Lung Cancer UPDATES
WCLC HIGHLIGHTS
06 - 09 SEPTIEMBRE 2025
Barcelona, Spain

Iniciativa científica de:
GECP lung cancer research

Cáncer de pulmón no microcítico en estadio temprano

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Hospital Universitari Son Espases

Guión

- QT/IO PERIOPERATORIA
- BM EN ENFERMEDAD LOCALIZADA
- OTROS:
  - TÉCNICAS QUIRÚRGICAS
  - STAS

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IASLC 2025 World Conference on Lung Cancer

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NADIM ADJUVANT trial

A phase III clinical trial of adjuvant chemotherapy vs chemo-immunotherapy for stage IB-IIIA completely resected non-small cell lung cancer (NSCLC) patients

First Interim Analysis

PL03.10

M. Provencio, R. Bernabé, E. Nadal, A. Martínez-Marti, E. Carcereny, A. Ortega, B. Campos, M. Dómine, B. Massuti, M. Martínez Aguillo, I. Sullivan, A. Padilla, J. González-Larriba, R. García Campelo, J. Bosch-Barrera, S. Sandiego, O. Juan-Vidal, D.Rodriguez, A. Blasco, L. Vilà, P. Martín-Martorell, R. Marsé, X. Mielgo, J. de Castro, J. Mane, J. Aires Machado, M. Sala, M. Lázaro-Quintela, R. Palmero, V. Calvo, on behalf of Spanish Lung Cancer Group.

BACKGROUND

- Patients with early-stage non-small cell lung cancer (NSCLC) have high recurrence rates, even following complete resection and/or adjuvant treatment.
- Several trials have explored the role of the adjuvant immunotherapy with variable results[1,2,3]. None of these studies had examined the combination of chemotherapy plus immunotherapy.
- Results of the NADIM and NADIM II trials[4,5] reinforced the use of perioperative chemo-immunotherapy in patients with potentially resectable NSCLC and supported its efficacy in patients with stages IB-IIIA NSCLC who are candidates for adjuvant treatment.
- NADIM ADJUVANT is a phase III study conducted to evaluate the efficacy and safety of the combination of chemo-immunotherapy in the adjuvant setting.

[1]Felip E, et al. Lancet. 2021 Oct 9;398(10308):1344-1357; [2]Goss G, et al. Ann Oncol (2024);35(suppl_2):1-72; [3]O'Brien M, et al. Lancet Oncol. 2022 Oct;23(10):1274-1286; [4]Provencio M, et al. Lancet Oncol. 2024 Nov;25(11):1453-1464; [5]Provencio M, et al. N Engl J Med. 2023 Aug 10;389(6):504-513.

NADIM ADJUVANT STUDY DESIGN

Open-label, randomized, phase III trial

Key Eligibility Criteria

- Histologically confirmed IB (≥4 cm), II or IIIA NSCLC per AJCC v8
- R0 resection
- No prior therapy
- ECOG PS 0 or 1
- Patients with **known** STK11, KEAP1 or EGFR mutations/ALK alterations were excluded

N=210
1:1

	ADJUVANT	MAINTENANCE
Experimental Arm	Nivolumab 360 mg Q3W + Chemotherapy[b] Q3W (4 cycles)	Nivolumab 480 mg Q4W 6 cycles (6 months)
Control Arm	Chemotherapy[b] Q3W (4 cycles)	Observation Q12W (6 months, 2 visits)

Follow up (5 years)

	Baseline	Post Cycle 2 adjuvant treatment	After adjuvant treatment	Every 3 months	Post maintenance treatment or observation	During FUP
PET-CT/ Brain MRI or CT	✓					
Tumor block / Blood samples[a]	✓					
Blood samples		✓	✓		✓	
CT SCAN			✓	✓		✓

During FUP
- Every 3 months for 2 years
- Every 6 months from 3rd to 5th year

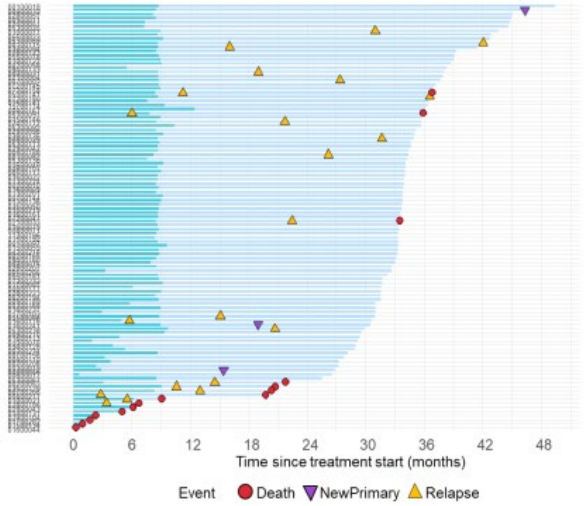
Primary Endpoint
Disease-Free Survival (DFS)[c] in ITT population.

Secondary Endpoints
- Overall Survival (OS)[d]
- Safety and Tolerability[e]

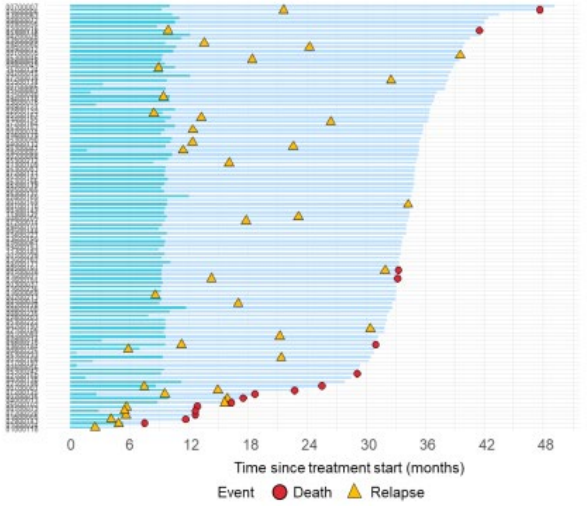
Exploratory Endpoints
Minimal Residual Disease (MRD)

Sensitivity Analysis for DFS
- Lung-cancer specific survival
- DFS from the last cycle of Ch

SWIMMER PLOT: EXPERIMENTAL GROUP

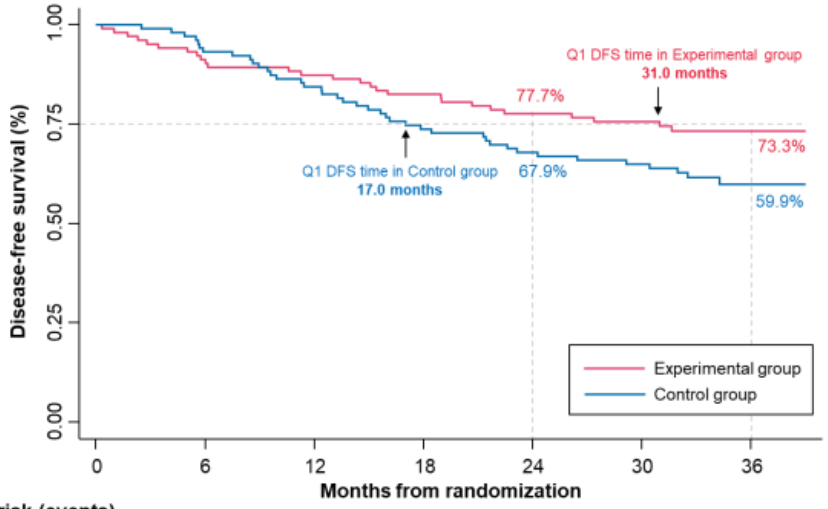


SWIMMER PLOT: CONTROL GROUP



A total of 61 events were reported, with 21 (20.4%) occurring in the experimental group and 40 (38.8%) in the control group.

PRIMARY ENDPOINT: DISEASE-FREE SURVIVAL (DFS)



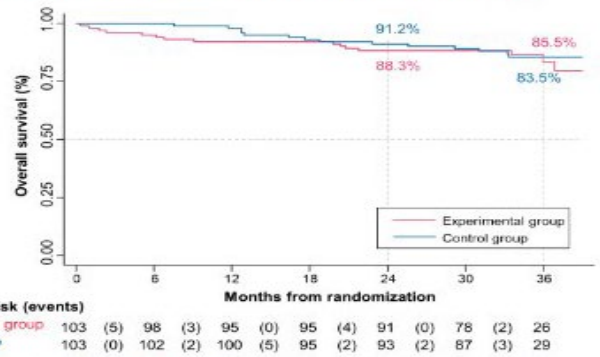
Number at risk (events)													
Experimental group	103	(9)	94	(4)	90	(5)	85	(5)	80	(2)	67	(2)	21
Control group	103	(7)	96	(9)	87	(11)	76	(6)	70	(3)	63	(4)	18

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

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

Maturity data: 57%

SECONDARY ENDPOINT: OVERALL SURVIVAL (OS)



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

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

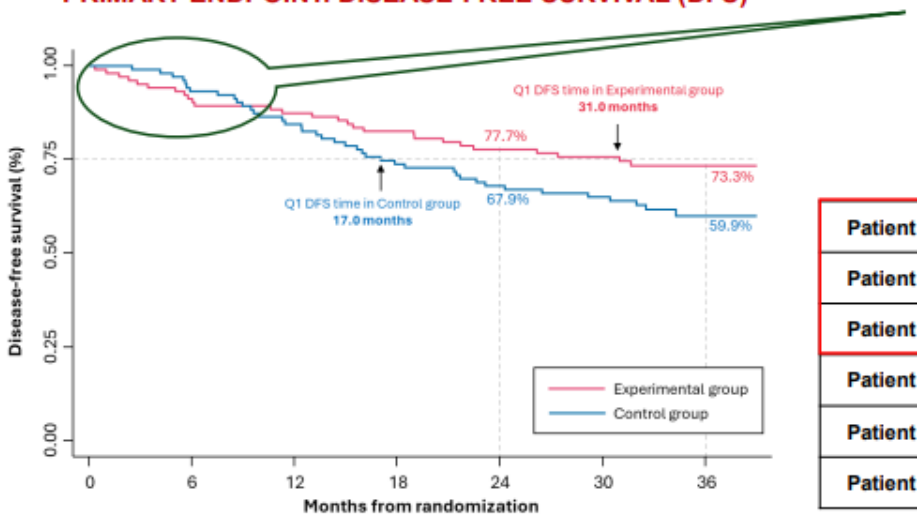
Median follow-up: 34.0 mo (IQR: 32.6-36.6)

Maturity data: 57%

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

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

PRIMARY ENDPOINT: DISEASE-FREE SURVIVAL (DFS)

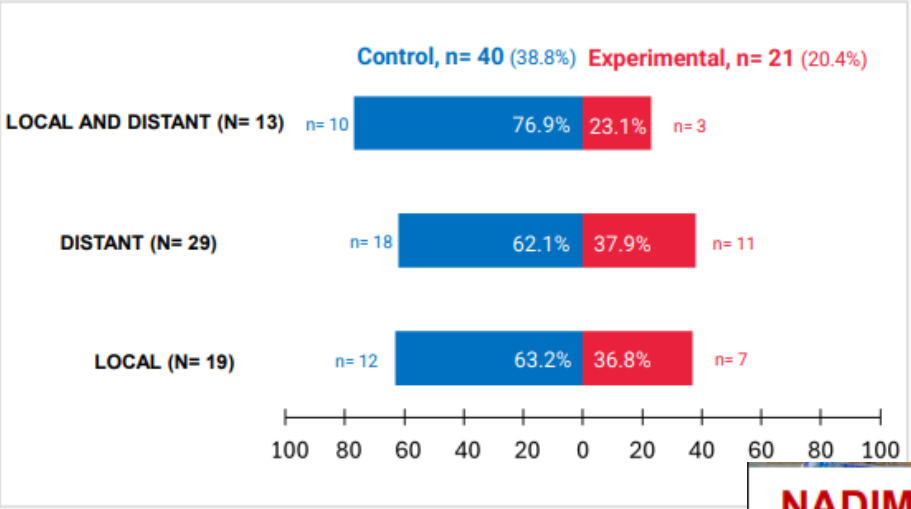


EARLY DEATHS IN EXPERIMENTAL ARM

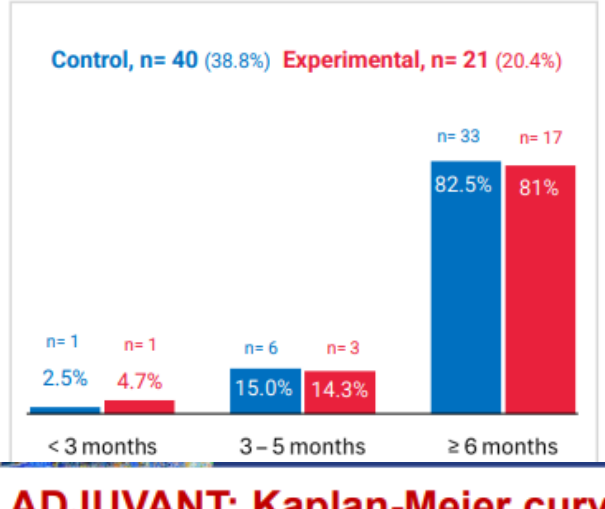
	Experimental arm				
	Treatment related	Age (years)	OS (months)	Type of surgery	Cause of death
Patient #1	No	77	1.5	Minor resection	Acute coronary syndrome
Patient #2	No	74	2.5	Pneumonectomy Left	Myocardial infarction
Patient #3	No	69	2.5	Lobectomy	Cardiac arrest
Patient #4	No	63	5.4	Pneumonectomy Left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

NADIM ADJUVANT: RELAPSES

TYPE OF RELAPSE



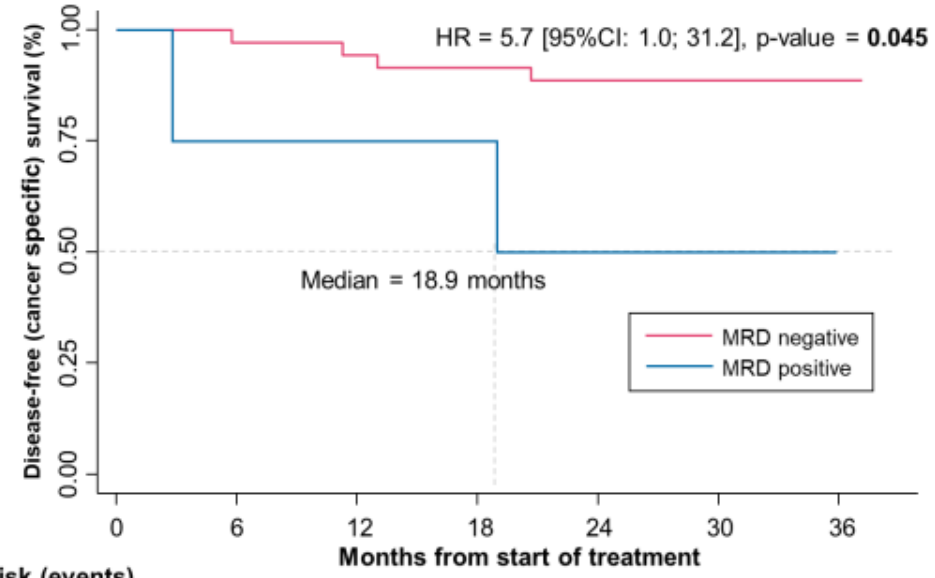
TIME OF RELAPSE



NADIM ADJUVANT: Kaplan-Meier curve based on baseline MRD status in patients from Experimental group

MRD negative	Experimental (n=36)	Control (n=37)
Median DFS (95% CI), mo	Not reached	Not reached
HR_{3years} (95% CI)	0.31 (0.10 - 0.97)	
P value	**0.043**	

MRD positive	Experimental (n=4)	Control (n=4)
Median DFS (95% CI), mo	18.9	21.3
HR_{3years} (95% CI)	1.19 (0.17 - 8.51)	
P value	0.863	



Number at risk (events)

MRD negative	37	(1)	34	(1)	33	(1)	32	(1)	31	(0)	27	(0)	5
MRD positive	4	(1)	3	(0)	3	(0)	3	(1)	2	(0)	2	(0)	0

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CONCLUSIONS

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

  20.4% in the experimental arm vs 38.8% in the control arm.

- The inclusion of **all patients after surgery** provides a **real-world evidence perspective**, since postoperative mortality and/or toxicity during the adjuvant period can affect DFS.

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

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SKYSCRAPER-05: phase II study of perioperative tiragolumab + atezolizumab ± chemotherapy in locally advanced resectable NSCLC

Harvey Pass[1], Enriqueta Felip[2], Catherine A. Shu[3], Martin Frueh[4], Andrea Ferris[5], Min Hee Hong[6], Alex Martinez-Marti[2], Ray Meng[7],

OA02.01

Study design

Eligibility criteria:
- Resectable Stage II, IIIA, or select IIIB (T3N2) NSCLC
- No prior immunotherapy, chemotherapy, or radiotherapy for lung cancer
- *EGFR/ALK* WT
- ECOG PS 0 or 1
- Tissue for PD-L1 status*

Cohort A PD-L1 high* n=8 → Tiragolumab 600mg IV Q3W + atezolizumab 1200mg IV Q3W for 4 cycles → Surgery MPR/pCR assessment → Tiragolumab 600mg IV Q3W + atezolizumab 1200mg IV Q3W for 16 cycles OR platinum-chemo Q3W for 4 cycles

CT assessment after 2 cycles to ensure treatment response or to evaluate if patients should proceed to surgery immediately

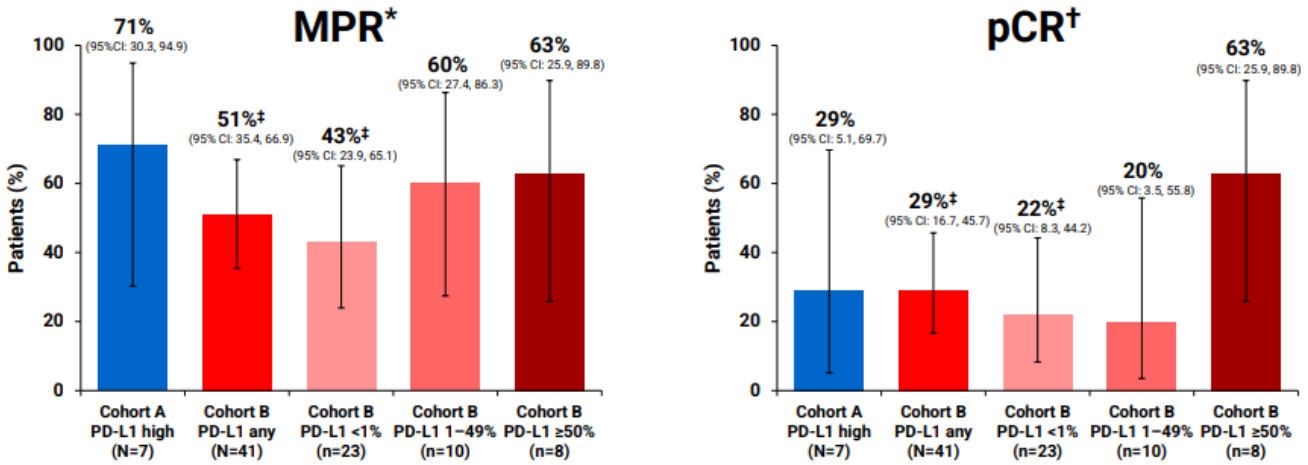
Postoperative radiotherapy optional for R1/R2 resection and/or ypN2 at time of surgical resection

Cohort B PD-L1 any n=42 → Tiragolumab 600mg IV Q3W + atezolizumab 1200mg IV Q3W + platinum-chemo Q3W for 4 cycles → Surgery MPR/pCR assessment → Tiragolumab 600mg IV Q3W + atezolizumab 1200mg IV Q3W for 16 cycles

Primary endpoints:
- Safety of neoadjuvant and adjuvant tiragolumab + atezolizumab treatment: **Incidence of AEs, surgical feasibility and outcomes**
- Efficacy of neoadjuvant treatment: **MPR by local pathology lab**

Secondary endpoints:
- Efficacy of neoadjuvant treatment: **pCR by local pathology lab**
- Efficacy of neoadjuvant and adjuvant treatment: **EFS by investigator**

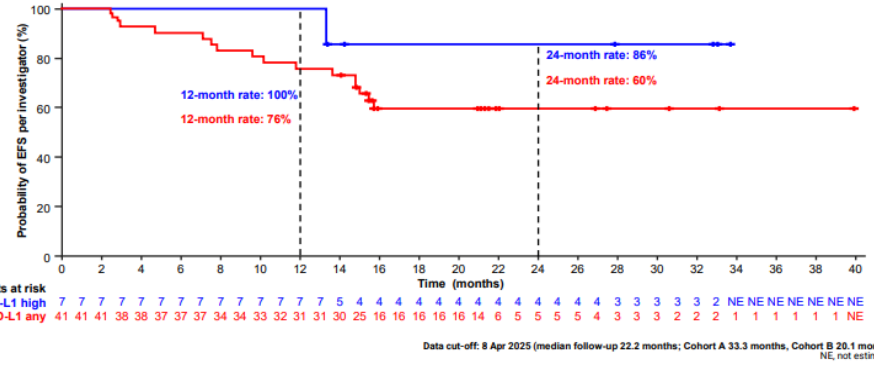
MPR and pCR



Data cut-off: 14 Feb 2024 (median follow-up 9.5 months)

*Defined as ≤10% residual viable tumour at the time of surgical resection in the primary tumour, as assessed by the local pathology laboratory
†Defined as the absence of any viable tumour cells in both the primary tumour and all sampled lymph nodes at the time of surgical resection, as assessed by the local pathology laboratory
‡2 patients did not undergo surgery and were counted as non-MPR and non-pCR
CI, confidence interval

EFS



Data cut-off: 8 Apr 2025 (median follow-up 22.2 months; Cohort A 33.3 months, Cohort B 20.1 months)
NE, not estimable

Safety summary

n (%)	Neoadjuvant		Adjuvant	
	Cohort A PD-L1 high (n=7)	Cohort B PD-L1 any (n=41)	Cohort A PD-L1 high (n=5)	Cohort B PD-L1 any (n=33)
Any grade AEs	7 (100)	40 (98)	5 (100)	30 (91)
Grade 3–4	3 (43)	16 (39)	0	9 (27)
Grade 5	0	2 (5)*†	0	2 (6)‡§
TRAEs	7 (100)	38 (93)	5 (100)	24 (73)
Grade 3–4	2 (29)	13 (32)	0	7 (21)
Grade 5	0	1 (2)*	0	1 (3)‡
AESIs	5 (71)	28 (68)	2 (40)	20 (61)
AE leading to treatment withdrawal				
Any treatment	0	4 (10)	0	11 (33)
Tiragolumab + atezolizumab	0	3 (7)	0	11 (33)
Chemotherapy	0	2 (5)	0	0
	Cohort A PD-L1 high (n=7)	**Cohort B PD-L1 any (n=41)**	**Cohort A PD-L1 high (n=7)**	**Cohort B PD-L1 any (n=39)**
Surgery-related AEs within 30 days after surgery	–	–	4 (57)	14 (36)
Grade 3–4	–	–	1 (14)	1 (3)
Grade 5	–	–	0	1 (3)‡

Data cut-off: 5 Mar 2025 (median follow-up 15.1 months)
Median treatment duration: 2.5 months for Cohort A and 13 months for Cohort B
*Infectious pleural effusion (n=1; related to chemotherapy); †Respiratory distress (n=1); ‡Unexplained death (n=1; related to tiragolumab + atezolizumab); §Acute pyelonephritis (n=1)
TRAE, treatment-related adverse event

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Conclusions

- The **SKYSCRAPER-05** study confirmed **surgical feasibility** after neoadjuvant treatment with tiragolumab + atezolizumab, with/without platinum-based chemotherapy, for patients with locally advanced resectable NSCLC
- MPR and pCR rates seen across PD-L1 subgroups with perioperative tiragolumab + atezolizumab were similar to other perioperative immunotherapy plus chemotherapy regimens[1–8]
- Tiragolumab + atezolizumab demonstrated an **acceptable safety profile consistent with expectations** for this treatment combination in an early disease setting

1. Forde et al. NEJM 2022; 2. Cascone et al. NEJM 2024; 3. Heymach et al. NEJM 2023; 4. Wakelee et al. NEJM 2023
5. Lu et al. JAMA 2024; 6. Yue et al. Lancet Respir Med 2025; 7. Provencio et al. NEJM 2023; 8. Henick et al. JITC 2024

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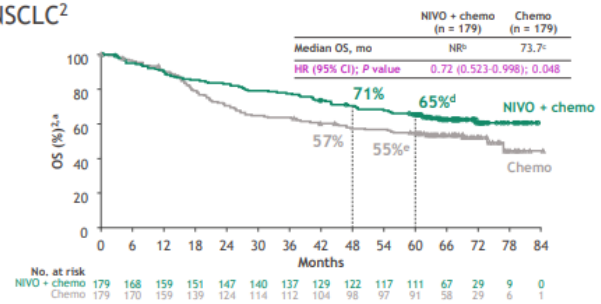
Overall survival with neoadjuvant nivolumab plus chemotherapy by surgical outcomes in the phase 3 CheckMate 816 study

Background

- The CheckMate 816 study demonstrated statistically significant and clinically meaningful improvements in EFS and pCR with neoadjuvant NIVO + chemo in patients with resectable NSCLC[1]
- NIVO + chemo is the sole neoadjuvant-only chemoimmunotherapy regimen to demonstrate statistically significant OS benefit in NSCLC[2]



- NIVO + chemo is an approved, standard of care neoadjuvant treatment in the United States, European Union, and several other countries for eligible patients with resectable NSCLC[3-7]
- Here, we report final 5-year OS and HRQoL by surgical outcomes in patients who had definitive surgery in CheckMate 816

OA02.03

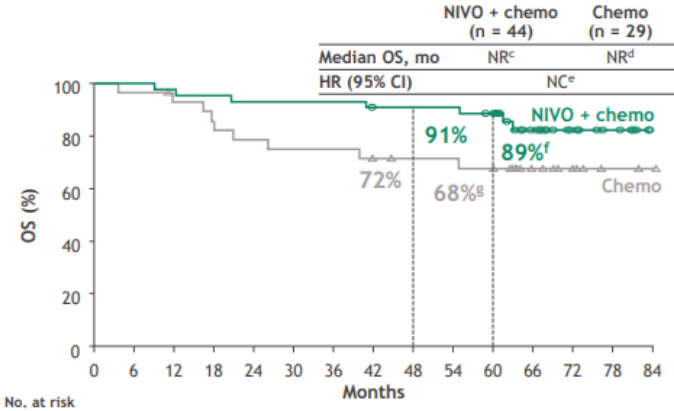
Summary

- In this final 5-year analysis from CheckMate 816, neoadjuvant NIVO + chemo demonstrated long-term survival benefit vs chemo in patients with resectable NSCLC, regardless of surgical approach or extent of resection, and in those with R0 resection
- NIVO added to neoadjuvant chemo did not negatively impact long-term HRQoL as assessed by EQ-5D-3L UI scores, whether patients had
  - Minimally invasive surgery or thoracotomy
  - Lobectomy or pneumonectomy
- These findings, together with previously reported results of significant OS benefit with NIVO + chemo, further support the use of this regimen as a standard neoadjuvant treatment in eligible patients with resectable NSCLC

OS by surgical approach

Minimally invasive[a]

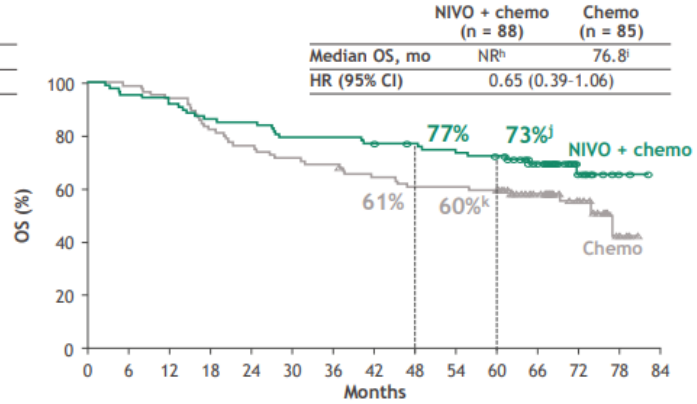
30% (NIVO + chemo) and 21% (chemo)[1]



	NIVO + chemo (n = 44)	Chemo (n = 29)
Stage III, n (%)	28 (64)	16 (55)

Thoracotomy[b]

59% (NIVO + chemo) and 63% (chemo)[1]



	NIVO + chemo (n = 88)	Chemo (n = 85)
Stage III, n (%)	56 (64)	50 (59)

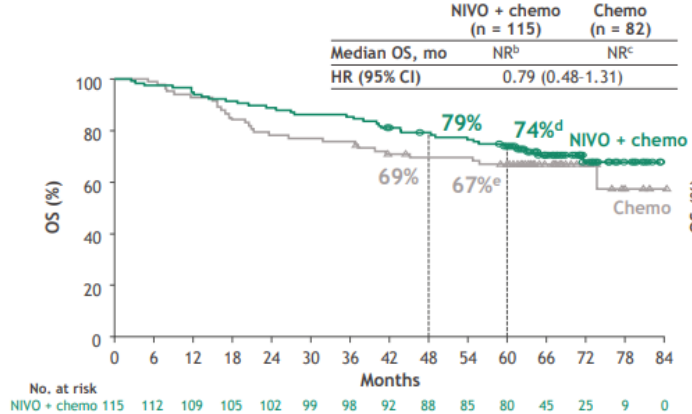
Minimum/median follow-up: 59.9/68.4 months.

[a]Includes minimally invasive therapeutic approaches (robotic approaches: n=105 (79%) patients in the NIVO + chemo arm and 10 (7%) patients in the chemo arm had thoracotomy as conversion from minimally invasive surgery to th
1.

OS by extent of resection[a]

Lobectomy

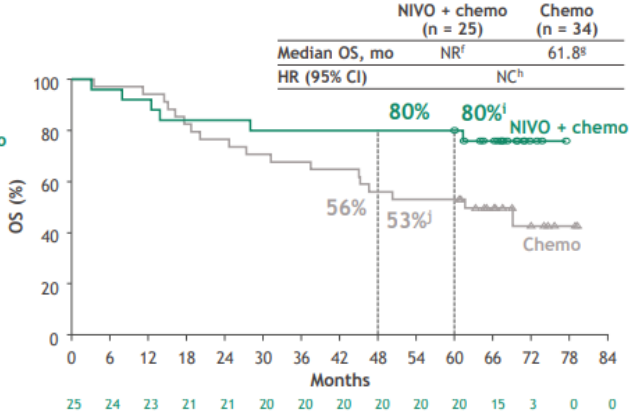
77% (NIVO + chemo) and 61% (chemo)[1]



	NIVO + chemo (n = 115)	Chemo (n = 82)
Stage III, n (%)	74 (64)	49 (60)

Pneumonectomy

17% (NIVO + chemo) and 25% (chemo)[1]



	NIVO + chemo (n = 25)	Chemo (n = 34)
Stage III, n (%)	16 (64)	25 (74)

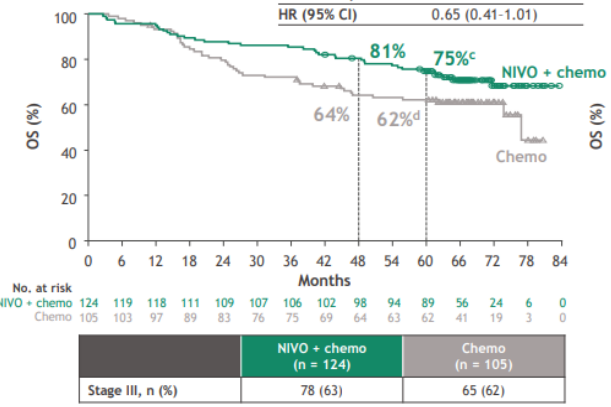
Minimum/median follow-up: 59.9/68.4 months.

[a]Patients may have had ≥ 1 surgery type. [b-e]95% CI: [b]NR-NR; [c]73.7-NR; [d]65-81; [e]55-76; [f]NR-NR; [g]31.2-NR. [h]HR was not calculated due to an insufficient number of events (< 10 per arm). [i,j]95% CI: [i]58-91; [j]35-68.
1. Forde PM, et al. *N Engl J Med* 2022;386:1973-1985.

OS by completeness of resection

R0

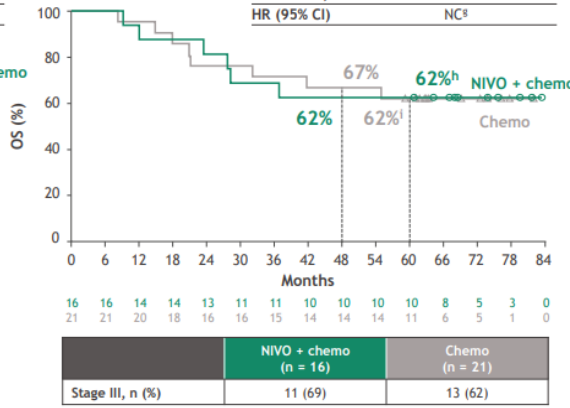
83% (NIVO + chemo) and 78% (chemo)[1]



	NIVO + chemo (n = 124)	Chemo (n = 105)
Stage III, n (%)	78 (63)	65 (62)

R1

11% (NIVO + chemo) and 16% (chemo)[1]



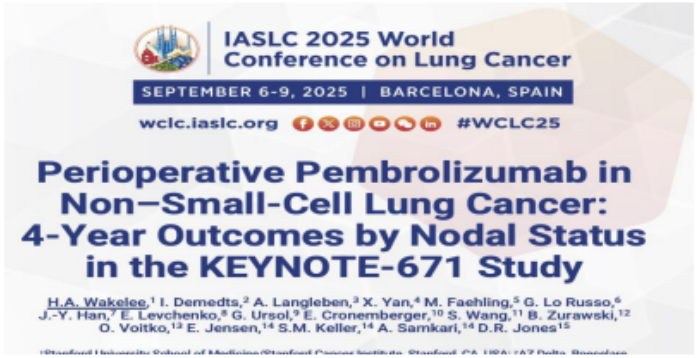
	NIVO + chemo (n = 16)	Chemo (n = 21)
Stage III, n (%)	11 (69)	13 (62)

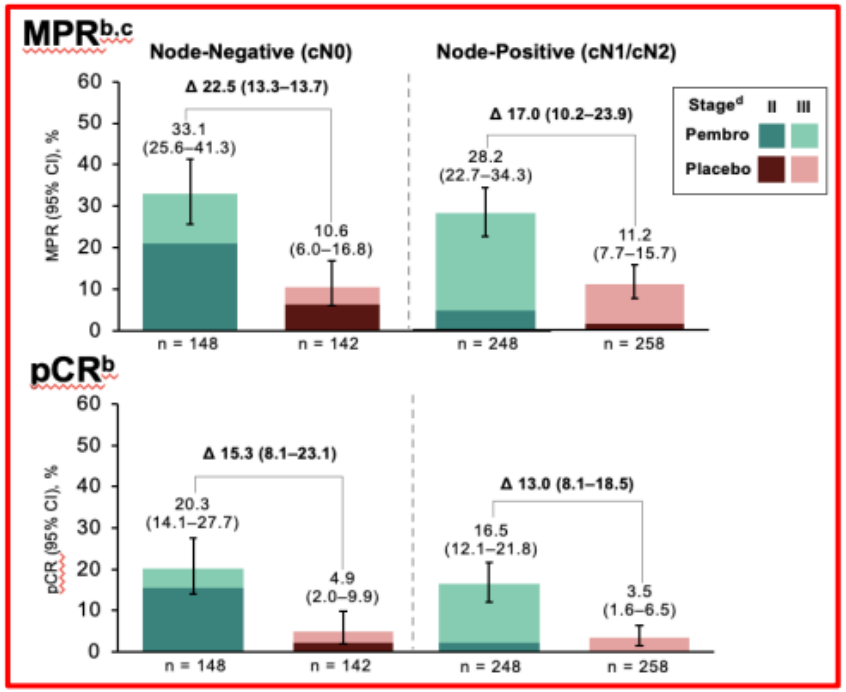
Minimum/median follow-up: 59.9/68.4 months.

Five patients in the NIVO + chemo arm and 4 in the chemo alone arm had R2 resection. [a-d]95% CI: [a]NR-NR; [b]73.7-NR; [c]66-82; [d]52-71. [e,f]95% CI: [e]27.6-NR; [f]31.9-NR. [g]HR was not calculated due to an insufficient number of events (< 10 per arm). [h,i]95% CI: [h]35-81; [i]38-79.

1. Forde PM, et al. *N Engl J Med* 2022;386:1973-1985.

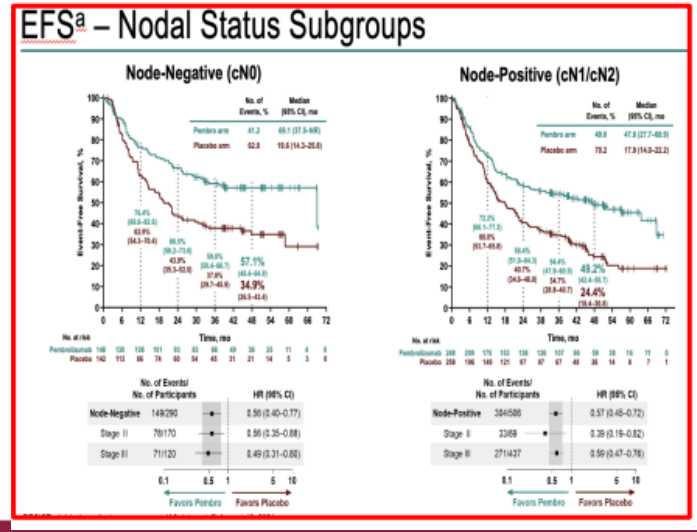
MA04.04

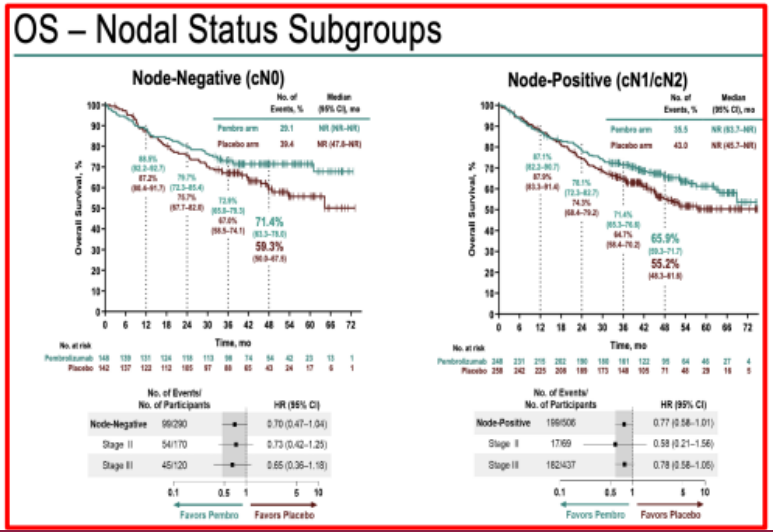




Perioperative Pembrolizumab in NSCLC: 4-Year Outcomes by Nodal Status in the KEYNOTE-671 Study

H. Wakelee





Patient-Reported Outcomes With Perioperative Nivolumab by Nodal Status in Patients With Resectable NSCLC From Checkmate 77T

J.D. Spicer

IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

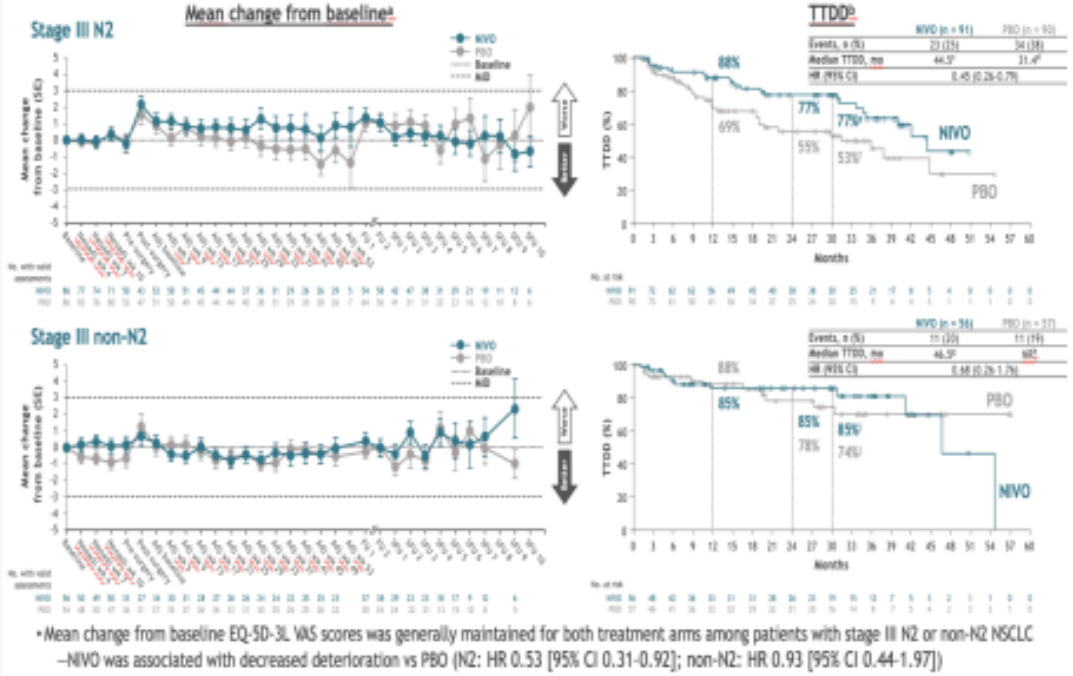
Patient-reported outcomes with perioperative nivolumab by nodal status in patients with resectable NSCLC from CheckMate 77T

Jonathan D. Spicer,[1] Mariano Provencio Pulla,[2] Tina Cascone,[3] Mark M. Awad,[4] Lubos B. Petruzelka,[5] Hiroyuki Ito,[6] Tudor-Eliade Ciuleanu,[7] Ludmila de Oliveira Muniz Koch,[8] Florian Guisier,[9] Nikolaj Frost,[10] T. Jeroen Nicolaas Hiltermann,[11] Shun Lu,[12] Sumeena Bhatia,[13] Steven I. Blum,[13] Stefano Lucherini,[14] Rachael Lawrance,[15] Christine Yip,[16] Gill Worthy,[15] Cinthya Coronado Erdmann,[17] Fumihiro Tanaka[18]

Summary

- In this exploratory analysis from CheckMate 77T, perioperative NIVO did not negatively impact HRQoL vs PBO, as measured by the NSCLC-SAQ or EQ-5D-3L VAS instruments, in patients with clinical stage III N2 or non-N2 resectable NSCLC
- Baseline PRO scores were generally maintained long-term, except at the postsurgical and preadjuvant visit as expected, regardless of nodal status
- Patients with stage III N2 NSCLC had a lower risk of HRQoL deterioration and delayed median TTDD with NIVO vs PBO, including those with simple lobectomy or complete resection

NSCLC-SAQ scores: stage III N2 or non-N2



- Mean change from baseline EQ-5D-3L VAS scores was generally maintained for both treatment arms among patients with stage III N2 or non-N2 NSCLC
  - NIVO was associated with decreased deterioration vs PBO (N2: HR 0.53 [95% CI 0.31-0.92]; non-N2: HR 0.93 [95% CI 0.44-1.97])

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

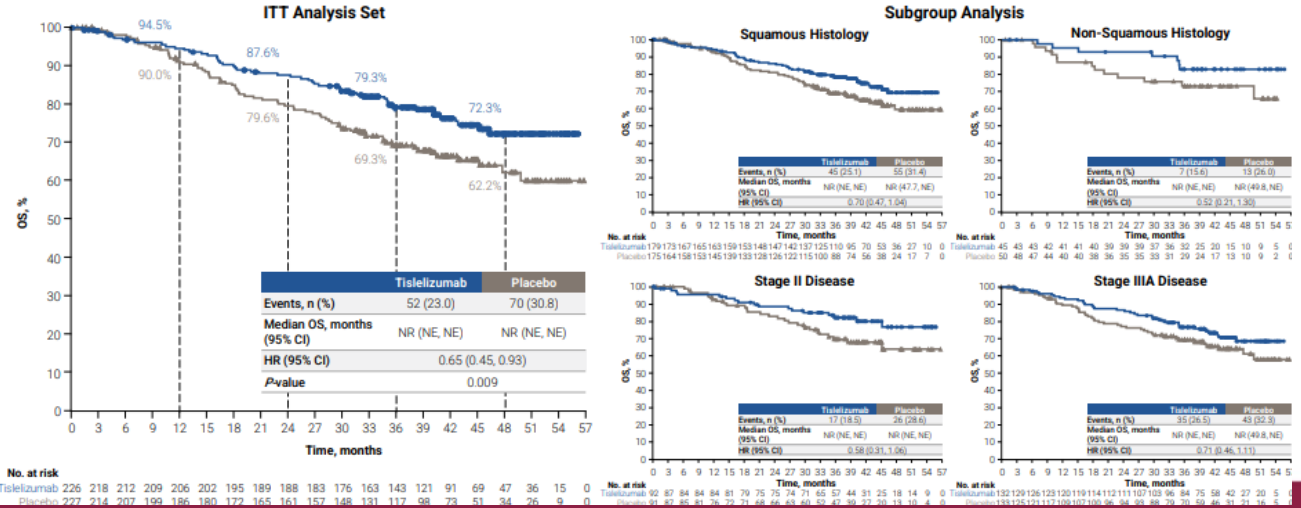
MA04.08

Conclusions

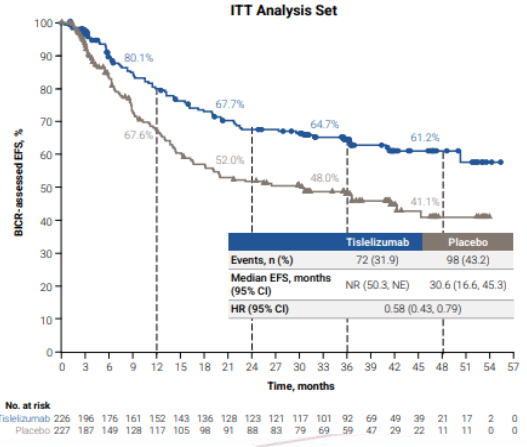
- A statistically significant and clinically meaningful benefit in OS was observed with perioperative tislelizumab plus PtDb chemotherapy vs placebo plus PtDb chemotherapy (HR=0.65 [95% CI: 0.45, 0.93]; one-sided *P*-value=0.009)
  - This benefit was consistent across prespecified and post-hoc subgroups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

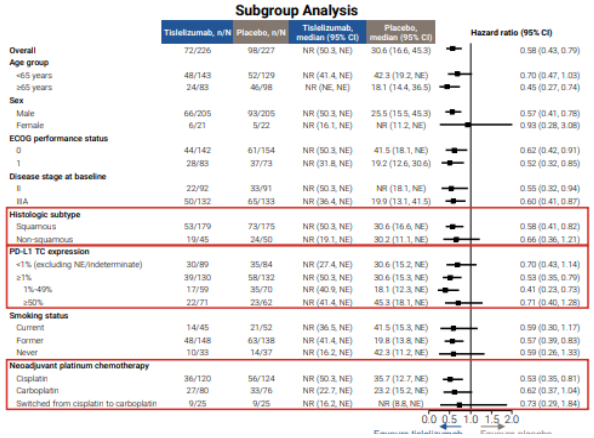
Results: Overall Survival

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



Results: Event-Free Survival



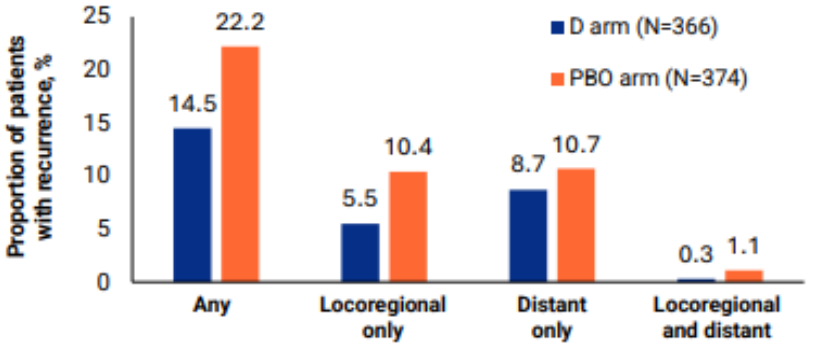


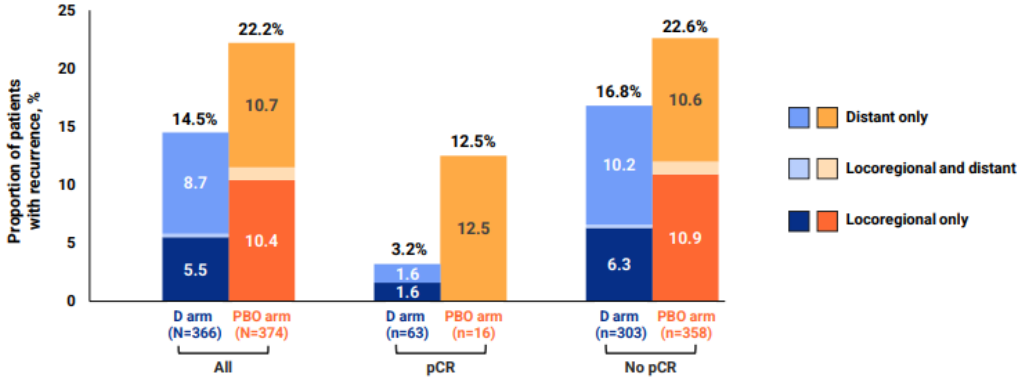
Patterns of Progression and Recurrence with Perioperative Durvalumab in Patients with Resectable NSCLC from AEGEAN

Manuel Cobo,[1] Martin Reck,[2] David Harpole,[3]
Tetsuya Mitsudomi,[4] Janis Taube,[5] Guilia Pasello,[6]
Thomas Winder,[7] Luis Leon Mateos,[8] Manuel Domine,[9]
Allen C. Chen,[10] Tamer M. Fouad,[10] Helen Mann,[11] John V. Heymach[12]

Sites of First EFS recurrence (mITT)

- Proportionally fewer patients in the D vs PBO arm had locoregional or distant only first recurrences





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Conclusions

- At a median follow-up of 25.9 months, proportionally fewer patients in the D vs PBO arm had any EFS events, including fewer patients in the D arm who had PD that precluded or prevented completion of surgery
- Proportionally fewer patients in the D vs PBO arm had any recurrences, including both locoregional and distant recurrences
  - Among patients with pCR in the D arm (n=63), only 2 patients had recurrences, one of which was distant (in the pleura)
- Median time to recurrence after surgery was longer in the D vs PBO arm, particularly for locoregional recurrences
- Of patients who completed surgery, approximately twice as many in the PBO vs D arm had subsequent Tx, primarily driven by differences in use of immunotherapy and radiotherapy

The addition of perioperative durvalumab to neoadjuvant CT reduced PD precluding or preventing completion of surgery and both locoregional and distant post-surgery recurrences

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Molecular Residual Disease (MRD) Analysis from NeoADAURA: Neoadjuvant Osimertinib ± Chemotherapy in Resectable EGFRm NSCLC

Collin M. Blakely,[1,2] Jacqulyne Robichaux, Sung Yong Lee, Jin-Yuan Shih, Kang-Yun Lee, Nguyen Viet Nhung, Somcharoen Saeteng, Jamie E. Chaft, Jianxing He, Walter Weder, Sanja Dacic, Yasushi Yatabe, Carles Escriu, Masahiro Tsuboi, Preetida Bhetariya, Balakumar Swaminathan, Yuri Rukazenkov, Ryan Hartmaier, Maximilian J. Hochmair

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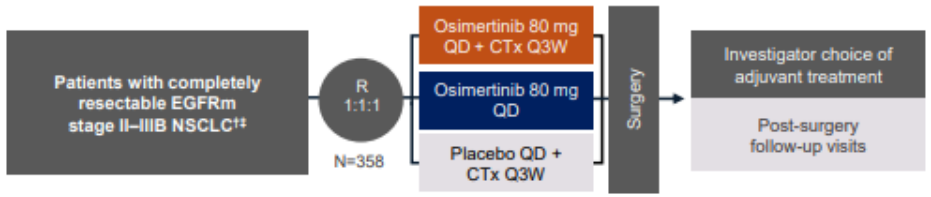
NeoADAURA: Neoadjuvant osimertinib ± CTx demonstrated significant improvements in MPR rates vs placebo + CTx in resectable EGFRm stage II–IIIB NSCLC[1]

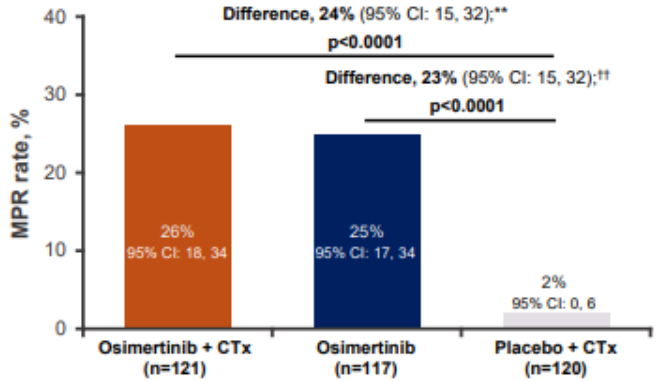
NeoADAURA study design*



CTx: carboplatin AUC5 or cisplatin 75 mg/m² + pemetrexed 500 mg/m²; 3 cycles

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

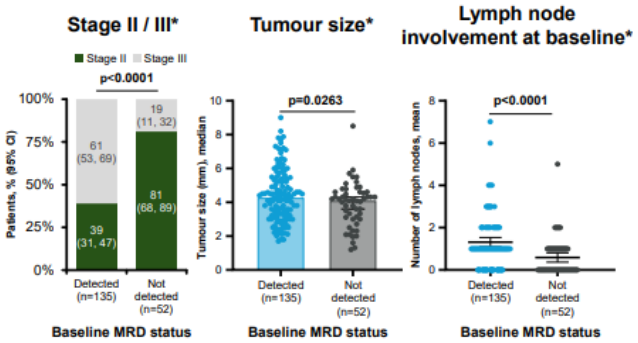
NeoADAURA primary endpoint: MPR rate¶

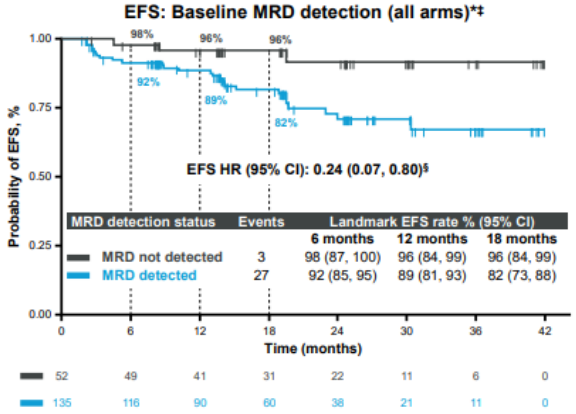


OA02.02

Patients with baseline MRD not detected vs MRD detected had less extensive disease and longer EFS

Sample tested: Baseline (C1D1)



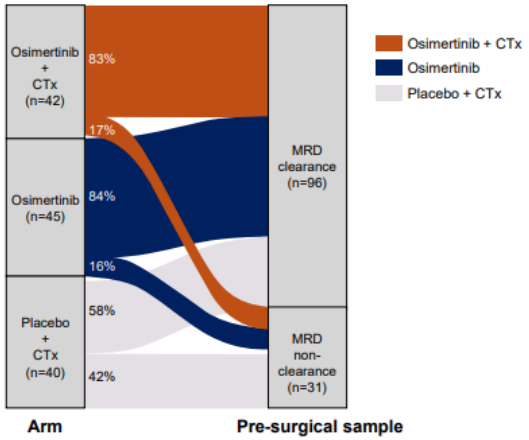


Other patient characteristics (EGFR mutation type, race, age, sex, smoking, WHO PS, surgery) were similar between the baseline MRD detected vs not detected groups†

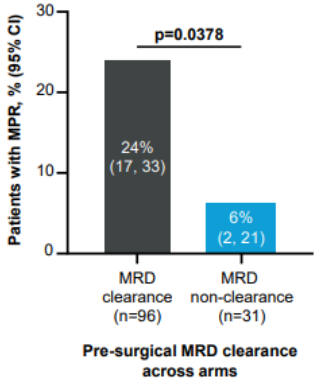
Pre-surgical MRD *clearance* was enriched with osimertinib-containing regimens and in patients with MPR

Samples tested: Baseline (C1D1)‡ Pre-surgical

Treatment with osimertinib-containing regimens led to higher rates of MRD clearance* vs placebo + CTx



MRD clearance was associated with MPR§ across arms

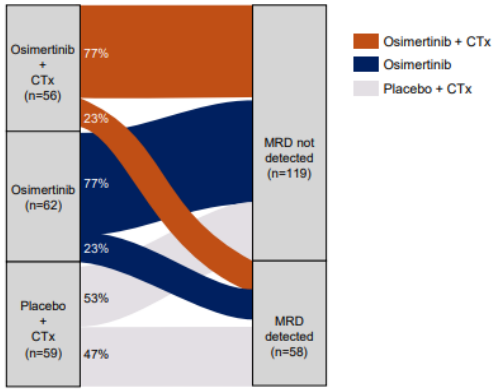


MRD clearance: 10-fold decrease in ctDNA or MRD not detected in the presurgical sample after baseline MRD detected

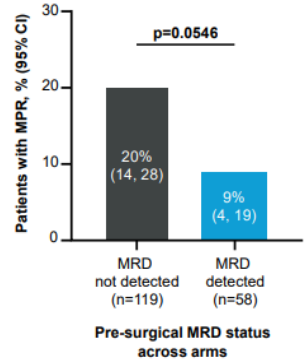
Pre-surgical MRD *not detected* rate was higher in osimertinib-containing regimens and in patients with MPR

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



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Conclusions

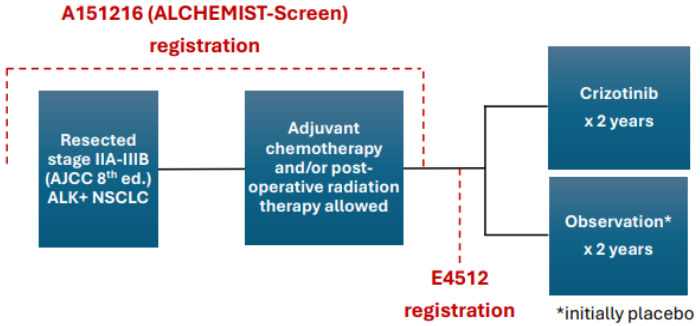
- In NeoADAURA, the tumour-informed, ctDNA-based MRD assay had greater sensitivity to detect tumour DNA vs single EGFR gene mutation testing
- Baseline MRD status was prognostic for EFS
- Osimertinib-containing regimens improved MRD clearance and reduced MRD detection before surgery vs placebo + CTx
- Pre-surgical MRD clearance and MRD not detected were associated with MPR
- Future NeoADAURA MRD analyses aim to understand the association of pre- and post-surgical MRD detection with long-term outcomes (EFS, DFS, OS), which will be presented at a later conference

These findings highlight the potential utility of MRD to complement MPR and support the use of neoadjuvant osimertinib-containing regimens in patients with resectable EGFRm stage II–III NSCLC

C Blakely. Molecular Residual Disease (MRD) Analysis from NeoADAURA: Neoadjuvant Osimertinib ± Chemotherapy in Resectable EGFRm NSCLC

ctDNA, circulating tumour DNA; CTx, chemotherapy; DFS, disease-free survival; EFS, event-free survival; EGFRm, epidermal growth factor receptor-mutated; MPR, major pathological response; MRD, molecular residual disease; NSCLC, non-small cell lung cancer; OS, overall survival.

E4512 design and endpoints



Endpoints

Primary
- DFS (in centrally ALK+ cases)

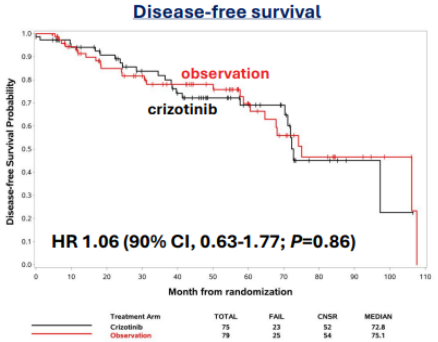
Secondary
- OS
- Toxicity

Stratification factors
- Stage: IIA/IIB/IIIA (T3N1) vs. IIIA (N2)/IIIB (N2) (AJCC 8th ed.)
- Prior RT: yes vs. no
- Sex: male vs. female

ALCHEMIST, Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials

GECP lung cancer research

Disease-free survival



Subgroup	DFS HR (90% CI)	*P* value
Sex		
Female	1.16 (0.61-2.18)	0.7
Male	0.73 (0.30-1.78)	0.6
Stage		
II-IIIA (N1)	0.65 (0.28-1.48)	0.4
IIIA (N2)-IIIB	1.48 (0.77-2.85)	0.3
Post-op RT		
Yes	1.86 (0.80-4.33)	0.2
No	0.68 (0.35-1.33)	0.3

Median follow-up = 58.3 months

PL02.18

Crizotinib toxicity and exposure

34 patients (43%) had grade ≥3 TRAE

Toxicity	Grade 3* N=79 n (%)
Diarrhea	6 (8)
Edema	4 (5)
Eye disorders	2 (3)
Abdominal pain	2 (3)
ALT ↑	2 (3)
Neutrophil count ↓	2 (3)

*One treatment-related grade 4 stroke occurred

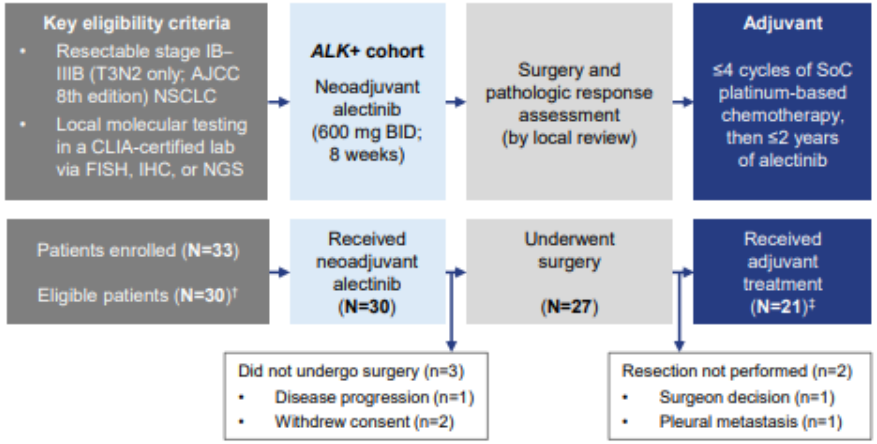
Duration of crizotinib [median (IQR)]
13.5 (3.4, 23.9) months

Reasons for treatment discontinuation

Reason	N=77 n (%)
Completed per protocol	31 (40)
Adverse event	21 (27)
Patient withdrawal / refusal	11 (14)
Other	7 (9)
Disease recurrence	4 (5)
Other treatment started	3 (4)

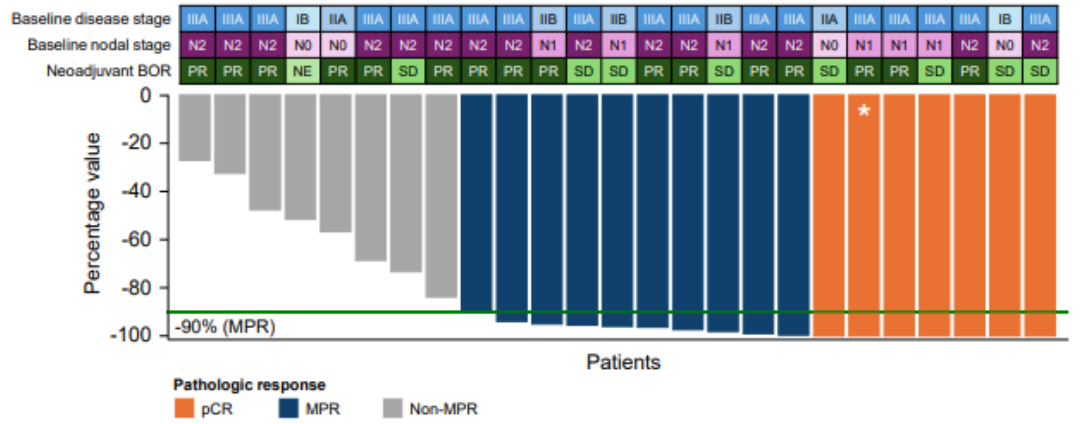
NAUTIKA1: Clinical Outcomes and Pathologic Regression with Neoadjuvant Alectinib in Resectable Stage IB–IIIB *ALK*+ NSCLC

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



Pathologic and radiographic response

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



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

Conclusions

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

MA04.02

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Otros

Survival outcome of VATS compared to open lobectomy for lung cancer
An individual patient data meta-analysis of randomised trials

- Video-assisted thoracoscopic surgery (VATS) is the most common approach for pulmonary lobectomy in early-stage lung cancer
- Widespread adoption is principally based on non-oncological benefits such as less pain, fewer complications, faster recovery and improved quality-of-life
- The oncological equivalence compared to open surgery remains assumed as no single randomised controlled trial to date has been adequately powered to detect an important difference in overall or disease-free survival
- Results from aggregate meta-analyses of predominantly non-randomized studies are limited by selection bias

- Three randomised controlled trial (RCT) included:

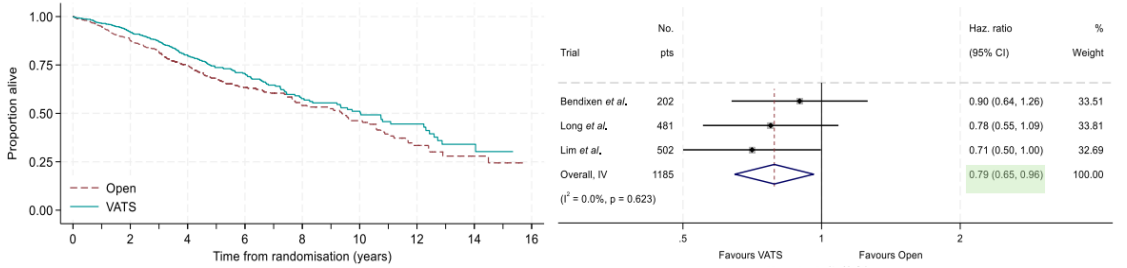
  Bendixen *et al.* (PLEACE trial, NCT01278888)

  Long *et al.* (NCT01102517)

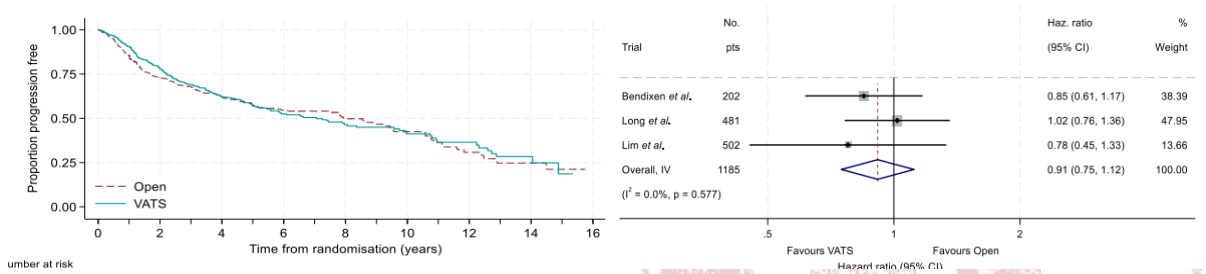
  Lim *et al.* (VIOLET trial, NCT03521375)

- 1185/1190 individual patient data obtained for all three trials - 586 randomized to VATS and 599 to open lobectomy

Primary Outcome-Overall Survival



Secondary Outcome-Disease Free Survival



PL03.13

- For the first time, we provide evidence in early-stage lung cancer, a simple change in surgical access to VATS:

  1. reduces the overall risk of death by 21%

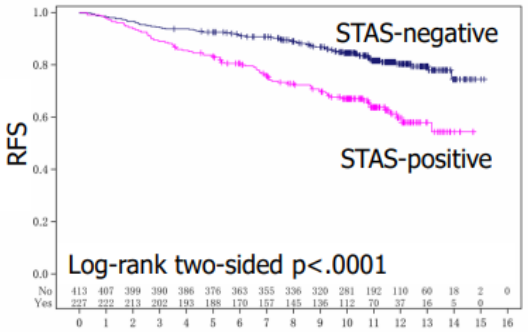
  2. without any compromise to disease-free survival

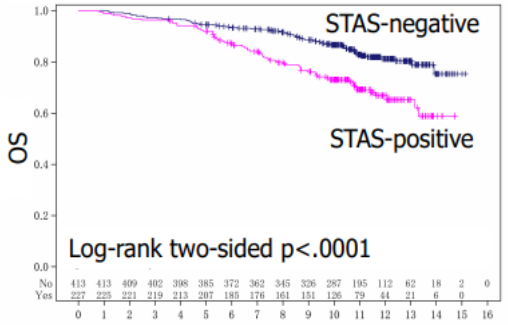
- Our results underscore the importance of prioritizing VATS (when technically feasible) as the access of choice for surgical resection of early-stage non-small cell lung cancer

Spread Through Airspaces (STAS) and Prognosis in the Phase III JCOG0802/WJOG4607L Trial of Segmentectomy vs Lobectomy in NSCLC

- Spread Through Airspaces (STAS) is a histological finding that represents an intra-alveolar invasion.
- Only a few study addressed STAS significance between lobectomy and limited resection, retrospectively.
- JCOG0802/WJOG4607L is a randomized phase III clinical trials for the patients with stage IA NSCLC, compared the patient outcome and local recurrence between lobectomy and segmentectomy.

RFS and OS by STAS status (n=640)





Pathology study cohort (n=640)

- Presence of STAS was identified as an independent prognostic factor for both RFS and OS.
- Local recurrent rate in in the tumors with STAS were higher in both lobectomy and segmentectomy subgroups.

Surgical type subgroups (lobectomy vs segmentectomy; n=321 and 318,respectively)
- STAS positive tumors had higher frequencies of local recurrences in both subgroups and distant recurrence only in segmentectomy
- Presence of STAS was confirmed to be shorter RFS in both subsets, but only shorter OS in the lobectomy subset.

Non-mucinous ADC subset assessing a histological grade (n=487)
- Grade 3 was confirmed as a poor prognostic factor for RFS and OS.
- Grade 3 demonstrated a strong association with presence of STAS
- In multivariate analysis, presence of STAS and grade 3 were both poor prognostic indicators for RFS, but only histological grade for OS.

While STAS was a negative prognostic indicator, the presence of STAS did not negate the original conclusion of the JCOG0802/WJOG4607L trial that segmentectomy was non-inferior to lobectomy in patients with stage IA NSCLC.

PL03.16

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Muchas gracias