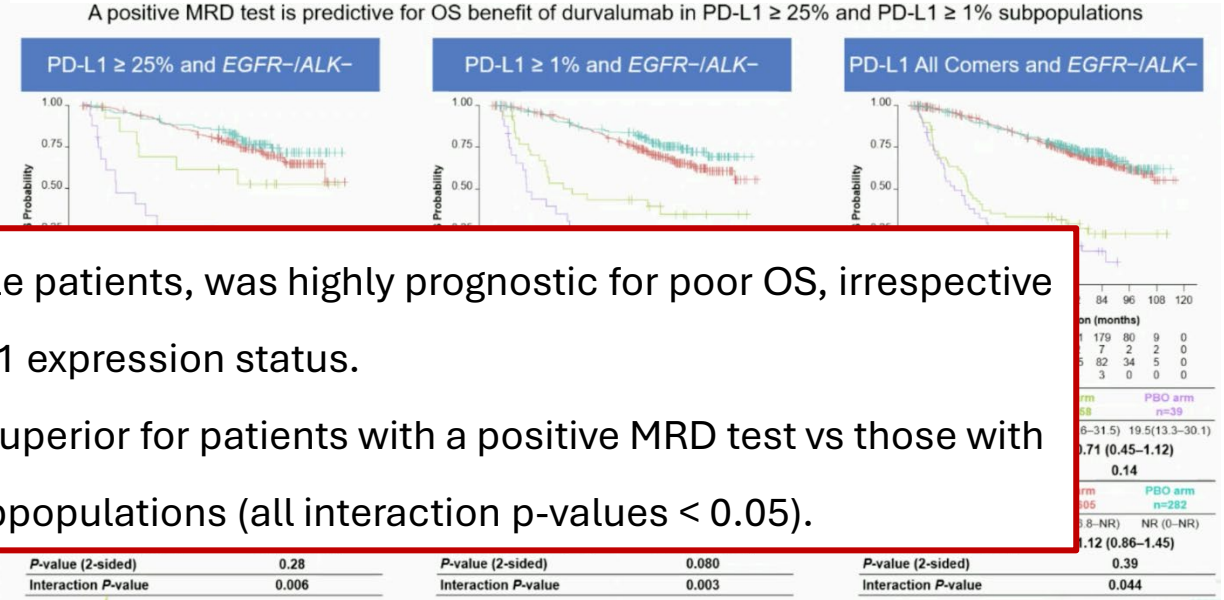

A positive MRD test observed in 10% of MRD-evaluable patients, was highly prognostic for poor OS, irrespective of tumour PD-L1 expression status.

The effects of durvalumab on OS were consistently superior for patients with a positive MRD test vs those with a negative MRD test across all PD-L1 subpopulations (all interaction p-values < 0.05).

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Article

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

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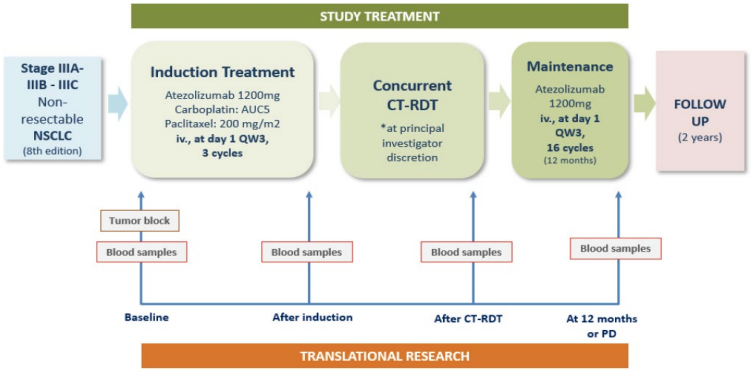

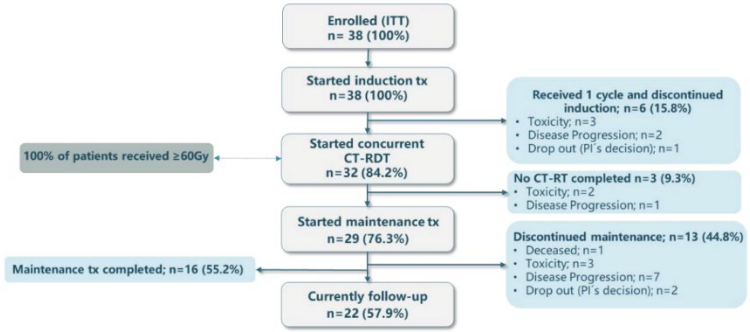

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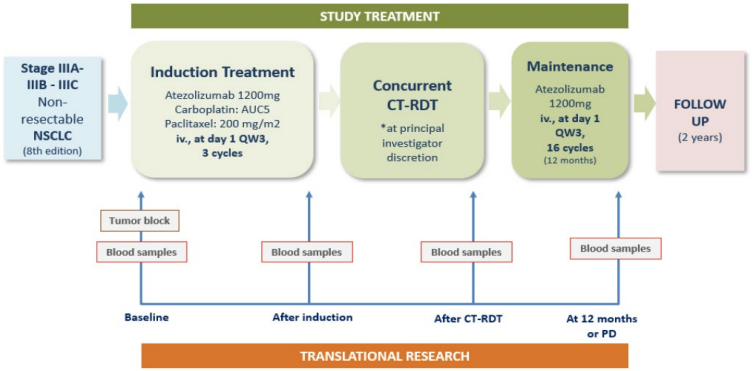
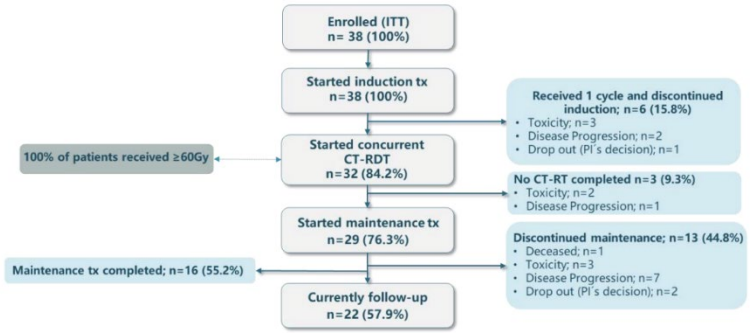
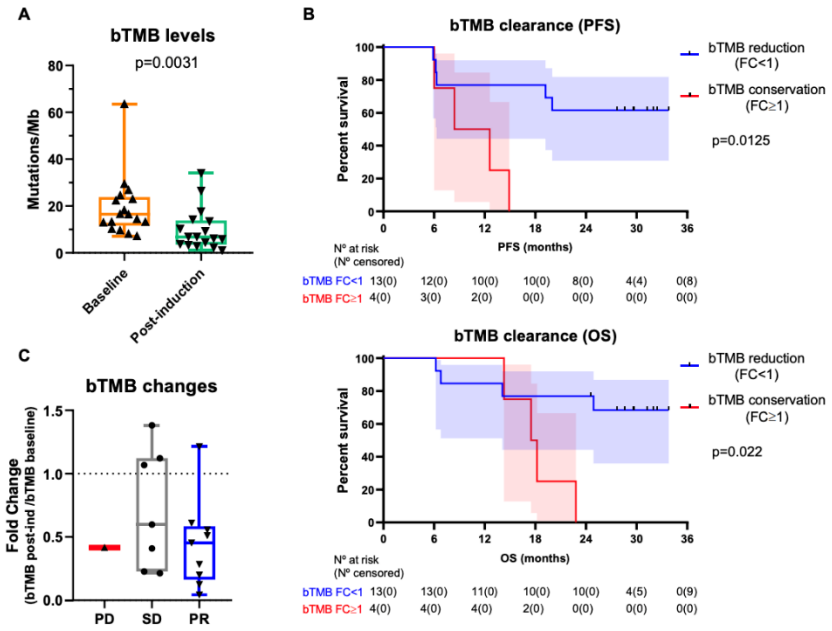




Supplementary Figure 11. Blood TMB reduction after induction in patients with available paired data.



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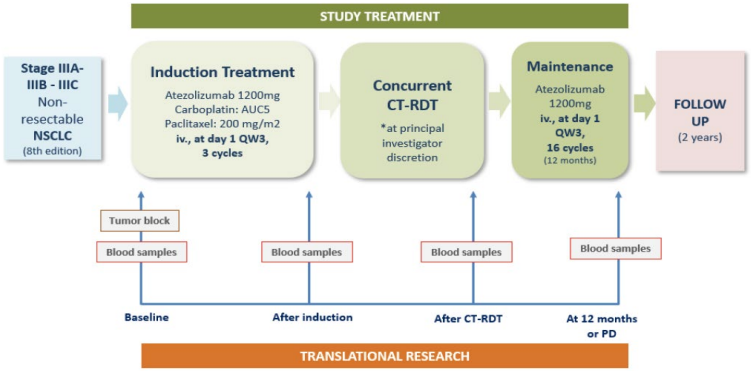

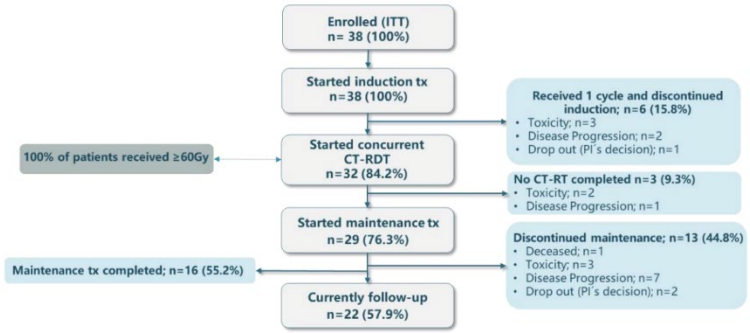

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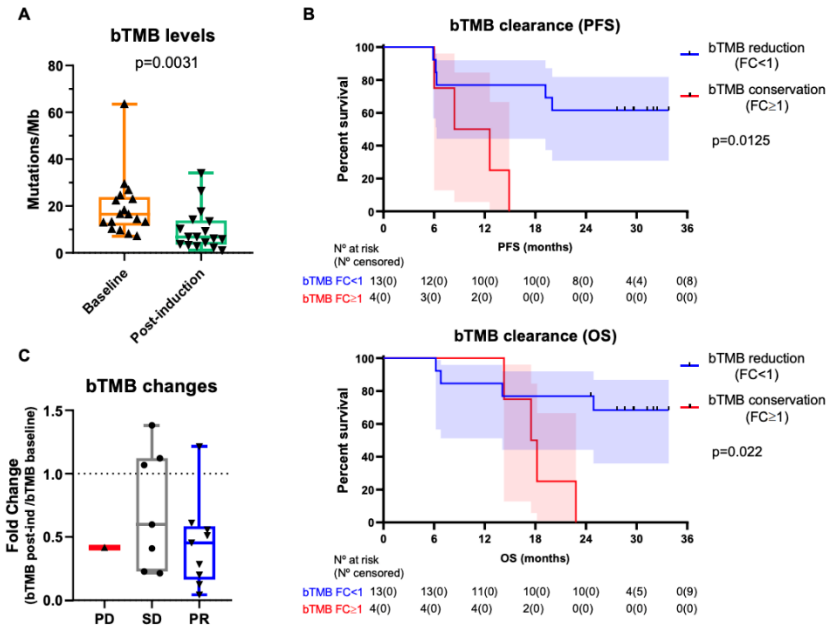
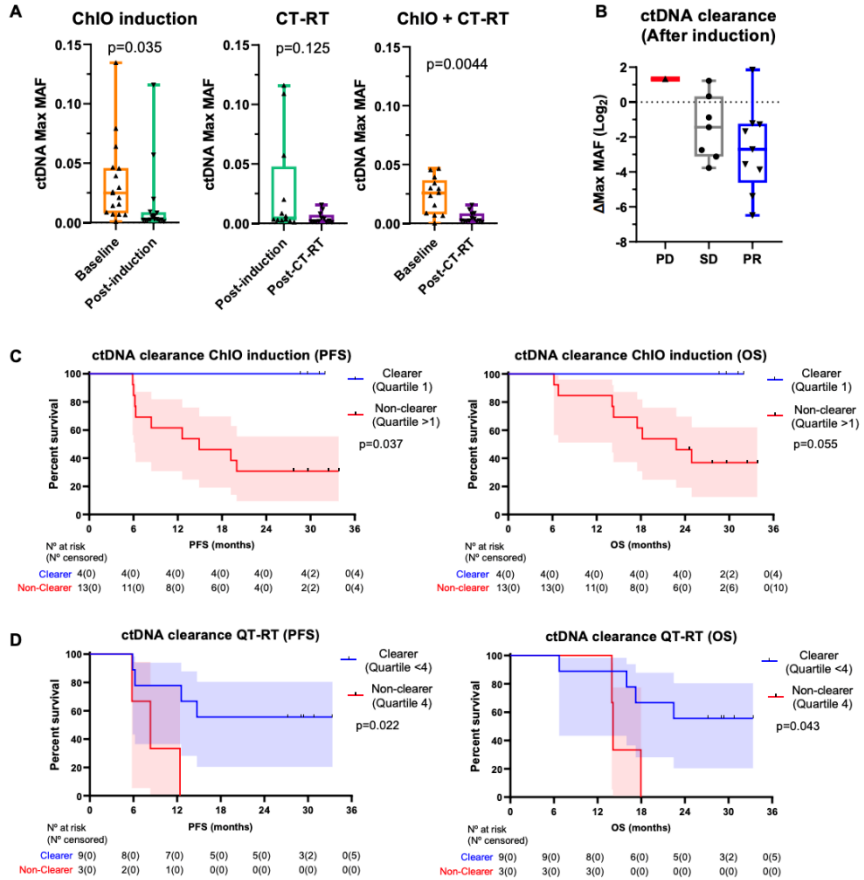


Supplementary Figure 10. ctDNA clearance in patients with available paired data.



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Median PFS to pembrolizumab + platinum doublet chemotherapy in PD-L1 positive NSCLC is 9.2 months (PD-L1 1–49%) to 11.1 months (PD-L1 ≥ 50%) (KEYNOTE-189 subsets). Median PFS to pembrolizumab in PD-L1 positive NSCLC is 5.4 months (KEYNOTE-042)[1]

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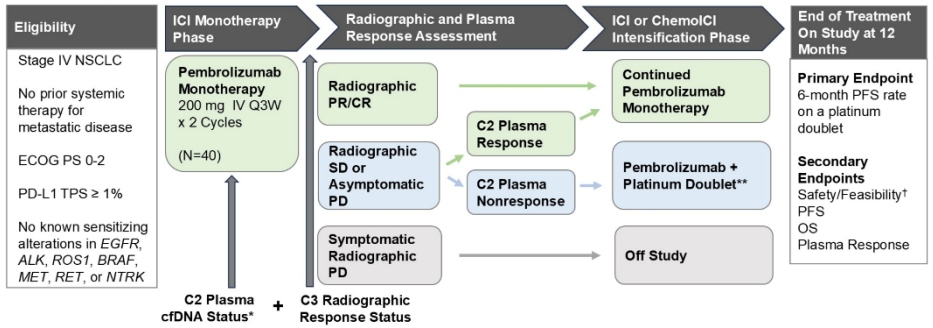

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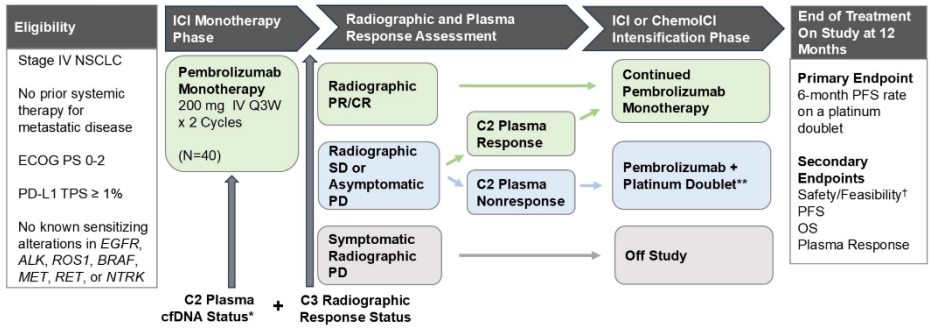
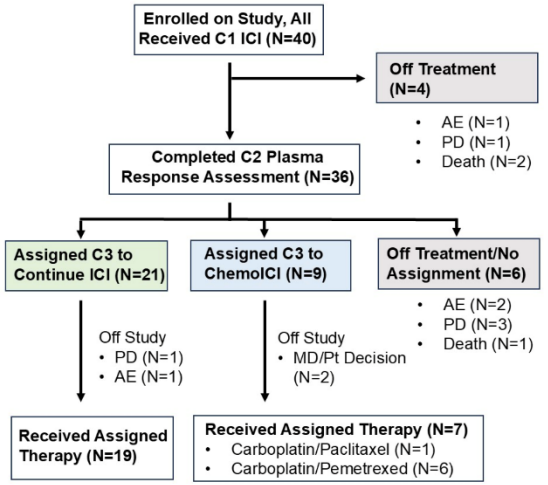


Treatment Allocation at Cycle Three



n (%)	Assigned ICI Monotherapy (N=21)	Assigned ChemoICI (N=9)	Off Rx Prior to Assignment (N = 10)
Age (mean)	68.4	69.8	72.2
Gender			
Male	11 (52.4%)	5 (55.6%)	6 (60.0%)
Female	10 (47.6%)	4 (44.4%)	4 (40.0%)
ECOG PS			
0	7 (33.3%)	2 (22.2%)	3 (30%)
1	14 (66.7%)	6 (66.7%)	6 (60%)
2	0 (0)	1 (11.1%)	1 (10%)
Histology			
NSQ	15 (71.4%)	7 (77.8%)	8 (80.0%)
SQ	6 (28.6%)	1 (11.1%)	2 (20.0%)
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Tobacco			
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PD-L1			
1-49%	8 (38.1%)	3 (33.3%)	4 (40.0%)
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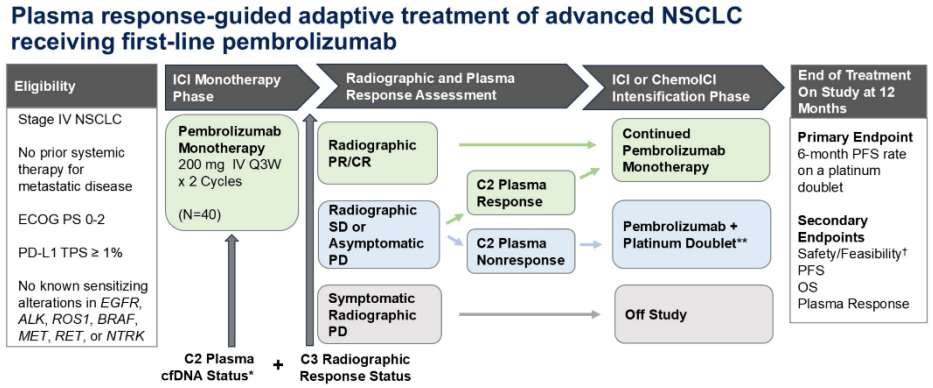

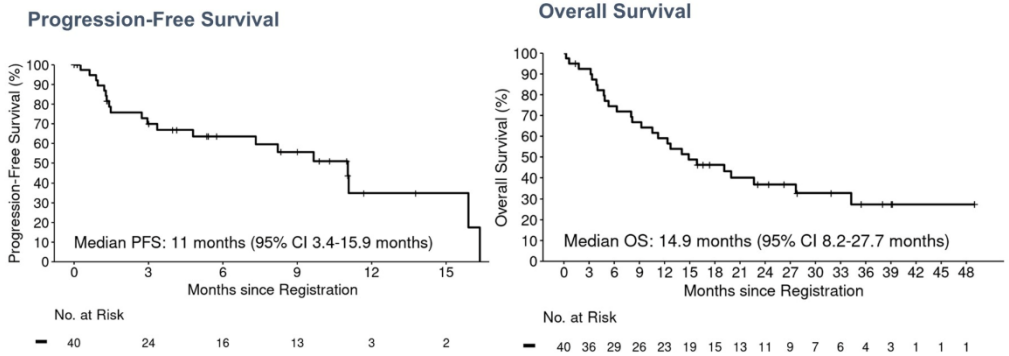

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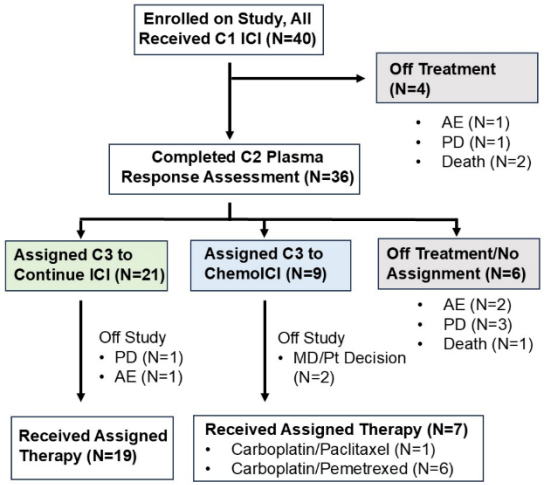

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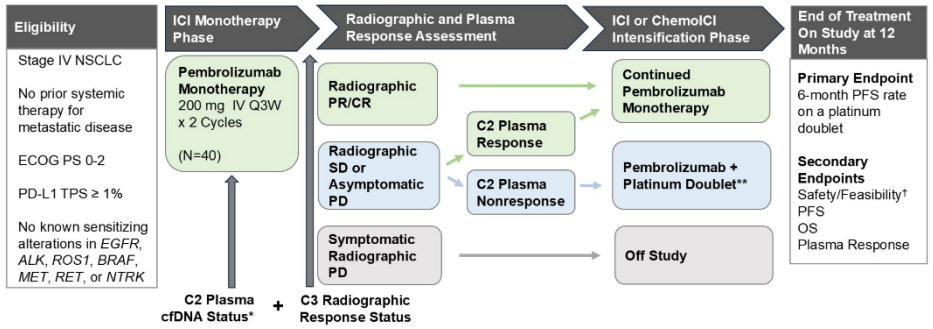
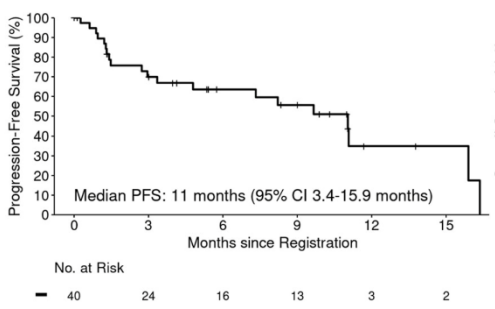
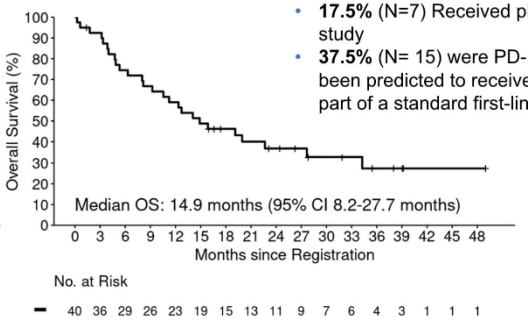


Progression-Free Survival



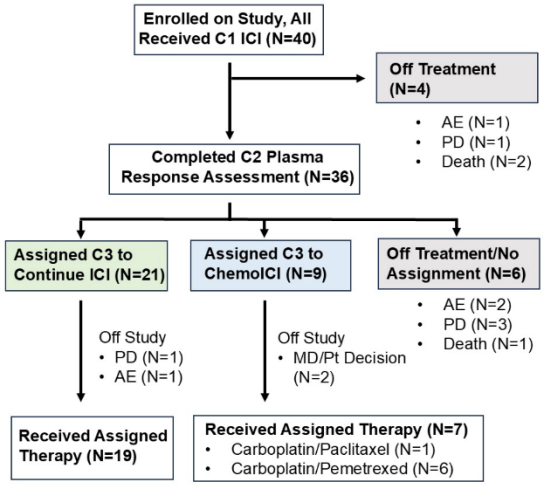
Overall Survival



Fewer patients received platinum doublet chemotherapy as part of their first-line regimen than would be predicted by PD-L1 score alone

- **17.5%** (N=7) Received platinum doublet on study
- **37.5%** (N= 15) were PD-L1 low and would have been predicted to receive platinum doublet as part of a standard first-line regimen

Treatment Allocation at Cycle Three



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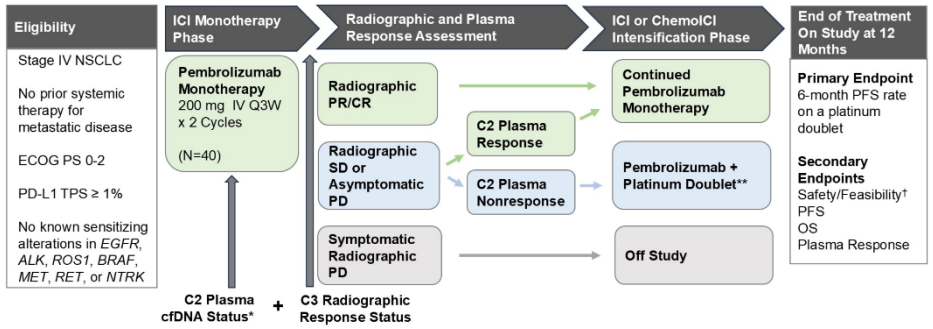
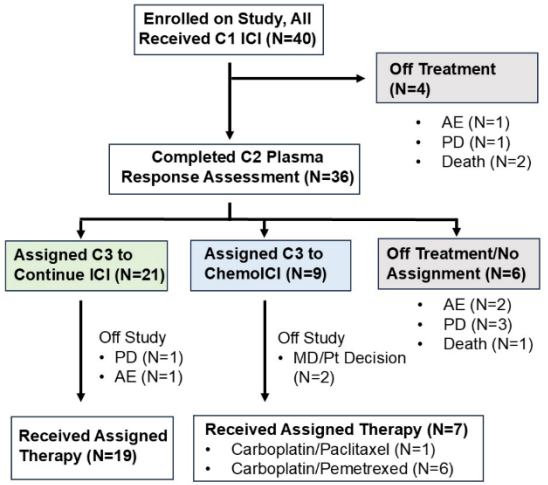


Treatment Allocation at Cycle Three

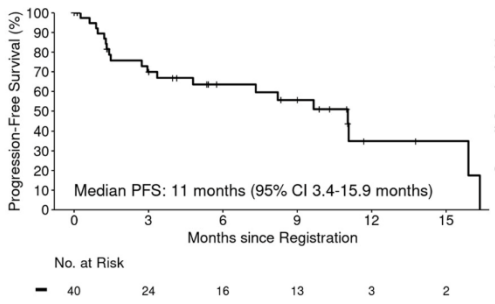


n (%)	Assigned ICI Monotherapy (N=21)	Assigned ChemoICI (N=9)	Off Rx Prior to Assignment (N = 10)
Age (mean)	68.4	69.8	72.2
Gender			
Male	11 (52.4%)	5 (55.6%)	6 (60.0%)
Female	10 (47.6%)	4 (44.4%)	4 (40.0%)
ECOG PS			
0	7 (33.3%)	2 (22.2%)	3 (30%)
1	14 (66.7%)	6 (66.7%)	6 (60%)
2	0 (0)	1 (11.1%)	1 (10%)
Histology			
NSQ	15 (71.4%)	7 (77.8%)	8 (80.0%)
SQ	6 (28.6%)	1 (11.1%)	2 (20.0%)
Adenosqua.	0 (0 %)	1 (11.1%)	0 (0%)
Tobacco			
Current	5 (23.8%)	3 (33.3%)	0 (0%)
Former	15 (71.4%)	5 (55.6%)	10 (100%)
Never	1 (4.8%)	1 (11.1%)	0 (0%)
PD-L1			
1-49%	8 (38.1%)	3 (33.3%)	4 (40.0%)
≥50%	13 (61.9%)	6 (66.7%)	6 (60.0%)
CNS+	4 (19.0%)	5 (55.6%)	1 (10.0%)

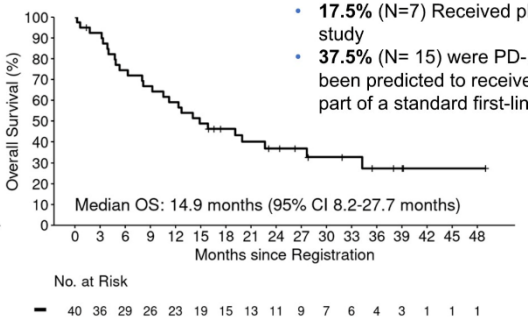
Fewer patients received platinum doublet chemotherapy as part of their first-line regimen than would be predicted by PD-L1 score alone

- **17.5%** (N=7) Received platinum doublet on study
- **37.5%** (N= 15) were PD-L1 low and would have been predicted to receive platinum doublet as part of a standard first-line regimen

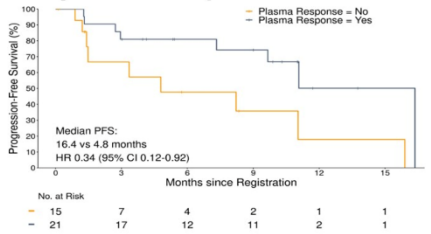
Progression-Free Survival



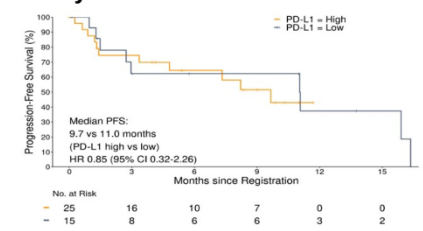
Overall Survival



PFS by Plasma Response



PFS by PD-L1 TPS



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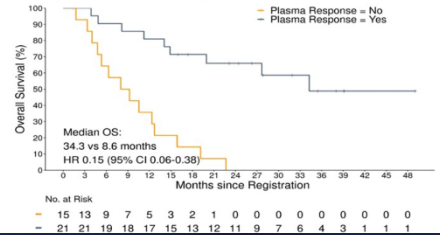

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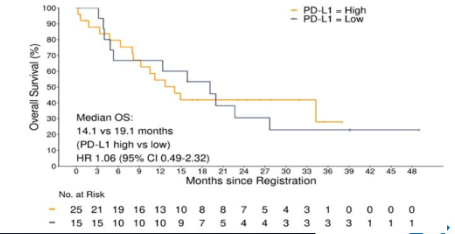

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Plasma-guided adaptive first-line CH-IO for NSCLC (ASCO 2025)

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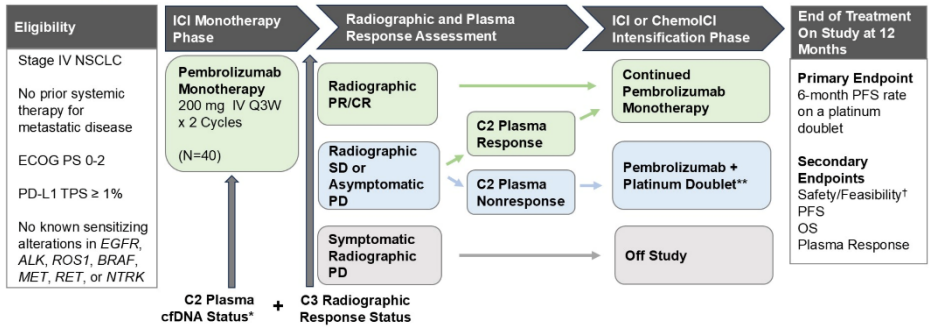

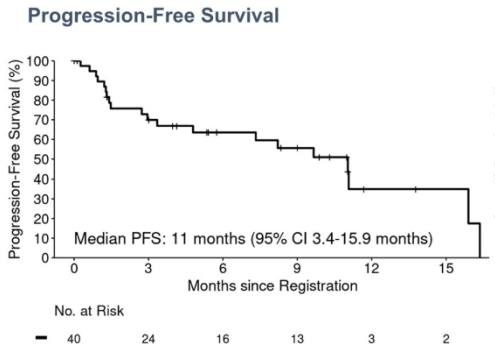

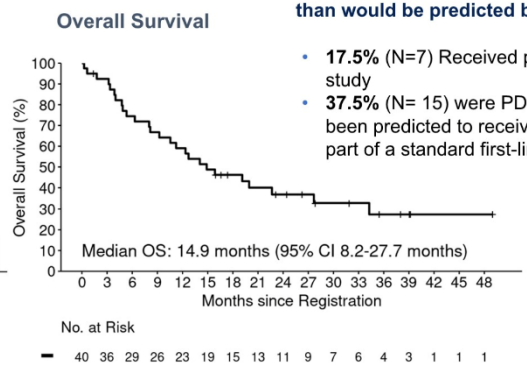

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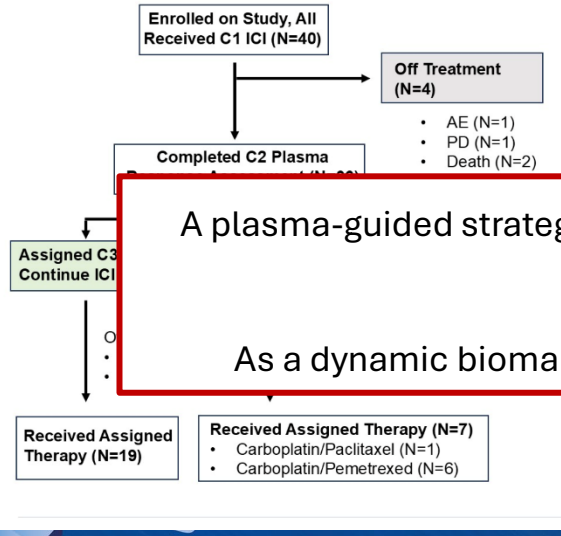

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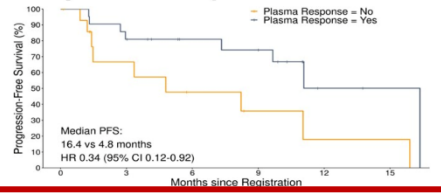

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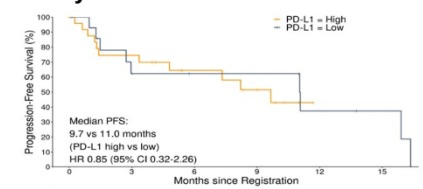
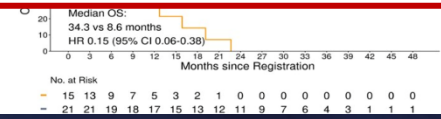
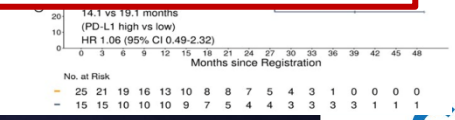


A plasma-guided strategy resulted in a median PFS of 11.0 months with fewer patients receiving first-line platinum doublet chemotherapy than would be predicted by PD-L1 TPS

As a dynamic biomarker, ctDNA kinetics are an important emerging tool to guide clinical decision making in NSCLC.





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AGENDA

1.- Dynamic based prognostic biomarkers (liquid biopsy)

2.- Integrated prognostic models and Artificial intelligence

3.- Host-immune based and genomic prognostic biomarkers

4.- Clinical and pathological biomarkers

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Integrated prognostic model and artificial intelligence

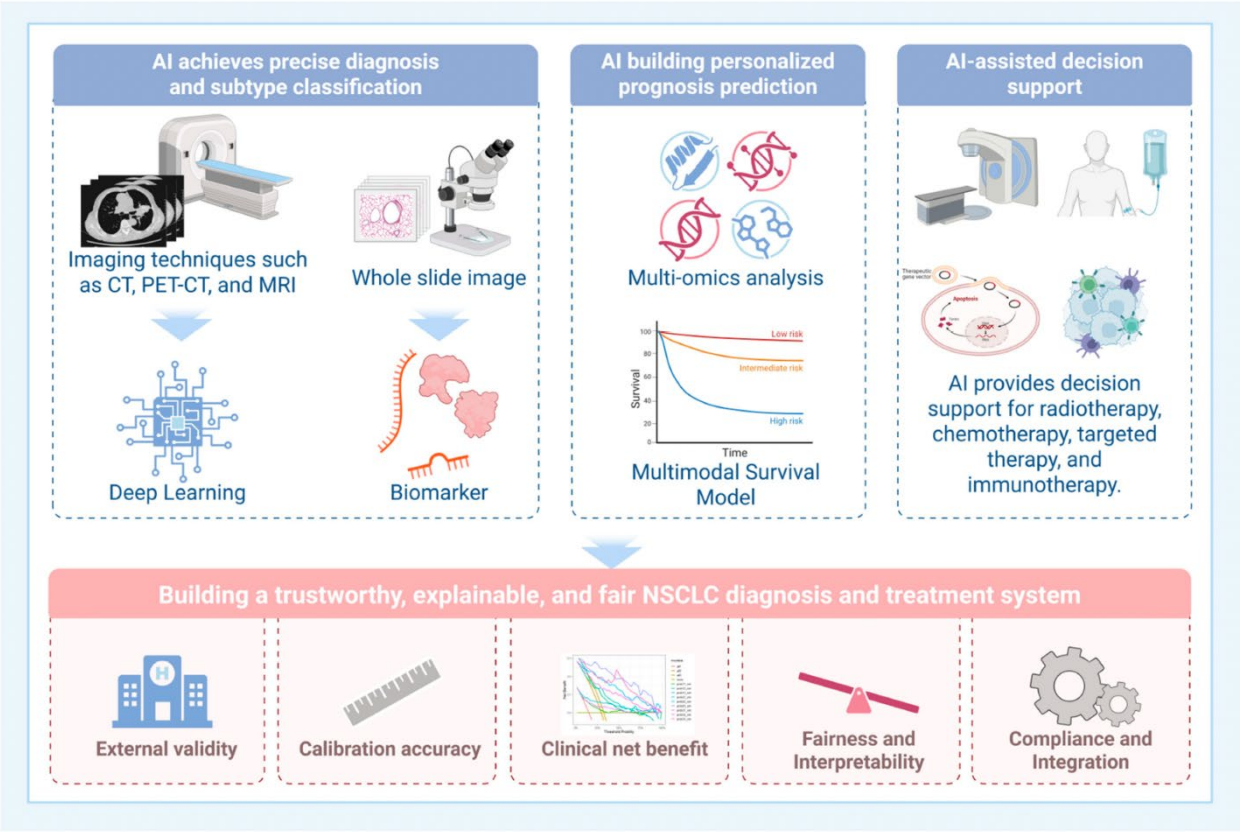

Figure 1 AI-enabled NSCLC pathway for precise diagnosis, personalized prognosis and clinical decision support

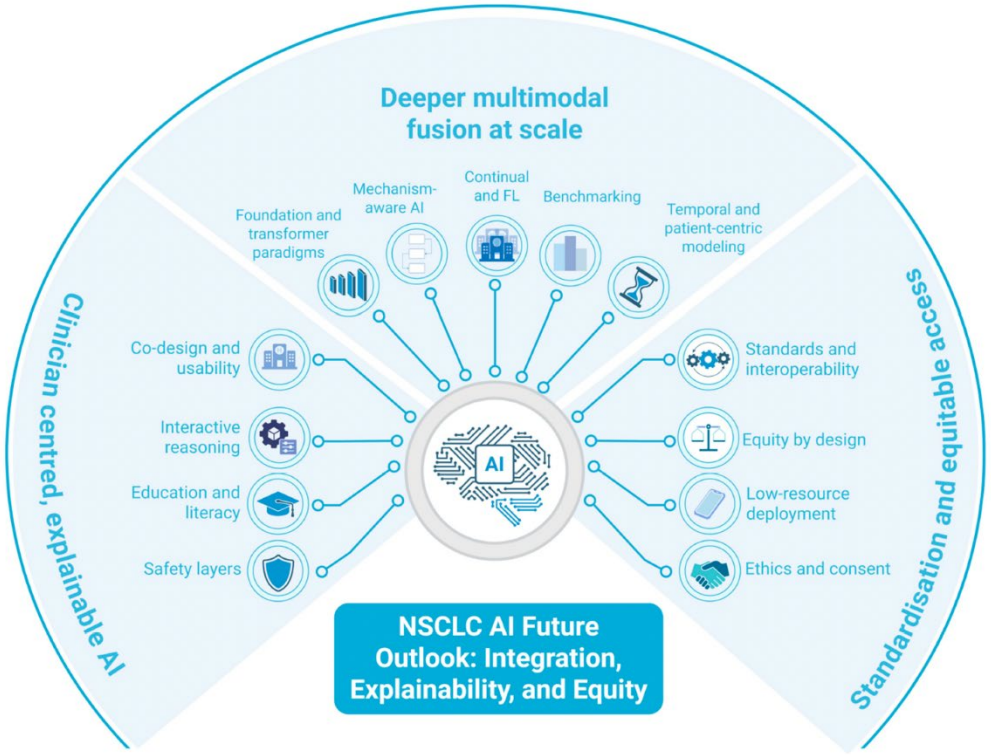

Figure 5 NSCLC AI Future Outlook: Integration, Explainability, and Equity

Chang L et al J Transl Med (2025)

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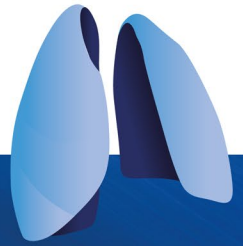
Association of radiomic features with DFS following neoadjuvant CH-IO in resectable NSCLC

- ✓ To identify radiomic texture features derived from pre-treatment CT scans that are associated with DFS in patients with NSCLC undergoing neoadjuvant
- ✓ 101 patients with locorregional NSCLC who received neoadjuvant Ch-IO at the Cleveland Clinic Foundation (Patient demographics, tumor characteristics and survival outcomes. Training (st; N=50) and validation (Sy; N = 51) cohorts for radiomic analyses



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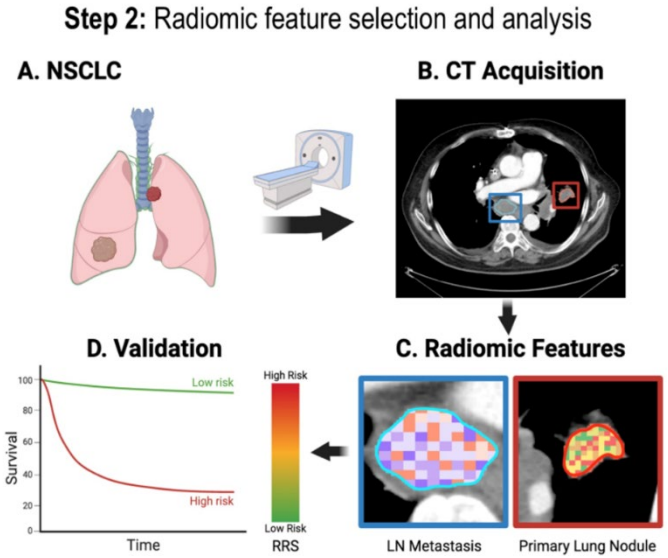

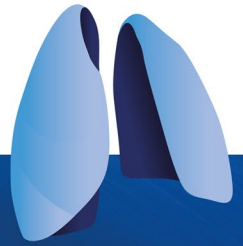

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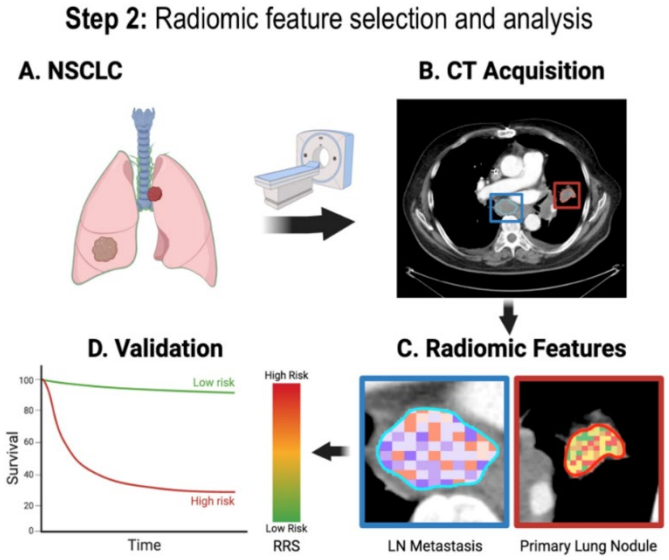
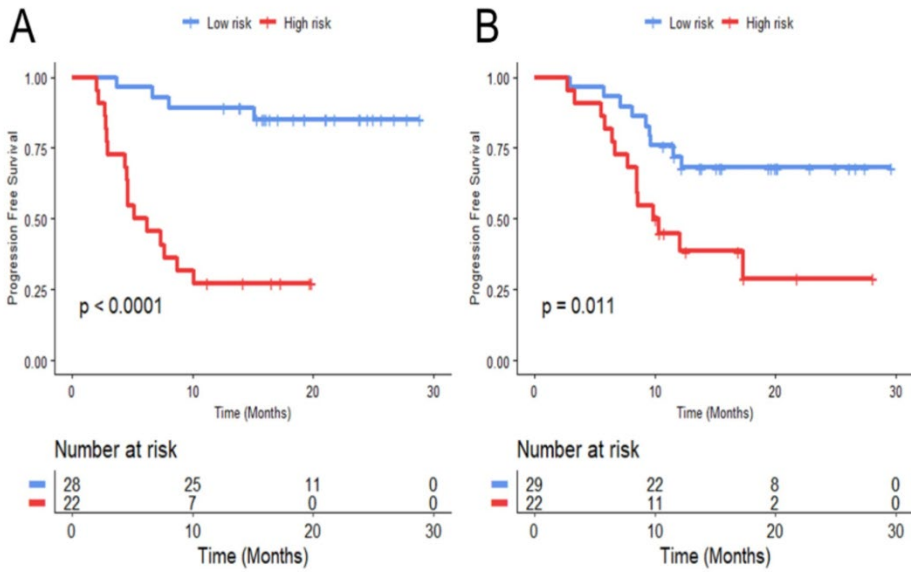




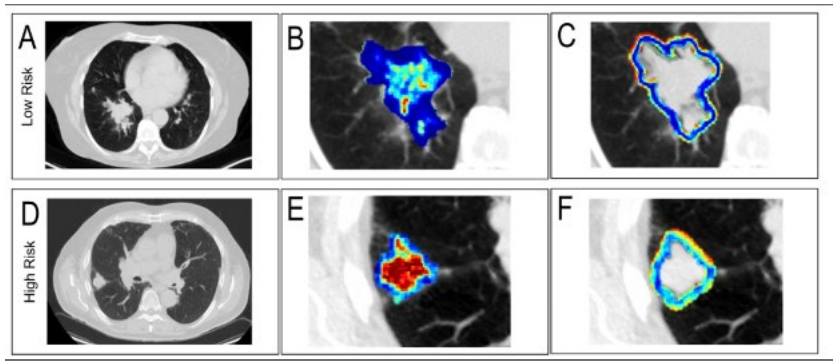
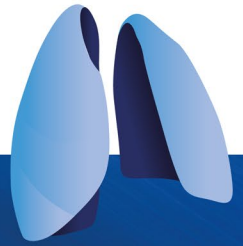


Fig. 2: Kaplan-Meier analyses between high- and low-risk groups determined by RRS in the training set (St; Fig 1A) and validation set (Sv; Fig 1B)



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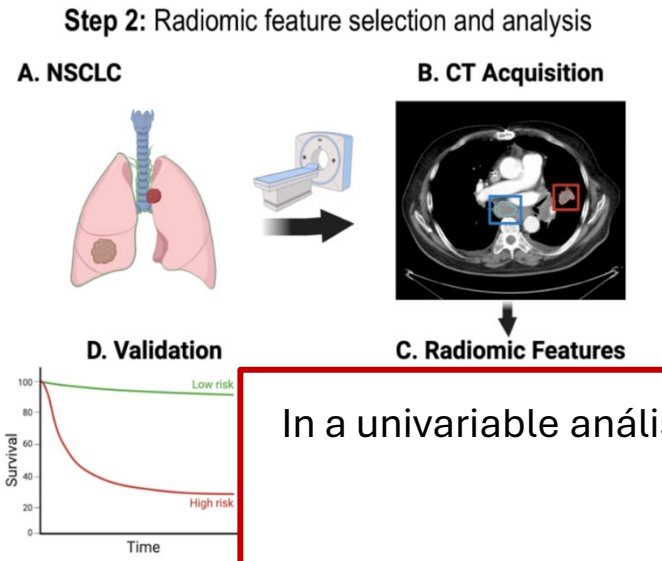
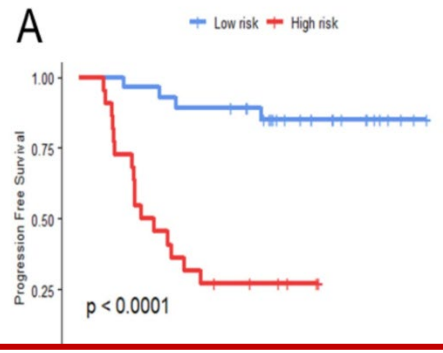
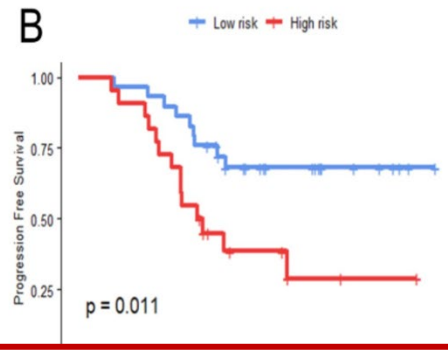
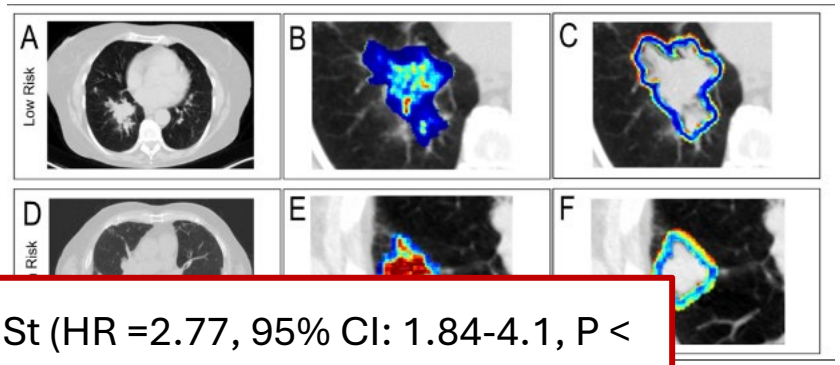


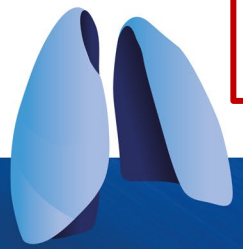






In a univariable análisis, RRS was significantly associated with DFS in both St (HR =2.77, 95% CI: 1.84-4.1, P < 0.0001) and Sv (HR = 2.28, 95% CI: 1.48-3.5, P = 0.0002)

These preliminary findings suggest that radiomic features hold promise as reliable, non-invasive biomarker for risk stratification and guiding treatment decisions



Enhancing survival prediction in aNSCLC: A comparison of AI derived prognostication and RECIST assessments in the MYSTIC Phase 3 trial

- ✓ To predict OS in aNSCLC patients with an AI-derived imaging biomarker model (IPRO-A) using differences between BL and early follow-up TC imaging, and to compare IPRO-A to RECIST v.1.1 response assessments
- ✓ IPRO-A is a Deep learning model trained on serial imaging data and survival outcomes from real-world aNSCLC patients, extracting and comparing spatial imaging biomarkers from BL and follow up CT scan data to generate a survival score.

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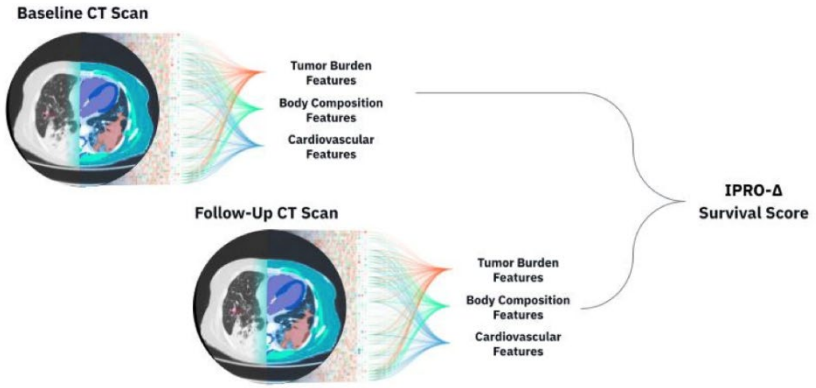

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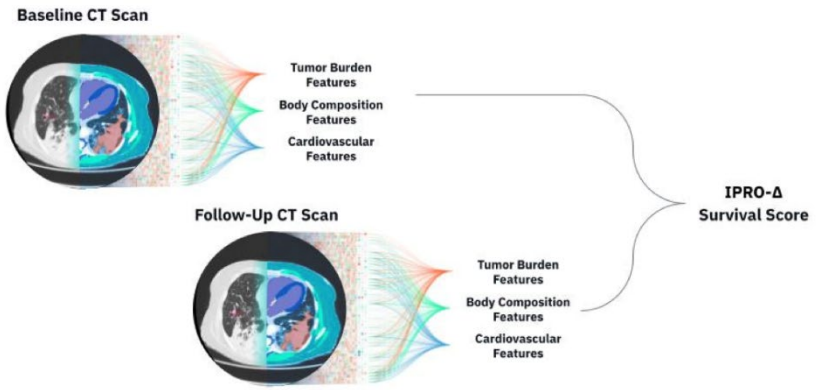
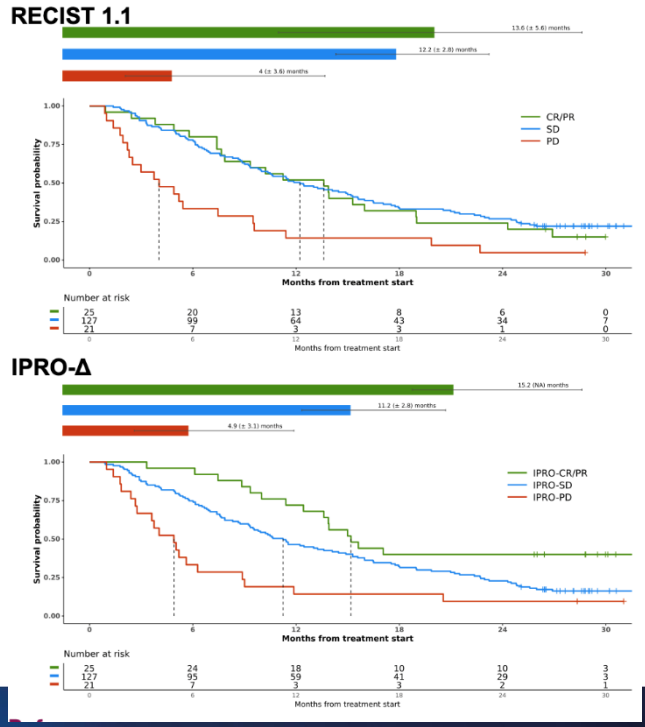


Figure 3. IPRO-Δ and RECIST v1.1 predictions of OS at W6 follow up.



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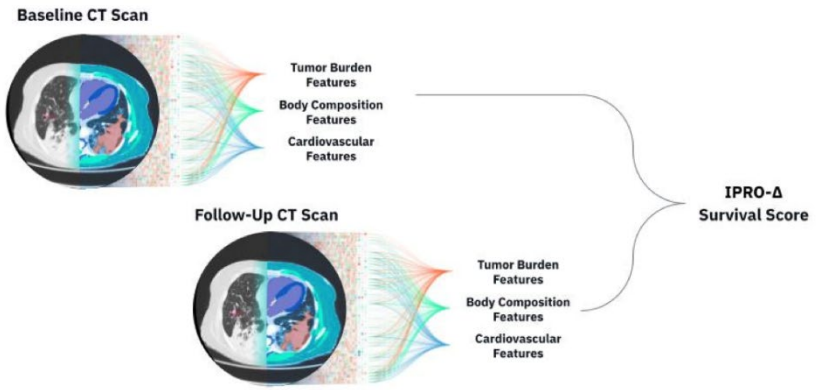

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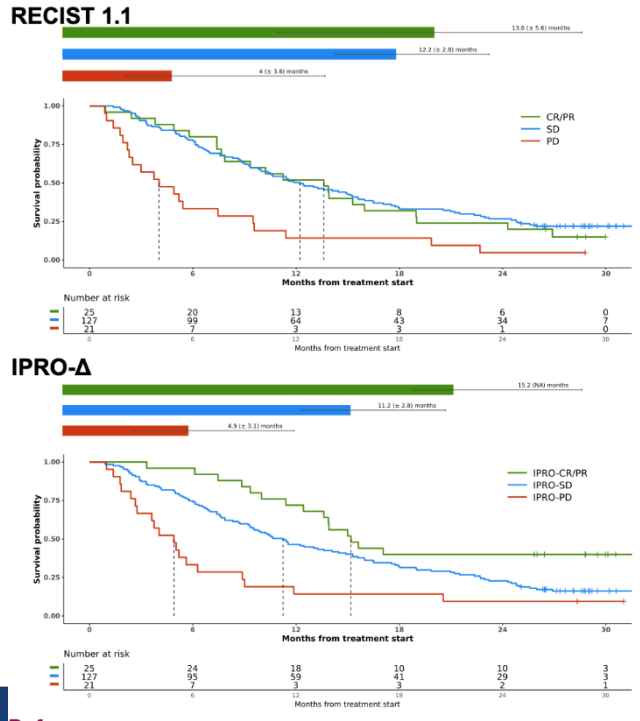
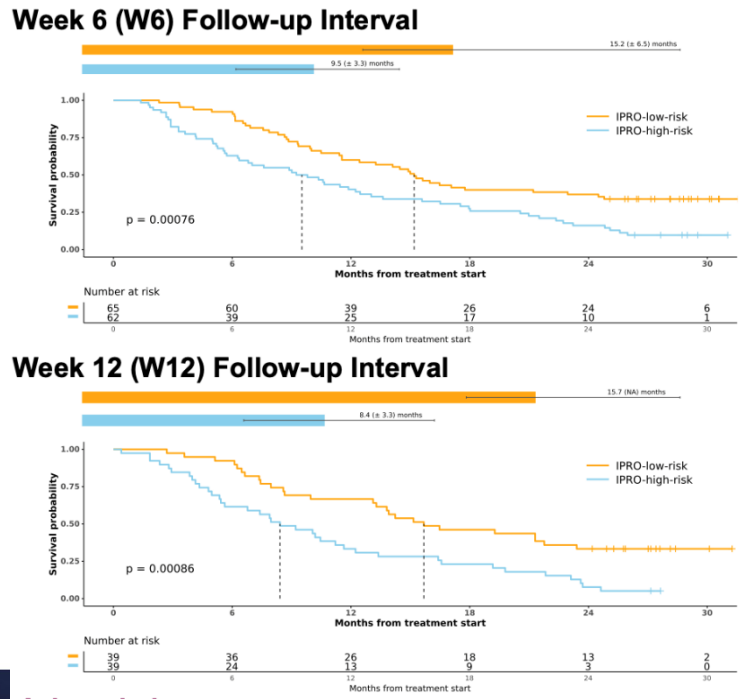


Figure 4. IPRO-Δ stratification of RECIST SD patients into high-risk and low-risk groups.



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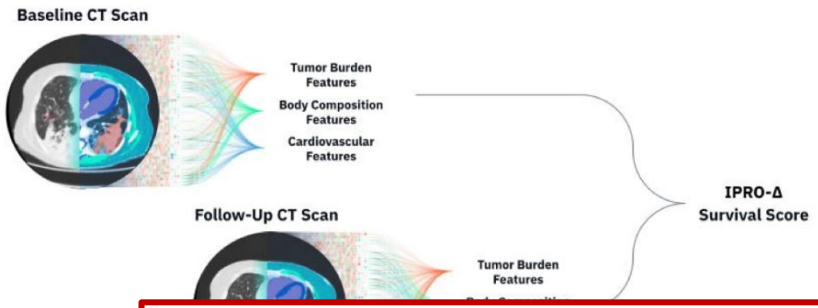

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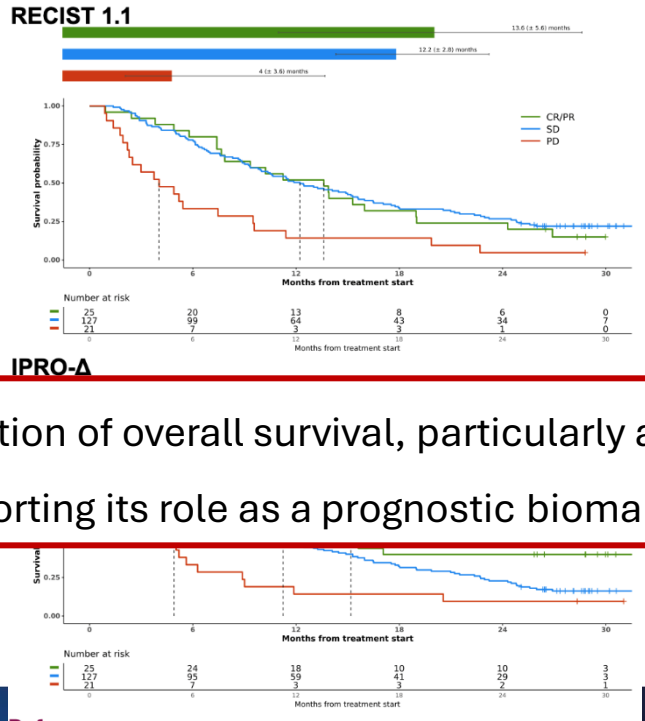

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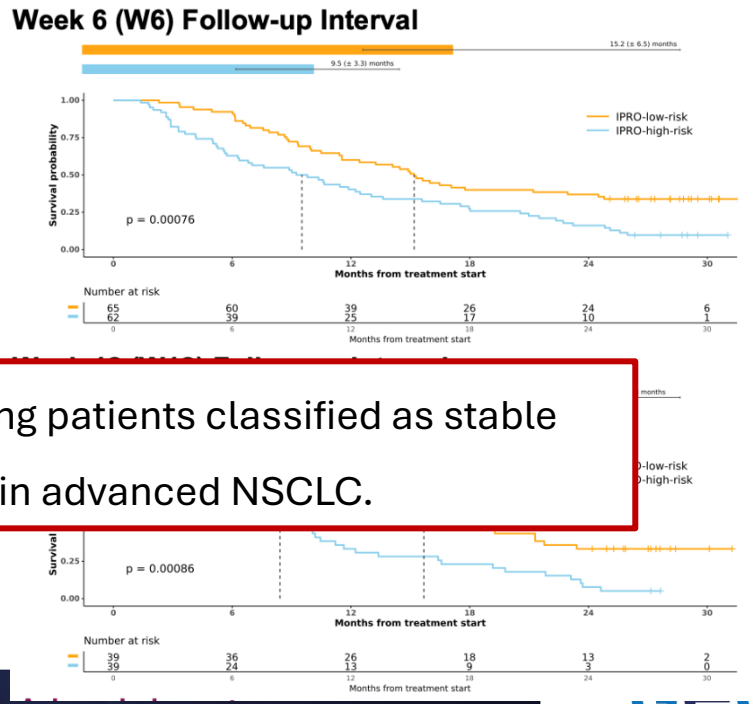


IPRO-A showed improved stratification of overall survival, particularly among patients classified as stable disease by RECIST, supporting its role as a prognostic biomarker in advanced NSCLC.

Integrated prognostic model and artificial intelligence

Open access Original research

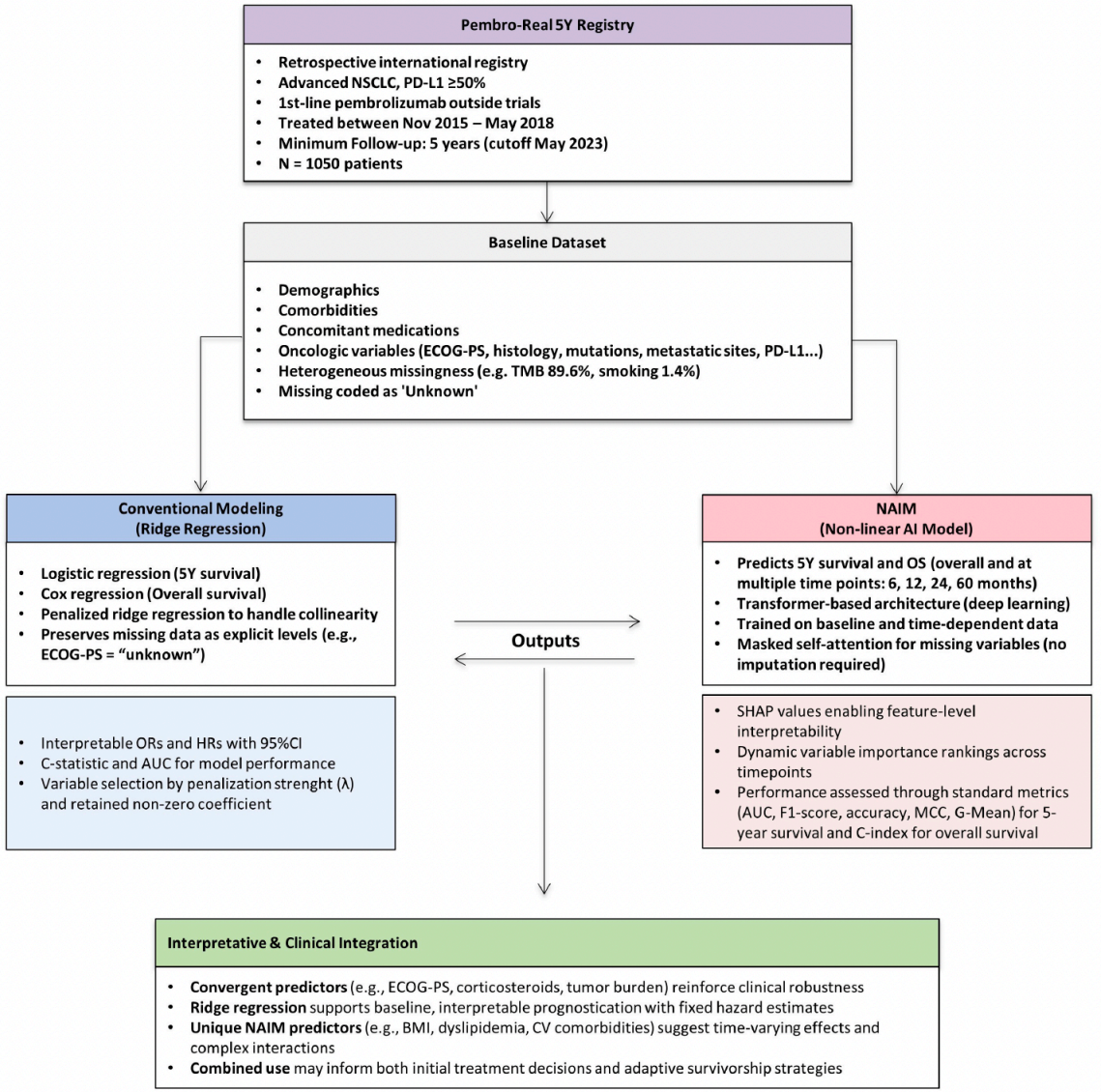
Journal for ImmunoTherapy of Cancer

Transformer-based AI approach to unravel long-term, time-dependent prognostic complexity in patients with advanced NSCLC and PD-L1 ≥50%: insights from the pembrolizumab 5-year global registry

Key Prognostic Factors

Early Mortality (≤6 months)	Long-Term Survival (5 years)
ECOG PS ≥2	No hypertension / cardiovascular disease
Baseline corticosteroid use	Dyslipidemia
Bone metastases	Higher BMI
High metastatic burden	No bone metastases

Analytical framework



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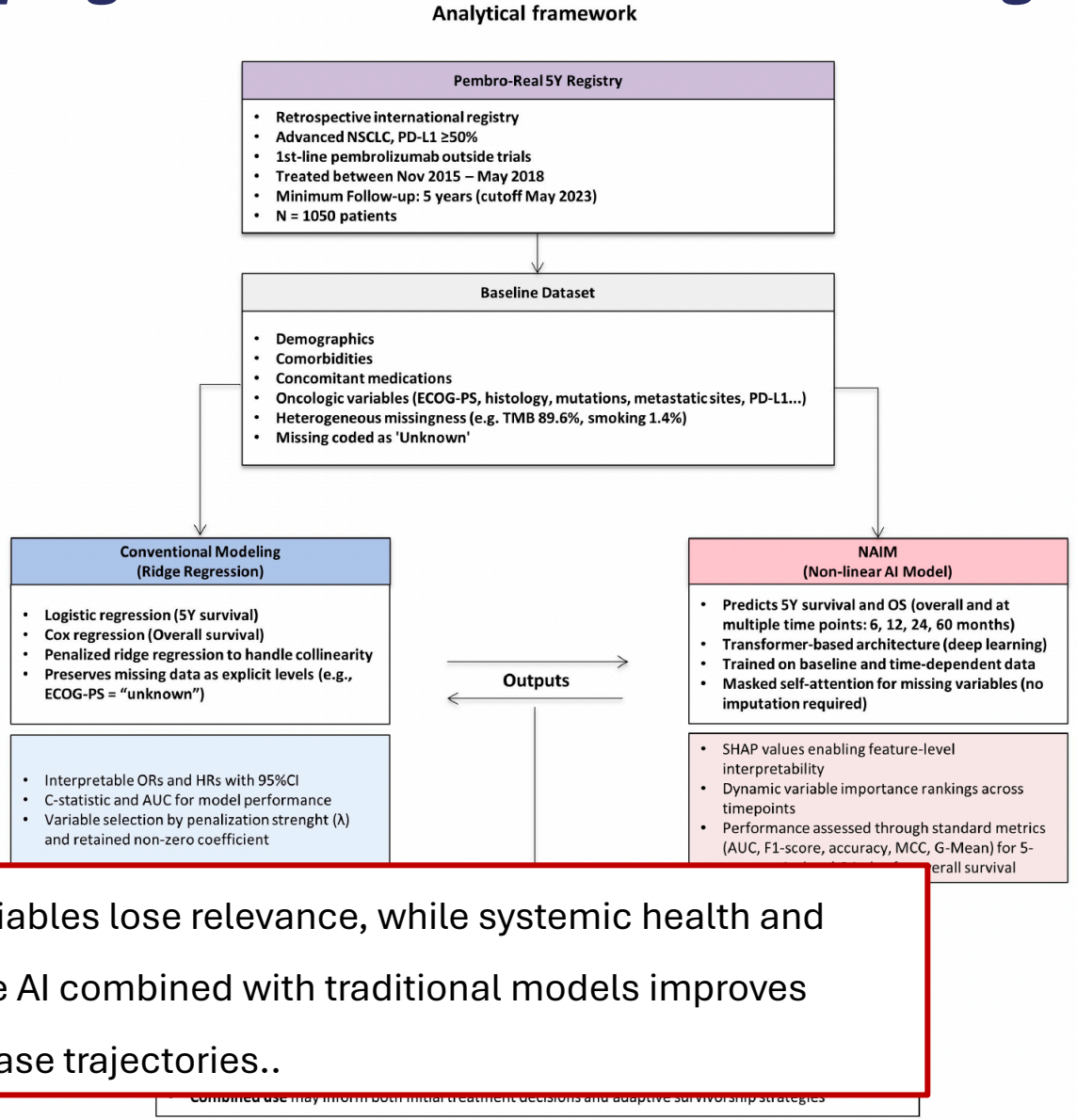

Prognostic factors evolve over time: tumor-related variables lose relevance, while systemic health and comorbidities drive long-term outcomes. Explainable AI combined with traditional models improves understanding of disease trajectories..

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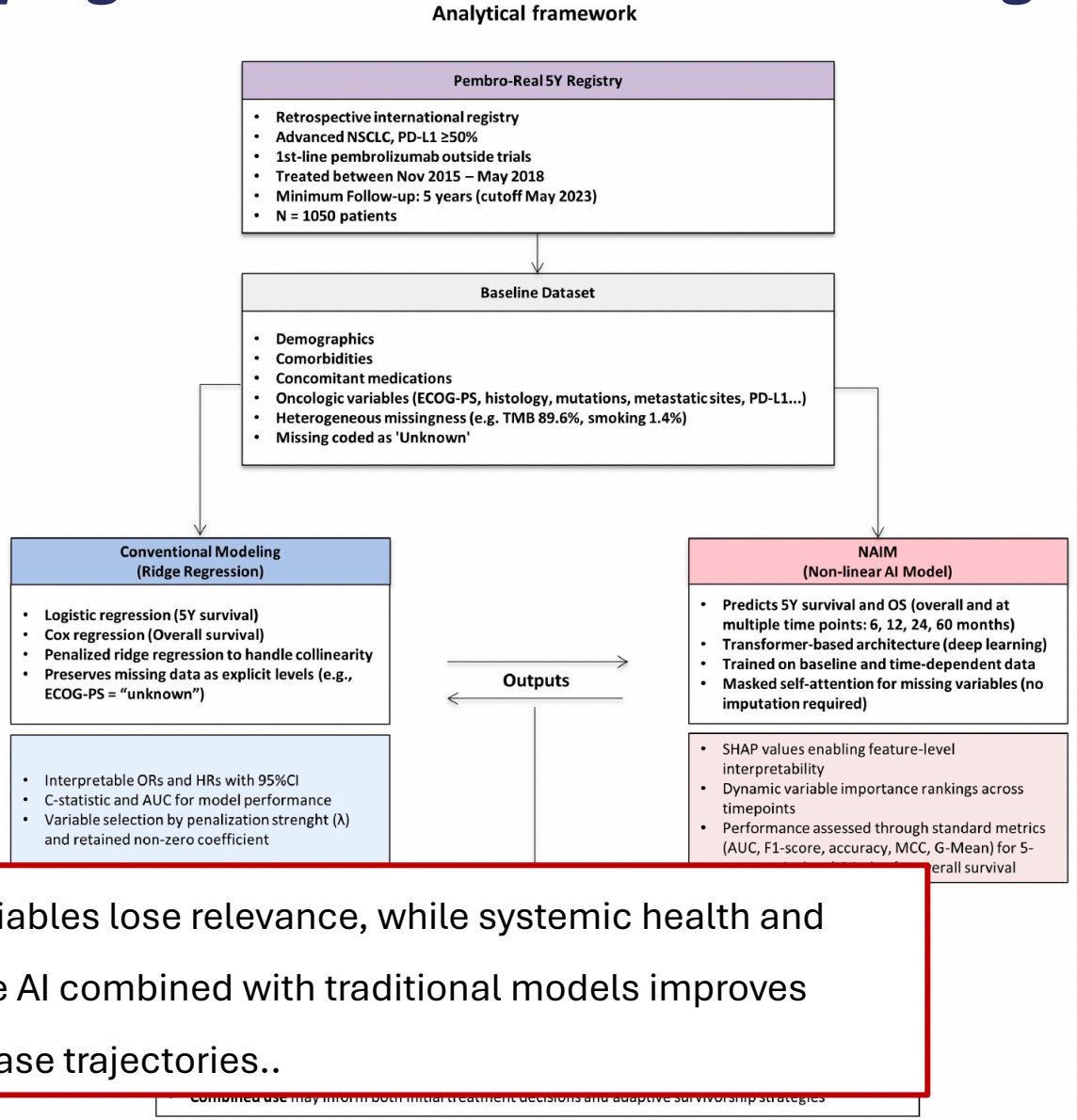

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GECP lung cancer research

AGENDA

1.- Dynamic based prognostic biomarkers (liquid biopsy)

2.- Integrated prognostic models and Artificial intelligence

3.- Host-immune based and genomic prognostic biomarkers

4.- Clinical and pathological biomarkers

GECP lung cancer research

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R 1:1

❖ Early ToD group

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Endpoints

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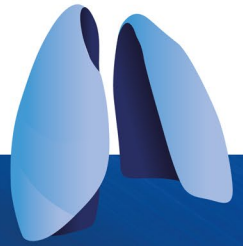

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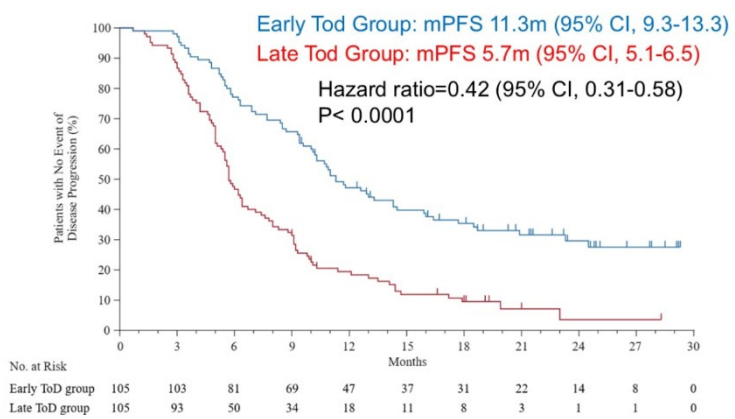

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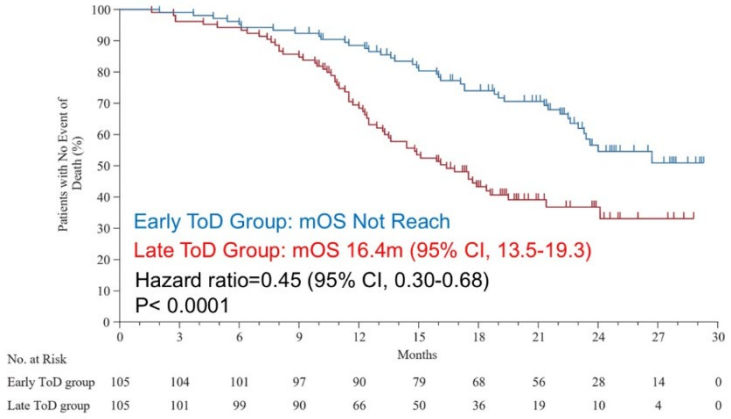

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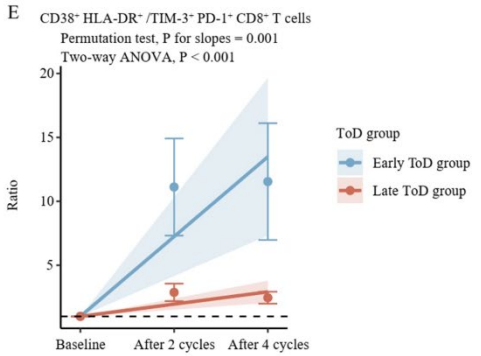

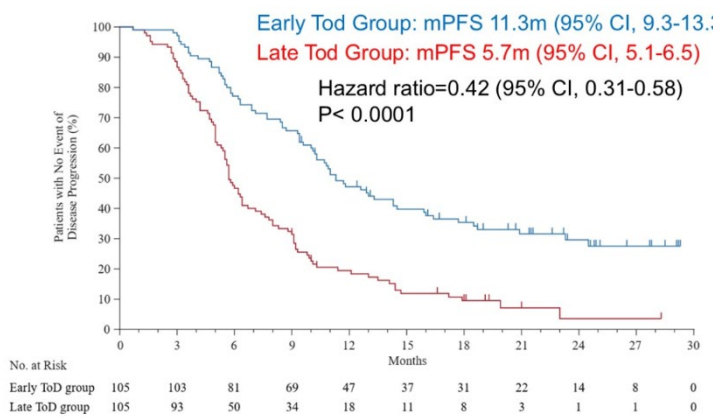

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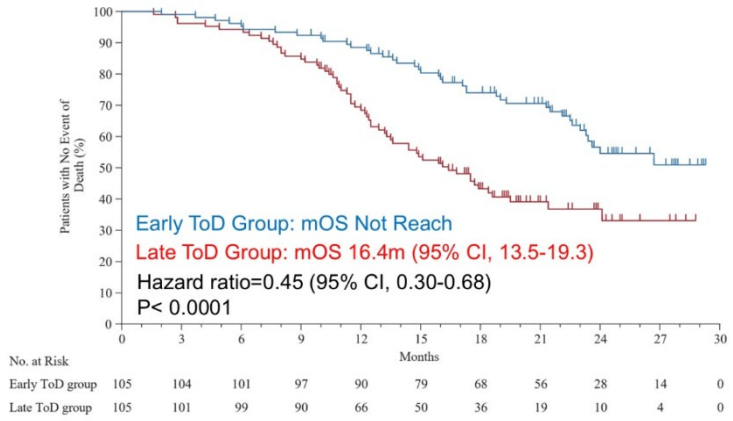

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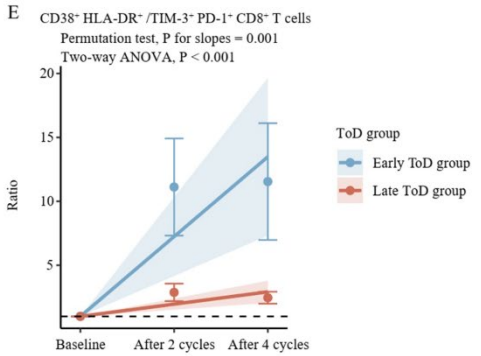

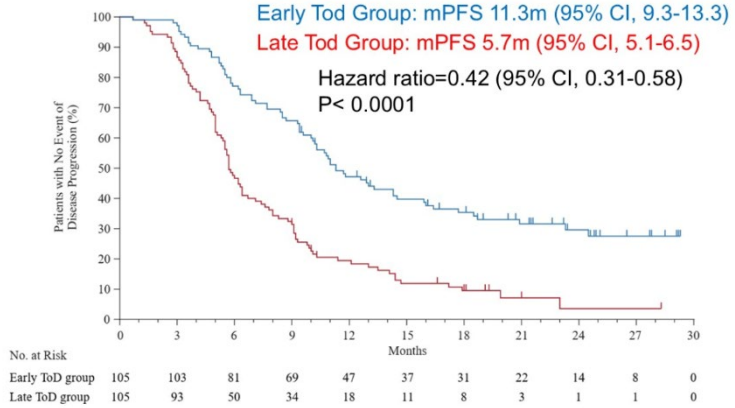

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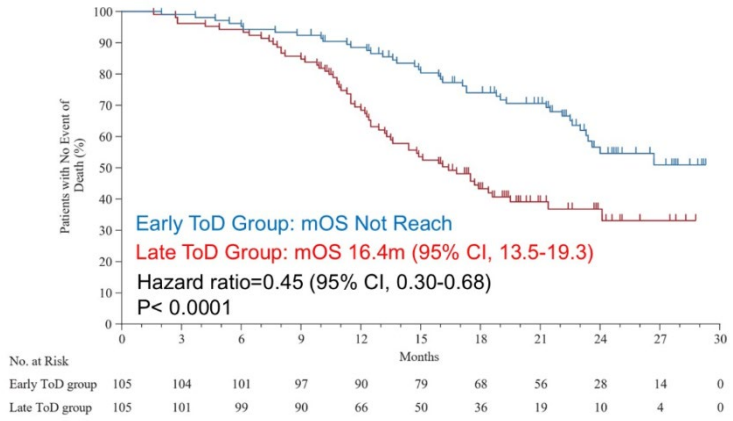

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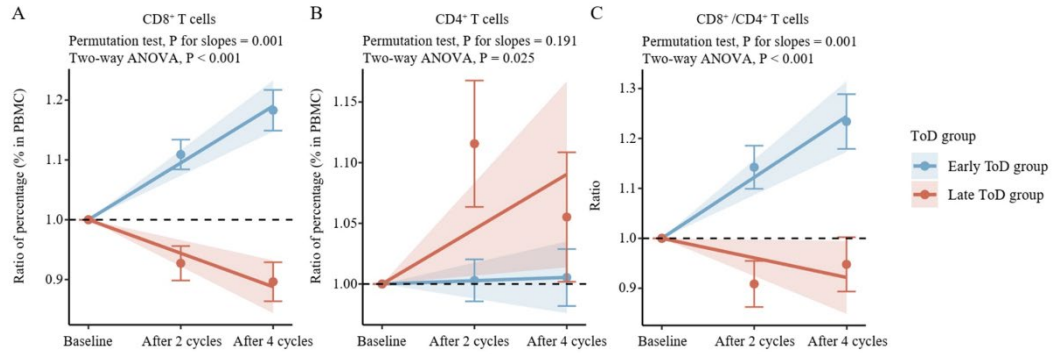
Increase of circulating CD8+ T cells in the early ToD group versus decrease in the late ToD group.



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lung cancer research

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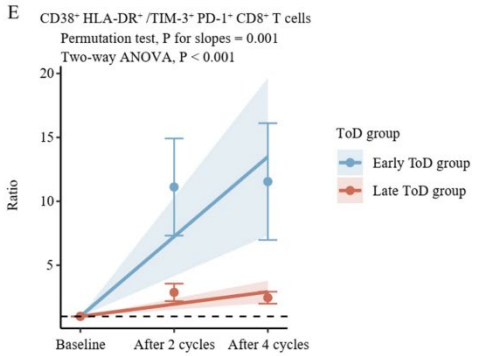
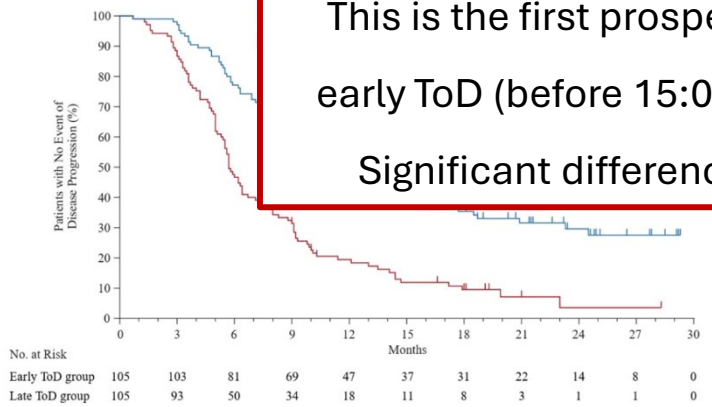


This is the first prospective randomized phase III study demonstrating infusion of immunochemotherapy at early ToD (before 15:00) improves PFS and OS in patients with advanced NSCLC irrespective of PDL1 status.

Significant difference in CD8⁺ T cell dynamics in peripheral blood comparing early with late ToD groups.



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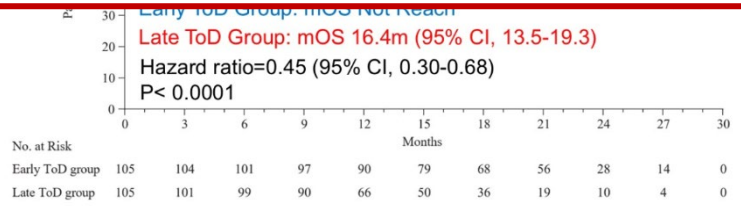

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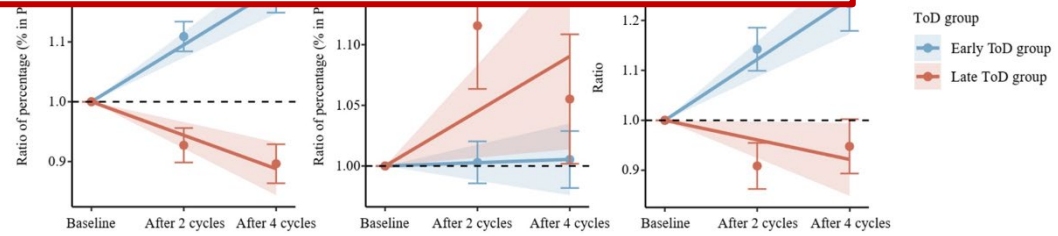

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lung cancer research

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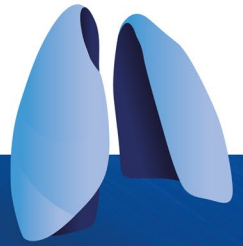

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Lung Immune Prognostic Index		
No factor	dNLR ≤3 and LDH≤ULN	Good
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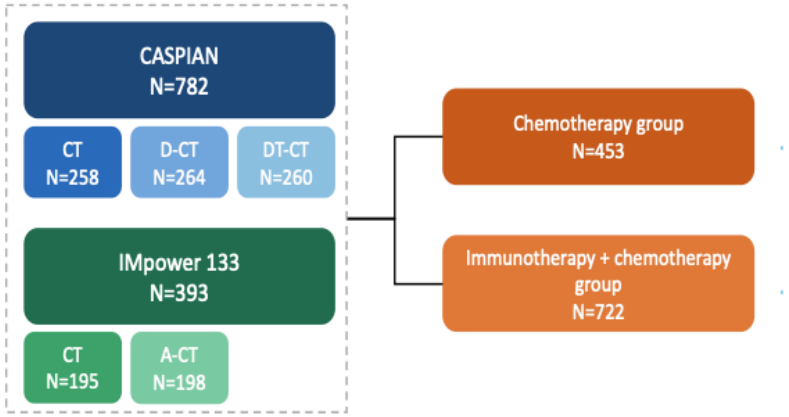
Table 1. LIPI calculation (1).



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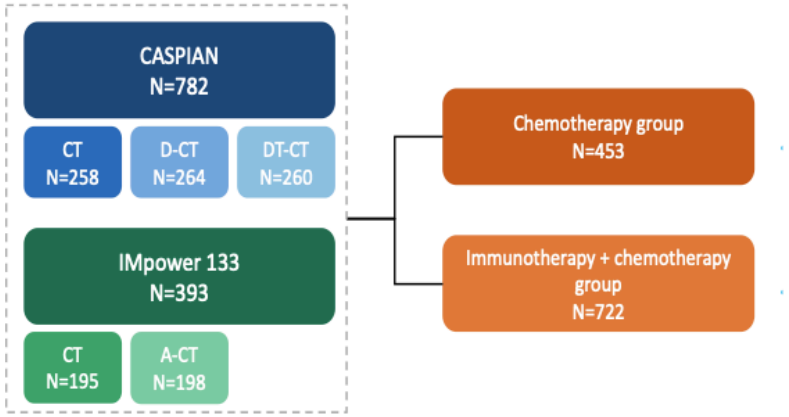

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independent prognostic factors.

		Progression free survival		Overall survival	
Variable		HR (95%CI)	p	HR (95%CI)	p
Gender	Male	1.28 (1.11-1.48)	<0.001	1.29 (1.11-1.49)	<0.001
Age	> 65 years	1.26 (1.10-1.45)	<0.001	1.26 (1.10-1.45)	<0.001
ECOG PS	≥ 1	1.30 (1.13-1.50)	<0.001	1.30 (1.13-1.49)	<0.001
Treatment arm	Chemotherapy	Ref	<0.001	Ref	<0.001
	Chemo-immunotherapy	0.78 (0.68-0.89)		0.78 (0.68-0.90)	
LIPI	Good	Ref		Ref	
	Intermediate	1.24 (1.07-1.44)	<0.001	1.24 (1.06-1.44)	<0.001
	Poor	1.76 (1.44-2.15)		1.76 (1.45-2.15)	
Metastatic site	Liver	1.72 (1.50-1.98)	<0.001	1.72 (1.50-1.98)	<0.001
	Peritoneal	-		1.19 (0.76-1.84)	0.40
	Bone	1.06 (0.91-1.25)	0.50	1.06 (0.91-1.24)	0.50
	Brain	1.33 (1.08-1.64)	0.008	1.32 (1.07-1.63)	0.01
Albumin	> 35 (g/L)	0.83 (0.70-0.99)	0.03	0.83 (0.70-0.99)	0.03

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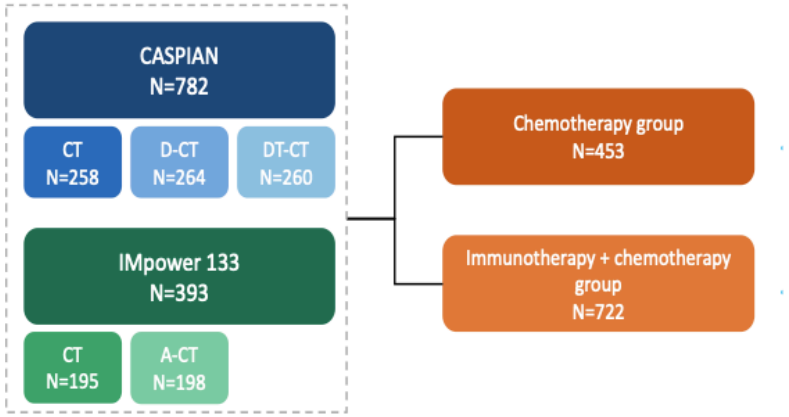

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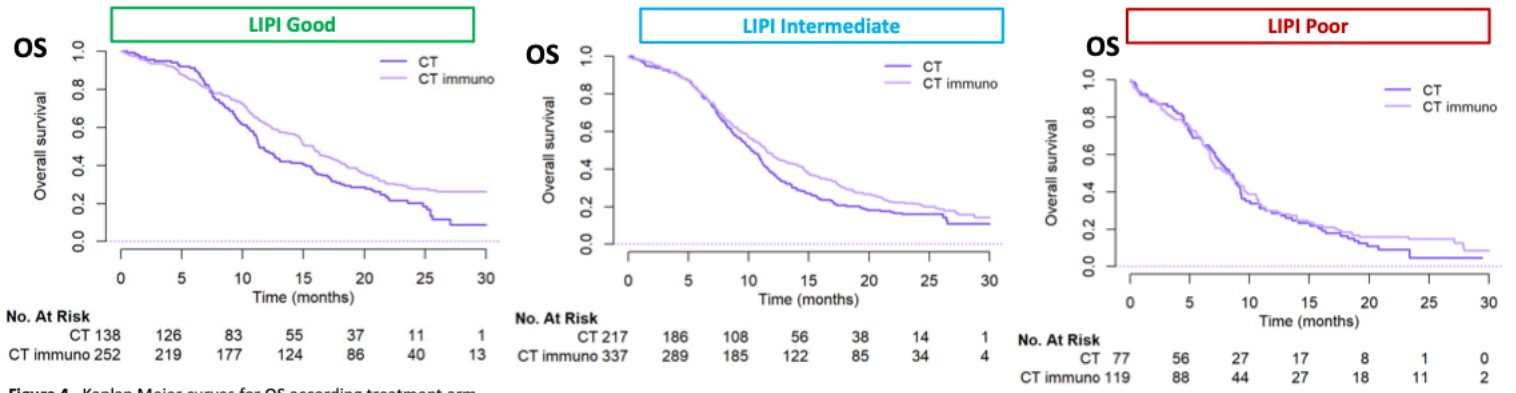

Figure 4. Kaplan Meier curves for OS according treatment arm, in each LIPI group.

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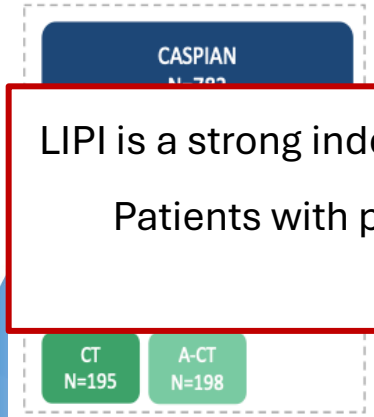

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		Progression free survival		Overall survival	
Variable		HR (95%CI)	p	HR (95%CI)	p
Gender	Male	1.28 (1.11-1.48)	<0.001	1.29 (1.11-1.49)	<0.001
Age	> 65 years	1.26 (1.10-1.45)	<0.001	1.26 (1.10-1.45)	<0.001
ECOG PS	≥ 1	1.30 (1.13-1.50)	<0.001	1.30 (1.13-1.49)	<0.001
Treatment arm	Chemotherapy	Ref	<0.001	Ref	<0.001
	Chemo-immunotherapy	0.78 (0.68-0.89)		0.78 (0.68-0.90)	
LIPI	Good	Ref		Ref	
	Intermediate	1.24 (1.07-1.44)	<0.001	1.24 (1.06-1.44)	<0.001
	Poor	1.76 (1.44-2.15)		1.76 (1.45-2.15)	
Metastatic site	Liver	1.72 (1.50-1.98)	<0.001	1.72 (1.50-1.98)	<0.001
	Peritoneal	-		1.19 (0.76-1.84)	0.40
	Bone	1.06 (0.91-1.25)	0.50	1.06 (0.91-1.24)	0.50
	Brain	1.33 (1.08-1.64)	0.008	1.32 (1.07-1.63)	0.01
Albumin	> 35 (g/L)	0.83 (0.70-0.99)	0.03	0.83 (0.70-0.99)	0.03

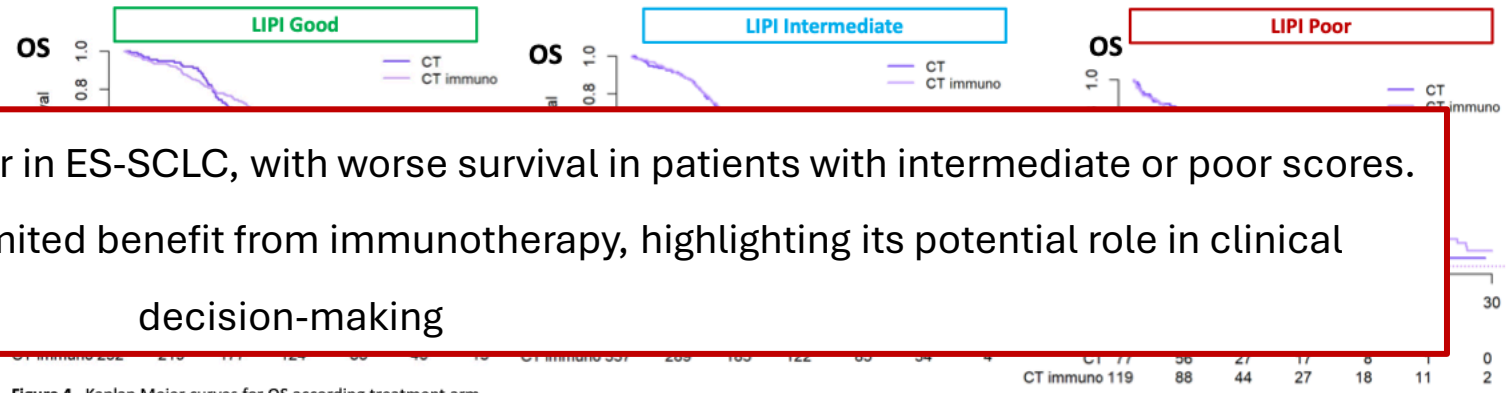

Figure 4. Kaplan Meier curves for OS according treatment arm, in each LIPI group.

LIPI is a strong independent prognostic marker in ES-SCLC, with worse survival in patients with intermediate or poor scores. Patients with poor LIPI appear to derive limited benefit from immunotherapy, highlighting its potential role in clinical decision-making

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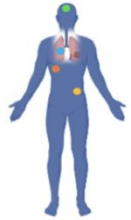
GECP lung cancer research

LIPI score in advanced NSCLC treated with ICIs: prognostic impact and blood immune-inflammatory correlations

Study Design



116 advanced NSCLC patients undergoing first-line CT-IO

Complete clinical records, including:

- Cardiovascular (CV) comorbidities;
- Immuno-metabolic disorders (i.e. mellitus diabetes)
- Concomitant medications (i.e. steroids, antibiotics, statins)

Baseline peripheral blood samples, including:

- Routine laboratory tests (including LDH, leukocytes, neutrophils)
- Flow cytometric analysis of T cell subpopulations
- Immuno-enzymatic assay for serum cytokines and soluble mediators

Patients stratification according to LIPI score

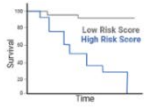
LIPI score	LDH (U/L)	dNLR*
GOOD LIPI	< 480	< 3
INTERMEDIATE LIPI	≥ 480	< 3
	< 480	≥ 3
POOR LIPI	≥ 480	≥ 3

Mezquita L. et al. The Lung Immune Prognostic Index (LIPI): a predictive score for immune checkpoint inhibitors in advanced non-small cell lung cancer (NSCLC) patients. Annals of Oncology, Volume 38, v473.

$$^{*}\text{dNLR} = \frac{\text{Neutrophils}}{(\text{Leukocytes} - \text{Neutrophils})}$$

Statistical analyses

- Impact of LIPI score on survival outcome (PFS and OS)



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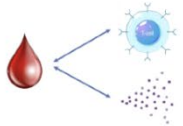

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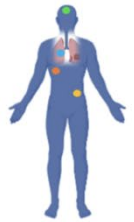

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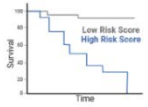

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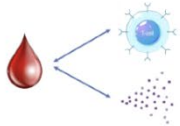
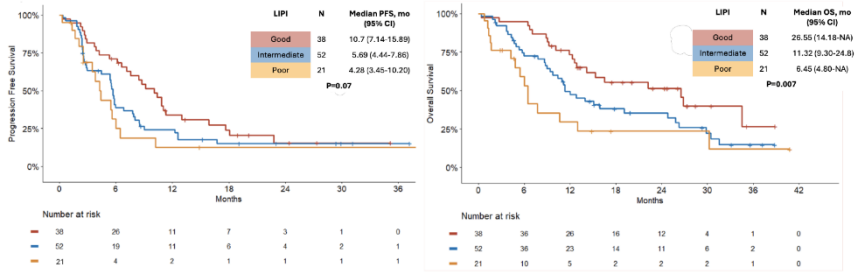
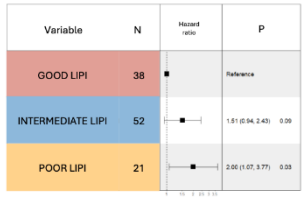


Impact of LIPI score on survival outcomes





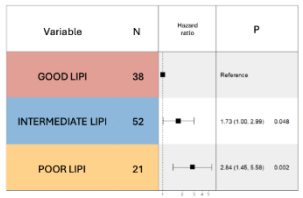


Figure 2. Among 116 patients treated with CT-IO, those with good LIPI (N=38) showed a longer median PFS (10.0 months [mo] for good LIPI vs 4.28 mo for poor LIPI [N=21]; p=0.03). Patients with good LIPI (N=38) showed significant longer median OS (26.55 mo for good LIPI vs 11.32 mo for intermediate LIPI [N=52] vs 6.45 mo for poor LIPI [N=21]; p=0.007).

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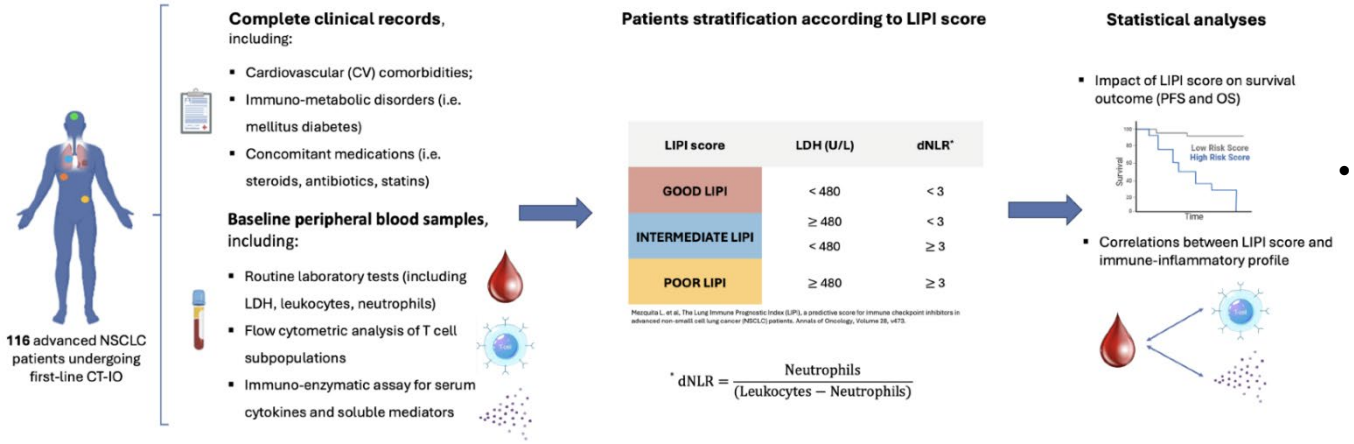
GECP lung cancer research

LIPI score in advanced NSCLC treated with ICIs: prognostic impact and blood immune-inflammatory correlations

Study Design



Correlations between LIPI score and immune-inflammatory profile

- Patients with good LIPI showed significantly lower levels of IL-12, IL-10, IL-2 and IL-6 compared to those with intermediate and poor LIPI.
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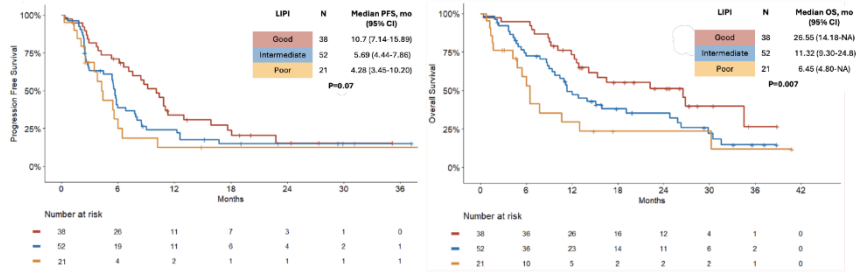

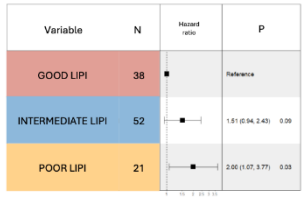

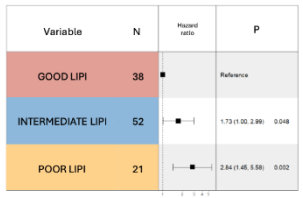

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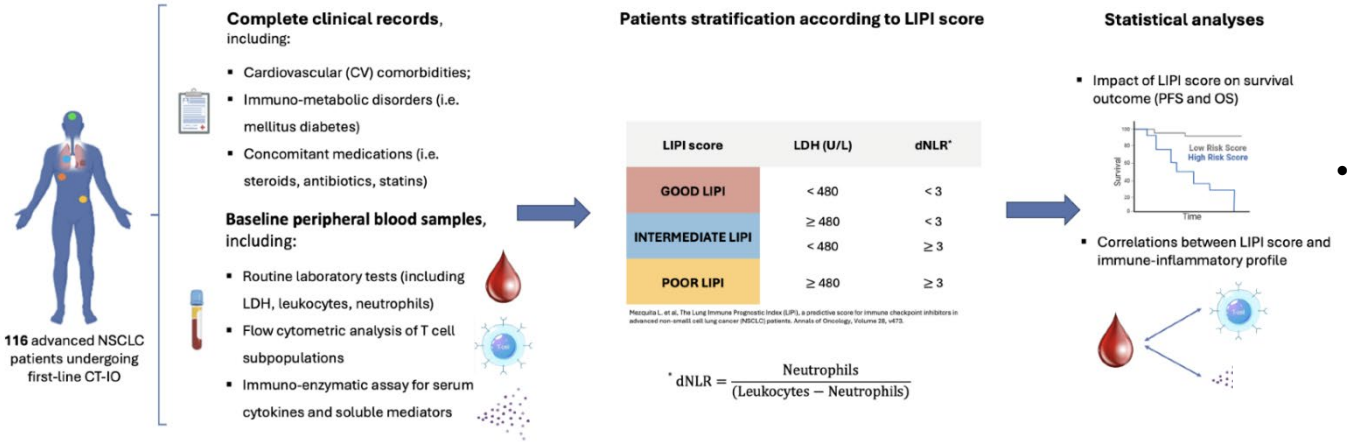

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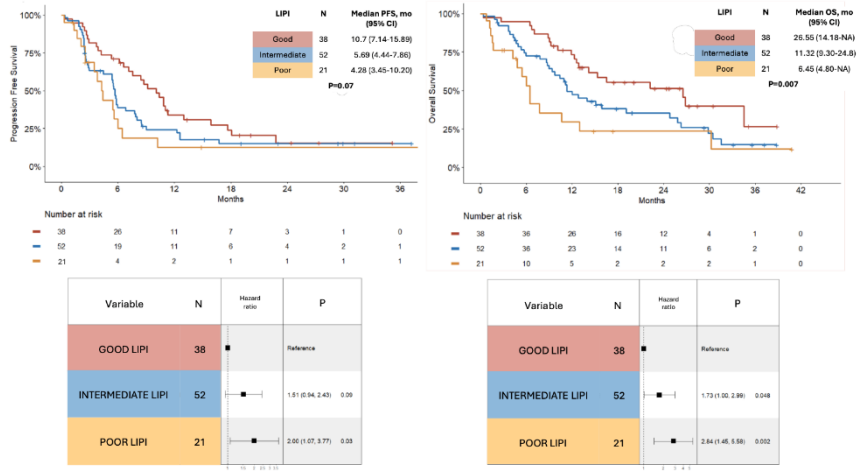

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LIPI score in advanced NSCLC treated with ICIs: prognostic impact and blood immune-inflammatory correlations

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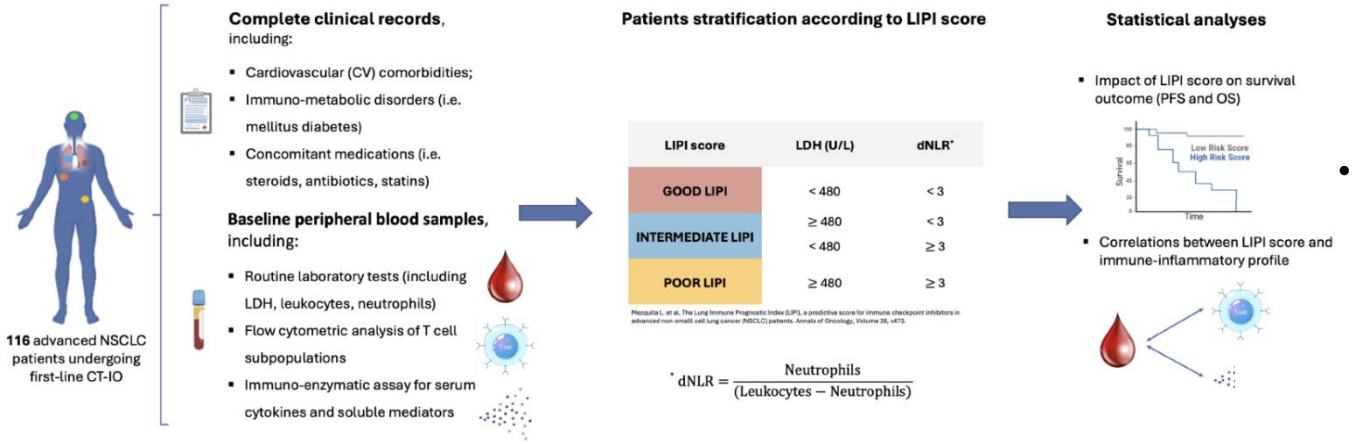

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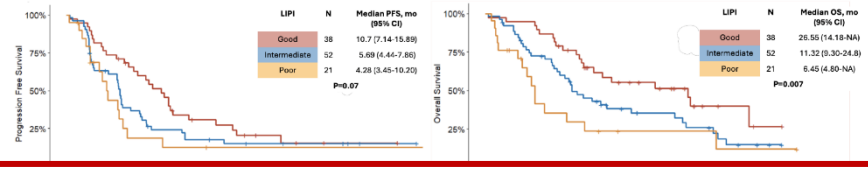

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Baseline LIPI score is a non-invasive clinical tool that predicts conveniently and reliably first-line CT-IO efficacy in advanced NSCLC and correlates with circulating cytokines and immune cell profiles, reflecting anti-tumour immune activity.

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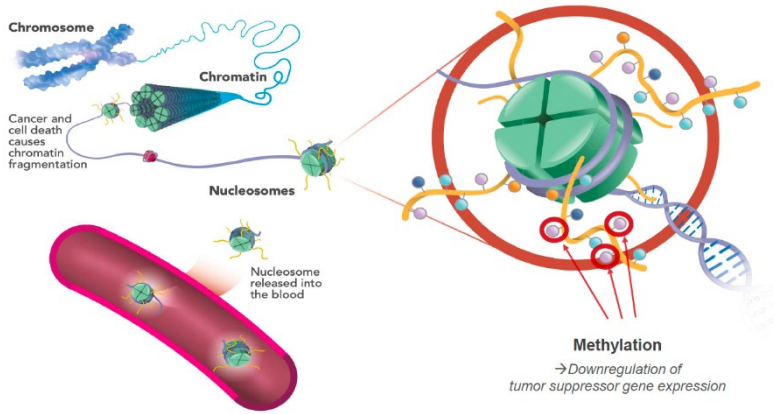
GECP lung cancer research

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.



Scheme 1: *Methylated nucleosomes (DNA wound around histone proteins carrying methylation marks) are released by cancer cells in bloodstream after cell death and can be detected in patients' plasma (figure from Volition©).*

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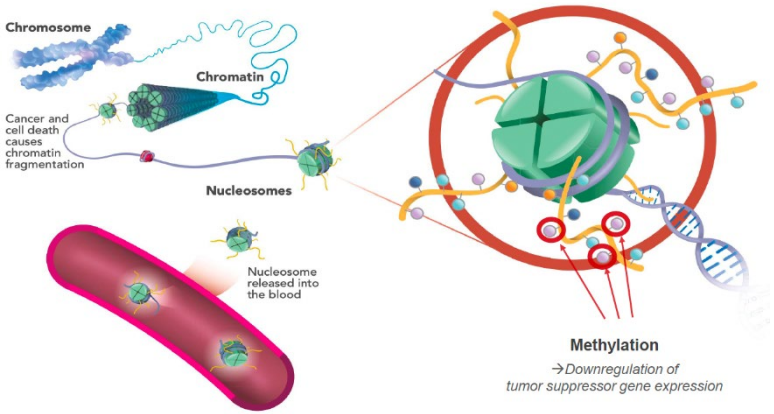

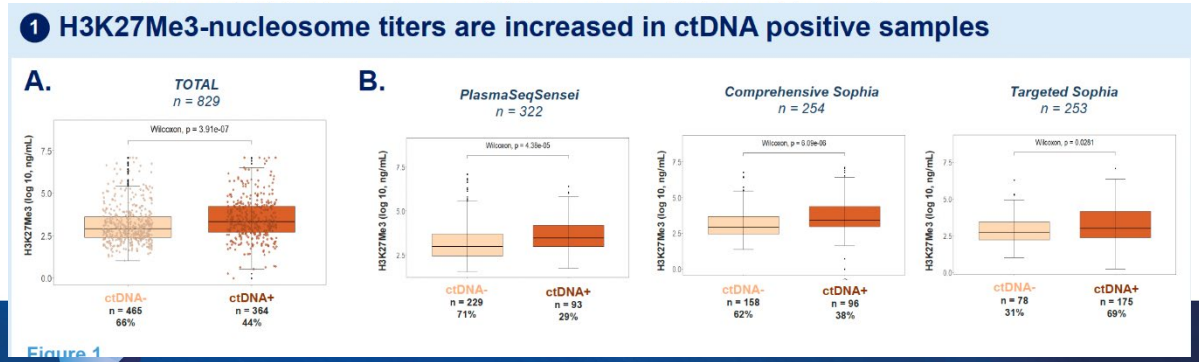

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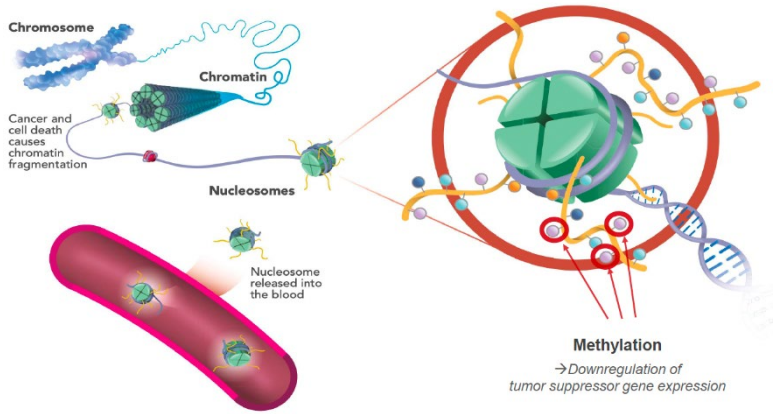


1 H3K27Me3-nucleosome titers are increased in ctDNA positive samples

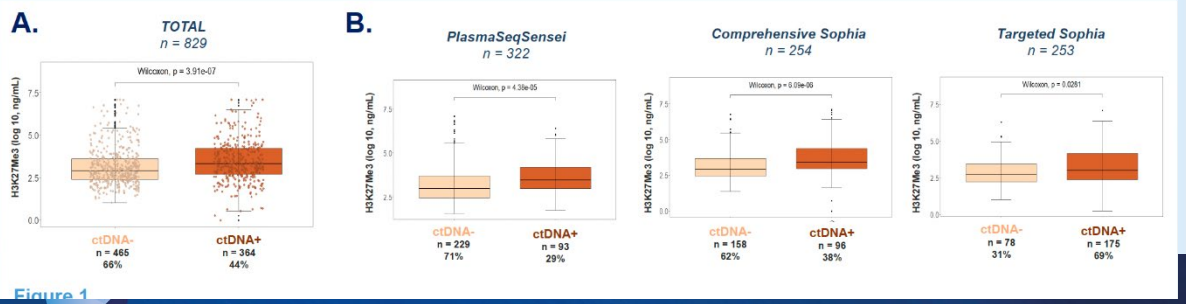
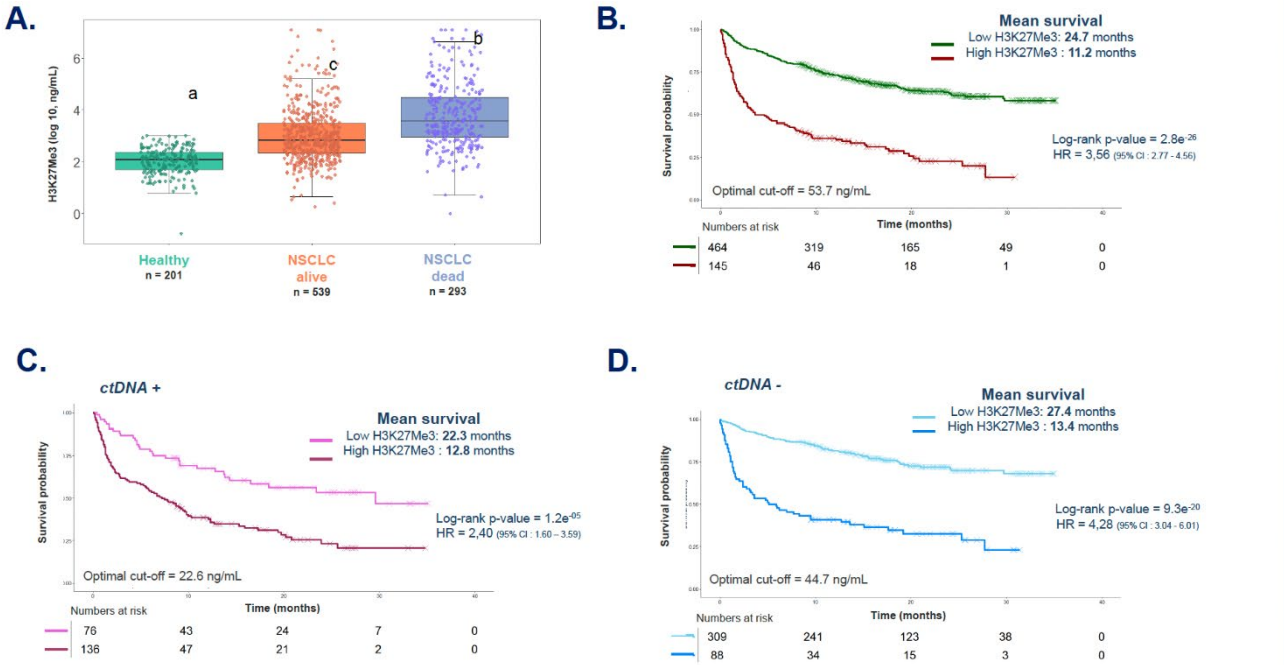


Figure 1

2 H3K27Me3-nucleosome titers are increased in patients with low survival probability, independently of molecular profiling results on ctDNA



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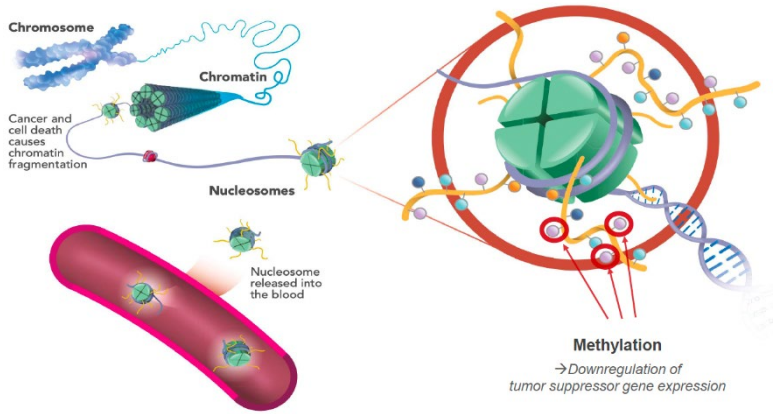

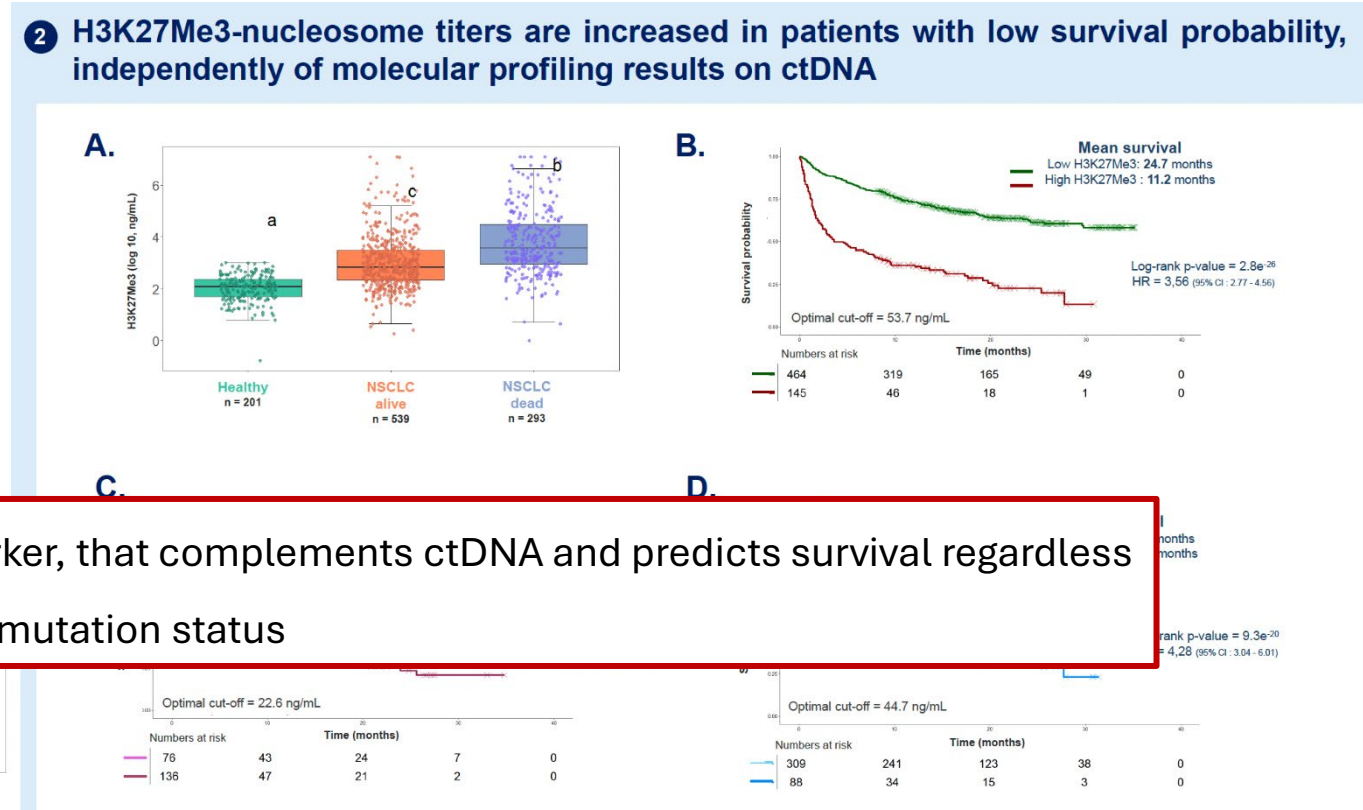

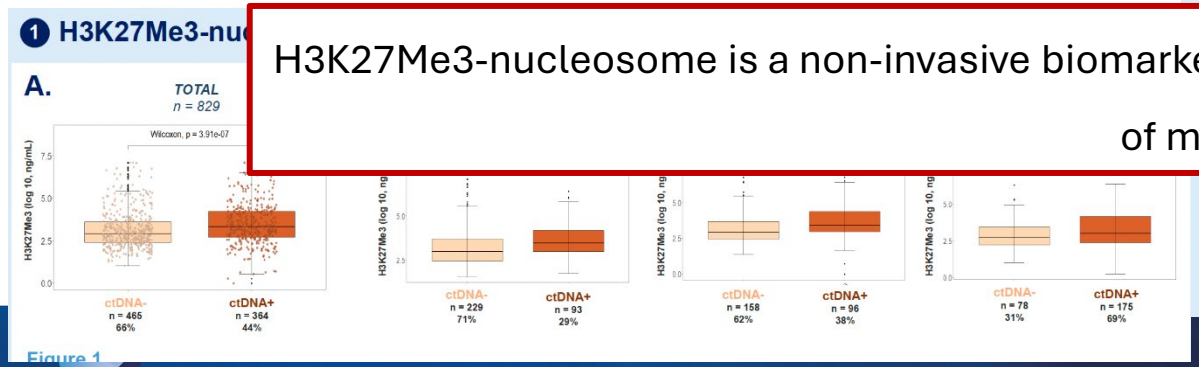

H3K27Me3-nucleosome is a non-invasive biomarker, that complements ctDNA and predicts survival regardless of mutation status

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GECP lung cancer research

AGENDA

1.- Dynamic based prognostic biomarkers (liquid biopsy)

2.- Integrated prognostic models and Artificial intelligence

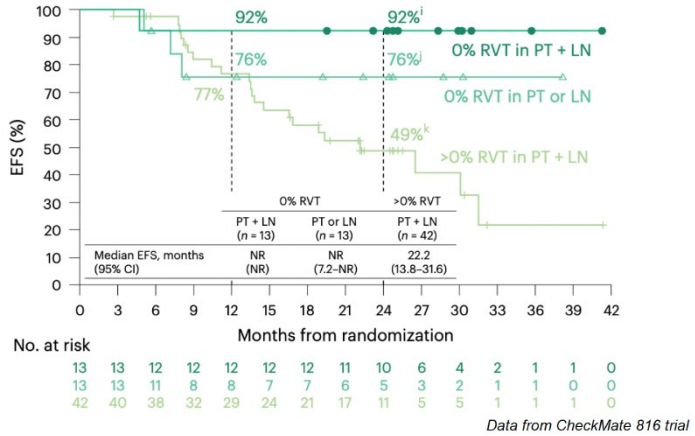
3.- Host-immune based and genomic prognostic biomarkers

4.- Clinical and pathological biomarkers

GECP lung cancer research

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).



Data from CheckMate 816 trial

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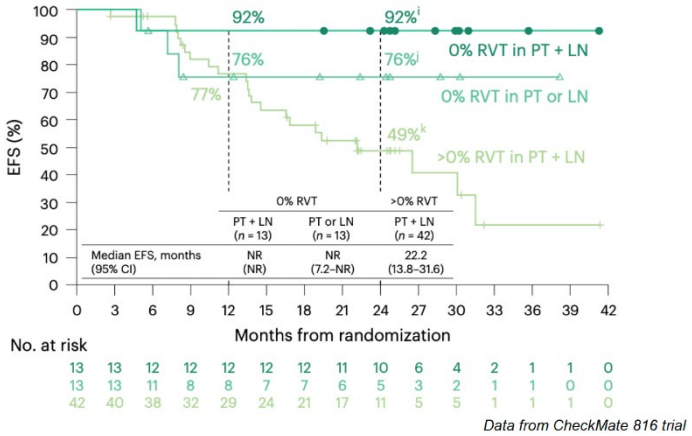

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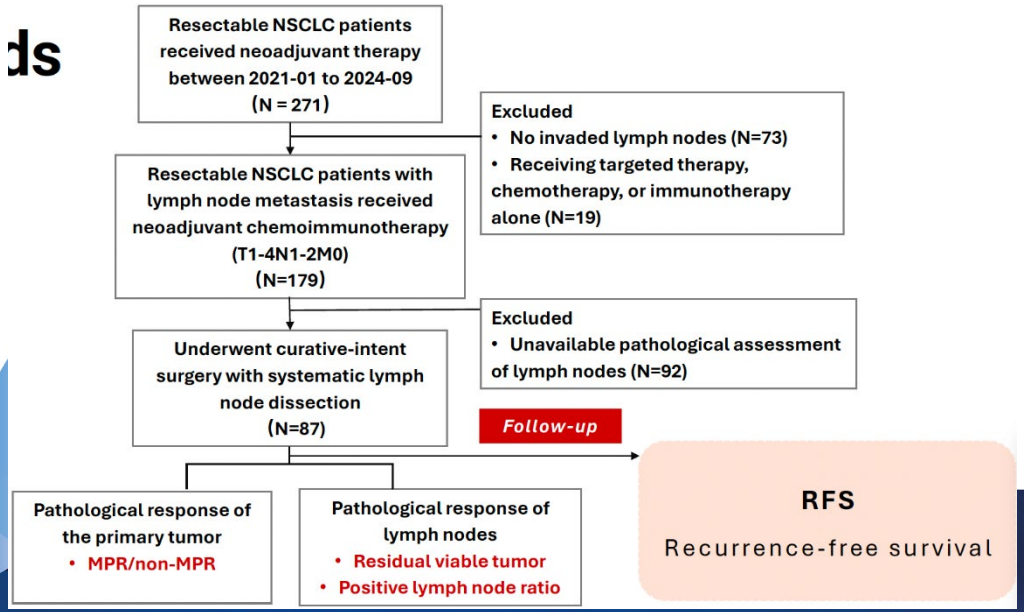

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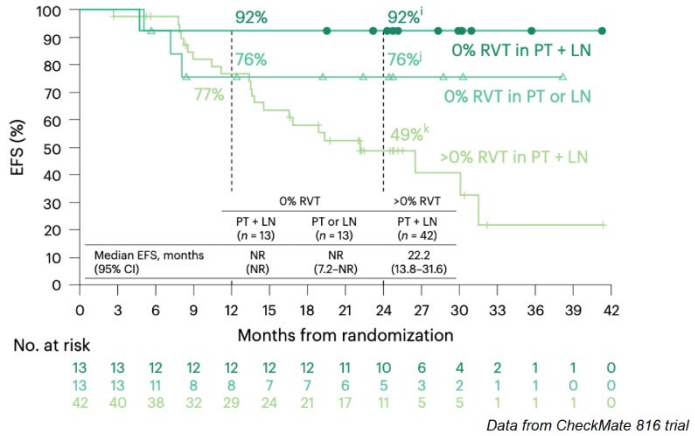
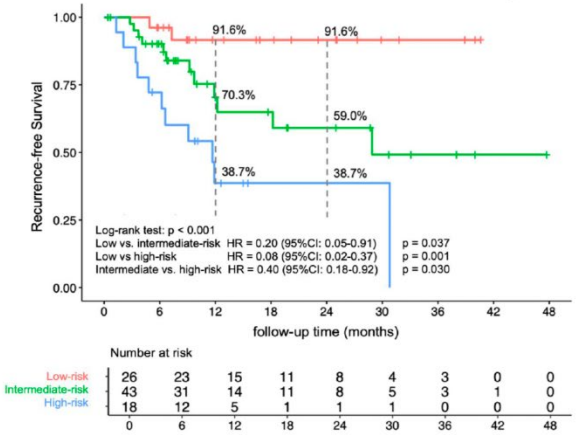


Data from CheckMate 816 trial

- 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

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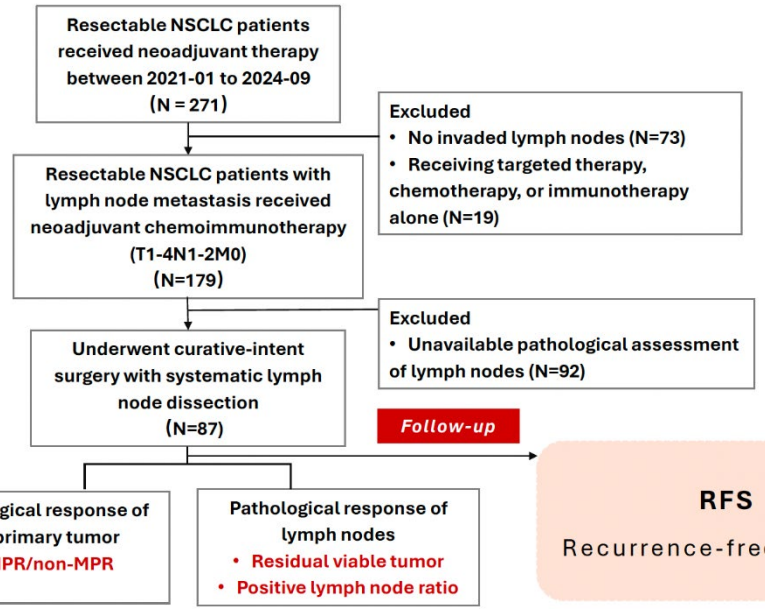

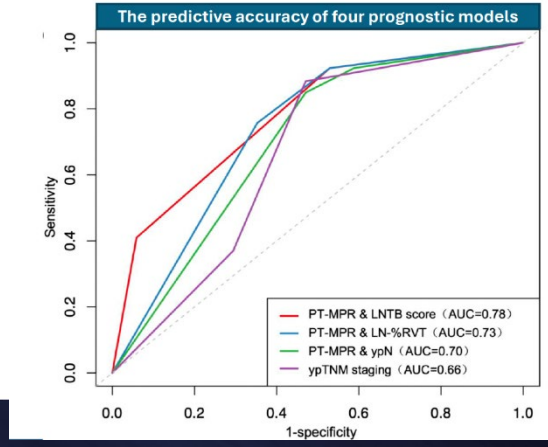

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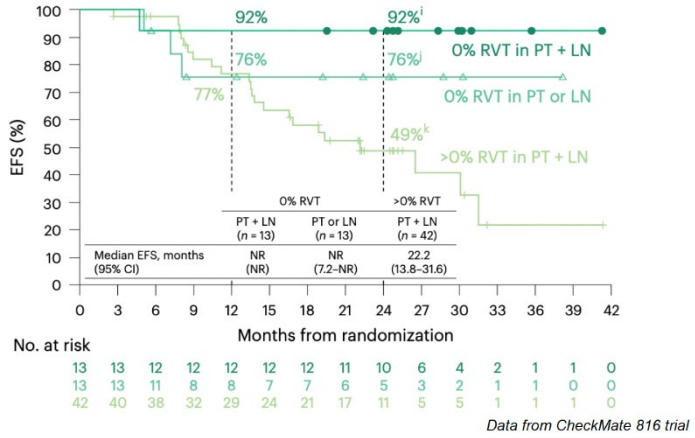
GECP lung cancer research

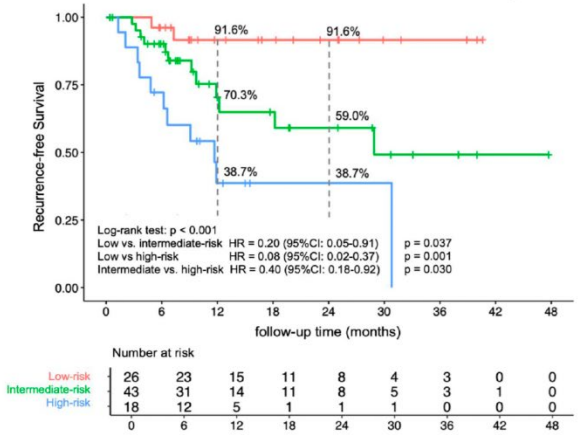
Prognostic value of residual viable tumor in lymph nodes of non-small cell lung cancer after neoadjuvant chemoimmunotherapy

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



Data from CheckMate 816 trial

- 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

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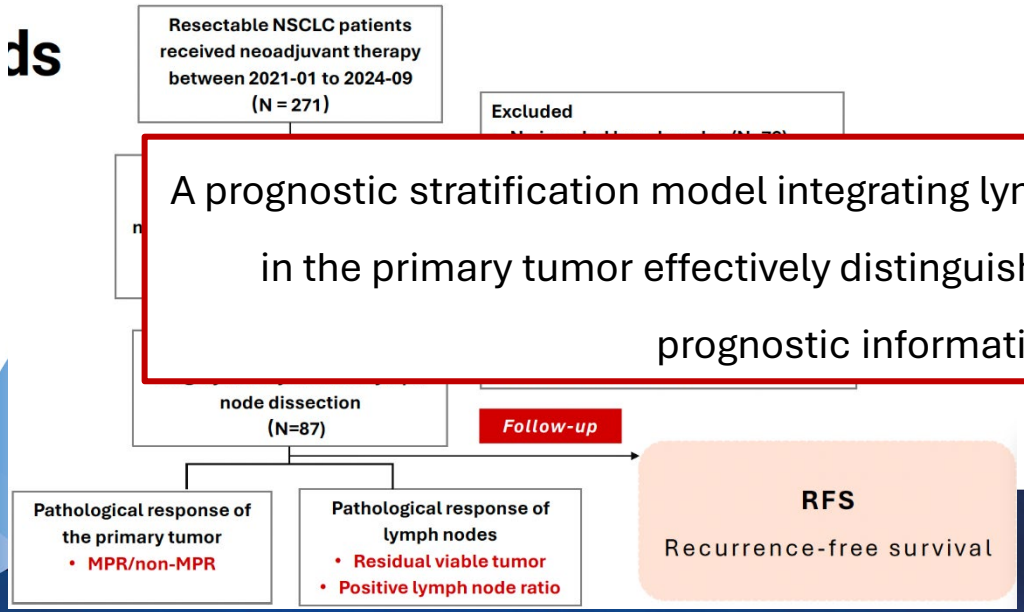
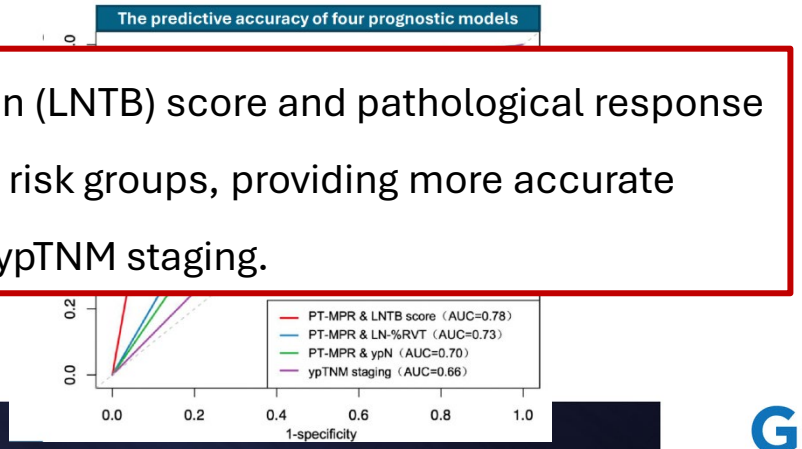


A prognostic stratification model integrating lymph node tumor burden (LNTB) score and pathological response in the primary tumor effectively distinguished patients into three risk groups, providing more accurate prognostic information than conventional ypTNM staging.



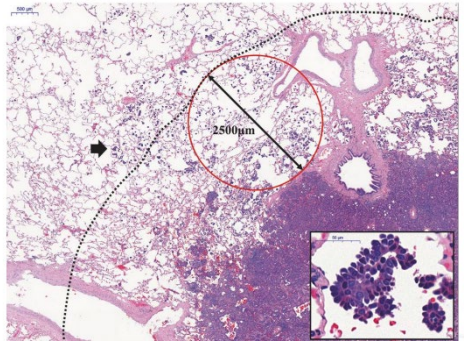
Han T et al WLCC 2025

GeCP lung cancer research

Grading system of Spread through Air Spaces (STAS) is an independent predictor of recurrence in stage I non-mucinous lung adenocarcinoma

Definition of STAS grading systems (since 2011, SNUBH)

- Grade I: tumor clusters **within 2500 μm** of tumor edge
- Grade II: clusters **beyond 2500 μm** from the tumor edge.



Han YB, et al. Mod Pathol. 2021 Mar;34(3):549-561.

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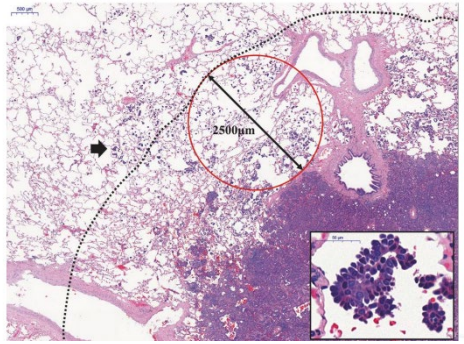

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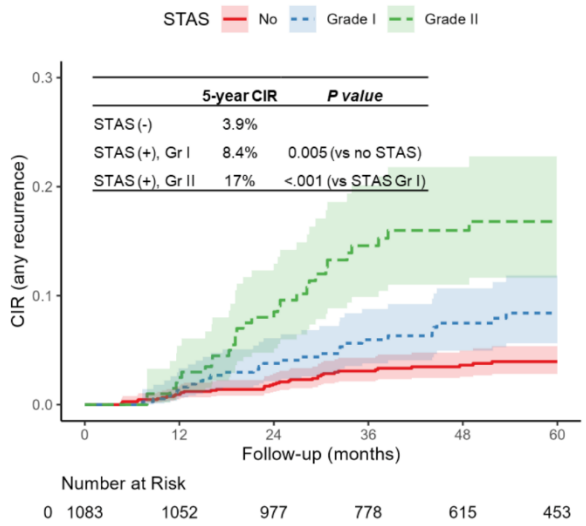
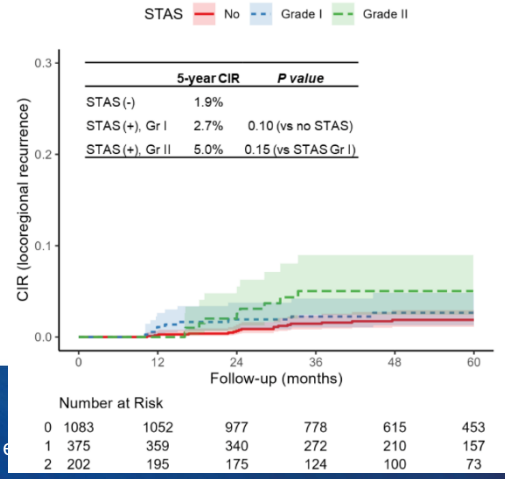
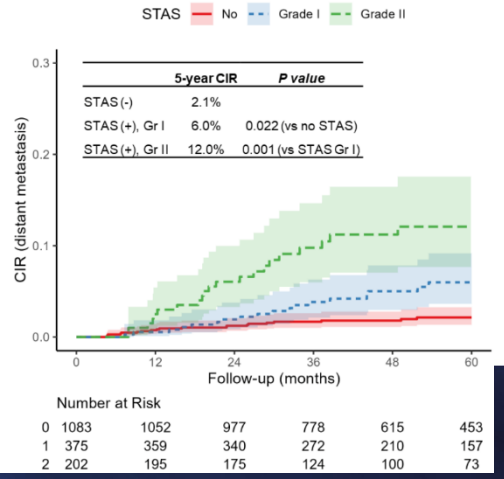
(A) Any Recurrence



(B) Loco-regional Recurrence



(C) Distant Metastasis



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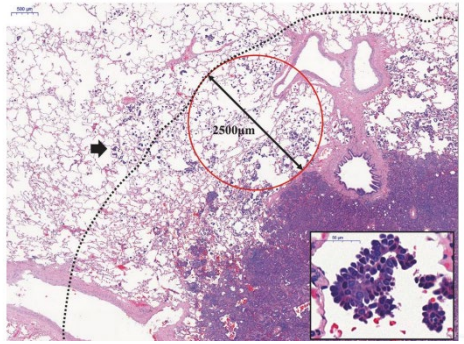

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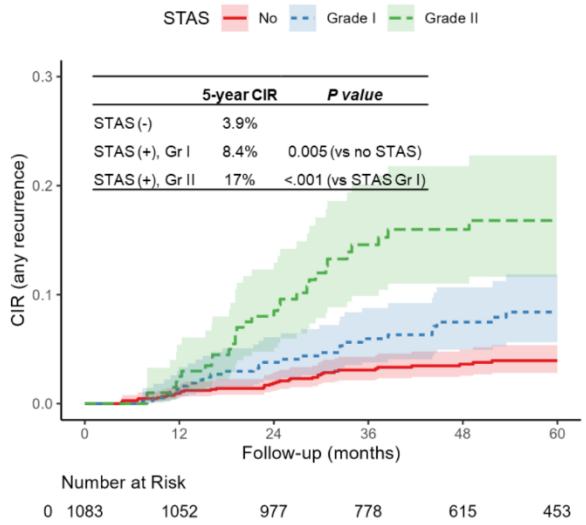

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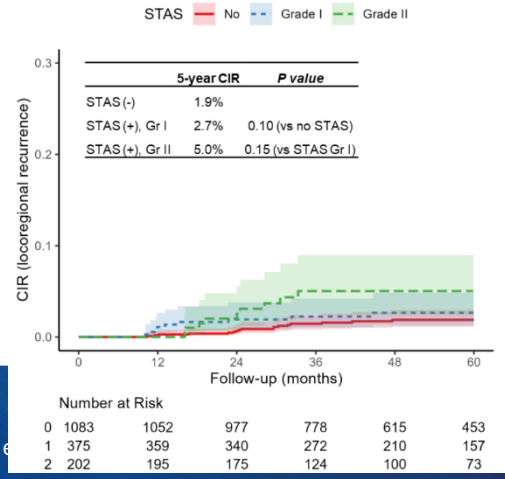

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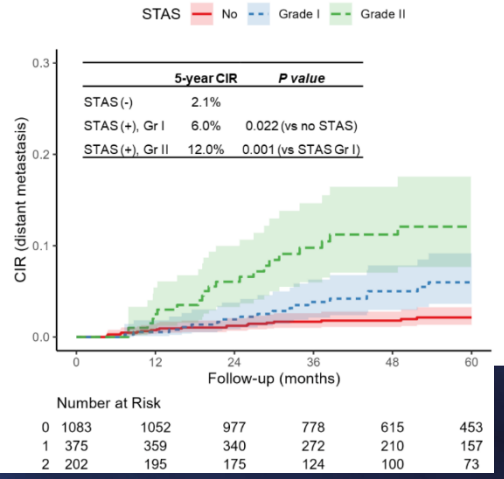

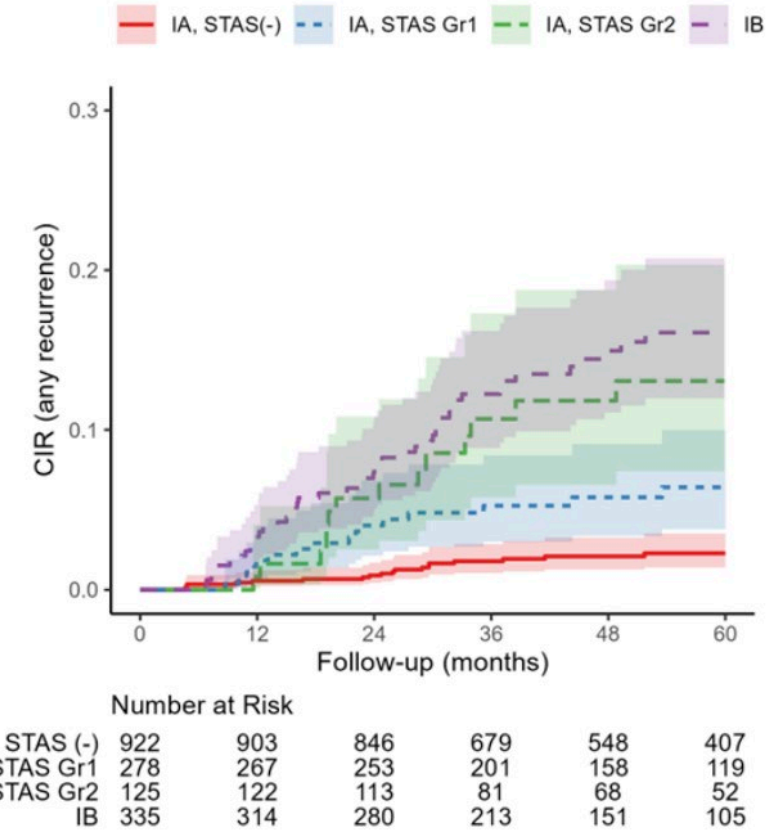

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GECP lung cancer research

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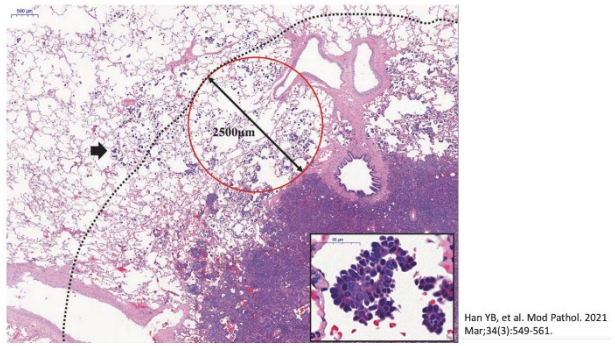

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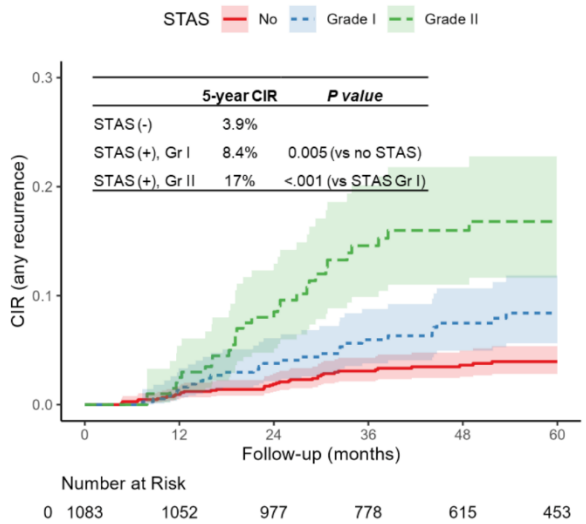

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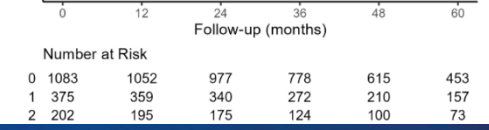

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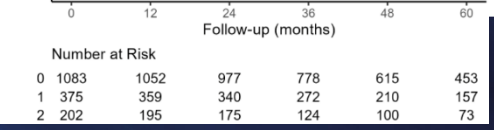

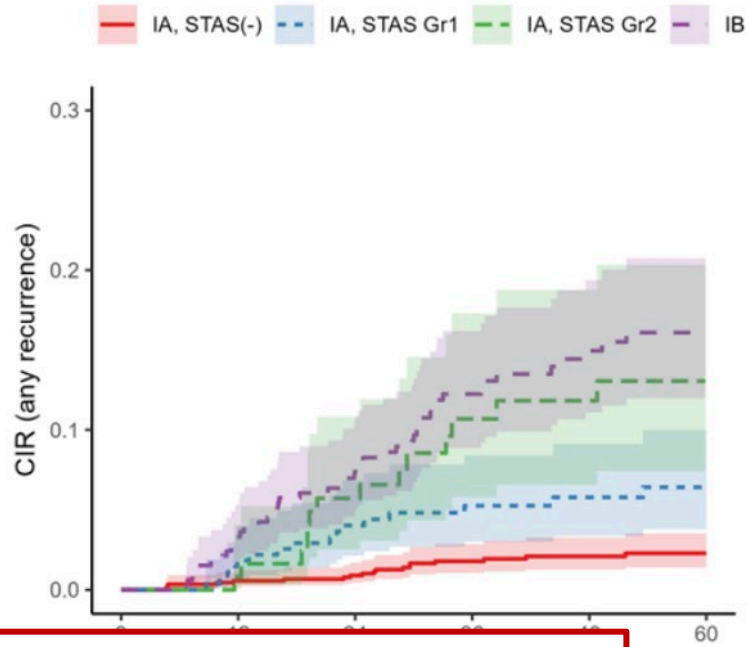

The STAS grading system might be associated with increased risk of recurrence in patients with pathologic stage I non-mucinous lung adenocarcinoma after lobectomy.

The STAS grade II in pathologic stage IA non-mucinous lung adenocarcinoma demonstrated a similar risk of recurrence to that of pathologic stage IB

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GECP lung cancer research

Genomic characterization of STAS in stage I EGFR-mutated NSCLC and prognostic implications

Consecutive patients with resected stage 1 NSCLC between 2016 –2021 with known EGFR and STAS status (n=300)

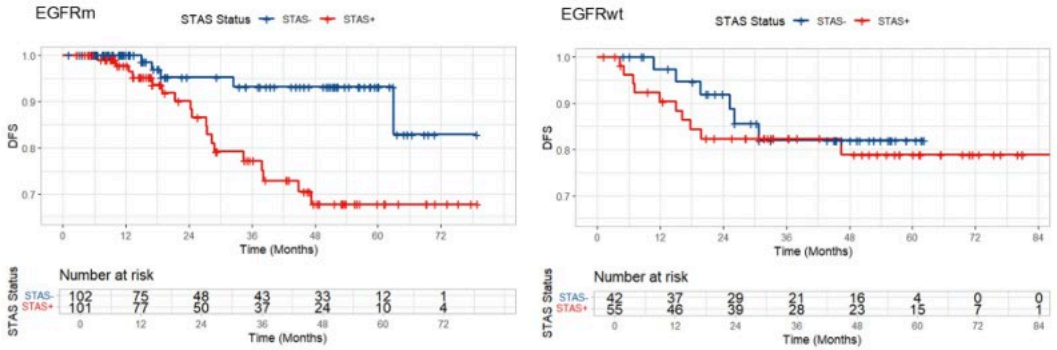
↓

Demographics and survival compared by STAS status (n=203 EGFRm; n=97 EGFR-wildtype [wt])

↓

Whole exome sequencing (WES) and RNA-seq performed for 193 EGFRm patients with correlation analyses (n=112 STAS+; n=81 STAS-)

Figure 1: DFS by STAS status among Stage 1 EGFRm and EGFRwt



5-year DFS was significantly worse for STAS+ vs STAS- EGFRm (67.8% vs 93.2%, p=0.005) but not EGFRwt (78.9% vs 82.0%, p=0.6)

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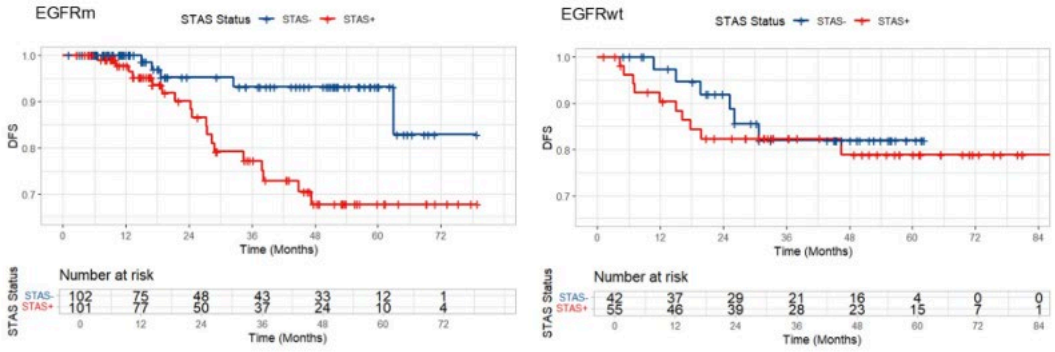

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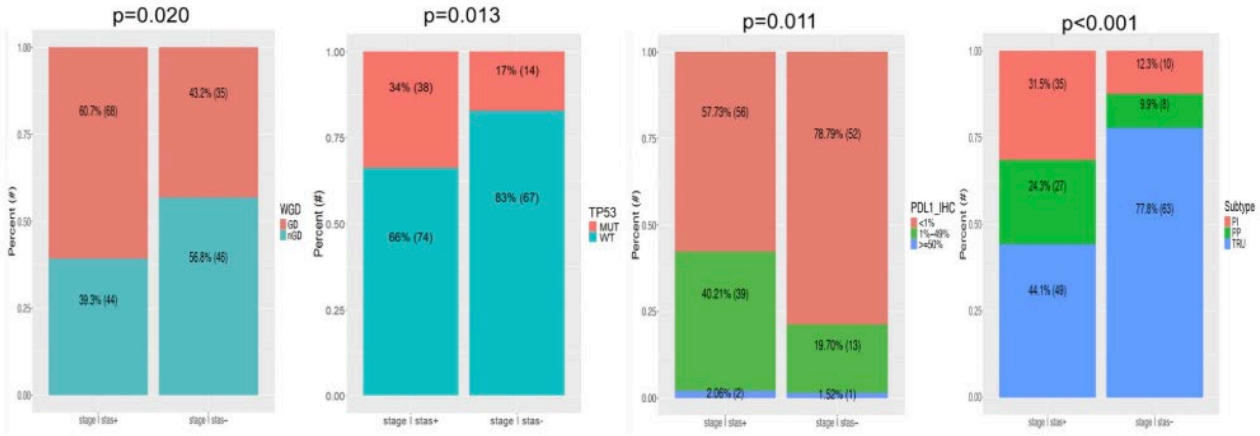

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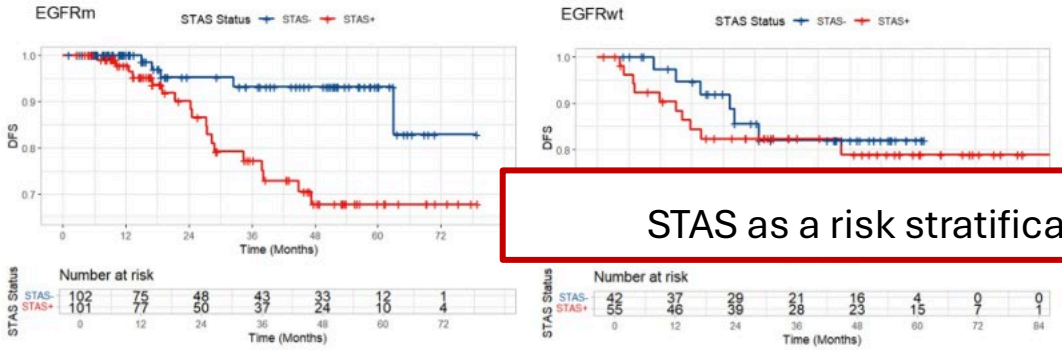

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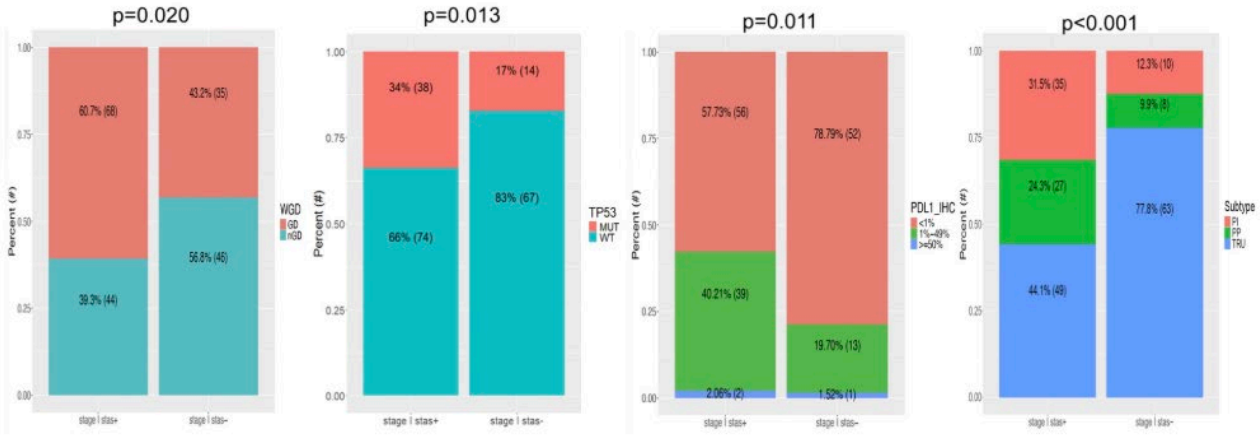
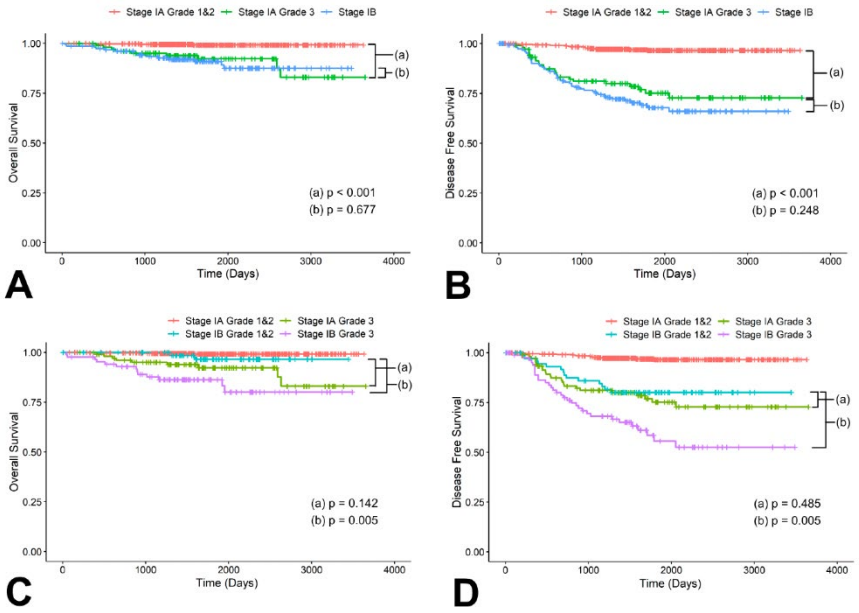


STAS as a risk stratification factor for stage I EGFRm NSCLC

148P Histological Grade 3 in Stage 1A Lung Cancer : Survival Risks Comparable to Stage 1B



Park G et al ASCO 2025; Koga H ELCC 2025; Liang S et al ELCC 2025

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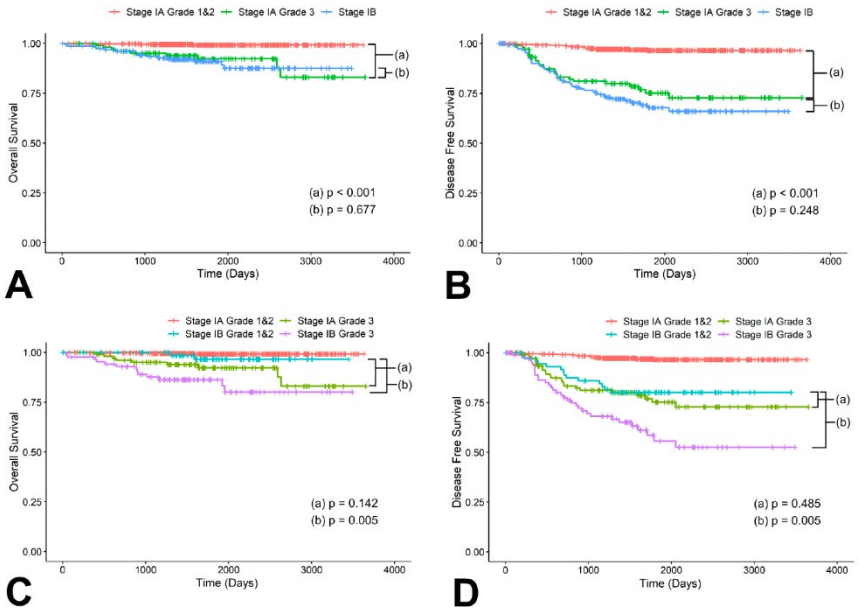

Prognostic Impacts of Skip Metastasis in N2a and N2b Subgroups in Non-Small Cell Lung Cancer: Insights from a Large Cohort

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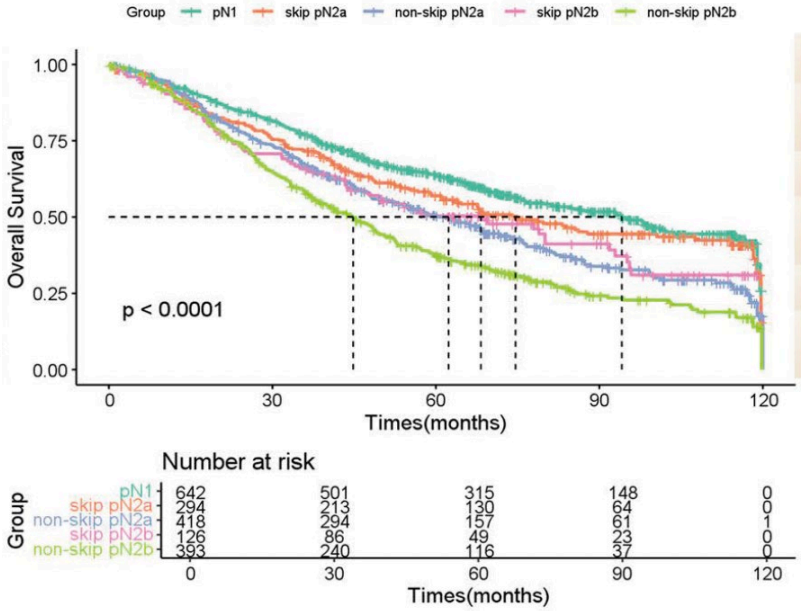
1.Department of Thoracic Surgery, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou, 510000, PR China. * indicates these authors contributed equally to this work.



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Park G et al ASCO 2025; Koga H ELCC 2025; Liang S et al ELCC 2025

Clinical and pathological biomarkers

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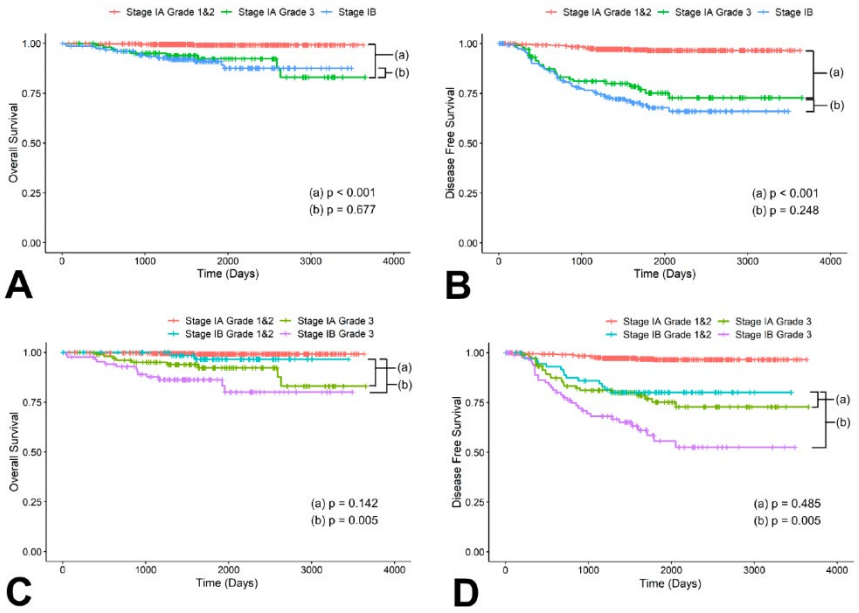

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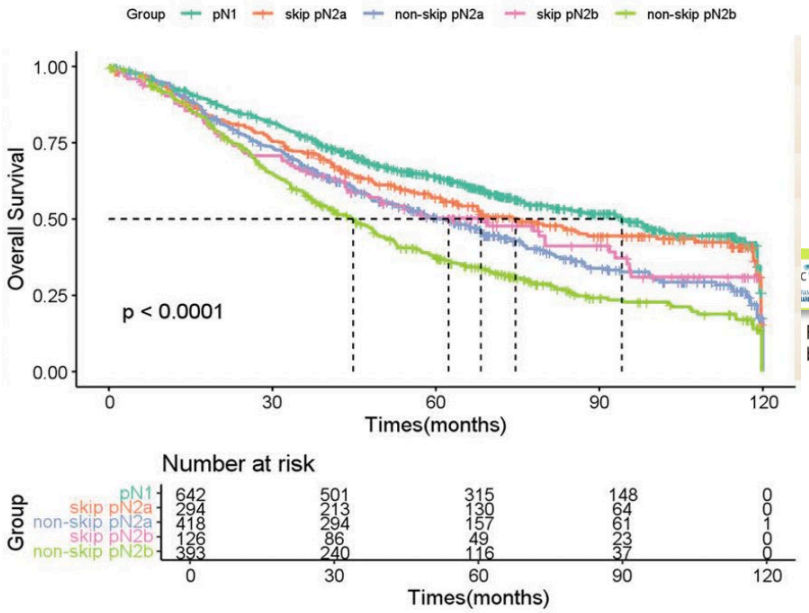
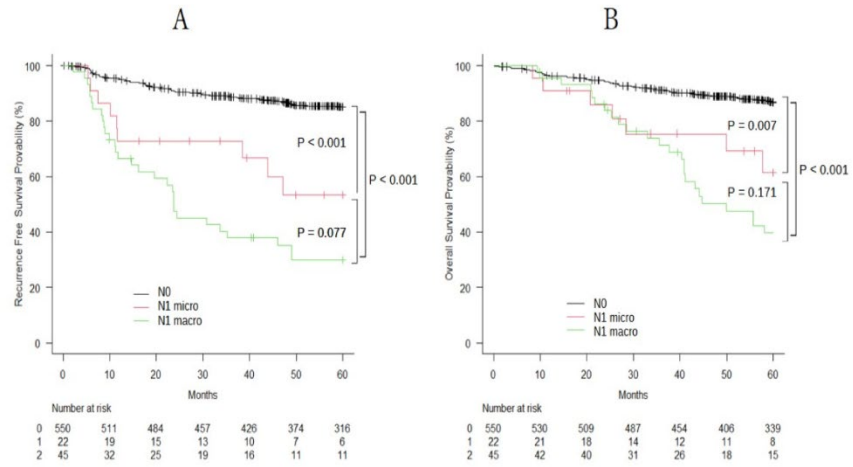


Prognostic Impact of N1 Lymph Node Micrometastasis in T1-2a Non-small Cell Lung Cancer

Figure 3. Recurrence-free survival and overall survival in patients stratified by lymph node micrometastasis or macrometastasis (A, B) .



Park G et al ASCO 2025; Koga H ELCC 2025; Liang S et al ELCC 2025

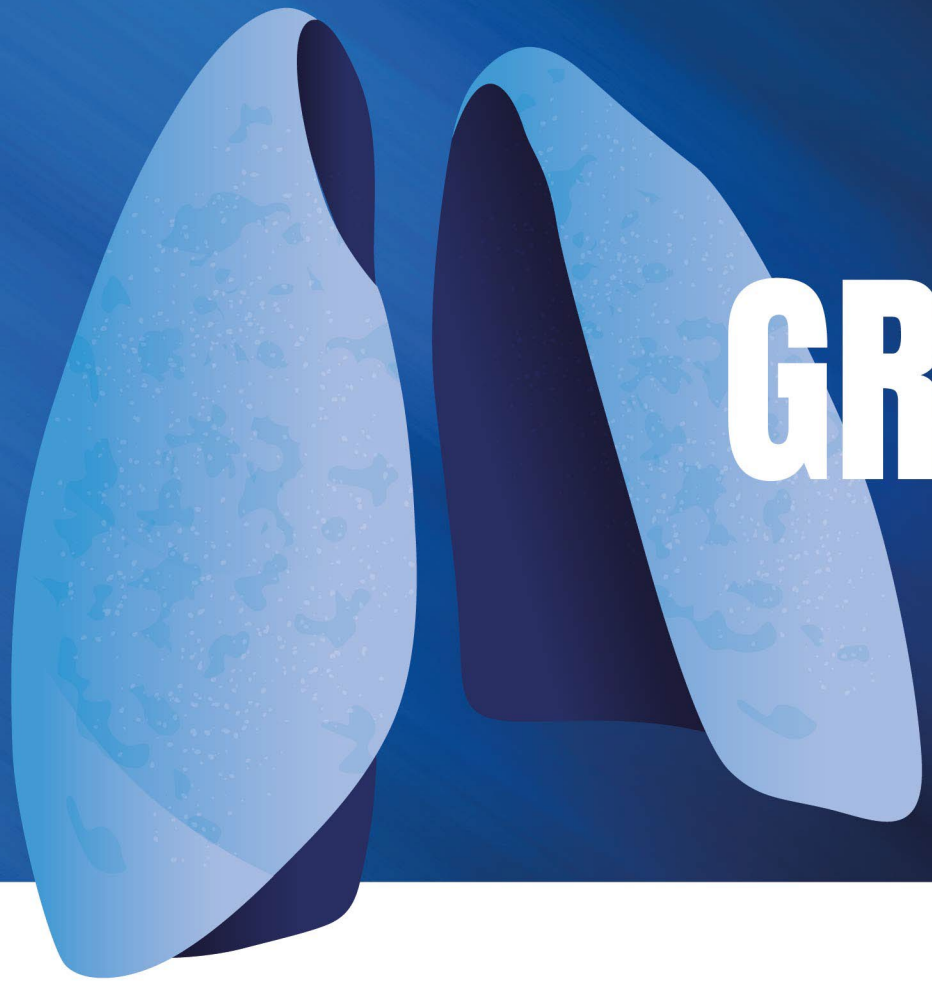
Conclusions

- Liquid biopsy is emerging as a key tool for monitoring treatment response and guiding therapeutic decision-making in a dynamic manner.

- Artificial intelligence and complex analytical models will enable the integration of multiple sources of information and improve the precision of clinical decision-making.

- Traditional immunological and clinical biomarkers continue to have significant value: they are easy to identify, widely accessible in routine clinical practice, and remain highly useful in supporting therapeutic decisions.

GECP lung cancer research



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