Iniciativa científica de:

GECP lung cancer research

Lung Cancer UPDATES

WCLC HIGHLIGHTS

12 - 15 **SEPTIEMBRE** 2026

Seoul, Republic of South Korea



#WCLCUPDATES

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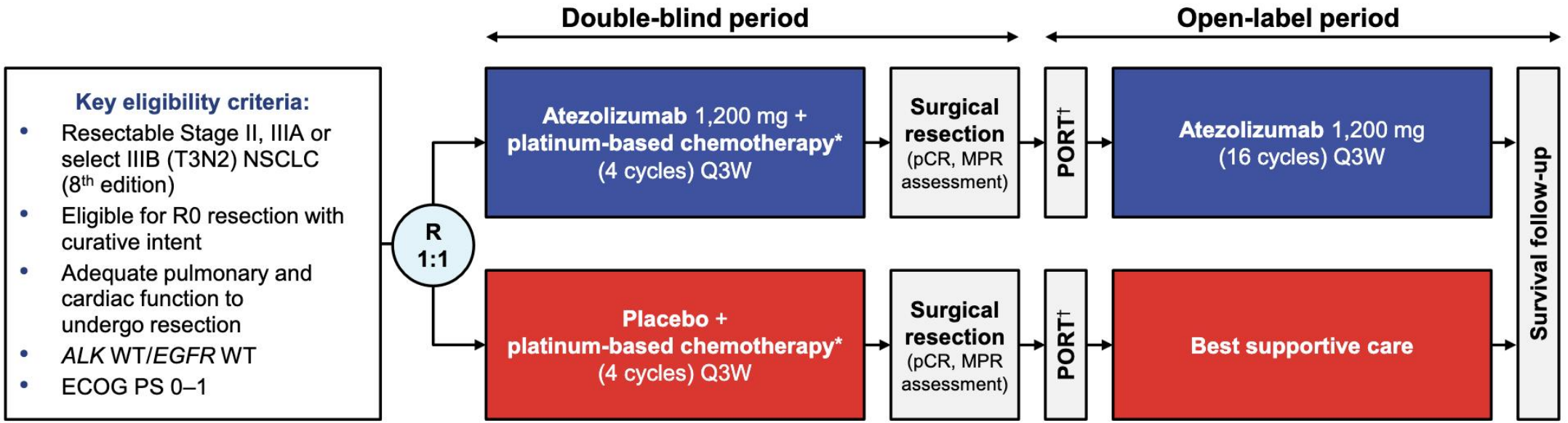
Seoul, Republic of South Korea

Biomarcadores, screening y cáncer de pulmón no microcítico estadio precoz - (Parte II)

Silvia Sequero Lopez

Hospital Universitario San Cecilio, Granada

Study Design



Stratification factors:
- Tumor Stage (II vs IIIA N2- vs IIIA/B N2+)
- Histology (non-squamous vs squamous)

Primary endpoint:
- IRF-EFS

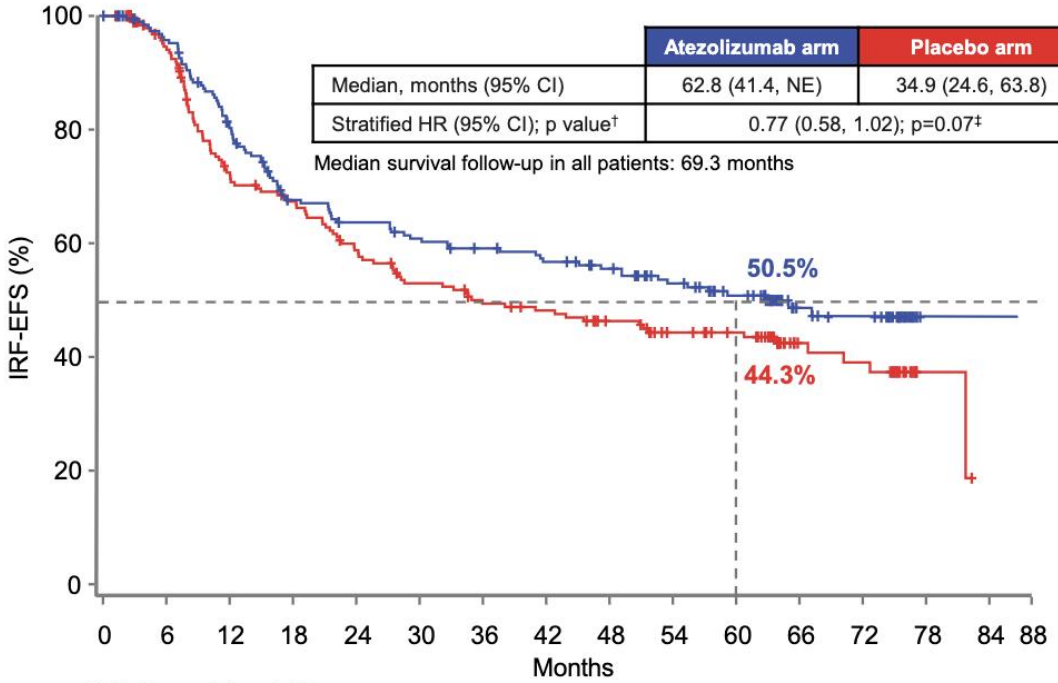
Key secondary endpoints:
- IRF-pCR
- IRF-MPR
- OS
- INV-EFS
- INV-DFS
- Safety

IRF-Assessed EFS

Stage IIB-IIIB-WT population (primary endpoint)*

	Atezolizumab arm	Placebo arm
Median, months (95% CI)	62.8 (41.4, NE)	34.9 (24.6, 63.8)
Stratified HR (95% CI); p value†	0.77 (0.58, 1.02); p=0.07‡	

Median survival follow-up in all patients: 69.3 months



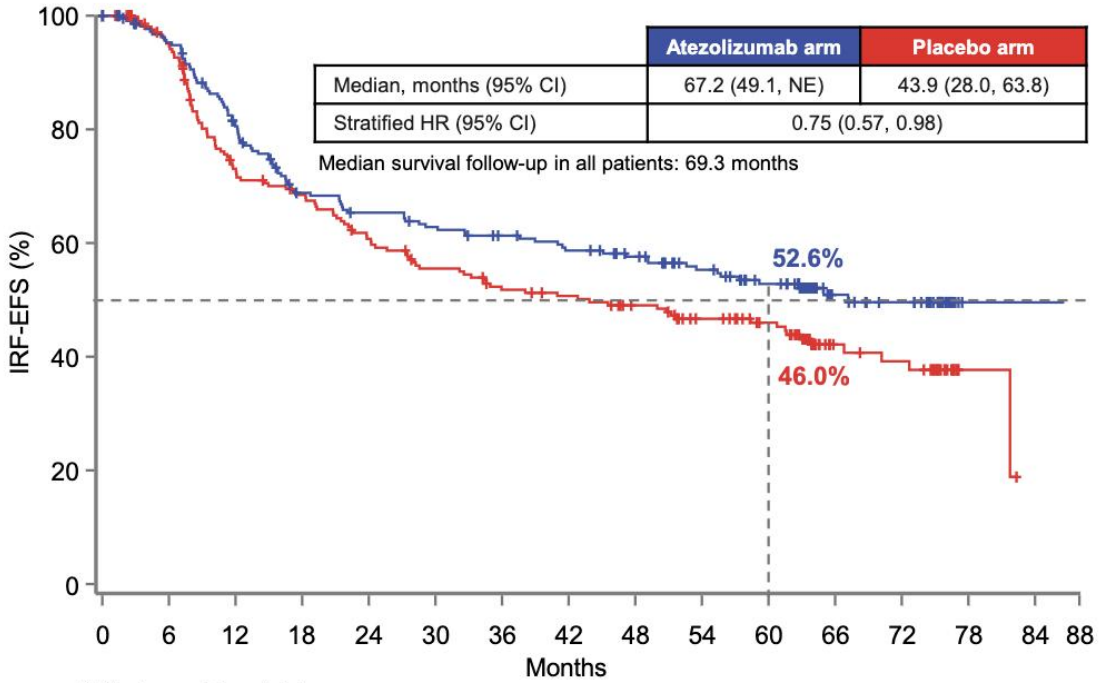
Patients remaining at risk

196	180	147	119	111	105	100	95	89	78	65	33	29	1	1
201	174	129	118	102	90	82	78	70	60	54	25	23	2	NE

ITT-WT population§

	Atezolizumab arm	Placebo arm
Median, months (95% CI)	67.2 (49.1, NE)	43.9 (28.0, 63.8)
Stratified HR (95% CI)	0.75 (0.57, 0.98)	

Median survival follow-up in all patients: 69.3 months



Patients remaining at risk

219	201	166	137	129	123	117	111	104	92	78	37	32	1	1
221	193	144	133	117	105	96	92	84	73	64	29	26	2	NE

Statistical significance was not met in the Stage IIB-IIIB-WT population

Benjamin Solomon

Neoadjuvant Divarasib Shows Manageable Safety and Promising Activity in Resectable KRAS G12C+ NSCLC: Updated NAUTIKA1 Data

IASLC 2026 World Conference on Lung Cancer
SEPTEMBER 12 – 15, 2026
SEOUL, REPUBLIC OF KOREA

Study design

Neoadjuvant treatment

Key eligibility
- Stage IB, IIA, IIB, IIIA, or select IIIB (T3N2 only) NSCLC per AJCC 8th edition
- Eligible for R0 resection
- ECOG PS 0/1
- *KRAS G12C+*

→ **Divarasib** (400 mg, QD; 8 weeks) → Surgery and pathological response assessment (by local review)

Adjuvant treatment

PD-L1 TC <1%:
Chemotherapy followed by ≤3 years of divarasib 400 mg, QD
OR ≤3 years of divarasib 400 mg, QD only
OR SoC*

PD-L1 TC ≥1%:
Chemotherapy followed by atezolizumab
OR SoC*

- **Primary endpoints:** safety and feasibility of neoadjuvant divarasib
- **Secondary endpoints:** MPR, pCR, ORR, and nodal downstaging
- **Exploratory endpoints:** pharmacokinetics

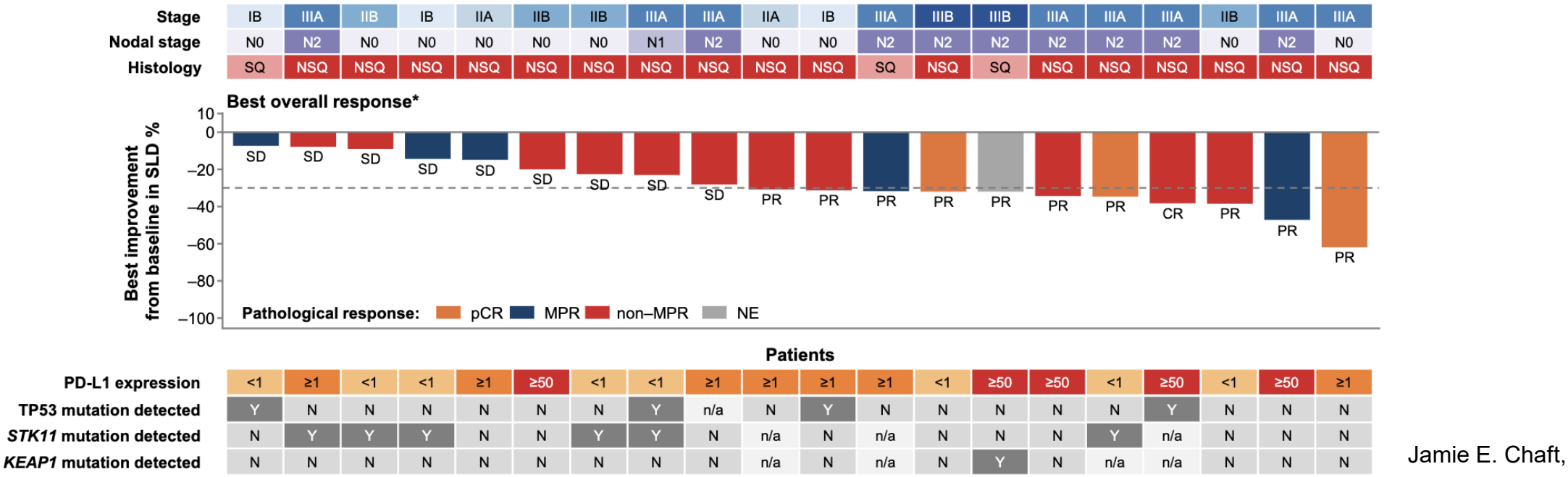
Jamie E. Chaft,

KRAS G12C mutation and PD-L1 expression determined by any FDA-approved assay performed in a CLIA-certified laboratory. *As per investigator's choice. CLIA, clinical laboratory improvement amendments; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, food and drug administration; MPR, major pathological response; ORR, overall response rate; pCR, pathological complete response; QD, once daily; R0, complete resection with negative margins; SoC, standard of care; TC, tumor cell. 1. Amin, et al. Springer 2017.

Neoadjuvant Divarasib Shows Manageable Safety and Promising Activity in Resectable KRAS G12C+ NSCLC: Updated NAUTIKA1 Data

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Best percent change in SLD from baseline with neoadjuvant divarasib



Stage	IB	IIIA	IIB	IB	IIA	IIB	IIB	IIIA	IIIA	IIA	IB	IIIA	IIIB	IIIB	IIIA	IIIA	IIIA	IIB	IIIA	IIIA
Nodal stage	N0	N2	N0	N0	N0	N0	N0	N1	N2	N0	N0	N2	N2	N2	N2	N2	N2	N0	N2	N0
Histology	SQ	NSQ	NSQ	NSQ	NSQ	NSQ	NSQ	NSQ	NSQ	NSQ	NSQ	SQ	NSQ	SQ	NSQ	NSQ	NSQ	NSQ	NSQ	NSQ
PD-L1 expression	<1	≥1	<1	<1	≥1	≥50	<1	<1	≥1	≥1	≥1	≥1	<1	≥50	≥50	<1	≥50	<1	≥50	≥1
TP53 mutation detected	Y	N	N	N	N	N	N	Y	n/a	N	Y	N	N	N	N	N	Y	N	N	N
STK11 mutation detected	N	Y	Y	Y	N	N	Y	Y	N	n/a	N	n/a	N	N	N	Y	n/a	N	N	N
KEAP1 mutation detected	N	N	N	N	N	N	N	N	N	n/a	N	n/a	N	Y	N	n/a	n/a	N	N	N

Jamie E. Chaft,

Tumor regression was observed across PD-L1, *TP53*, and *STK11* status

NAUTIKA1: study schema and baseline characteristics

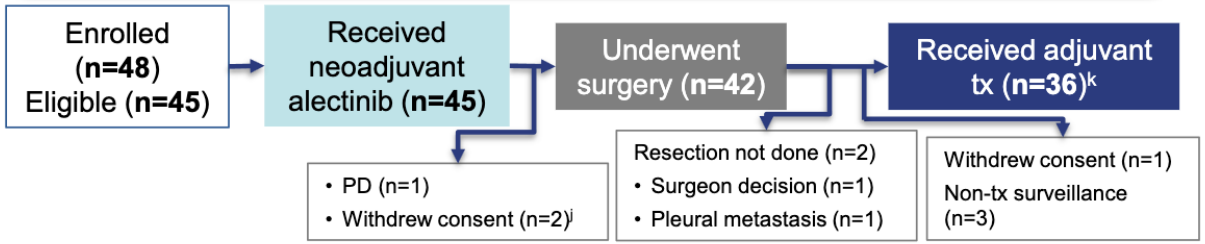
- Phase II umbrella study of targeted neoadjuvant tx in patients with early-stage NSCLC harbouring study-eligible oncogenic drivers[1]
- We present the primary analysis of the ***ALK*+ cohort**[a]

Key eligibility criteria
- Stage IB-IIIA/select IIIB[b] (T3N2 only) NSCLC
- *ALK*+
- Eligible for R0 resection
- Local molecular testing[c]

→ ***ALK*+ cohort** Neoadjuvant alectinib (600 mg BID; 8 weeks) → Surgery and pathologic response assessment by local review → **Adjuvant tx** ≤4 cycles SOC platinum-based chemotherapy,[d] then ≤2 years alectinib

Key Endpoints

Primary: MPR[e,f] **Secondary:** MPR,[e,g] pCR,[f,g] pathologic regression,[h] ORR, DFS, EFS, OS, nodal downstaging, ctDNA clearance rate[i]
Exploratory: ctDNA status over time, correlation with outcomes



Baseline characteristics	*ALK*+ cohort (N=48)
Age, median (range) years	**62** (30–80)
Female | **male**, n (%)	24 (**50**) | 24 (**50**)
Race, n (%) Asian | American Indian/Alaska | White | Unknown	 7 (**15**) | 1 (**2**) | 31 (**65**) | 9 (**19**)
Smoking history, n (%) Current | Former | Never	 1 (**2**) | 11 (**23**) | 36 (**75**)
ECOG PS 0 | 1, n (%)	33 (**69**) | 15 (**31**)
Lung cancer histology, n (%) Non-squamous | squamous	 45 (**94**) | 3 (**6**)
Clinical staging[a], n (%) IB | IIA | IIB IIIA | IIIB	 4 (**8**) | 2 (**4**) | 8 (**17**) 29 (**60**) | 5 (**10**)
Lymph node stage, n (%) N0 | N1 | N2	 8 (**17**) | 11 (**23**) | 29 (**60**)
Primary tumour, n (%) T1a | T1b | T1c | T2a | T2b | T3 | T4	 1 (**2**) | 11 (**23**) | 6 (**13**) | 12 (**25**) | 6 (**13**) | 10 (**21**) | 2 (**4**)

NCT04302025. [a]Fully enrolled *ALK*+ cohort who completed/discontinued the neoadjuvant/surgical phases. [b]American Joint Committee on Cancer 8th edition. [c]Local biomarker testing in Clinical Laboratory Improvement Amendments–certified lab via fluorescence in situ hybridization, immunohistochemistry or next-generation sequencing. [d]Unless contraindicated/patient declined. [e]Defined as ≤10% residual viable tumour cells. [f]Locally assessed. [g]Centrally assessed by consensus committee. [h]Based on weighted % of viable tumour cells; [i]Prior to surgery in patients with detectable ctDNA at start of therapy. [j]One patient withdrew consent after discontinuing neoadjuvant treatment due to adverse event. [k]At the cutoff, 33 patients had received chemotherapy then alectinib while 3 had received only chemotherapy at that point. *ALK*, anaplastic lymphoma kinase; BID, twice daily; ctDNA, circulating tumour DNA; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EFS, event-free survival; MPR, major pathologic response; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; pCR, pathological complete response; PD, disease progression; R0, complete resection; SOC, standard of care; tx, treatment. 1. Lee JM, et al. J Thorac Oncol 2025;20:S66.

Jay M. Lee,

Pathologic and radiographic[a] responses and 2-year time-to-event outcomes[b]

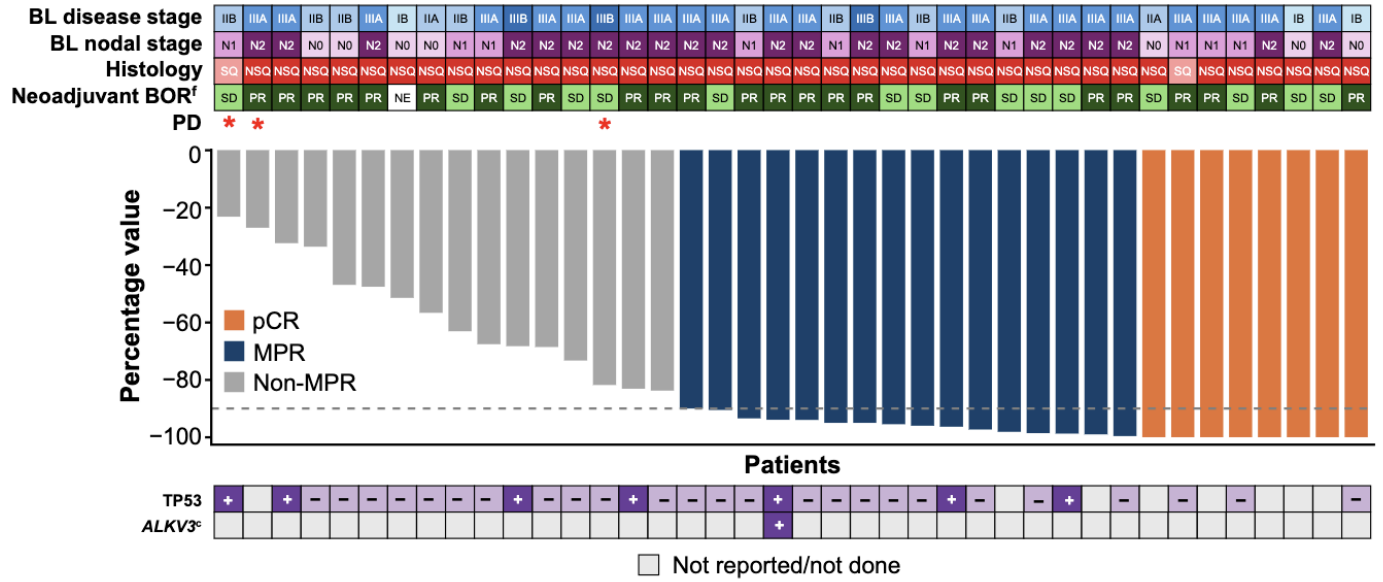
Jay M. Lee,

Response endpoint	
Pathological response, n[c]	**43[d]**
MPR, n (%) [95% CI]	24 (**56**) [40, 71]
pCR, n (%) [95% CI]	8 (**19**) [8, 33]
Radiographic response, n	**45[e]**
ORR, n (%) [95% CI]	27 (**60**) [44, 74]
PR	27 (**60**) [44, 74]
SD	16 (**36**) [22, 51]
PD, n (%) [95% CI]	1 (**2**) [<1, 12]
NE,[f] n (%)	1 (**2**)

2-year event rates, % (95% CI)	
EFS (n=45)	**90** (81, 99)
DFS (n=39)[g]	**97** (91, 100)
OS rate (n=45)	**98** (93, 100)

Median follow-up: 23.0 months

Weighted percentage pathologic regression (n=40)[h]



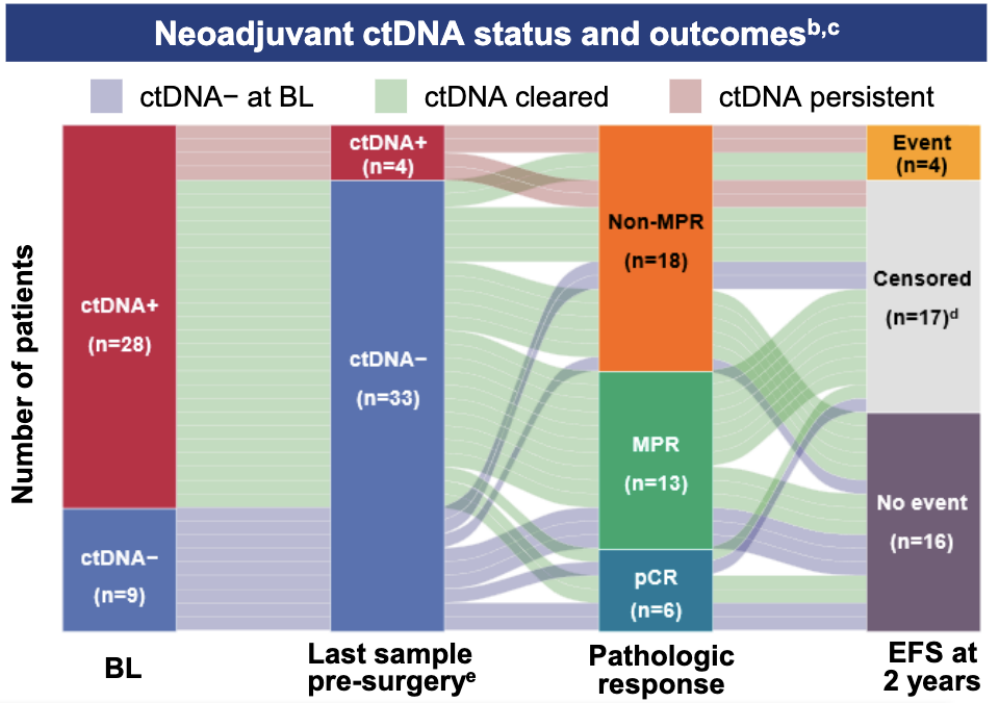
Robust pathologic regression and radiographic responses were observed with neoadjuvant alectinib

Data snapshot: 30 June 2026. [a]Among all treated, eligible patients. [b]From neoadjuvant alectinib initiation through surgery, then adjuvant treatment with chemotherapy and alectinib in 33 patients (73%) and chemotherapy only in 3 patients (7%). [c]Locally assessed. [d]Included all treated, eligible patients who either underwent post-neoadjuvant surgery (with or without resection) or discontinued due to AE or PD with pathologic response for patients without R0 resection set to non-MPR. [e]Assessed in eligible efficacy-evaluable patients; unconfirmed. [f]One patient with BOR of NE had SD at cycle 2 day 1 but no pre-surgery scan. [g]Efficacy-evaluable population who had R0 resection and were deemed disease-free. [h]In the pathologic response analysis population; weighted % viable tumour regression values were set to "missing" for patients who did not have primary tumour R0 resection.
AE, adverse event; *ALKV3*, *ALK* variant 3; BL, baseline; BOR, best overall response; NE, not evaluable; NSQ, non-squamous; PR, partial response; SD, stable disease; SQ, squamous; TP53, tumour protein p53.

ctDNA clearance status post neoadjuvant tx and pathologic/clinical outcomes

Jay M. Lee,

- Plasma-only/tumour-agnostic ctDNA was analysed by PredicineWES+ (BL) and PredicineBEACON (MRD) with whole blood germline control subtraction
  - BEP[a] included 39/45 patients (87% of eligible and efficacy-evaluable patients)
  - 77% of BEP (30/39) was ctDNA+ at BL
  - *ALK* fusions detected in 26% of BEP (10/39)
- ctDNA clearance prior to surgery was observed in 86% of patients (24/28) who were ctDNA+ at BL
- All patients who had MPR (n=13) or pCR (n=6) were either ctDNA− at BL or cleared ctDNA prior to surgery[b]
- All patients who were event free at 2 years (n=16) were either ctDNA− at BL or cleared ctDNA prior to surgery



These data suggest that ctDNA MRD clearance after neoadjuvant alectinib may be associated with favourable outcomes

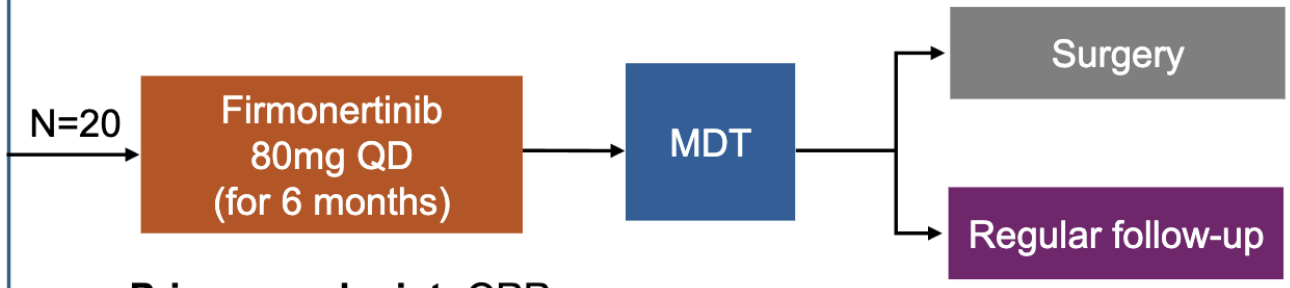
[a]Includes patients who had BL ctDNA data. [b]1 patient was excluded from outcomes analysis due to missing MPR/pCR. [c]Includes patients who had BL and longitudinal ctDNA data. [d]Patients' last disease assessment date has not been 2 years since first treatment date, but they were event-free at the time of the snapshot. [e]Last sample collected post-BL, during neoadjuvant phase before surgery. 2 patients only had Cycle 2 Day 1 sample.
BEP, biomarker-evaluable population; MRD, molecular residual disease.

Background and study design

- The management of early-stage, multiple primary lung cancer (MPLC) presents a significant clinical challenge, as a single radical surgery cannot eradicate all lesions
- While the efficacy of third-generation EGFR-TKIs in the adjuvant setting for early-stage NSCLC with high-risk clinicopathological features is well-established, their role in managing unresectable residual GGOs remains unclear

Key Eligibility Criteria

- Age 18-75 years
- Preoperative chest CT scan diagnosed MPLC
- ≥10 contralateral GGO (≥4 mm) not be resected simultaneously
- Confirmed EGFR mutations (19del or L858R)
- ECOG PS 0-1



Primary endpoint: ORR

Secondary endpoints: pCR、MPR、DFS、OS、Safety

Exploratory endpoint: RR (CT attenuation change by lesion)

Ye Wang

Efficacy

Ye Wang

- A median follow-up was 19.5 months (range: 8.1-32.2 months), **8/14** patients underwent surgical resection

Primary endpoint

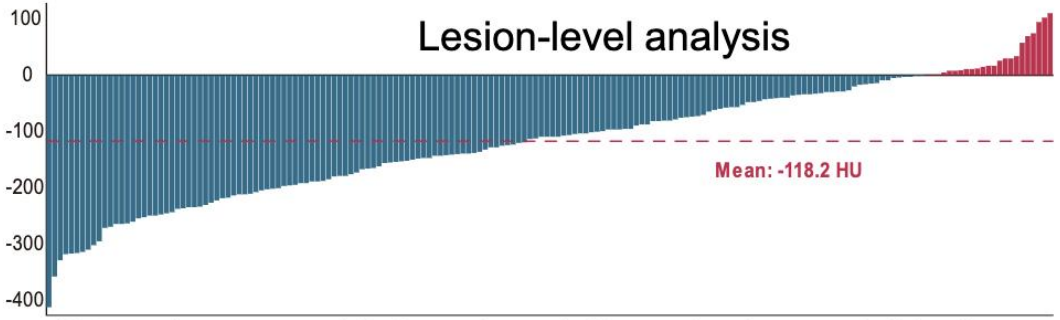
Best overall response, n (%)	N = 14
CR	1 (7.1)
PR	4 (28.6)
SD	9 (64.3)
PD	0
ORR, % (95%CI)	**35.7 (12.8-64.9)**
DCR, % (95%CI)	**100 (76.8-100)**

Secondary endpoints

- Among **8** surgically treated patients: **pCR 4**, **MPR 1**, **non-MPR 3**
- The 1-year DFS rate was 100%

Exploratory endpoint

Numerical range (Hu)	No. of lesions, n (%)
≥0	23 (12.8)
0 to -100	58 (32.2)
-200 to -100	57 (31.7)
-300 to -200	33 (18.3)
≤-300	9 (5)
CT attenuation response rate*: **157/180 (87.2%)**	



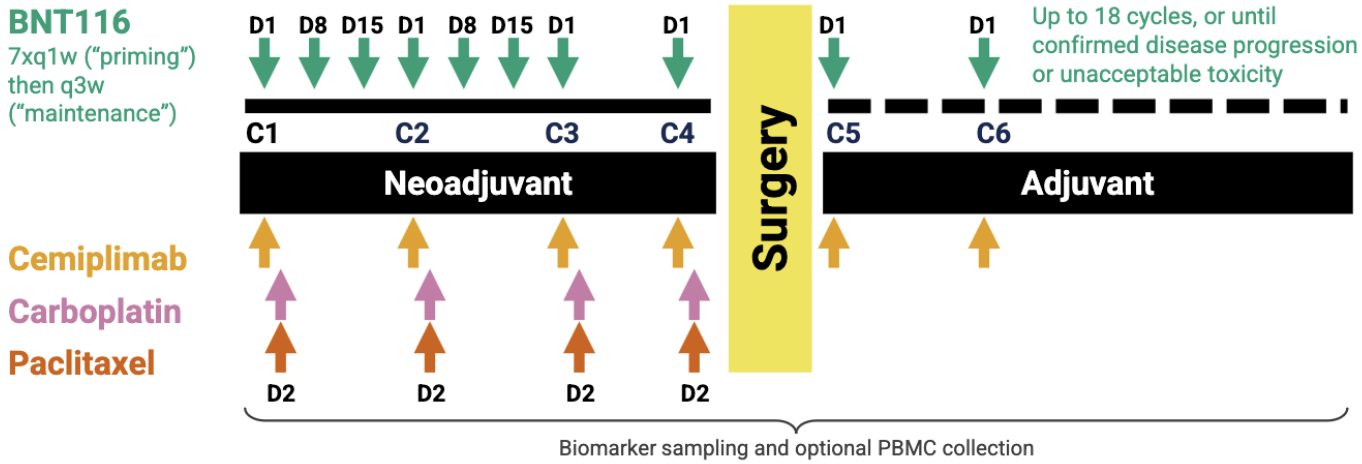
*CT attenuation response was defined as any decrease in CT attenuation value compared with baseline, meaning the HU value became more negative.

LuCa-MERIT-1 (NCT05142189) Cohort 6: Neoadjuvant BNT116 + cemiplimab + chemotherapy in patients with resectable NSCLC

Rafal Dziadziuszko

- RNA-LPX-based investigational BNT116 combines targeted RNA delivery to professional APCs with antigen-specific T-cell induction, supported by a TLR-mediated type 1 interferon response.
- LuCa-MERIT-1 (NCT05142189) is an ongoing open label Phase I dose confirmation trial with multiple expansion cohorts to determine safety and clinical activity of BNT116 ± immunotherapy or chemotherapy in NSCLC.
- **This cohort evaluates neoadjuvant treatment with BNT116 + cemiplimab + carboplatin + paclitaxel in patients with resectable NSCLC.**
- Results from adjuvant treatment with BNT116 + cemiplimab will be reported separately.

Treatment schedule



Patients

Key inclusion criteria

- Resectable Stage II/III NSCLC
- Measurable disease by RECIST v1.1
- Eligible for neoadjuvant treatment
- Able to tolerate anti-PD-1
- ECOG PS ≤1

Key exclusion criteria

- Prior systemic therapy
- Disease localization or symptoms requiring immediate surgical intervention

Endpoints (selected)

Primary	Safety and tolerability
Secondary	Pathologic response rate, ORR, OS
Exploratory	Predictive and pharmacodynamic biomarkers

Abbreviations: APC, antigen-presenting cell; C, cycle; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; LPX, lipoplex; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PBMC, peripheral blood mononuclear cell; PD-1, programmed cell death protein 1; q1w, once weekly; q3w, every 3 weeks; RECIST v1.1, response evaluation criteria in solid tumors version 1.1; TLR, toll-like receptor.

Rafal Dziadziuszko

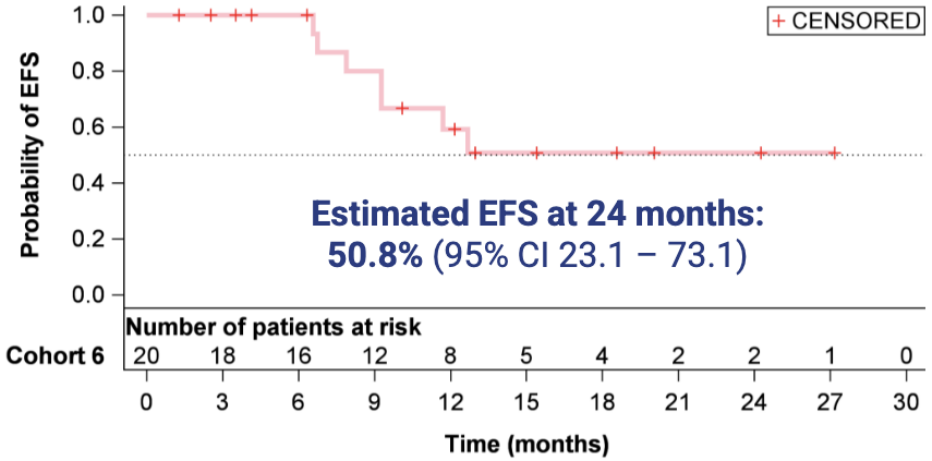
Clinical activity

Clinical activity	BNT116 + cemiplimab + chemotherapy N = 20[1]
Best overall response[2], n (%)	
PR	13 (65)
SD	7 (35)
PD	0
Objective response rate[2], n (%)	13 (65)
95% CI	40.8, 84.6
Disease control rate[2], n (%)	20 (100)
95% CI	83.2, 100.0
Median event-free survival (months)	NE
95% CI	9.3, NE
Median overall survival (months)	NE
95% CI	NE, NE
Median follow-up time (months)	14.5
Min – max	2.4 – 28.1

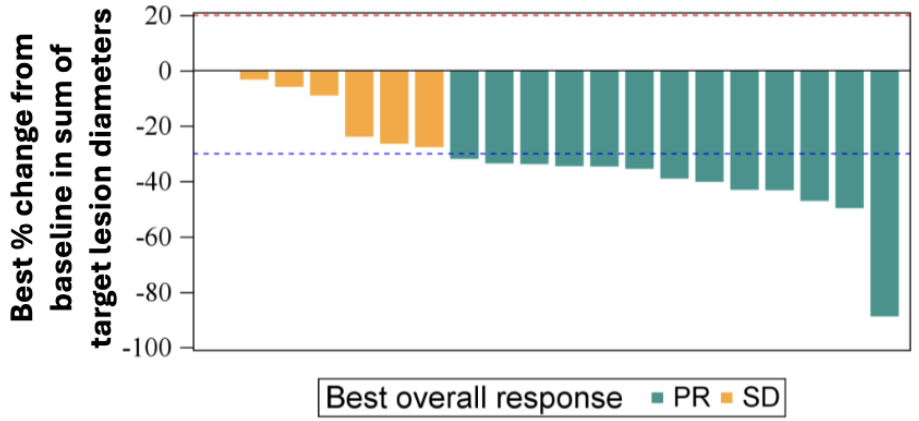
[1] Two patients had the post neoadjuvant therapy scan per protocol, but discontinued prior to surgery (one inoperable, one had a better therapeutic option available); [2] Neoadjuvant treatment, before surgery.

- **An objective radiologic response prior to surgery was observed in 65% of patients.**
- **No progressive disease events occurred during the neoadjuvant treatment.**
- **Neoadjuvant BNT116 + cemiplimab + carboplatin + paclitaxel followed by adjuvant treatment achieved an estimated EFS rate of 51% at 24 months.**

BNT116 + cemiplimab + carboplatin + paclitaxel



BNT116 + cemiplimab + carboplatin + paclitaxel



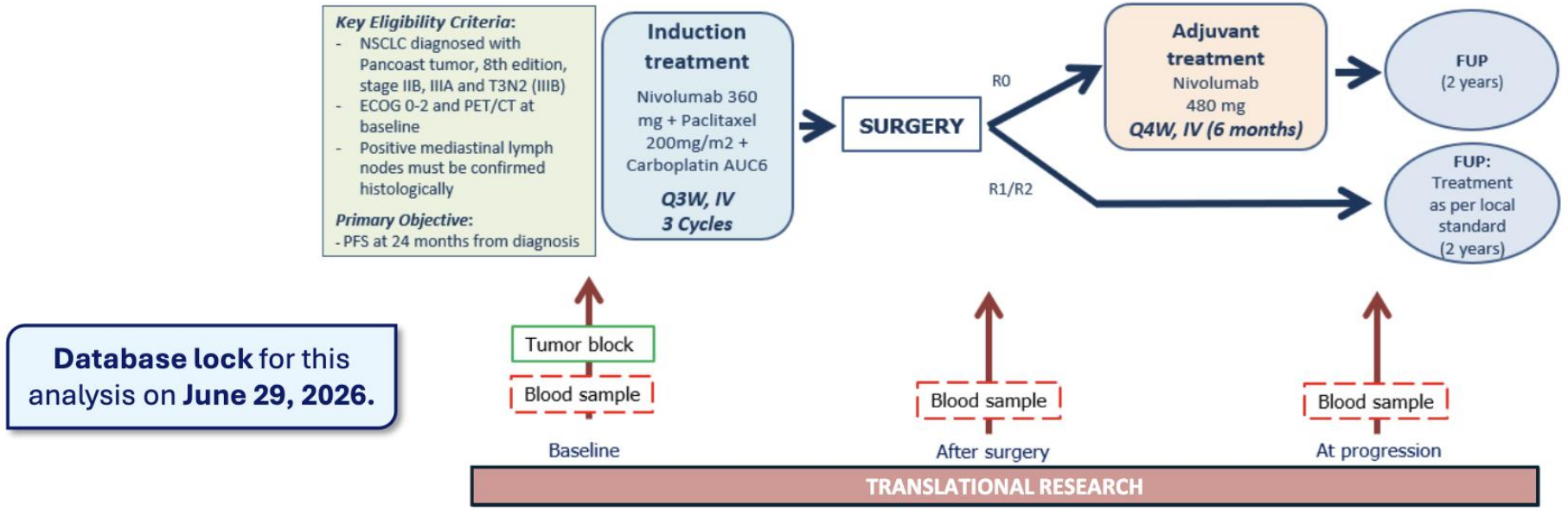
Abbreviations: CI, confidence interval; EFS, event-free survival; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Data cut-off date: July 1, 2026

Study design

Open-label, prospective, single-arm, multicentre, phase II clinical trial.

GECP lung cancer research



Database lock for this analysis on **June 29, 2026.**

The 22 patients were enrolled across 14 centers. The **recruitment period lasted approximately 2 years and 5 months**, from June 2023, to November 2025.

Baseline: CT, PET-CT, brain MRI/CT, blood and FFPE tumour tissue.; **Radiological assessments**: after neoadjuvant therapy (CT + PET-CT), after surgery, every 12 weeks during adjuvant treatment, and every 3 months during FUP.

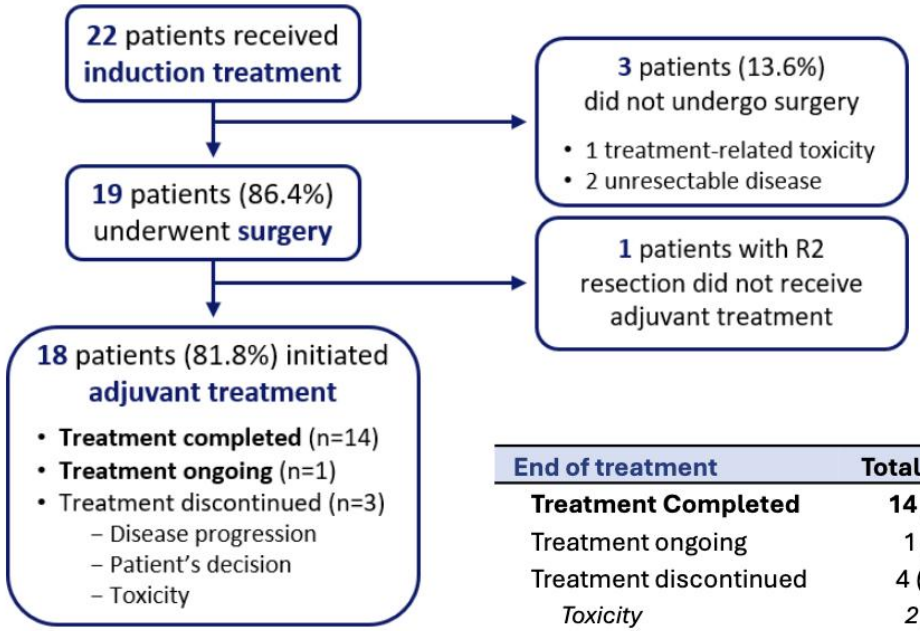
Primary endpoint: 24-month PFS.; **Secondary endpoints:** OS, R0 resection rate, ORR, DCR, DOR, pCR, MPR, safety.; **Exploratory endpoints:** Prognostic value of ctDNA, MRD dynamics.

A total of 22 patients was required to detect an improvement in 24-month PFS from 55% (null hypothesis) to 75% (alternative hypothesis), with 80% power and a one-sided α of 0.05. The null hypothesis was rejected if the lower bound of the two-sided 90% CI for PFS24 exceeded 55%.

NSCLC: Non-small cell lung cancer; **IV:** Intravenously; **ECOG PS**: Eastern Cooperative Oncology Group performance status; **PET:** Positron emission tomography; **CT:** Computed tomography; **R0 resection:** complete resection; **FUP:** Follow-up; **MRI:** Magnetic resonance imaging; **FFPE**: Formalin-Fixed Paraffin-Embedded; **PFS:** Progression-free survival (defined as time from enrolment to relapse, progression or death); **OS:** Overall survival; **ORR:** Objective response rate; **DCR:** Disease control rate; **DOR:** Duration of response; **pCR:** Pathological complete response; **MPR:** Major pathological response; **MRD:** Minimal residual disease.

Surgical aspects and treatment completion

GECP lung cancer research



End of treatment	Total (N = 22)
Treatment Completed	**14 (63.6%)**
Treatment ongoing	1 (4.5%)
Treatment discontinued	4 (18.1%)
Toxicity	*2 (9.1%)*
Disease Progression	*1 (4.5%)*
Patient's decision	*1 (4.5%)*
Other	3 (13.6%)
Unresectable	*2 (9.1%)*
R2 patient	*1 (4.5%)*

2 patients with unresectable tumour post-induction.
1 patient with grade 3 treatment-related toxicity.

	Total (N = 22)
No surgery	3 (13.6%)
Surgical approach	
Open: Shaw-Paulson	11 (50.0%)
VATS	6 (27.3%)
Open: posterolateral thoracotomy	1 (4.5%)
Open: anterior (Dartavelle)	1 (4.5%)
Open: other (Spare Muscle MIOS)	2 (9.1%)
Major resection *	**17 (77.3%)**
Lobectomy	17 (77.3%)
Right	11 (50.0%)
Left	6 (27.3%)
Minor/other resection†	**16 (72.7%)**
Exploratory thoracotomy	3 (13.6%)
Typical segmentectomy	2 (9.1%)
Atypical segmentectomy	1 (4.5%)
Others	12 (54.5%)
Costal arch / ribs only	9 (40.9%)
Costal arch / ribs + vertebral body	2 (9.1%)
Parietal pleura + brachial plexus	1 (4.5%)

All results are shown as n (%) unless otherwise indicated. *Of the 19 resected patients, 17 (89.5%) underwent major resection (lobectomy) and 2 (10.5%) underwent minor resection only (one atypical segmentectomy plus typical segmentectomy, and one typical segmentectomy); both achieved pathological complete response (ypT0, R0). 16 patients had minor/other procedures, most in combination with major resection.

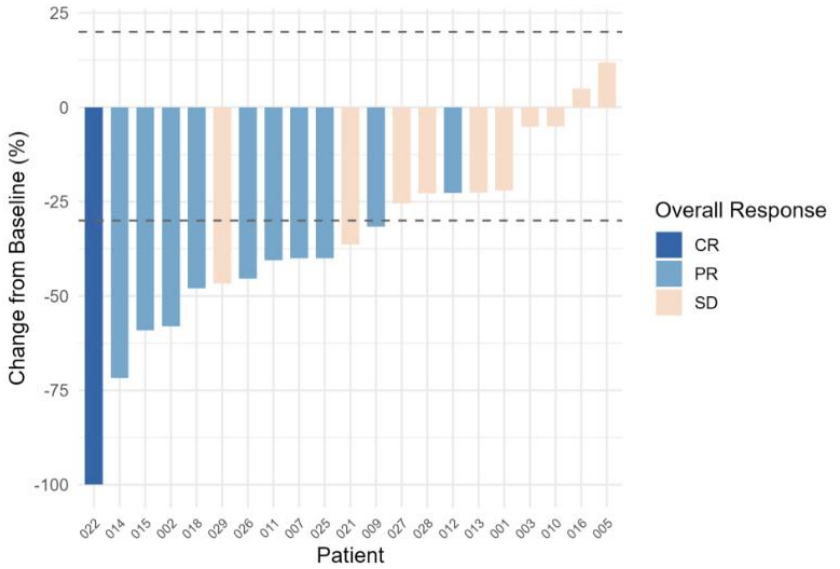
Radiological response to neoadjuvant treatment

GECP lung cancer research

Median **primary tumour diameter decreased** from 61 mm (IQR 45–85) at baseline to 42 mm (IQR 24–56), representing a **median relative reduction of 38%** (IQR −48 to −23).

	Total (N = 22)
Sum of primary tumour diameter (mm), median (IQR)	42 (24, 56)
Min., Max.	0, 84
Relative change (%), median (IQR)	-38 (-48, -23)
Min., Max.	-100, 12
SUVmax primary tumour, median (IQR)	5.5 (3.9, 7.0)
FEV1 pre-surgery (%), median (IQR)	88.0 (68.6, 105.8)
DLCO pre-surgery (%), median (IQR)	61.0 (54.0, 72.0)
Response after induction treatment	
CR	1 (4.5%)
PR	10 (45.5%)
SD	10 (45.5%)
PD	0 (0.0%)
NE/NR	1 (4.5%)
ORR	**11 (50.0%)**
DCR	**21 (95.4%)**

All results are shown as n (%) unless otherwise indicated. IQR, Interquartile Range; SUVmax, Maximum Standardized Uptake Value; FEV1, Forced Expiratory Volume in 1 second; DLCO, Diffusing Capacity of the Lung for Carbon Monoxide; CT, Computed Tomography; PET, Positron Emission Tomography; VATS, Video-assisted Thoracic Surgery.



Each bar represents one patient (n = 21; one patient not assessable excluded). The y-axis shows the percentage change in sum of diameters from baseline to post-neoadjuvant assessment. Dashed lines indicate the RECIST 1.1 thresholds for partial response (−30%) and progressive disease (+20%). CR: complete response; PR: partial response; SD: stable disease. Patients are ordered by magnitude of response.

Surgery and pathological data

GECP lung cancer research

Pathological downstaging included ypT0 disease in 11 patients (57.9%) and ypN0 status in 18 (94.7%).

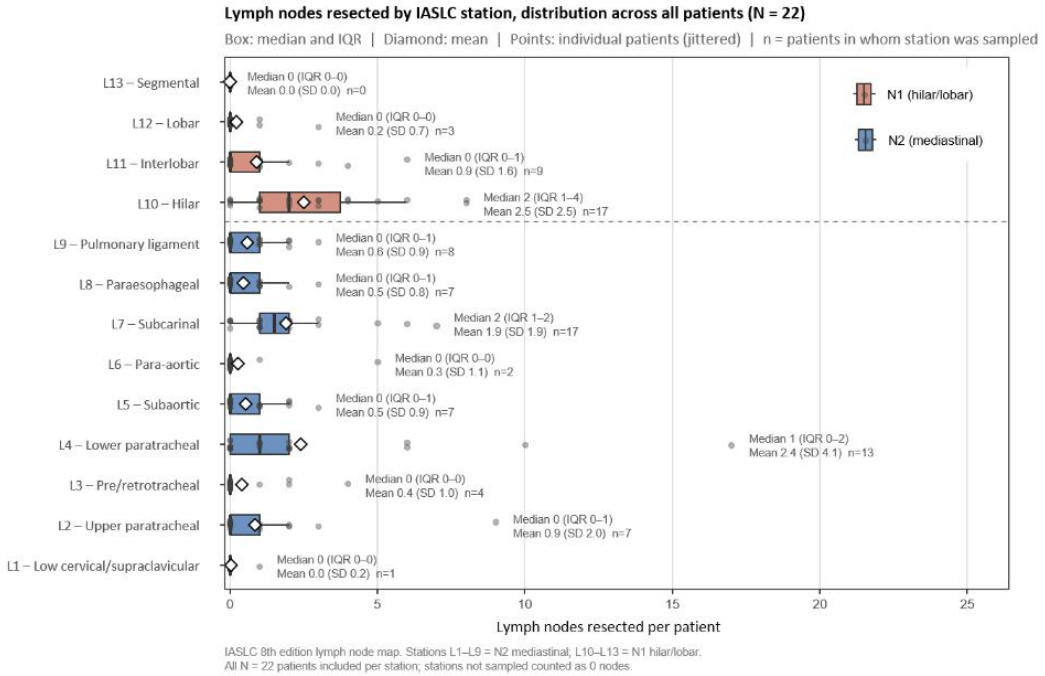
	Total (N = 19)
Resection degree	
R0	18 (94.7%)
R2	1 (5.3%)
Pathological response	
Complete	11 (57.8%)
Major	4 (21.1%)
< Major	4 (21.1%)
Residual tumour viability (%)	
No viability (= 0%)	11 (57.9%)
Some viability (> 0%)	8 (42.1%)
Median RTV (IQR) in > 0%	10.0 (8.0 – 26.0)
Median tumour size in mm (IQR) in > 0%	9.5 (3.3 – 42.8)
Intraoperative complications	0 (0.0%)
Post-surgical complications	10 (52.6%)
Post-surgical effusion	4 (21.1%)
Persistent air leak	4 (21.1%)
Post-surgical 30-day mortality	0 (0.0%)
Post-surgical 90-day mortality	0 (0.0%)

Overall pathological response rate of 78.9%

All results are shown as n (%) unless otherwise indicated. *Of the 19 resected patients, 17 (89.5%) underwent major resection (lobectomy) and 2 (10.5%) underwent minor resection only (one atypical segmentectomy plus typical segmentectomy, and one typical segmentectomy); both achieved pathological complete response (ypT0, R0). **IQR,** Interquartile range; **R0,** Complete resection; **pCR,** Pathological complete response.

Highest nodal sampling in stations L10 and L4.

Pathological nodal involvement was identified in two patients.

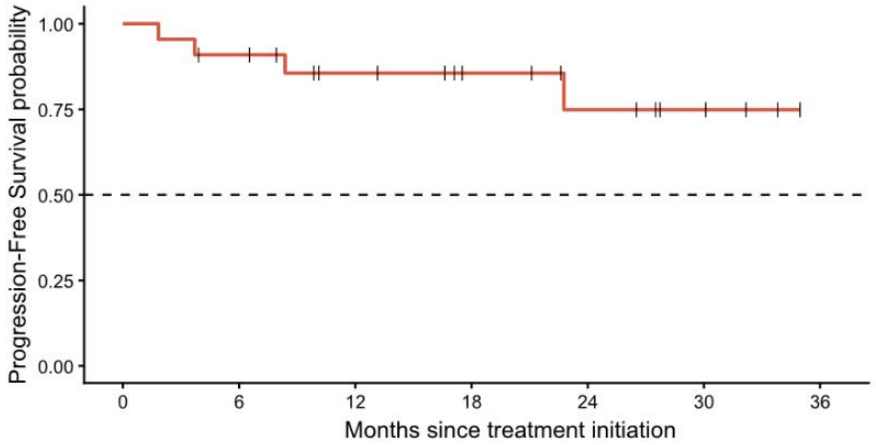


Blue = tumor-free nodes; red = tumor-positive nodes. n = number of patients in whom the station was sampled. Dashed line separates N2 mediastinal stations (L1–L9) from N1 hilar/lobar stations (L10–L13), according to the IASLC 8th edition lymph node map. Diamond: mean. N = patients in whom station was sampled.

Preliminary survival outcomes

Median follow-up of 21.1 months
Data maturity of 19.4%

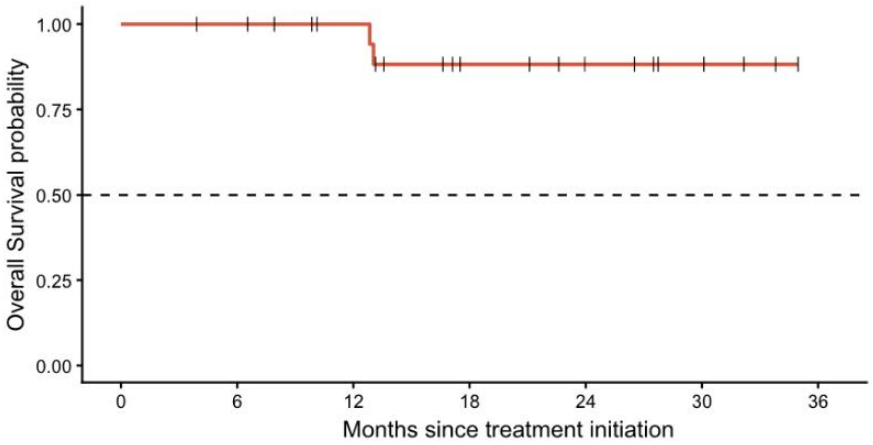
At this data cut-off, the **primary endpoint has been met.**



Median PFS not reached at cut-off.

Estimated PFS rate at 6 months: 90.9% (95% CI 79.7–100%)
Estimated PFS rate at 12 months: 85.6% (95% CI 71.6–100%)
Estimated PFS rate at 24 months: **74.9% (90% CI 57.4-97.6%;** 95% CI 54.6–100%)

PFS24 >55% and lower bound of 90% CI >55% → Primary endpoint met



Median OS not reached at cut-off.

Estimated OS rate at 6 months: 100%
Estimated OS rate at 12 months: 100%
Estimated OS rate at 24 months: 88.2% (95% CI 74.2–100%)

4 disease progressions (PFS events); 2 deaths, both after disease progression.

Results: Metabolic response predict Survival

Follow up 56.9 months

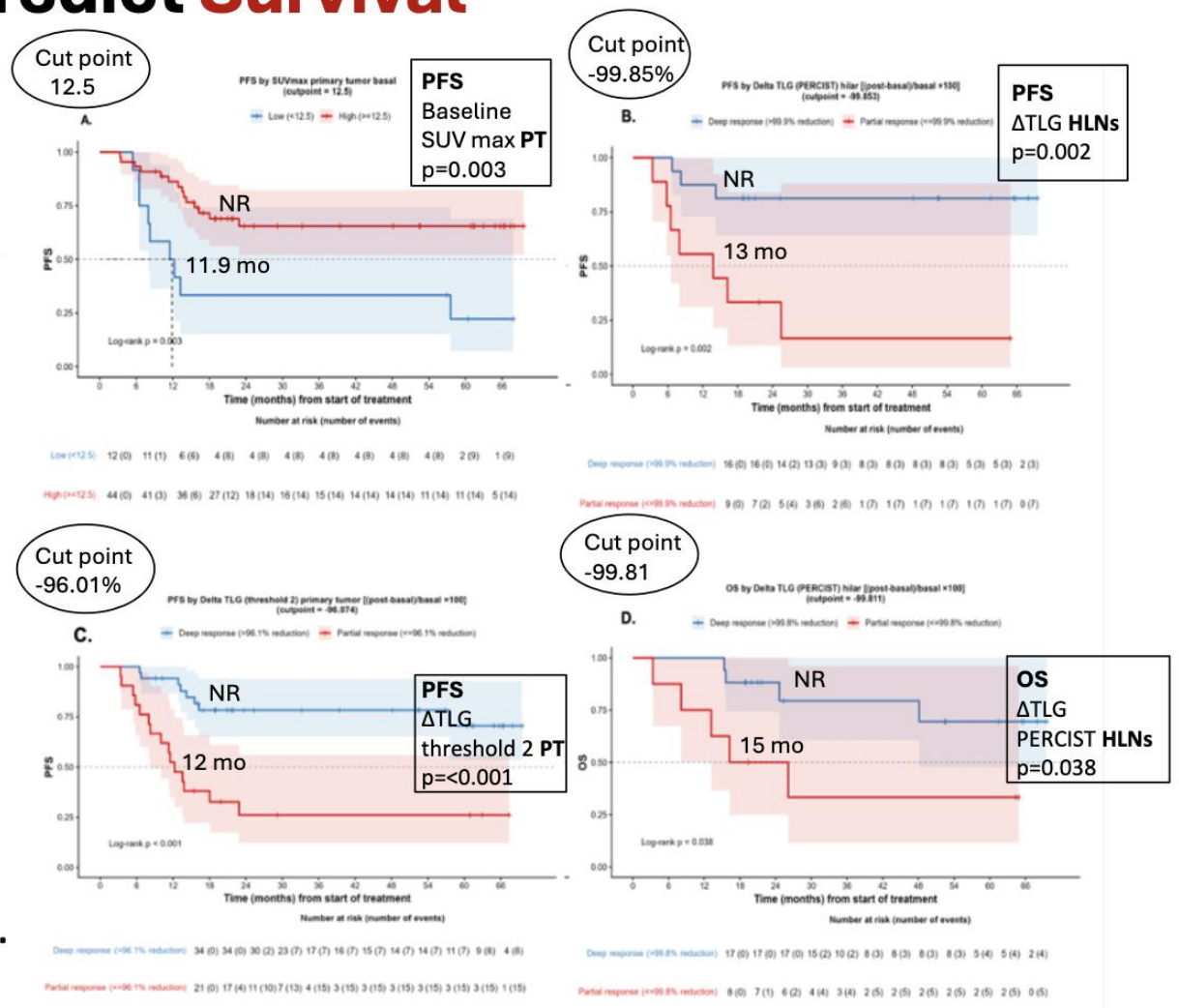
Baseline SUVmax and **SUVpeak** cut points **12.5** (log-rank p=0.003) and **9.4** (log-rank p=0.010), in **PT** were associated with **PFS.** AUC at 6 months **0.651.**

Non-linear association between baseline **SUVmax** and **PFS** (p = 0.034).

Patients achieving **deeper metabolic responses (Δ>95%)** had **PFS NR** vs. **12.3–18 mo**. AUC 0.70. HR 1.06; 95% CI, 1.02-1.09; p=0.001.

HLNs Δ parameters predicted **PFS** (p<0.032) and **OS** (p<0.047). HR 1.02; 95% CI, 1.00-1.03.

MLNs pos-treatment TLG PERCIST and MTVPERCIST had **limited** performance to predict PFS (AUC 0.586).



PFS: Progression free survivall, **OS:** Overal survivall. **PT :** primary tumor, **HLNs**: Hilar lymph nodes.

Rafael Jimeno, Aylen Vanessa Ospina-Serrano

14-gene Assay is Prognostic of Survival

200+ candidate genes

↓

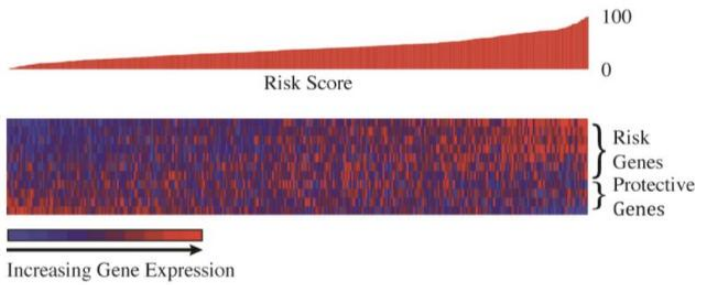
$L_{1,2}$-penalized Cox PH Modeling

↓

Prognostic Algorithm

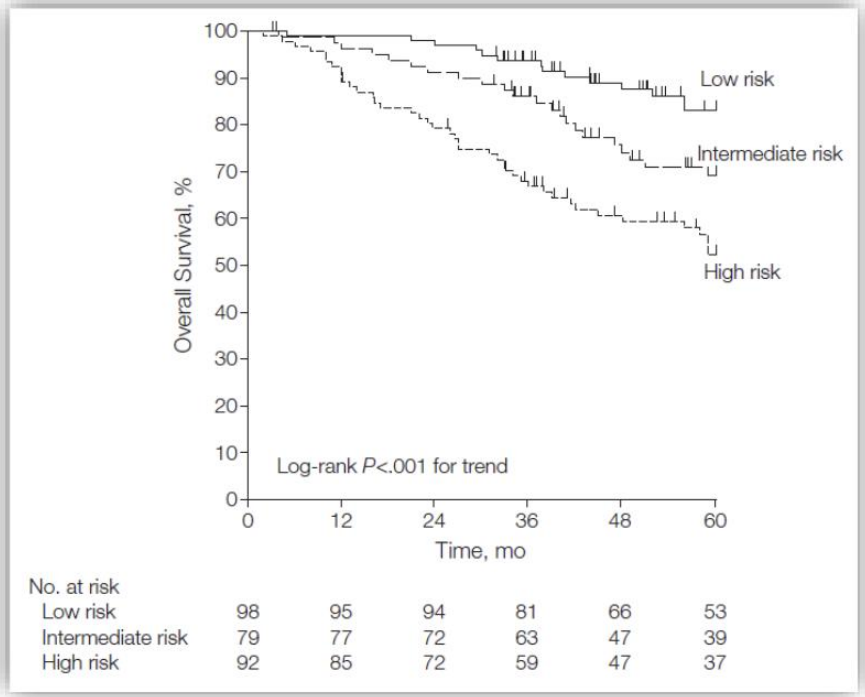
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Risk Score (1-100)



	Gene name	Relevant biological functions and pathways
BAG1	BCL2-associated athanogene	Apoptosis; cell surface receptor linked signalling
BRCA1	Breast cancer 1, early onset	Induction of apoptosis; protein ubiquitination; regulation of G2/M transition DNA damage checkpoints; regulation of DNA repair
CDC6	Cell division cycle 6 homolog	Regulation of transcription involved in G1/S phase of mitotic cell cycle; regulation of cell proliferation
CDK2AP1	Cyclin-dependent kinase 2 associated protein 1	Regulation of S phase of mitotic cell cycle; DNA-dependent DNA replication
ERBB3	V-erb-b2 erythroblastic leukemia viral oncogene homolog 3	Regulation of cell adhesion; transmembrane receptor protein tyrosine kinase signalling; regulation of phosphoinositide 3-kinase cascade; regulation of cell proliferation
FUT3	Fucosyltransferase 3	Carbohydrate metabolism; protein aminoacid glycosylation
IL11	Interleukin 11	Regulation of cell proliferation; B-cell differentiation; megakaryocyte differentiation; regulation of peptidyl-serine phosphorylation; regulation of MAPKKK cascade
LCK	Lymphocyte-specific protein tyrosine kinase	Induction of apoptosis; activation of caspase activity; regulation of T-cell receptor signalling; leucocyte migration
RND3	Rho family GTPase 3	Cell adhesion; small GTPase mediated signal transduction; actin cytoskeleton organisation
SH3BGR	SH3 domain binding glutamic acid-rich protein	Protein complex assembly
WNT3A	Wingless-type MMTV integration site family, member 3A	Canonical Wnt receptor signalling; multicellular organismal development; regulation of cell proliferation and differentiation; regulation of catenin protein nuclear translocation
ESD	Esterase D	Recycling of sialic acids; serine hydrolysis
TBP	TATA box binding protein	Transcription initiation from RNA polymerase II promoter; RNA elongation from RNA polymerase II promoter; transcription from RNA polymerase III promoter
YAP1	Yes-associated protein 1	Hippo signalling cascade; regulation of transcription; contact inhibition

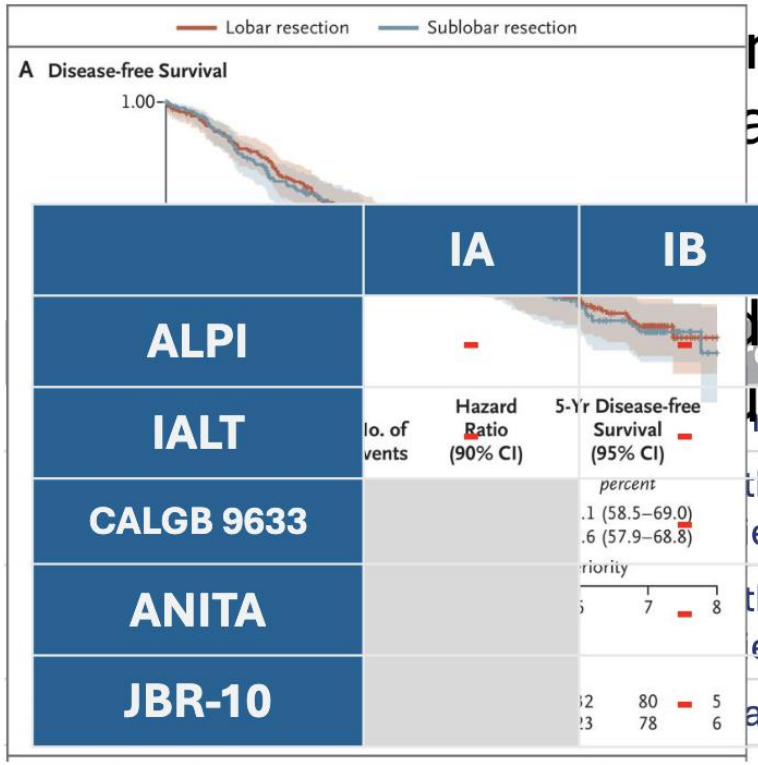
Table 4: **Algorithm genes**



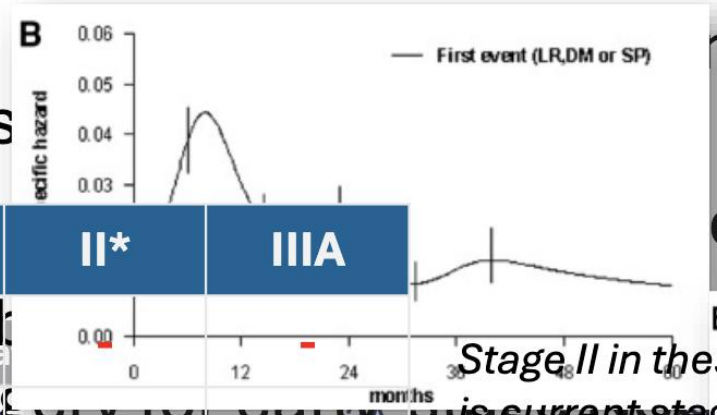
Kratz et. al *Lancet* 2012; Kratz et. al *JAMA* 2012; Woodard et. al *Clin Lung Cancer* 2018; Kratz et al. *J Thor Onc* 2019; Haro et al. *JAMA Network Open* 2019; Woodard et. al *Clin Lung Cancer* 2021

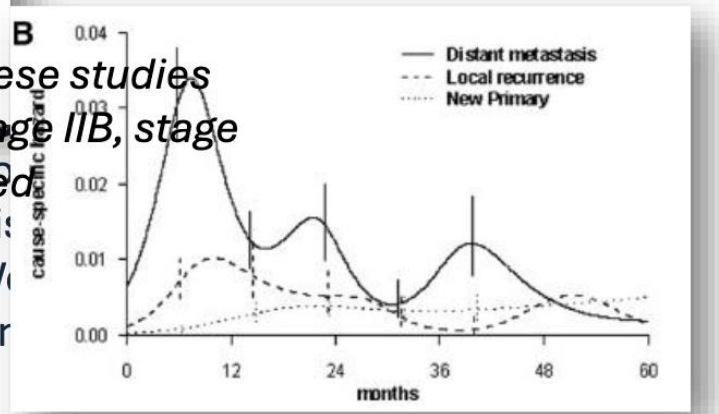
Background

- 30-50% recurrence rate in stage I-II NSCLC despite surgery
- n not improve
  - Occult metastases at time of surgery
- as
- e
- H



	IA	IB	II*	IIIA
ALPI	-	-	-	-
IALT	No. of Events	Hazard Ratio (90% CI)	5-Yr Disease-free Survival (95% CI)	-
CALGB 9633			percent .1 (58.5–69.0) .6 (57.9–68.8)	
ANITA			riority 5 7 - 8	+ 2A
JBR-10			32 80 - 5 23 78 6	





Stage II in these studies is current stage IIB, stage IIA not studied

- Pe
- Vis
- W
- Ur

ichell et al. *J c Oncol* 2012)

therapy for ents

apy

64% DFS in Stage IA NSCLC < 2cm
(Altorki et al. *NEJM* 2023)

Gavitt A. Woodard

AIM-HIGH Trial Study Design

45 international centers, randomized control trial

Do molecular high-risk patients benefit from adjuvant chemotherapy?

Patients with completely resected IA, IB, IIA* non-squamous non-small cell lung cancer

Key inclusion criteria:
- ≥ 18 years old
- Confirmed primary non-squamous NSCLC
- ECOG performance status 0 / 1
- Anatomical lung resection (segmentectomy, lobectomy or bilobectomy) with negative margins

→ Risk stratification by 14-gene expression profile
- Molecular low-risk
- Molecular high-risk (int- or high-risk) → Randomization (N=200)§
  - Observation
  - 4 cycles platinum-based doublet +/- immunotherapy, TKI if EGFR+

→ Follow up: Routine CT surveillance until 5 years or event (recurrence or death)

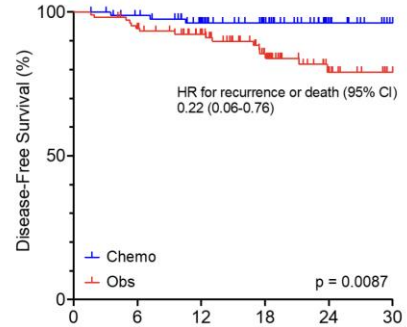
Primary outcome DFS

ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer
*American Joint Committee on Cancer 8th edition. §Randomization stratified according to age, sex and tumor size ≥4 cm.

AIM-HIGH Results

24-month disease-free survival

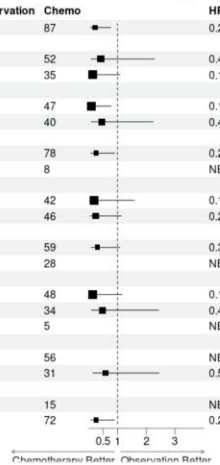
- 24-month DFS
  - **Chemo 96%** (95% CI 0.92-1.00) **vs.**
  - **Obs 79%** (95% CI 0.70-0.90)
- 3 events vs. 16 events
- 78% reduction in recurrence or death



Number at Risk						
Chemotherapy	107	99	81	54	28	14
Observation	87	81	65	48	26	15

AIM-HIGH DFS by subgroup

Subgroup	Observation	Chemo	HR (95% CI)
All Patients	107	87	0.22 (0.06 to 0.76)
Age			
< 65 yr	48	52	0.42 (0.08 to 2.28)
≥ 65 yr	59	35	0.14 (0.02 to 1.09)
Sex			
Male	58	47	0.10 (0.01 to 0.78)
Female	49	40	0.45 (0.09 to 2.24)
Smoking history			
Yes	92	78	0.26 (0.07 to 0.90)
No	15	8	NE
Pack-years			
< 35	50	42	0.19 (0.02 to 1.58)
≥ 35	59	46	0.25 (0.05 to 1.13)
ECOG status			
ECOG 0	71	59	0.30 (0.09 to 1.07)
ECOG 1	36	28	NE
Stage			
IA	58	48	0.15 (0.02 to 1.16)
IB	44	34	0.47 (0.09 to 2.43)
IIA	5	5	NE
Minimally invasive surgery			
Yes	74	56	NE
No	33	31	0.58 (0.14 to 2.44)
Type of resection			
Sublobar	19	15	NE
Lobar	88	72	0.26 (0.07 to 0.89)



Benefit likely ***independent*** of smoking history, ECOG status, stage, type of surgery

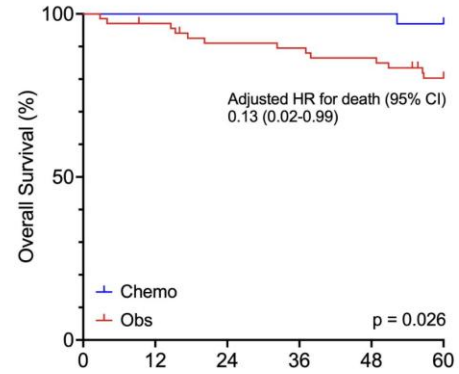
	Univariate Analysis		Multivariate Analysis	
	HR	P value	HR	P value
Chemotherapy*	0.22 (0.06-0.76)	0.009	0.22 (0.06-0.77)	0.018
Age ≥ 65	2.27 (0.86-5.98)	0.088	1.85 (0.69-4.96)	0.219
Male Sex	1.15 (0.46-2.87)	0.765	1.25 (0.49-3.19)	0.635
Tumor Size > 4 cm	2.10 (0.49-9.12)	0.309	3.36 (0.74-15.26)	0.117

*Compared to Observation

Molecular High-Risk Population (n=101)

5-Year Overall Survival

- Median follow-up: 90.8 months (IQR 84.9-100 months)
- 60-month Overall Survival
  - **Chemo 97%** (95% CI 0.91-1.00) **vs.**
  - **Obs 80%** (95% CI 0.71-0.91)
- 87% reduction in death



Number at Risk						
Chemotherapy	33	33	33	33	33	32
Observation	68	65	60	59	57	51


Gracias