Iniciativa científica de:

GECP lung cancer research

# Lung Cancer UPDATES

## ASCO HIGHLIGHTS

29 MAYO - 02 JUNIO 2026

Chicago, USA

#ASCOUPDATES

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Lung Cancer UPDATES

ASCO HIGHLIGHTS

29 MAYO - 02 JUNIO 2026

Chicago, USA

# Cáncer de pulmón no microcítico. Estadios iniciales y localmente avanzados

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The science and practice of translation: Improving cancer outcomes worlwide

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# Mensajes resumen

**La quimio-inmunoterapia preoperatoria (+/- postoperatoria) se consolida como la estrategia de mayor eficacia en estadios iniciales**

**En la fusion de RET el tto adyuvante con Selpercatinib deberá integrarse en la práctica clínica. En la fusion ALK el tto neoadyuvante con Lorlatinib obtiene una tasa significative de pCR**

**La detección de la MRD mediante ctDNA es el área de investigación preferente para permitir individualizar el tratamiento**

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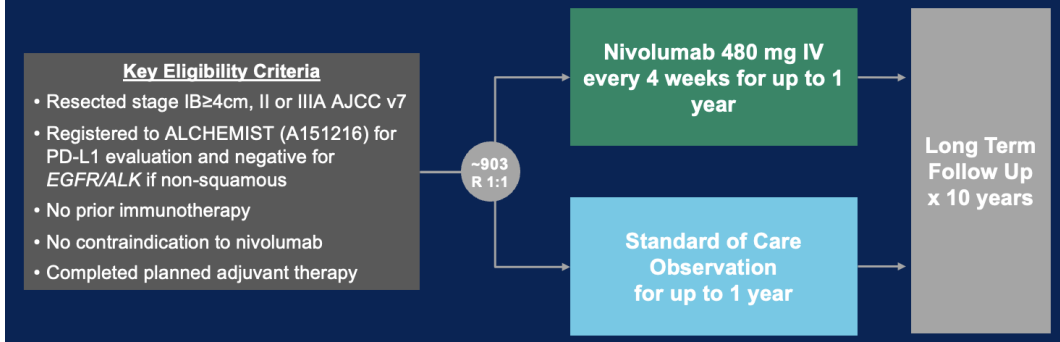
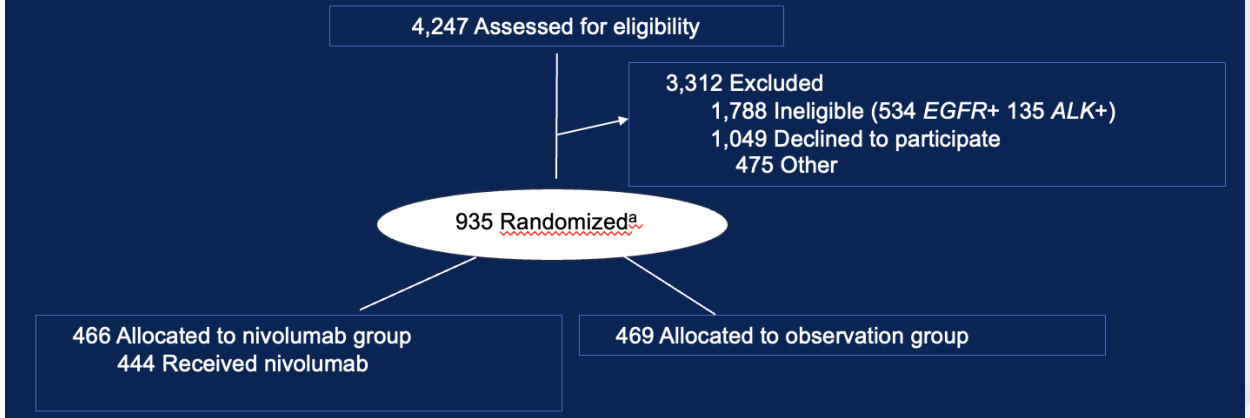
# EA5142 Schema




**Stratification Factors**
- Disease stage (IB/IIA vs IIB/III)
- PD-L1 expression by Dako 28-8 (<1% vs ≥1%)
- Histology (squamous vs non-squamous)
- Prior adjuvant treatment (none vs chemo vs chemo & radiation

**Dual primary end points:** DFS (in ITT and in PD-L1 ≥50%. OS tested hierarchically if DFS significant.

**Key secondary end points:** safety, DFS in prespecified subsets




| Characteristic | Nivolumab (n = 466) | Observation (n = 469) |
|---|---|---|
| Median age, years (range) | 66 (33-85) | 67 (39-92) |
| Sex, no. (%) | | |
| Male | 241 (52) | 245 (52) |
| Female | 225 (48) | 224 (48) |
| Smoking History, no. (%) | | |
| Current (quit < 1 year ago) | 143 (31) | 154 (33) |
| Former (quit ≥ 1 year ago) | 274 (59) | 271 (58) |
| Never (< 100 lifetime cigarettes) | 49 (11) | 44 (9) |
| Histology, no. (%) | | |
| Adenocarcinoma | 301 (65) | 293 (63) |
| Squamous cell carcinoma | 136 (29) | 134 (28) |
| Combined, large cell, not otherwise specified | 29 (6) | 42 (9) |
| AJCC 7th edition stage[b], no. (%) | | |
| IB (T ≥4 - 5 cm + no LN) | 47 (10) | 58 (12) |
| IIA (T ≤5 cm + hilar LN or 5-7cm + no LN) | 182 (39) | 174 (37) |
| IIB (T 5-7 cm + hilar LN or >7 cm + no LN | 82 (18) | 90 (19) |
| IIIA (T >7 cm + hilar LN or any T + mediastinal LN) | 155 (33) | 147 (31) |
| Prior Adjuvant Treatment, no. (%) | | |
| Chemotherapy | 405 (88) | 408 (87) |
| Radiotherapy | 74 (16) | 73 (16) |
| PD-L1 Tumor Proportion Score, no. (%) | | |
| <1% (negative) | 140 (30) | 137 (29) |
| 1 - <50% (positive) | 190 (40) | 195 (42) |
| ≥50% (high) | 136 (29) | 137 (29) |

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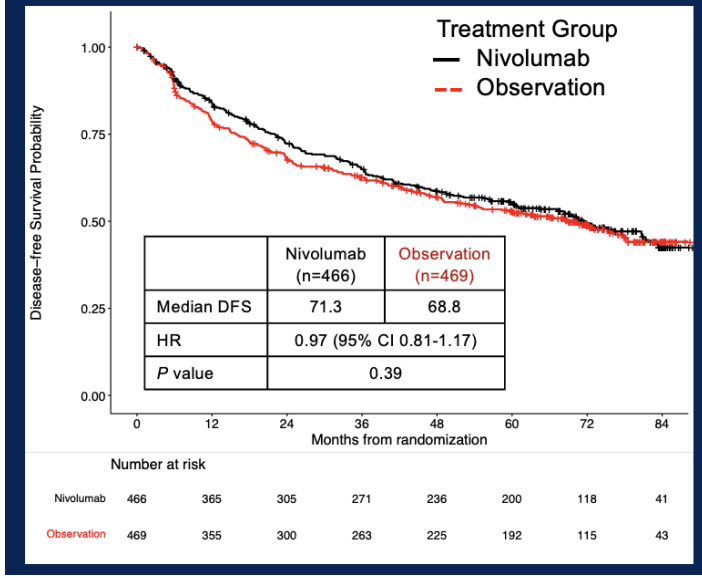
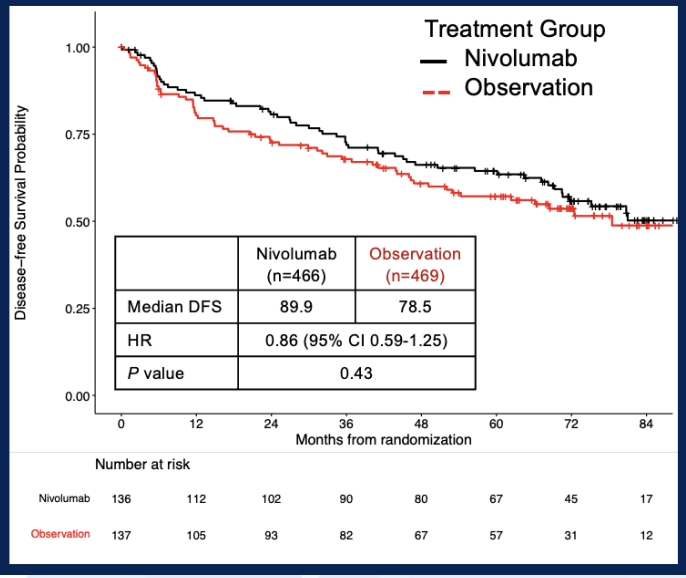
## Intention to Treat Population



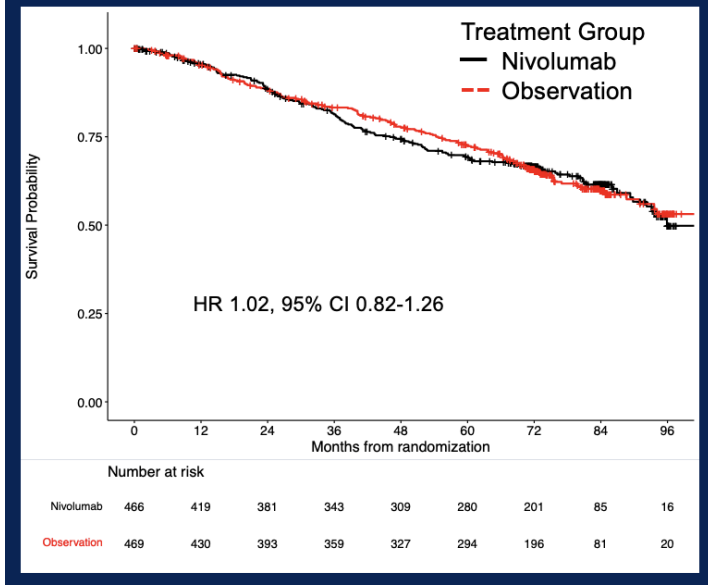

| | Nivolumab (n=466) | Observation (n=469) |
|---|---|---|
| Median DFS | 71.3 | 68.8 |
| HR | 0.97 (95% CI 0.81-1.17) | |
| *P* value | 0.39 | |

## Population with tumor PD-L1 ≥ 50%

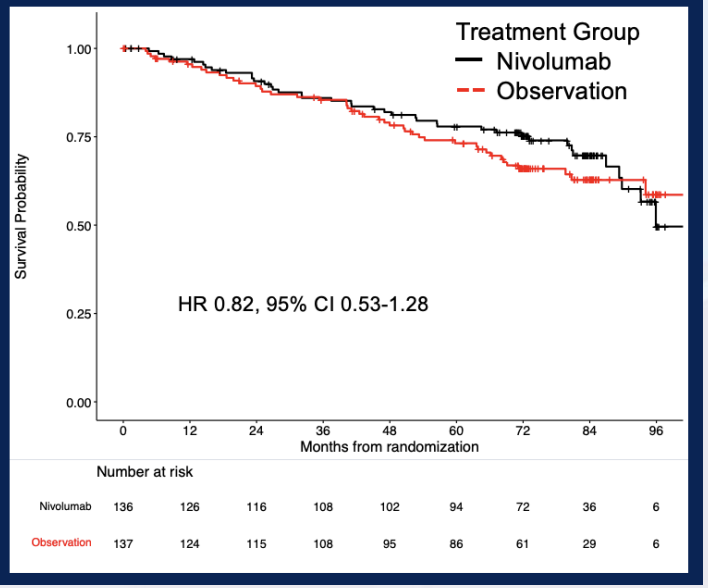



| | Nivolumab (n=466) | Observation (n=469) |
|---|---|---|
| Median DFS | 89.9 | 78.5 |
| HR | 0.86 (95% CI 0.59-1.25) | |
| *P* value | 0.43 | |

## Intention to Treat Population

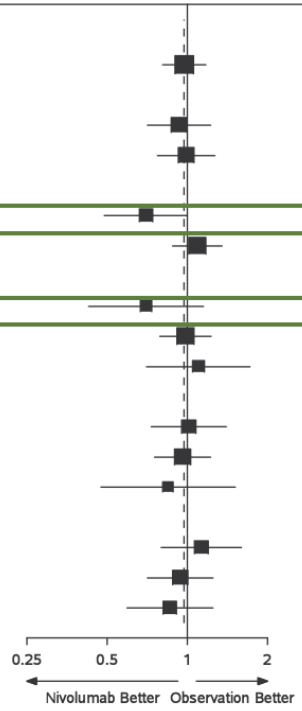


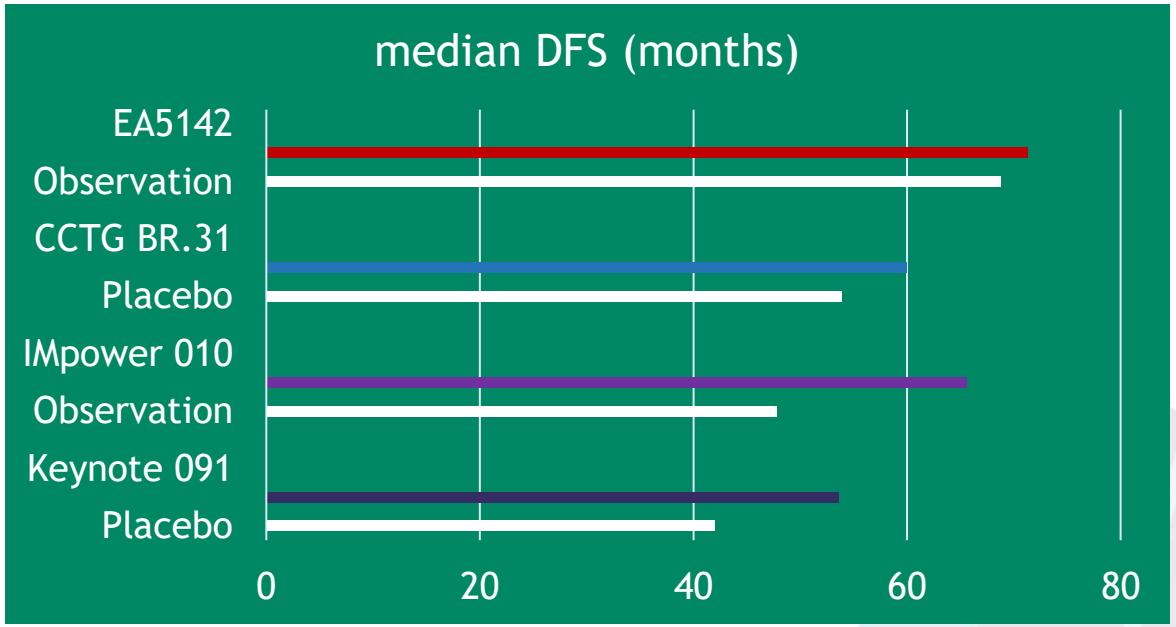

## Population with tumor PD-L1 ≥ 50%




DFS Hazard Ratio (Nivolumab/Observation) Subgroup Analysis

| Variable | Nivolumab Events | Nivolumab Total | Observation Events | Observation Total | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|---|---|
| Disease-free Survival | | | | | | |
| All patients | 225 | 466 | 230 | 469 | 0.97 (0.81±1.17) | 0.78 |
| Stage (AJCC 7th edition) | | | | | | |
| IB/IIA | 100 | 229 | 107 | 232 | 0.93 (0.71±1.22) | 0.61 |
| IIB/IIIA | 125 | 237 | 123 | 237 | 0.99 (0.77±1.27) | 0.94 |
| Histology | | | | | | |
| Squamous | 53 | 136 | 68 | 133 | 0.70 (0.49±1.00) | 0.051 |
| Non-squamous | 172 | 330 | 162 | 336 | 1.09 (0.88±1.35) | 0.43 |
| Prior adjuvant treatment | | | | | | |
| None | 29 | 61 | 34 | 60 | 0.70 (0.43±1.15) | 0.16 |
| Chemotherapy | 155 | 331 | 160 | 336 | 0.99 (0.79±1.23) | 0.90 |
| Chemotherapy + radiation | 41 | 74 | 36 | 72 | 1.10 (0.70±1.72) | 0.68 |
| Smoking Status | | | | | | |
| Current(quit<1 year ago) | 72 | 143 | 76 | 154 | 1.01 (0.73±1.40) | 0.94 |
| Former(quit>=1 year ago) | 129 | 274 | 132 | 271 | 0.96 (0.75±1.22) | 0.74 |
| Never(<100 lifetime cigarettes) | 24 | 49 | 22 | 44 | 0.85 (0.47±1.51) | 0.57 |
| PD-L1 status | | | | | | |
| Negative/non-evaluable | 71 | 140 | 65 | 137 | 1.13 (0.80±1.60) | 0.49 |
| 1-49% | 96 | 190 | 105 | 195 | 0.94 (0.71±1.25) | 0.67 |
| >=50% | 58 | 136 | 60 | 137 | 0.86 (0.59±1.25) | 0.43 |






### IMpower 010

- All patients received cisplatin/platinum-based chemotherapy.
- Enriched population by design: Stage II-IIIA, PD-L1+; strongest signal in high PD-L1 tumors.
- Biologically coherent benefit (higher PD-L1 = higher benefit)

**Interpretation**: This supports the use of atezolizumab in a selected niche, rather than as a universal approach.

### KEYNOTE 091

- Positive in the overall population, but without a clearly defined driving subgroup.
- More heterogeneous population; prior chemotherapy not mandatory for all patients.
- No clear signal in PD-L1 ≥ 50%

**Interpretation**: Signal appears more dependent on study design than on a clearly defined sensitive population.

### BR.31 & ANVIL

- **BR.31:** Durvalumab does not confirm a universal adjuvant monotherapy benefit.
- **ANVIL:** Sequential nivolumab as monotherapy after all therapy does not improve DFS.

  Negative in ITT and PD-L1 ≥ 50%; no rescue subgroup emerges.

**Interpretation**: Challenges the idea of a homogeneous class effect and routine "end-of-pathway" monotherapy.

Greater enrichment by risk, PD-L1, and chemotherapy integration → **Gradient of biological plausibility** → Lower biological coherence of isolated adjuvant-IO benefit

### My hypothesis: Timing + enrichment explain the divergence

**IMpower 010**: Enriched and integrated. → **KEYNOTE 091**: Positive but biologically less coherent. → **ANVIL**: late and less integrated.

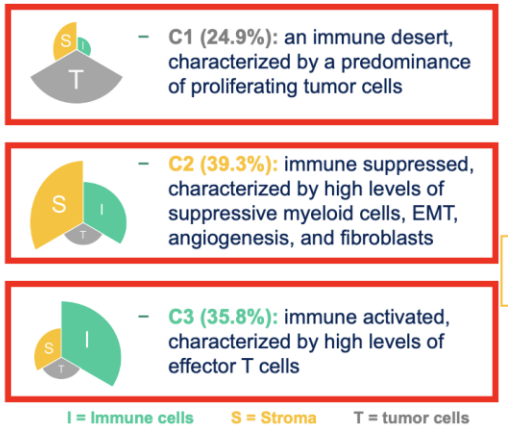
### Clinical read

IMpower 010 and KEYNOTE 091 open the door, BR.31 and ANVIL define the limits.

| | Population | Adjuvant IO start / duration with time from surgery |
|---|---|---|
| NADIM Adjuvant | R0 IB (≥4 cm)-IIIA | Sx → ChT+IO → IO 6 mo; ~4–8 wk after surgery |
| BR.31 | EGFR/ALK–; PD-L1 TC ≥25% (primary population) | Sx → ChT → IO 12 mo; ~4–7 mo after surgery |
| ANVIL / ALCHEMIST | IB ≥4 cm–IIIA, EGFR/ALK WT; post-adjuvant therapy | Sx → ChT/RT → IO 12 mo; ~4–7 mo after surgery |
| IMpower 010 | II–IIIA, PD-L1 TC ≥1% (primary population) | Sx → ChT → IO 12 mo; ~4–7 mo after surgery |
| KEYNOTE 091 | IB ≥4 cm–IIIA, ITT | Sx → ChT → IO 12 mo; ~4–8 mo after surgery |

# TME Phenotypic Clusters at Baseline

- At baseline, 3 distinct phenotypic clusters (C) based on TME features were identified* (% of patients across both arms):




- **C1 (24.9%):** an immune desert, characterized by a predominance of proliferating tumor cells

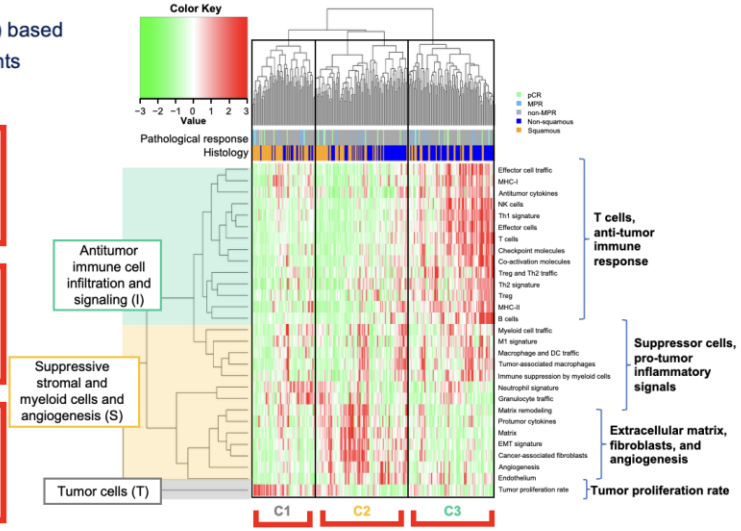



- **C2 (39.3%):** immune suppressed, characterized by high levels of suppressive myeloid cells, EMT, angiogenesis, and fibroblasts




- **C3 (35.8%):** immune activated, characterized by high levels of effector T cells

I = Immune cells  S = Stroma  T = tumor cells




*Samples were clustered based on expression signatures reported in Bagaev A, et al. Cancer Cell 2021;39:845–65.

| Characteristic, % | | C1: immune desert (n=64) | C2: immune suppressed (n=101) | C3: immune activated (n=92) |
|---|---|---|---|---|
| **Histology** | Squamous | 70.3 | 47.5 | 29.3 |
| | Non-squamous | 29.7 | 52.5 | 70.7 |
| **Smoking status** | Current | 34.4 | 25.7 | 25.0 |
| | Former | 57.8 | 57.4 | 63.0 |
| | Never | 7.8 | 16.8 | 12.0 |
| **Disease stage (AJCC 8th ed.)** | II | 20.3 | 38.6 | 20.7 |
| | III | 79.7 | 61.4 | 79.3 |
| **TNM stage, regional lymph nodes** | N0 | 26.6 | 47.5 | 21.7 |
| | N1 | 12.5 | 15.8 | 8.7 |
| | N2 | 60.9 | 36.6 | 69.6 |
| **PD-L1 expression** | TC <1% | 28.1 | 42.6 | 25.0 |
| | TC 1–49% | 39.1 | 34.7 | 32.6 |
| | TC ≥50% | 32.8 | 22.8 | 42.4 |

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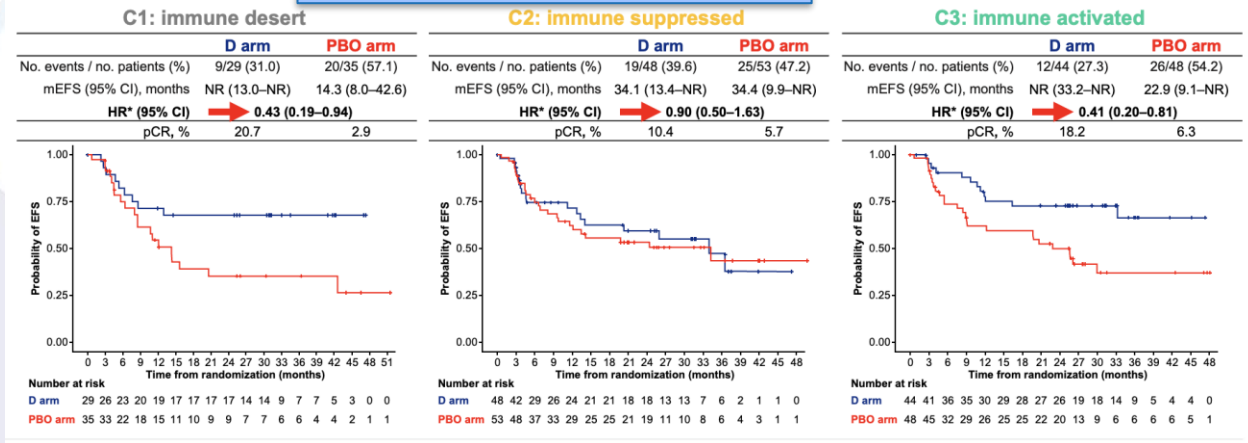
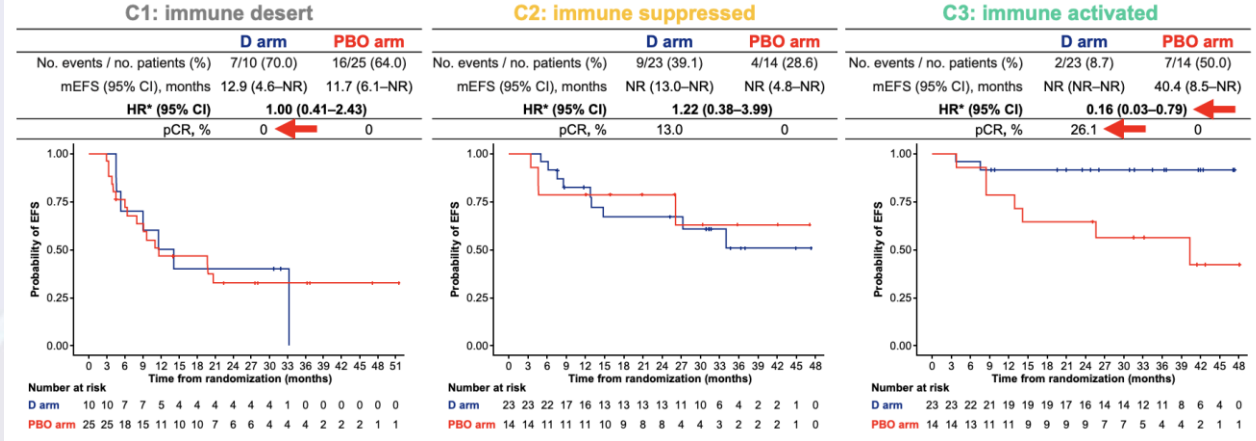
## Cluster al diagnóstico



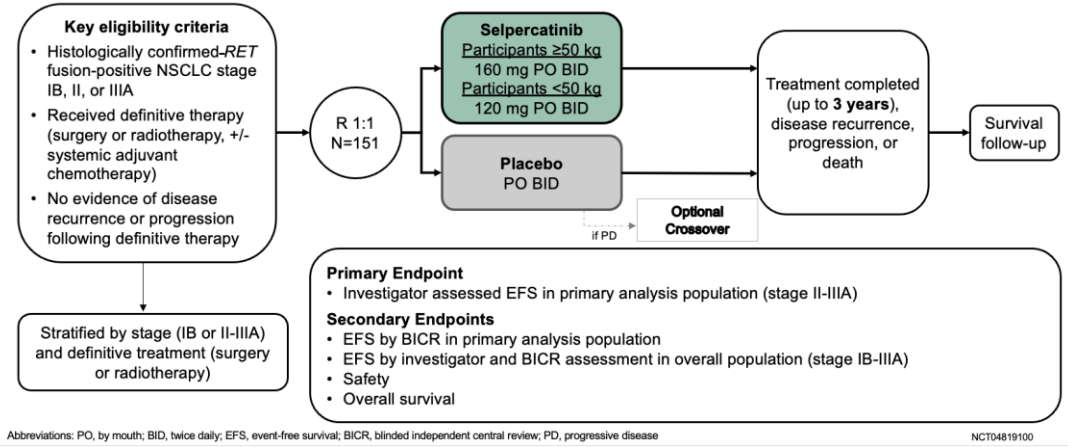

## Cluster a la cirugía

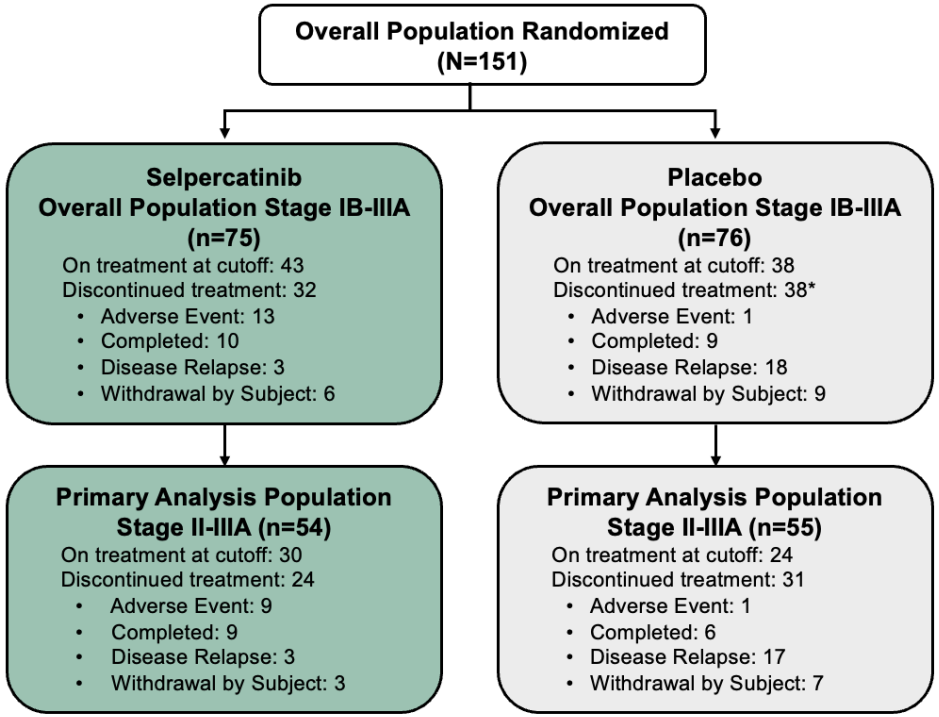


Nueva diapositiva con Copilot

# LIBRETTO-432 Study Design

## A global, multicenter, phase 3, double-blind, randomized, placebo-controlled study

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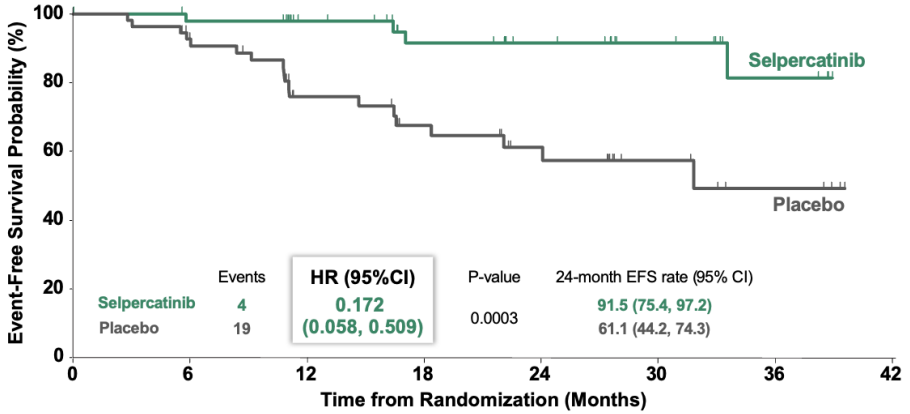
| | | Selpercatinib N=54 | Placebo N=55 |
|---|---|---|---|
| **Age, years** | Median (range) | 59.5 (41.0-84.0) | 61.0 (26.0-78.0) |
| **Sex, n (%)** | Female | 34 (63.0) | 30 (54.5) |
| | Male | 20 (37.0) | 25 (45.5) |
| **Race, n (%)[a]** | Asian | 33 (61.1) | 32 (58.2) |
| | White | 21 (38.9) | 21 (38.2) |
| **Geographic Region, n (%)** | East Asia | 31 (57.4) | 31 (56.4) |
| | Europe/North America | 18 (33.3) | 21 (38.2) |
| | Other | 5 (9.3) | 3 (5.5) |
| **Smoking Status, n (%)** | Never | 37 (68.5) | 38 (69.1) |
| | Former / Current | 17 (31.5) | 17 (30.9) |
| **ECOG PS, n (%)[b]** | 0 | 30 (55.6) | 36 (65.5) |
| | 1 | 24 (44.4) | 18 (32.7) |
| **RET fusion, n (%)** | KIF5B:: RET | 33 (61.1) | 34 (61.8) |
| | CCDC6:: RET | 14 (25.9) | 11 (20.0) |
| | Other | 7 (13.0) | 10 (18.2) |
| **PD-L1, n (%)[c]** | Negative | 11 (20.4) | 16 (29.1) |
| | Positive | 25 (46.3) | 28 (50.9) |
| | Unknown | 17 (31.5) | 11 (20.0) |
| **Prior anti-cancer therapy, n (%)** | Surgery | 54 (100.0) | 54 (98.2) |
| | Radiotherapy | 2 (3.7) | 6 (10.9) |
| | Systemic therapy | 50 (92.6) | 50 (90.9) |

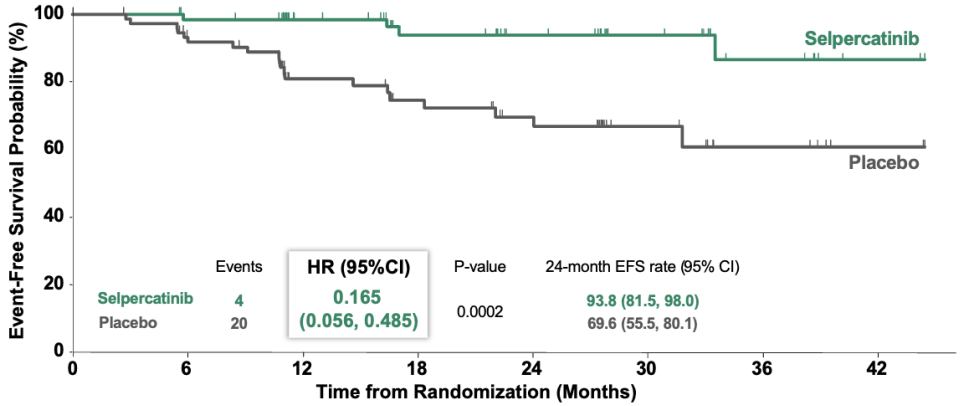
| **Events, n (%)** | Selpercatinib N=75 | Placebo N=76 |
|---|---|---|
| Any TEAE | 75 (100) | 74 (97.4) |
| Grade ≥3 TEAEs | 50 (66.7) | 18 (23.7) |
| Serious TEAEs ≥1 | 17 (22.7) | 10 (13.2) |
| Discontinued study treatment due to TEAEs* | 13 (17.3) | 1 (1.3) |
| Discontinued due to SAE | 2 (2.7) | 1 (1.3) |
| Dose modifications | 66 (88.0) | 35 (46.1) |
| Dose interruptions due to TEAEs | 58 (77.3) | 20 (26.3) |
| Dose reductions due to TEAEs | 41 (54.7) | 6 (7.9) |
| TEAEs leading to death, on study treatment | 0 | 0 |

# Primary Analysis Population, Stage II-IIIA *RET* fusion-positive NSCLC

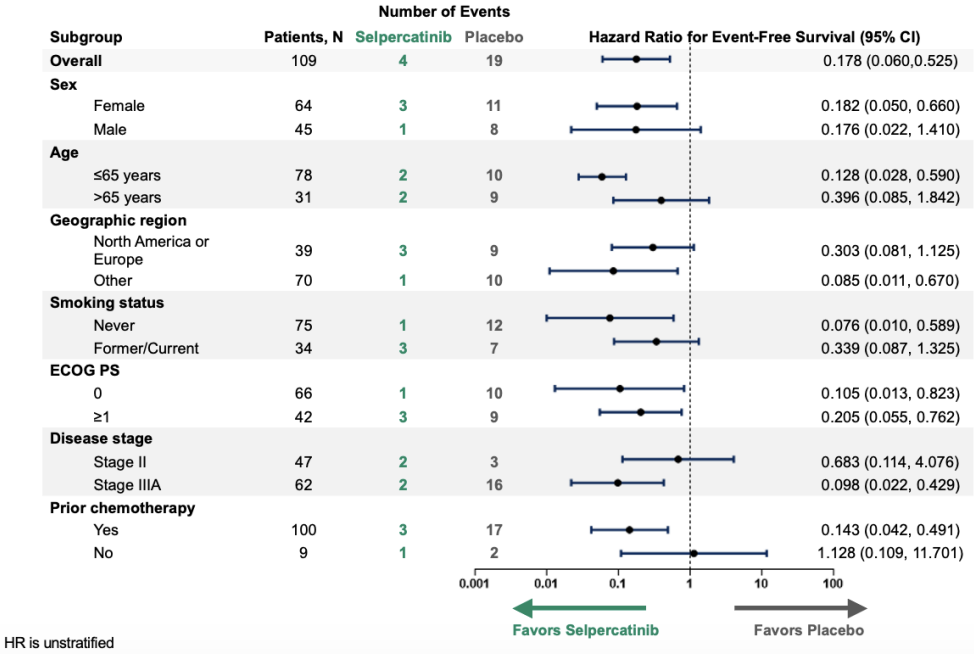



| Number at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Selpercatinib | 54 | 45 | 37 | 27 | 22 | 15 | 7 | 0 |
| Placebo | 55 | 47 | 28 | 22 | 16 | 8 | 4 | 0 |

# Overall Population, Stage IB-IIIA *RET* fusion-positive NSCLC




| Number at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Selpercatinib | 75 | 63 | 51 | 37 | 30 | 20 | 10 | 2 |
| Placebo | 76 | 64 | 40 | 31 | 25 | 12 | 6 | 2 |




HR is unstratified

| | Selpercatinib N=54 | Placebo N=55 |
|---|---|---|
| Number of EFS events, n | 4 | 19 |
| Locoregional | 1 | 10 |
| Local | 1 | 3 |
| Regional | 0 | 7 |
| Distant | 5 | 18 |
| Brain | 1 | 3 |

| | Selpercatinib N=54 | Placebo N=55 |
|---|---|---|
| Median follow-up, months (IQR) | 25 (13.9, 33.2) | 27 (15.8, 34.1) |
| On treatment, n (%) | 30 (55.6) | 24 (43.6) |
| Off treatment, n (%) | 24 (44.4) | 31 (56.4) |
| Death, n | 0 | 3 |

16 stage II-IIIA patients crossed over to selpercatinib following disease recurrence

- 12 of these patients remain on selpercatinib at data cutoff
- 3 deaths occurred in patients who crossed over*

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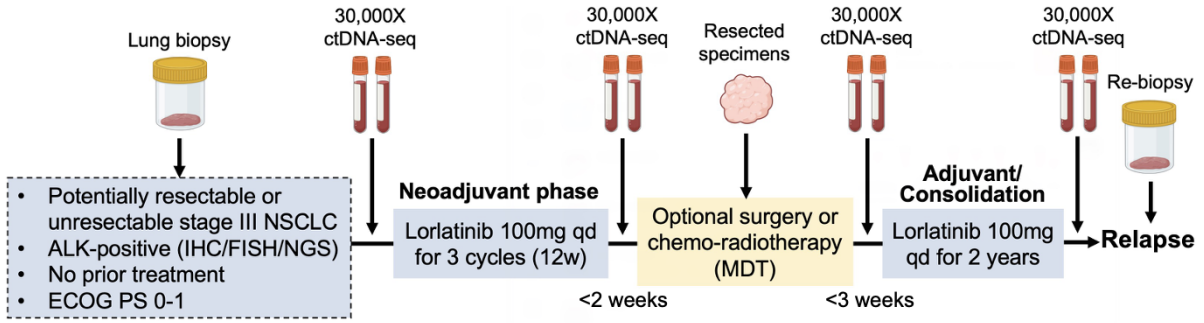
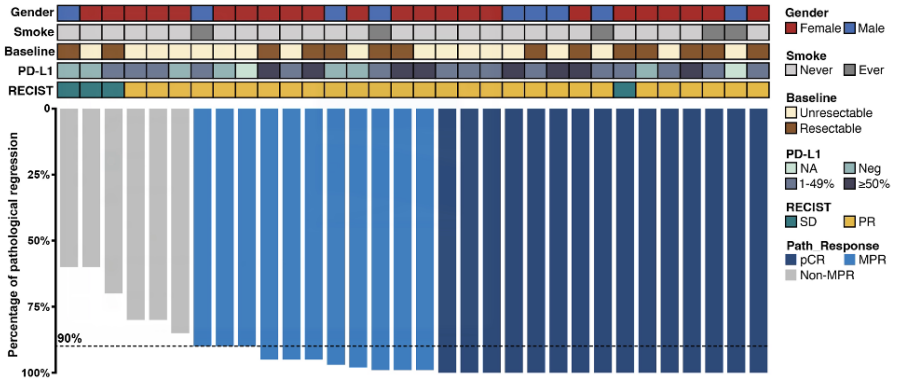



**Primary endpoint**: pCR (IASLC criteria)
**Secondary endpoints**: MPR (IASLC criteria), ORR, EFS, OS, AEs

**Exploratory analysis**: (Spatial transcriptomics & proteomics) Characterization of DTPCs after lorlatinib and the correlation between dynamic changes in the tissue immune microenvironment and pathological response

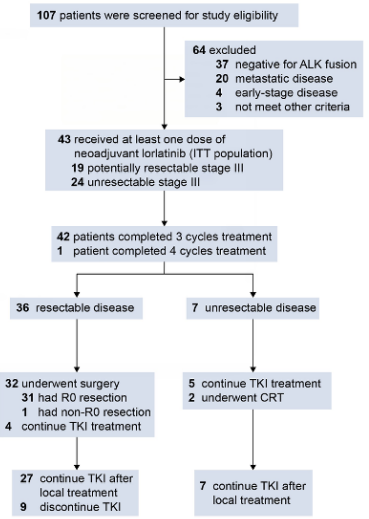



Among patients who underwent surgery, the pCR and MPR rates were **46.9% (15/32) (95%CI, 29.1%-65.2%) [34.9% for ITT]** and **81.3% (26/32) [60.5% for ITT]**, respectively, reaching the primary endpoint.

| Overall | N=32 (n, %) |
|---|---|
| pCR | 15 (47) |
| MPR | 26 (81) |
| Median/Mean RVT | 1%/7% |

| Resectability | pCR/MPR |
|---|---|
| Resectable | 50%/86% |
| Unresectable | 44%/78% |

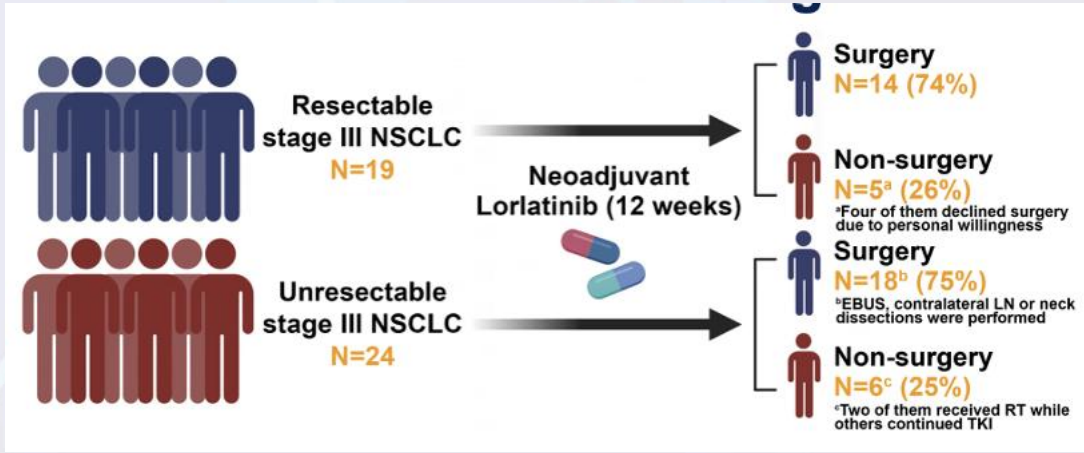
| | Median PD-L1 exp. |
|---|---|
| MPR/pCR | 25% |
| Non-MPR | 1% |
| *p* value <0.01 | |

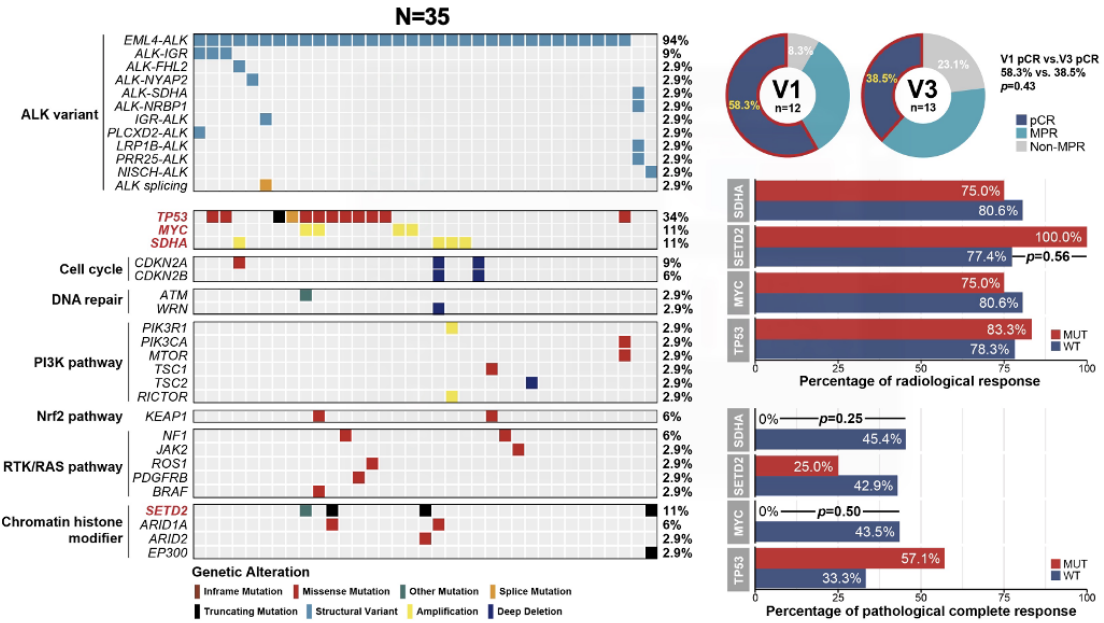



| Characteristic | N=43 |
|---|---|
| Age, median (IQR) | 52 (41.5, 62) |
| Gender, n (%) | |
| Male | 12 (27.9%) |
| Female | 31 (72.1%) |
| Smoking status, n (%) | |
| Ever-smoker | 7 (16.3%) |
| Non-smoker | 36 (83.7%) |
| cN status, n (%) | |
| N0 | 1 (2.3%) |
| N1 | 2 (4.7%) |
| N2 | 16 (37.2%) |
| N3 | 24 (55.8%) |
| cTNM, n (%)[a] | |
| IIIA | 16 (37.2%) |
| IIIB | 22 (51.2%) |
| IIIC | 5 (11.6%) |

| Characteristic | N=43 |
|---|---|
| Resectability, n (%) | |
| Unresectable | 24 (55.8%) |
| Resectable | 19 (44.2%) |
| Histology, n (%) | |
| Adeno | 42 (97.7%) |
| Squamous | 1 (2.3%) |
| ALK status, n (%) | |
| NGS | 40 (93%) |
| IHC/FISH only | 3 (7%) |
| PD-L1, n (%) (n=39) | |
| Negative | 9 (23.1%) |
| Low exp. | 17 (43.6%) |
| High exp. | 13 (33.3%) |

[a]All patients underwent PET/enhanced CT plus brain MRI for staging except for one patient only underwent PET/CT

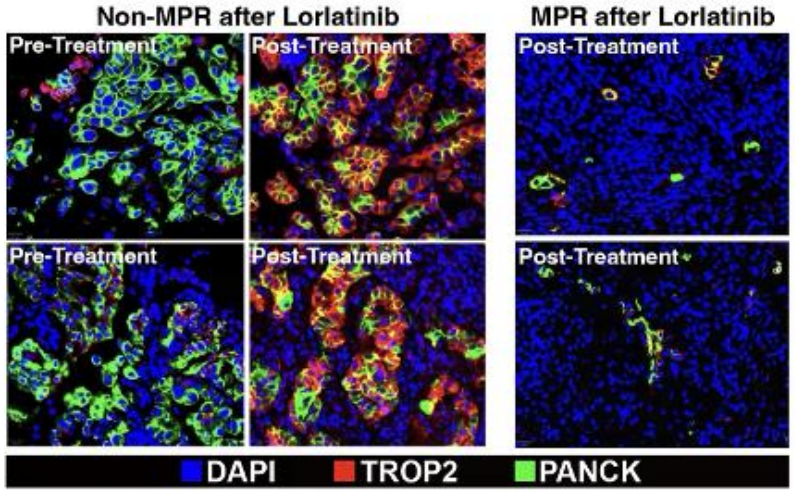


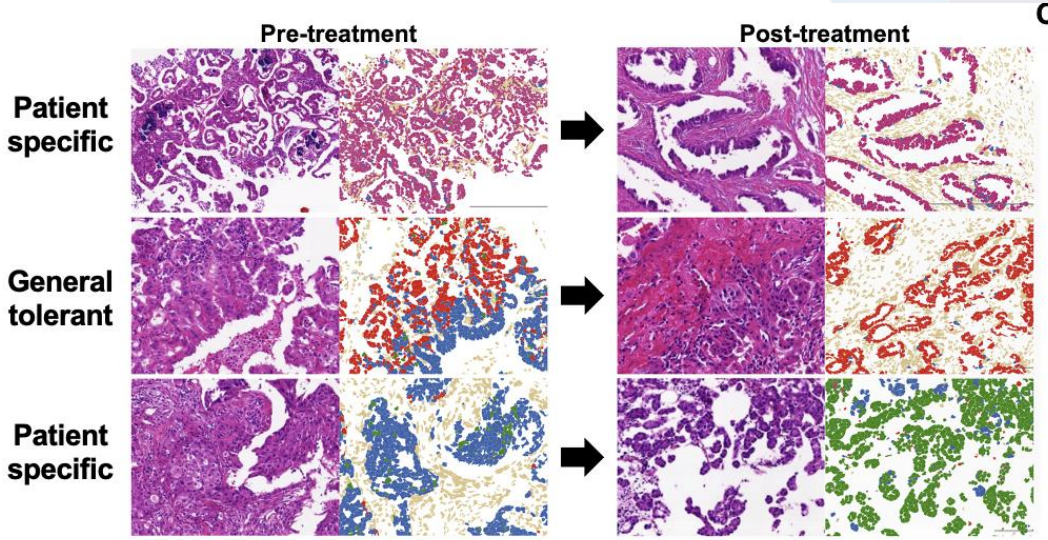






- Co-mutations: TP53 (34%), MYC (11%), SETD2 (11%), SDHA (11%), CDKN2A (9%)
- No significant impact of co-mutations on clinical outcomes
- Numerically improved pathological response in V1 compared to V3 subtype




**Changes of insensitive/resistant tumor clones for Non-MPR**

LAPTM4B-DTPCs (MDM2$^{hi}$) (44.2% vs. 88.2%, $p$<0.001)
**Chemoresistance need novel regimens**

FOLR1-DTPCs (FRα) (60.9% vs. 84.3%, $p$<0.001)
**PC regimen combination**

MET-DTPCs (8.0% vs. 88.4%, $p$<0.001)
**MET-TKI combination**

For **MPR** patients, **FOLR1-DTPCs** and **MMP14-DTPCs** are the dominant residual tumor subtypes with median proportions of **40% (range, 14-88%)** and **23% (range, 3-63%)**, respectively

| Neoadjuvant phase | N=43 |
|---|---|
| Any TRAEs, n (%) | 43 (100) |
| Grade 3-4, n (%) | 10 (23) |
| TRAE lead to dose reduction, n (%) | 7 (16) |
| TRAE lead to discontinuation, n (%) | 1 (2)[a] |

| Adjuvant/consolidation phase | N=34 |
|---|---|
| Any TRAEs, n (%) | 32 (94) |
| Grade 3-4, n (%) | 7 (21) |
| TRAE lead to dose reduction[b], n (%) | 8 (24) |
| TRAE lead to treatment switch[c], n (%) | 4 (12) |

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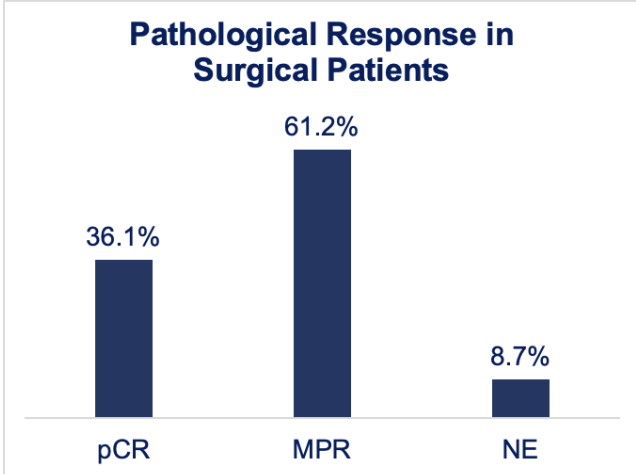
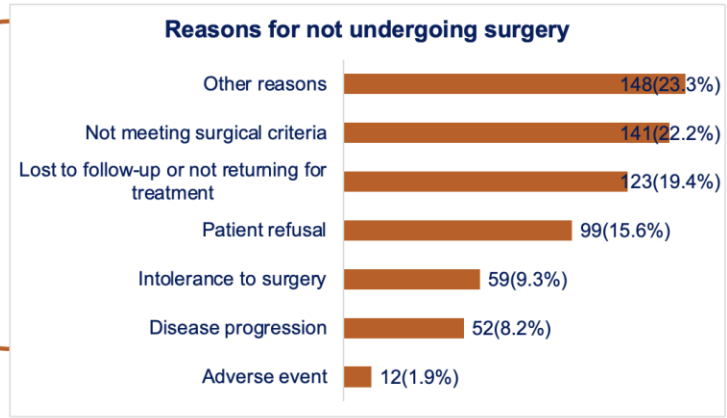
| Baseline Characteristics | | N | Proportion (%) |
|---|---|---|---|
| Gender | Male | 1430 | 82.8 |
| Age | ≥65 years | 888 | 51.4 |
| ECOG PS | 0 | 746 | 43.2 |
| | 1 | 940 | 54.4 |
| | 2 | 41 | 2.4 |
| Histology | Non-squamous | 316 | 18.3 |
| | Squamous | 1233 | 71.4 |
| | NSCLC-others* | 178 | 10.3 |
| Stage # | IIA | 29 | 1.7 |
| | IIB | 179 | 10.4 |
| | IIIA | 912 | 52.8 |
| | IIIB | 570 | 33.0 |
| | IIIC | 37 | 2.1 |
| N stage | N0 | 236 | 13.7 |
| | N1 | 337 | 19.5 |
| | N2 | 831 | 48.1 |
| | N3 | 79 | 4.6 |
| | Missing | 244 | 14.1 |

| | | N | Proportion (%) |
|---|---|---|---|
| Patient underwent surgery | | 551 | 100 |
| Neoadjuvant treatment | Completed ≤2 cycles | 215 | 39 |
| | Completed 3 cycles | 250 | 45.4 |
| | Completed ≥4 cycles | 86 | 15.6 |

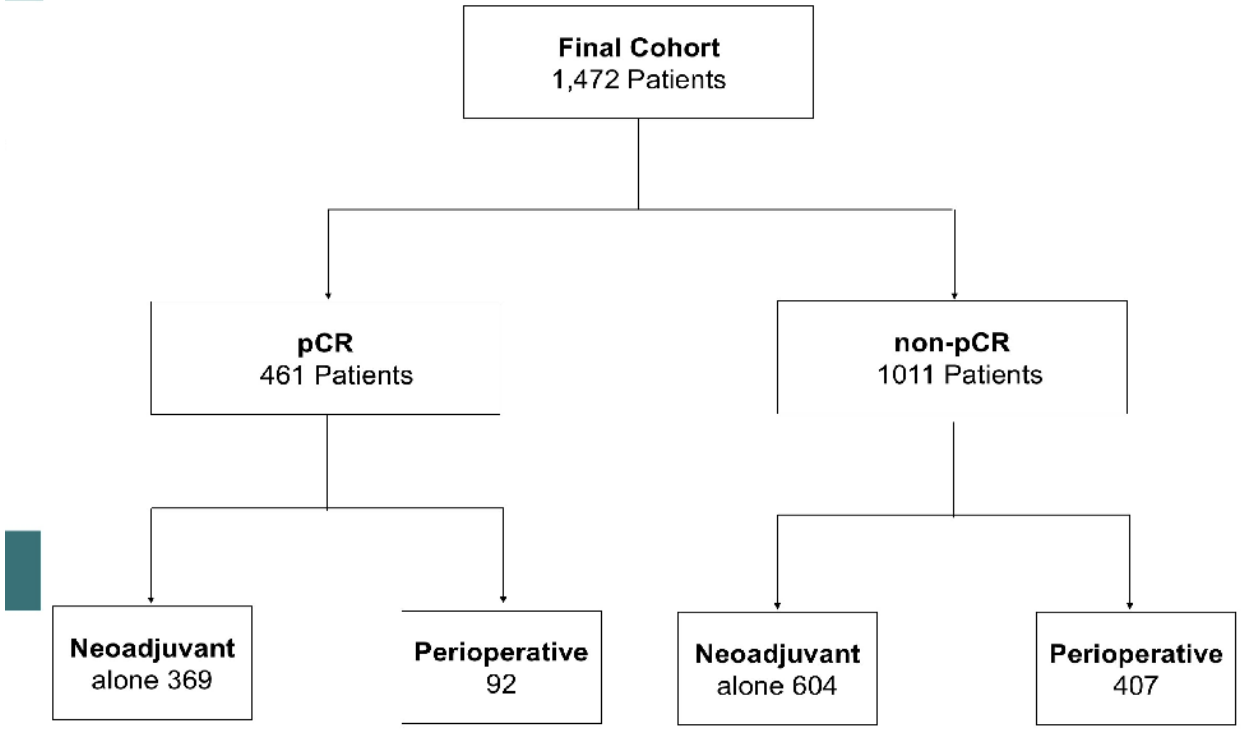



| Surgical Completion Status | N | Proportion (%) |
|---|---|---|
| Non-surgical patients | 634 | 53.5 |
| Surgical patients | 551 | 46.5 |
| Total | 1185 | 100.0 |




| | | N | Proportion (%) |
|---|---|---|---|
| Patient underwent surgery | | 551 | 100 |
| Adjuvant treatment | Received treatment | 278 | 50.5 |
| | Ongoing treatment | 239 | 43.4 |
| | Discontinued treatment | 38 | 6.9 |
| | Completed 14 cycles | 1 | 0.2 |

Figure 1 : Study Cohort Selection and Stratification by Pathologic Response

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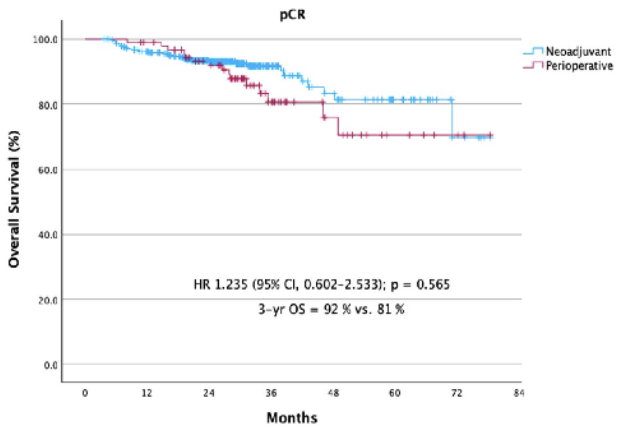


Figure 2A : Overall Survival in Patients Achieving pCR: Neoadjuvant vs Perioperative Therapy

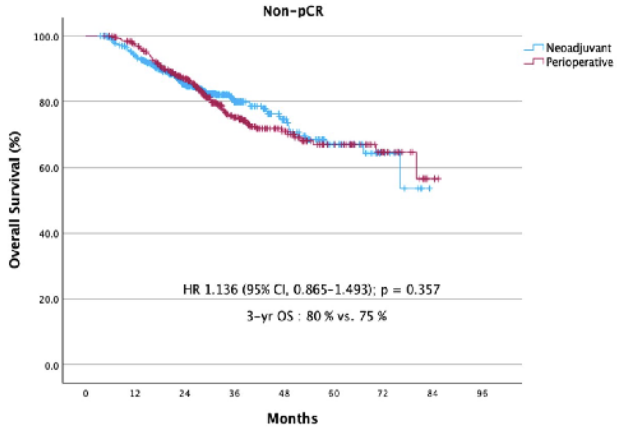


Figure 2B : Overall Survival in Patients not Achieving pCR: Neoadjuvant vs Perioperative Therapy

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Completely resected stage IB (≥4 cm), II or IIIA non-squamous NSCLC with negative margins standard post-operative therapy (if applicable)

- **Previously registered to A151216 screening trial**
- **EGFR exon 19 deletion or L858R mutation (local/central)**
- Age ≥18 years
- ECOG Performance Status 0-1
- No prior cancers per Protocol Section 3.2
- Non-pregnant and non-lactating
- No history of cornea abnormalities

**RANDOMIZE** 1:1

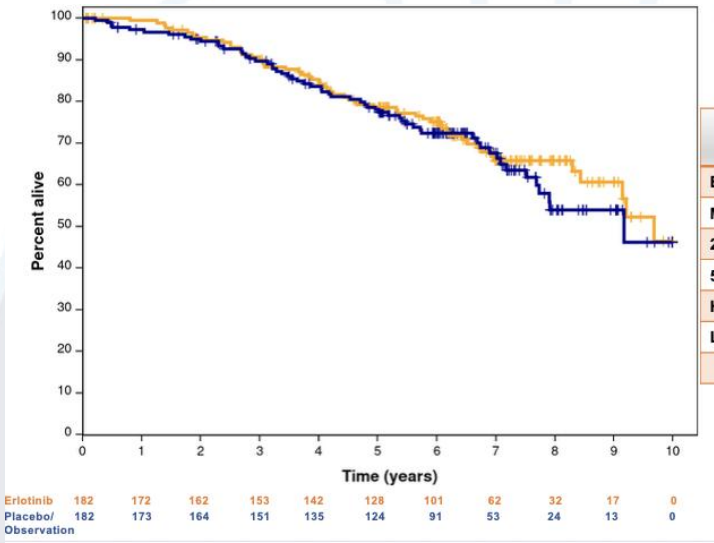
- Erlotinib* 150 mg once daily up to 2 years
- Placebo† / Observation*

† 150 mg once daily up to 2 years
***Before 6/15/2017: Blinded erlotinib vs placebo; After: Open Label erlotinib vs observation**

**Stratification Factors**
- stage (IB≥4 cm, II vs. IIIA),
- prior chemotherapy (yes vs. no),
- exon 19 deletion (yes vs. no) and
- ECOG performance status (PS) (0 vs. 1)

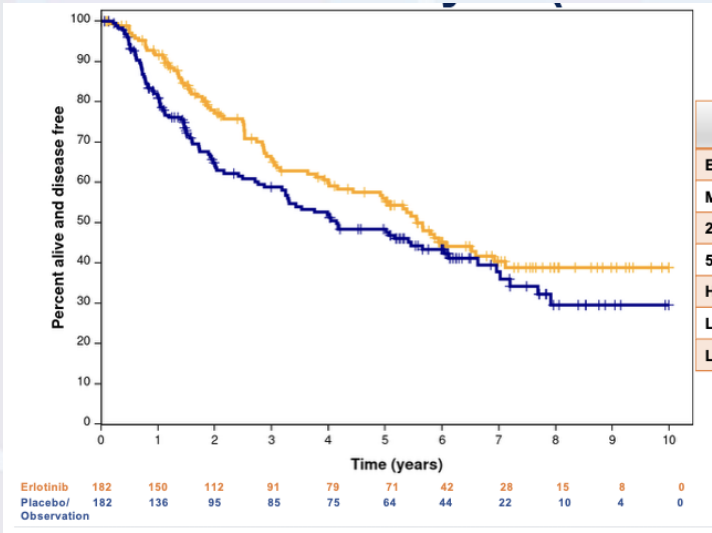
| | Erlotinib (N=191) | Placebo/ Observation (N=188) |
|---|---|---|
| **Stage** | | |
| IB>=4cm | 25 (13.1%) | 21 (11.2%) |
| II | 97 (50.8%) | 96 (51.1%) |
| IIIA | 69 (36.1%) | 71 (37.8%) |
| **Prior Chemotherapy** | | |
| Yes | 159 (83.2%) | 153 (81.4%) |
| No | 32 (16.8%) | 35 (18.6%) |
| **Exon 19 Deletion*** | | |
| Yes | 108 (56.5%) | 107 (56.9%) |
| No | 83 (43.5%) | 81 (43.1%) |
| **ECOG Performance Status (PS)** | | |
| 0 | 117 (61.3%) | 110 (58.5%) |
| 1 | 74 (38.7%) | 78 (41.5%) |

* Based on local result or central if local not available




| | Erlotinib | Placebo / Observation |
|---|---|---|
| **Events** | 56/182 | 58/182 |
| **Median OS, years (95% CI)** | **9.7** (8.4-NE) | **9.2** (7.7-NE) |
| **2-years OS, % (95% CI)[a]** | 95.4 (90.9-97.6) | 94.4 (89.8-96.9) |
| **5-years OS, % (95% CI)[a]** | 78.6 (71.6-84.1) | 78.0 (70.9-83.6) |
| **Hazard ratio (95% CI)** | 0.89 (0.62-1.29)[b]; | 0.86 (0.58-1.28)[c] |
| **Log rank 1-sided P value** | 0.2755[b]; | 0.2316[c] |

CI=confidence interval
[a] Kaplan-Meier method
[b] Unstratified Cox model
[c] Stratified Cox model by stage, prior chemotherapy, Exon 19 Deletion and ECOG PS



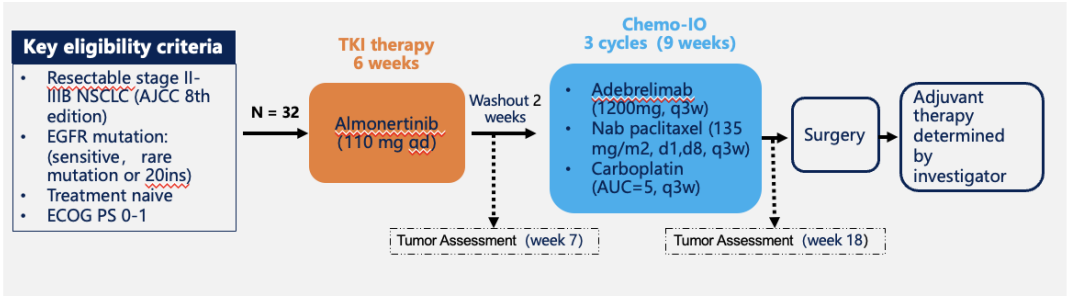

| | Erlotinib | Placebo / Observation |
|---|---|---|
| **Events** | 82/182 | 96/182 |
| **Median DFS, years (95% CI)** | **5.6** (4.2-6.9) | **4.1** (3.2-6.1) |
| **2-years DFS, % (95% CI)[a]** | 77.2 (69.8-83.0) | 64.3 (56.4-71.1) |
| **5-years DFS, % (95% CI)[a]** | 56.0 (47.4-63.7) | 48.4 (40.3-56.0) |
| **Hazard ratio (95% CI)** | 0.78 (0.58-1.04)[b]; | 0.75 (0.55-1.02)[c] |
| **Log rank 1-sided P value** | **0.0461**[b]; | **0.0337**[c] |
| **Log rank 2-sided P value** | 0.0922[b]; | 0.0674[c] |

CI=confidence interval
[a] Kaplan-Meier method
[b] Unstratified Cox model
[c] Stratified Cox model by stage, prior chemotherapy, Exon 19 Deletion and ECOG PS

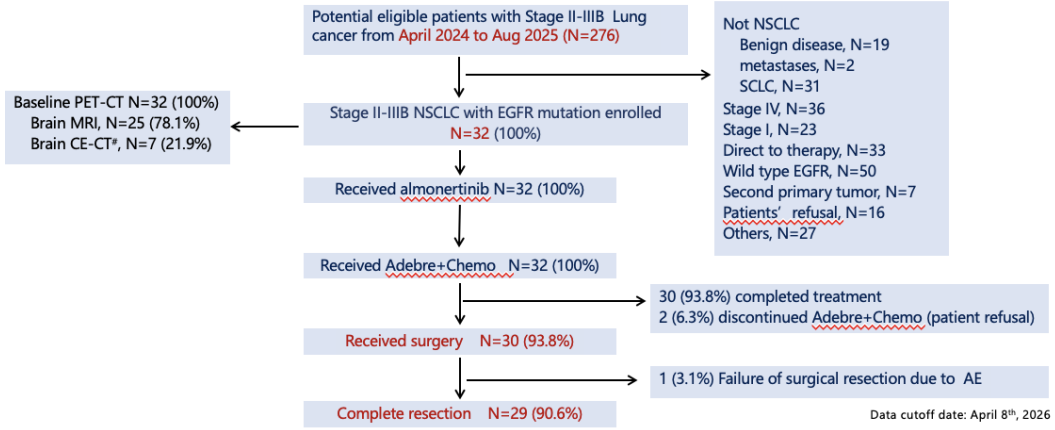
Iniciativa científica de:

GECP lung cancer research

# A single-arm phase II study of Neoadjuvant Almonertinib (3rd gen EGFR-TKI) → Adebrelimab (an anti-PD-L1 antibody) + Chemotherapy for Stage II–IIIB EGFR-Mutant NSCLC (NCT06300424, NEOVADE)

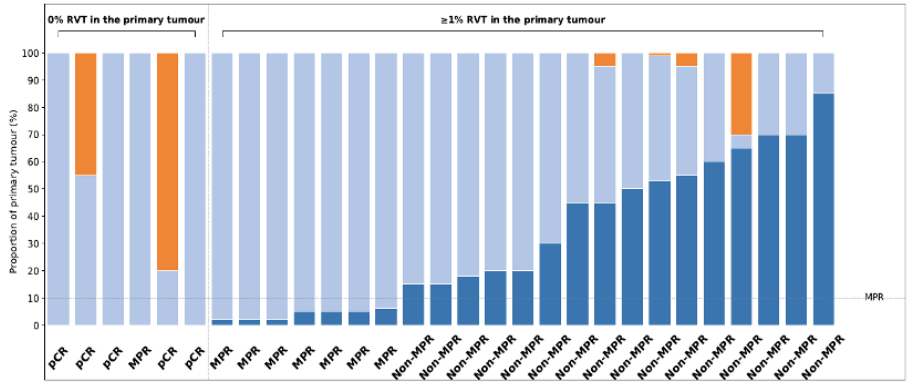



**Primary endpoint:** MPR
**Secondary endpoints**: pCR, safety, ORR after TKI, ORR after chemo-IO, resectability, EFS, OS.
**Exploratory endpoints**: ctDNA-MRD and biomarker
**Statistical**: Simon' s optimal two-stage design (P0=15%, P1=35% , $\alpha_{one\text{-}sided}$=0.05, power=80%, $N_{stage\ I}$ =17 (R1>2), $N_{total}$ = 32 (R>7))




#CE-CT, Contrast-Enhanced CT were included in PET-CT.
NSCLC, non small cell lung cancer; SCLC, small cell lung cancer; SCC, squamous cell carcinoma; EGFR, Epidermal Growth Factor Receptor; AE, adverse event.

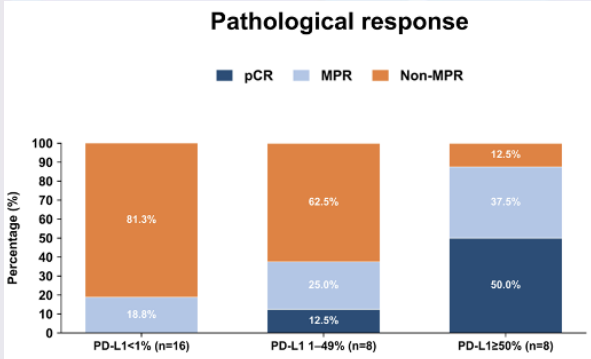
| Surgical outcomes | Patients (N=32) |
|---|---|
| Time from 3rd cycle of neoadjuvant chemo-IO, median (range), weeks | 4.8 (3.9-7.4) |
| Patient decision to refuse surgery | 2 (6.6%) |
| Discontinuation surgery due to AE* | 1 (3.3%) |
| **R0 resection** | 29 (90.6%) |

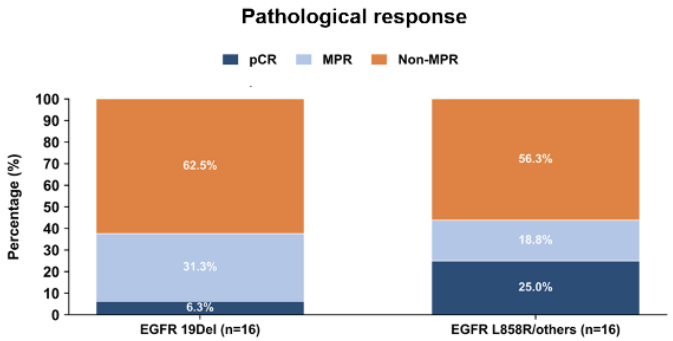



| | ITT (N=32) | PP#(N=29) |
|---|---|---|
| MPR | 40.6% (13/32) | 44.8% (13/29) |
| pCR | 15.6% (5/32) | 17.2% (5/29) |

ITT, Intention-To-Treat; pCR, pathological complete response; MPR, major pathological response; RVT, residual viable tumor

#PP, Per-Protocol Population: those who underwent resection and eligible for pathological response evaluation



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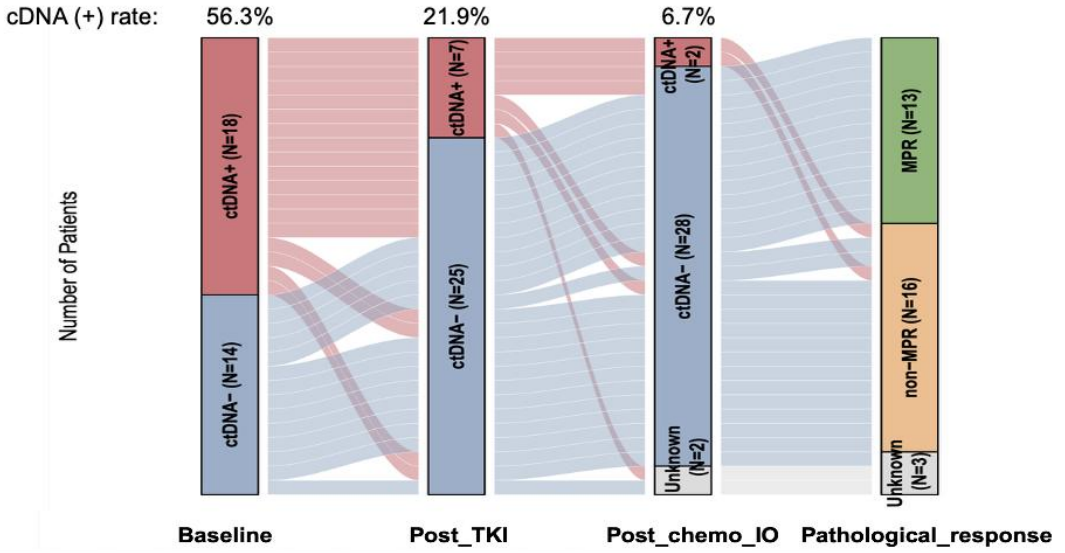
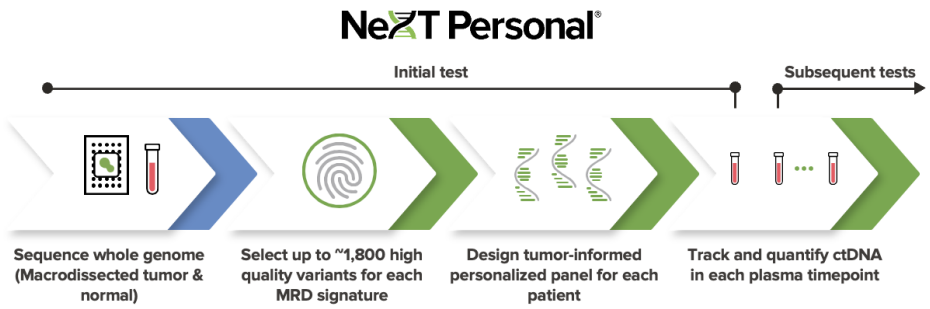
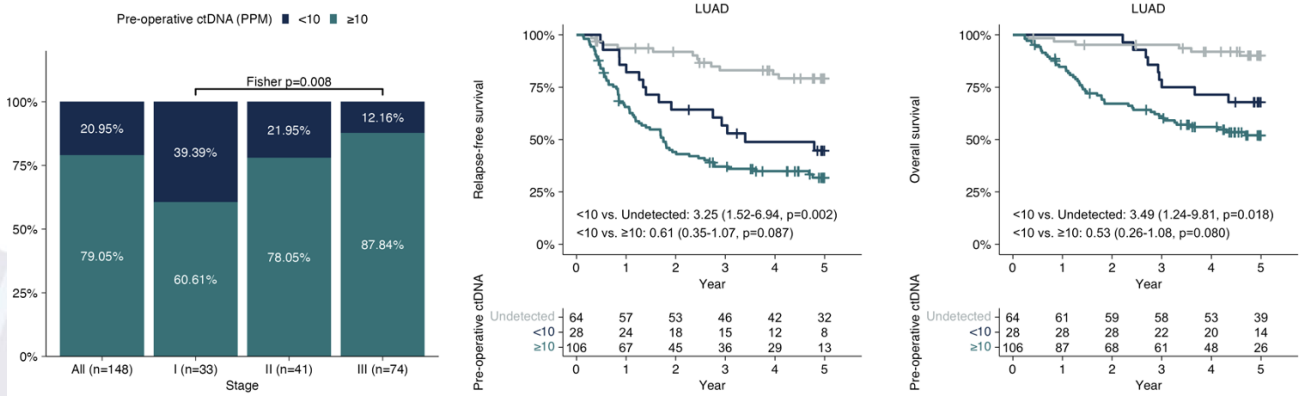


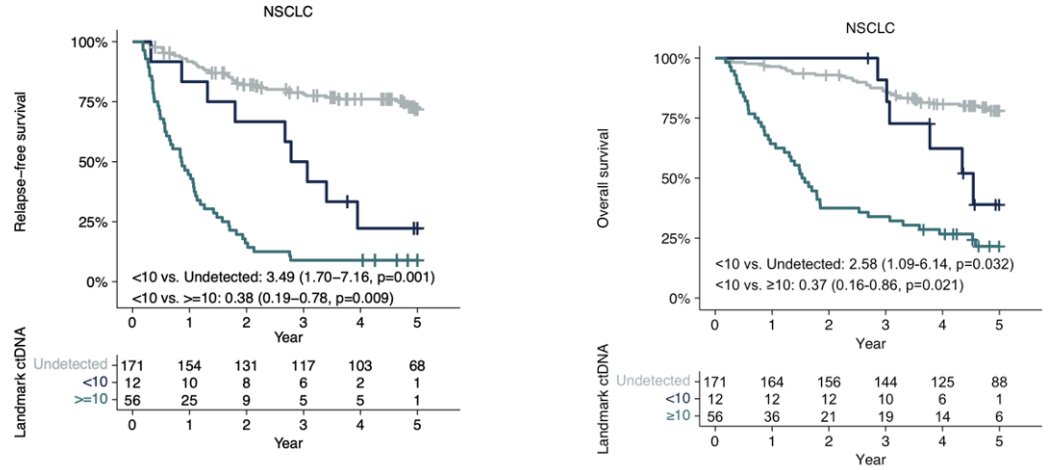

# Ultrasensitive tumour informed MRD assay powered by whole genome sequencing and advanced analytics




- Published* analytical validation demonstrating limit of detection (LOD) in the 1-3 PPM range
- In this study, median LOD across 2,994 samples = 1.66 PPM




- 21% of all preoperative ctDNA detections in LUAD occurred below 10 PPM
- Patients with Sub 10 PPM ctDNA levels detected preoperatively are at 3 fold greater risk for recurrence and death, similar to >10 PPM




- Patients with Sub 10 PPM ctDNA levels at the post-operative landmark are at 3 fold greater risk for recurrence

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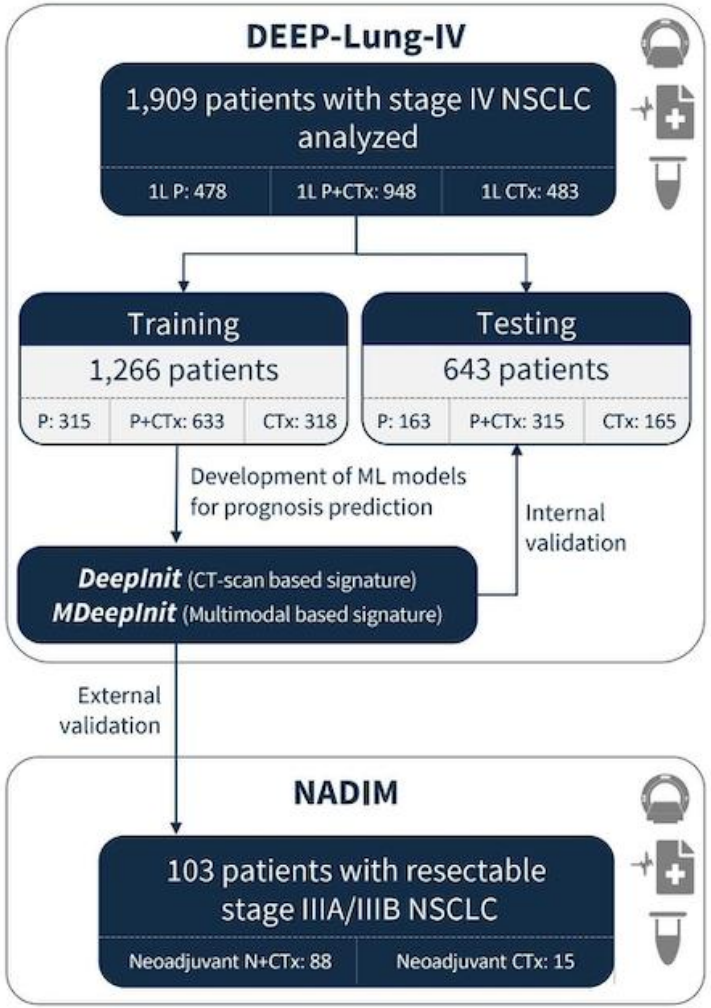


**DEEP-Lung-IV**[1]

- Observational, international, multicentric study collecting multimodal RWD.
- Study goal: Develop AI-powered predictive models for response to therapy in 1L metastatic NSCLC.
- Enrollment of patients treated with 1L pembrolizumab monotherapy (P), pembrolizumab plus chemotherapy (P+CTx) or chemotherapy doublet (CTx).
- **Multimodal ML models developed and validated for prediction of prognosis in mNSCLC: *DeepInit* (leveraging CT-scan only) & *MDeepInit* (leveraging multimodal clinical, biological, radiology imaging data) ML models**

**NADIM**[2,3]

- Randomized, open-label, phase II, multicentric clinical trial.
- Study goal: Assess pCR after neoadjuvant chemo-IO in resectable stage III NSCLC.
- Patients enrolled treated with either nivolumab plus chemotherapy (N+CTx) or chemotherapy alone (CTx) before surgery.
- **External & cross-stage validation of *DeepInit* & *MDeepInit* on 103 stage III NSCLC patients** (selected based on multimodal data availability at treatment initiation and documented surgery).

## Predictive performance

| | All patients | Arm N + CTx |
|---|---|---|
| | n = 103 | n = 88 |
| ***pCR prediction*** | | |
| *DeepInit* | **0.646** (0.538, 0.752) | **0.625** (0.515, 0.745) |
| *MDeepInit* | **0.745** (0.641, 0.835) | **0.701** (0.601, 0.801) |

## Risk-group stratification

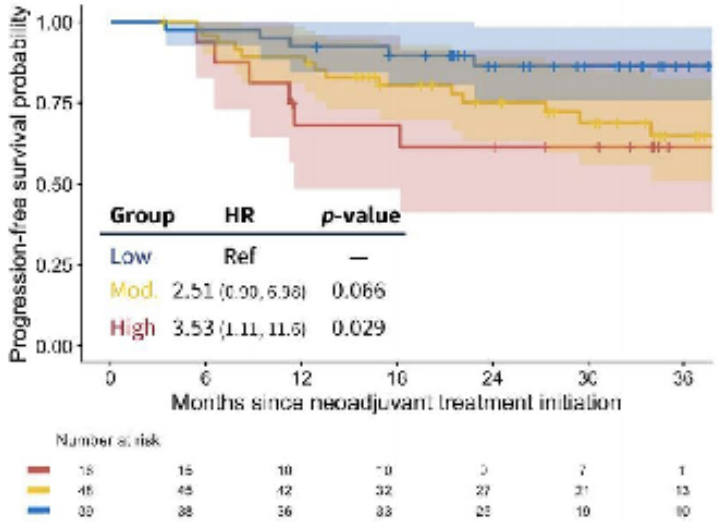


**Figure 3. Kaplan-Meier PFS curves stratified by *MDeepInit*-based risk groups, for all NADIM patients.**

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# Mensajes resumen

**La quimio-inmunoterapia preoperatoria (+/- postoperatoria) se consolida como la estrategia de mayor eficacia en estadios iniciales**

**En la fusion de RET el tto adyuvante con Selpercatinib deberá integrarse en la práctica clínica. En la fusion ALK el tto neoadyuvante con Lorlatinib obtiene una tasa significative de pCR**

**La detección de la MRD mediante ctDNA es el área de investigación preferente para permitir individualizar el tratamiento**

# Abstracts utilizados en la presentación

Iniciativa científica de:
GECP
lung cancer research

- Chaft J et al :Abstract 8000. Oral Presentation Session Lung Cancer Non Small Cell Local-Regional
- Provencio M: Discussant Session Lung Cancer Non Small Cell Local-Regional
- Goldman JW et al: Abstract LBA3 Oral Presentation Plenary Session
- Govindan R et al :Abstract 8001 Oral Presentation Session Lung Cancer Non Small Cell Local-Regional
- Zhang C et al: Abstract 8002 Oral Presentation Session Lung Cancer Non Small Cell Local-Regional
- Song P et al: Abstract 8010 Oral Presentation Session Lung Cancer Non Small Cell Local-Regional
- Zhong W et al: Abstract 8509. Oral Presentation Clinical Science Symposium Challenges in combination therapy for Non-Small Cell Lung Cancer
- Wan J et al: Abstract 8017 Oral Presentation Session Lung Cancer Non Small Cell Local-Regional
- Huang Z et al: Abstract 8031 Poster
- Zouein J et al: Abstract 8060 Poster
- Zouein J et al: Abstract 8062 Poster
- Ferrer L et al: Abstract 551298 Poster

# Gracias