16th CONGRESS Lung ON CANCER

BARCELONA 27 / 28 NOVEMBER 2025

GECP lung cancer research

Surgical messages from NADIM II

Ricard Ramos Izquierdo

Hospital Clinic. Barcelona

CONFLICTO DE INTERESES

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Nivolumab and Chemotherapy in Stage III Non–Small-Cell Lung Cancer

M. Provencio, E. Nadal, J.L. González-Larriba, A. Martínez-Martí, R. Bernabé, J. Bosch-Barrera, J. Casal-Rubio, V. Calvo, A. Insa, S. Ponce, N. Reguart, J. de Castro, J. Mosquera, M. Cobo, A. Aguilar, G. López Vivanco, C. Camps, R. López-Castro, T. Morán, I. Barneto, D. Rodríguez-Abreu, R. Serna-Blasco, R. Benítez, C. Aguado de la Rosa, R. Palmero, F. Hernando-Trancho, J. Martín-López, A. Cruz-Bermúdez, B. Massuti, and A. Romero

N Engl J Med 2023;389:504-513, DOI: 10.1056/NEJMoa2215530, VOL. 389 NO. 6 2023

Study Objectives

- Evaluate the efficacy and safety of

  Nivolumab + chemotherapy
  vs
  Chemotherapy alone

  } in resectable stage IIIA/IIIB NSCLC

- Key endpoints:
  - Pathological complete response (pCR)
  - Progression-free survival (PFS)
  - Overall survival (OS)

  and

  - Surgical feasibility and complications

Study Design

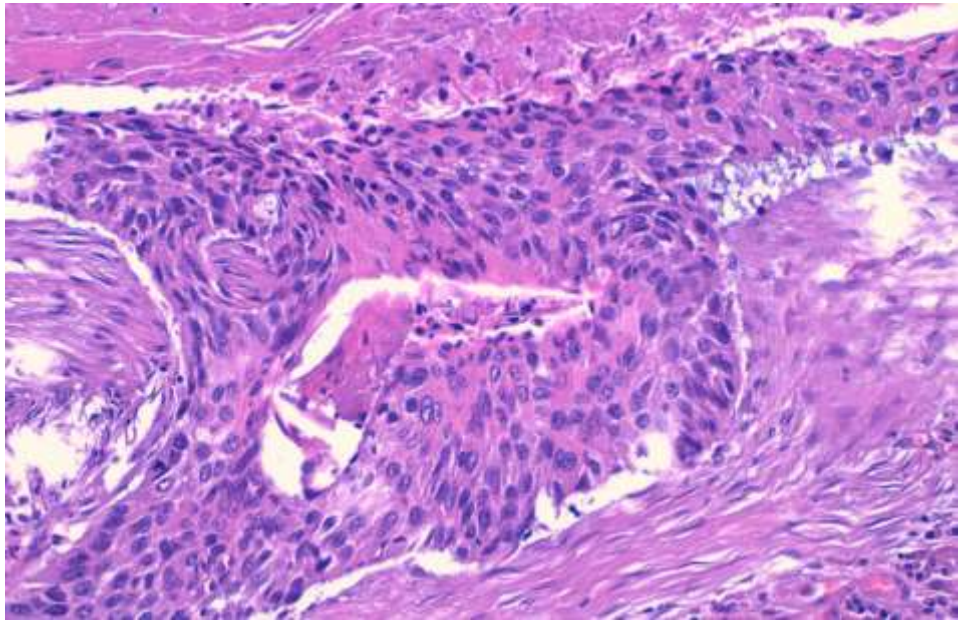
Phase 2, open-label, randomized (2:1)

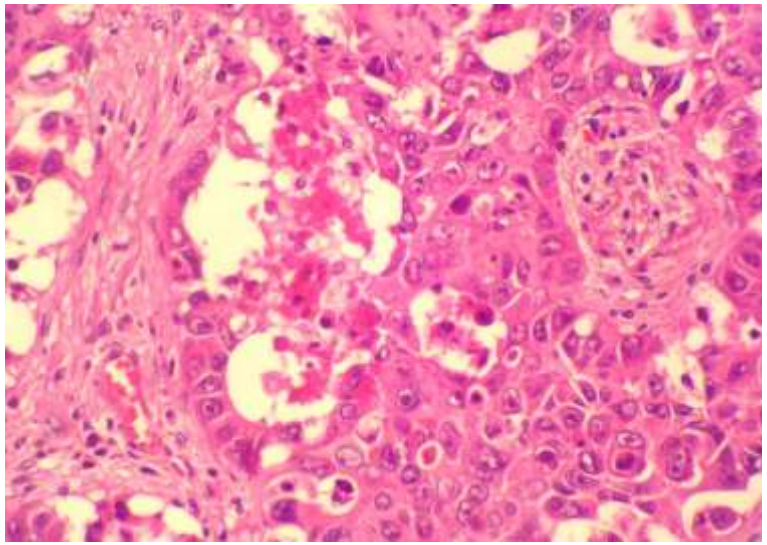
Patients with resectable stage IIIA–IIIB (T3N2) NSCLC

Treatment arms:

- Experimental:
  Nivolumab + paclitaxel + carboplatin (3 cycles)
  → surgery
  → adjuvant nivolumab (6 months)

- Control:
  Chemotherapy alone → surgery





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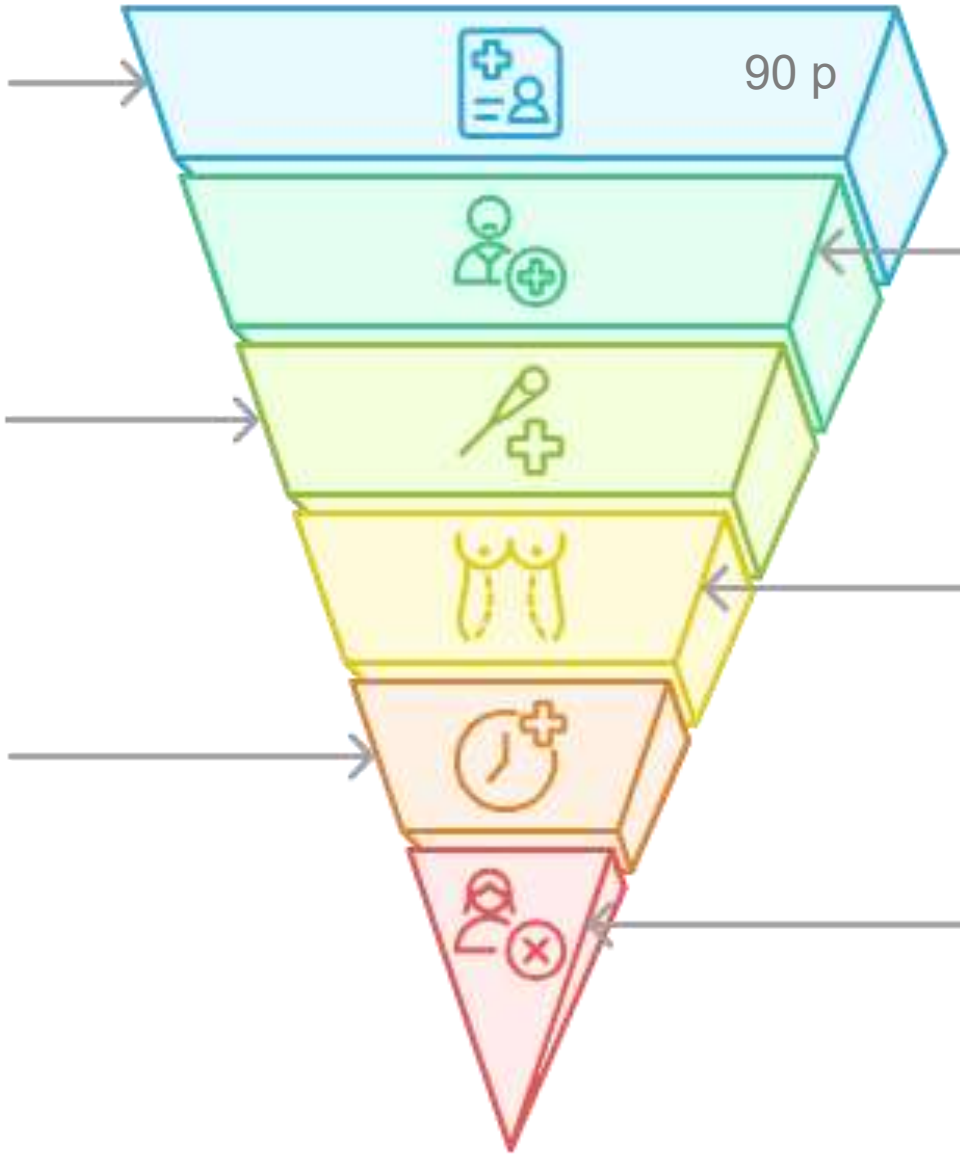
Patient Flow



Excluded Patients

4 patients excluded due to eligibility

Experimental Arm

57 patients in nivolumab + chemo group

Control Arm

29 patients in chemo alone group

Treated Patients

86 patients received treatment

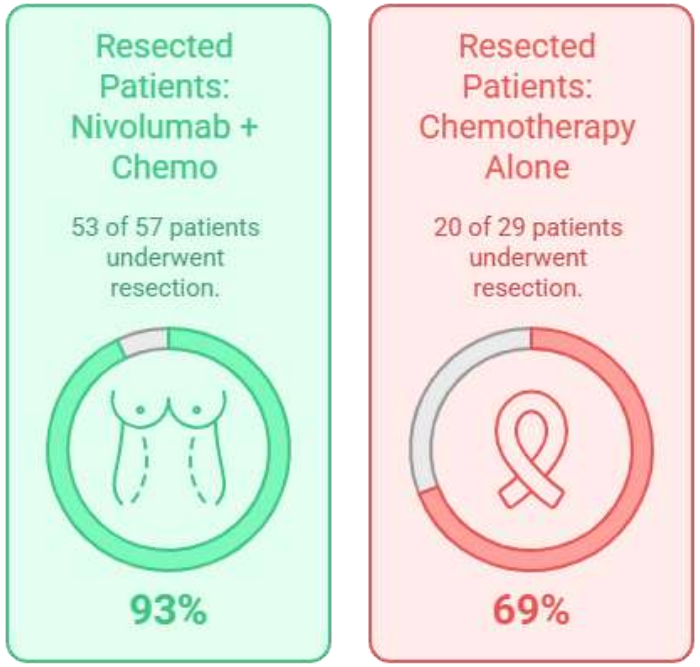
Resected Experimental

53 patients underwent resection

Resected Control

20 patients underwent resection

Resection Rates: Nivolumab + Chemo vs Chemo Alone



Nivolumab + chemotherapy significantly improves resection rates compared to chemotherapy alone.

Comparing Non-Resection Reasons in Lung Cancer Groups

Survival Outcomes

Progression-Free Survival:

Nivolumab + Chemo:

89.5% at 12 m, 67.2% at 24 m

Chemo Alone:

58.6% at 12 m, 40.9% at 24 m

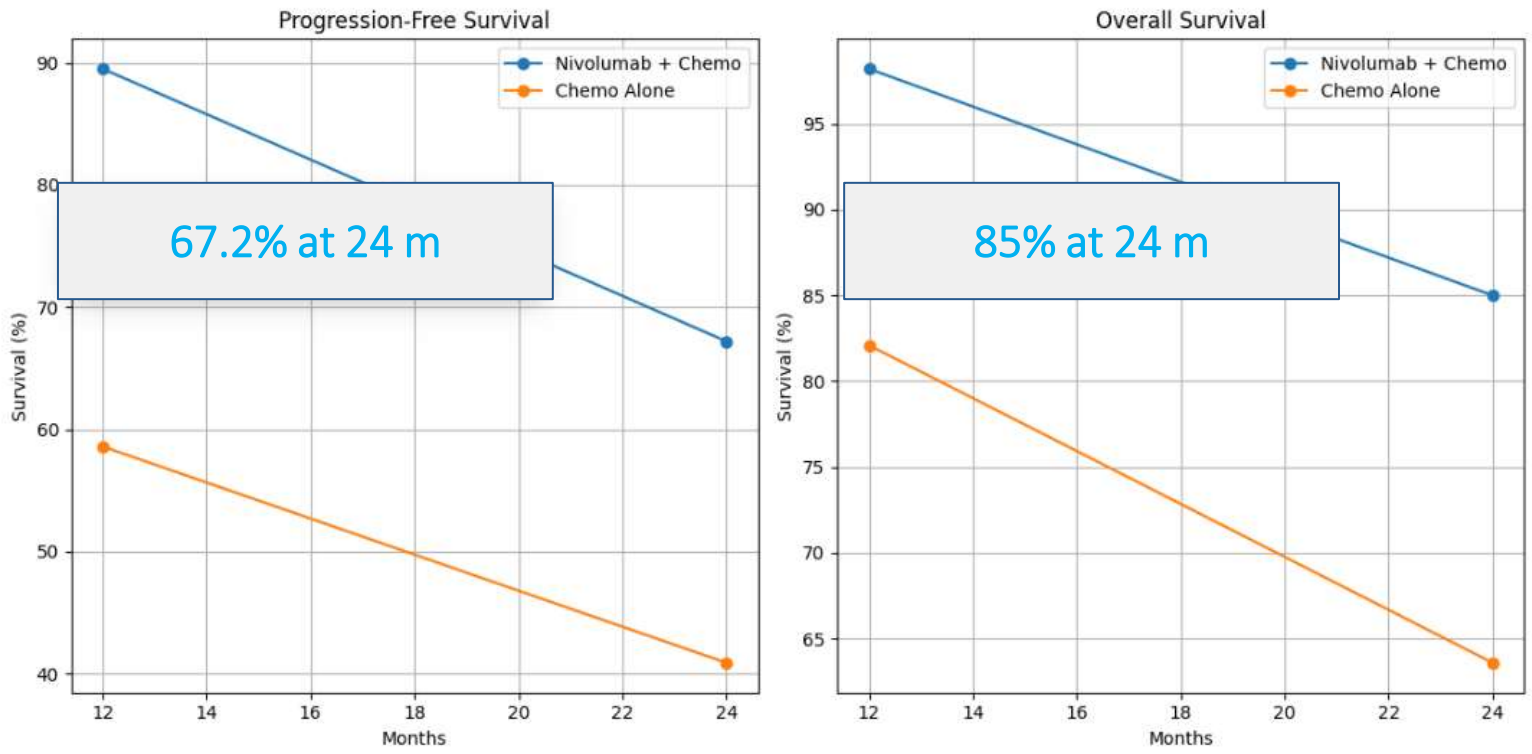
Overall Survival:

Nivolumab + Chemo:

98.2% at 12 m, 85.0% at 24 m

Chemo Alone:

82.1% at 12 m, 63.6% at 24 m



Survival Outcomes

Progression-Free Survival:
Nivolumab + Chemo:
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Overall Survival:
Nivolumab + Chemo:
98.2% at 12 m, 85.0% at 24 m
Chemo Alone:
82.1% at 12 m, 63.6% at 24 m

All patients with pCR were alive
and
progression-free at 2 years

Pathological Outcomes

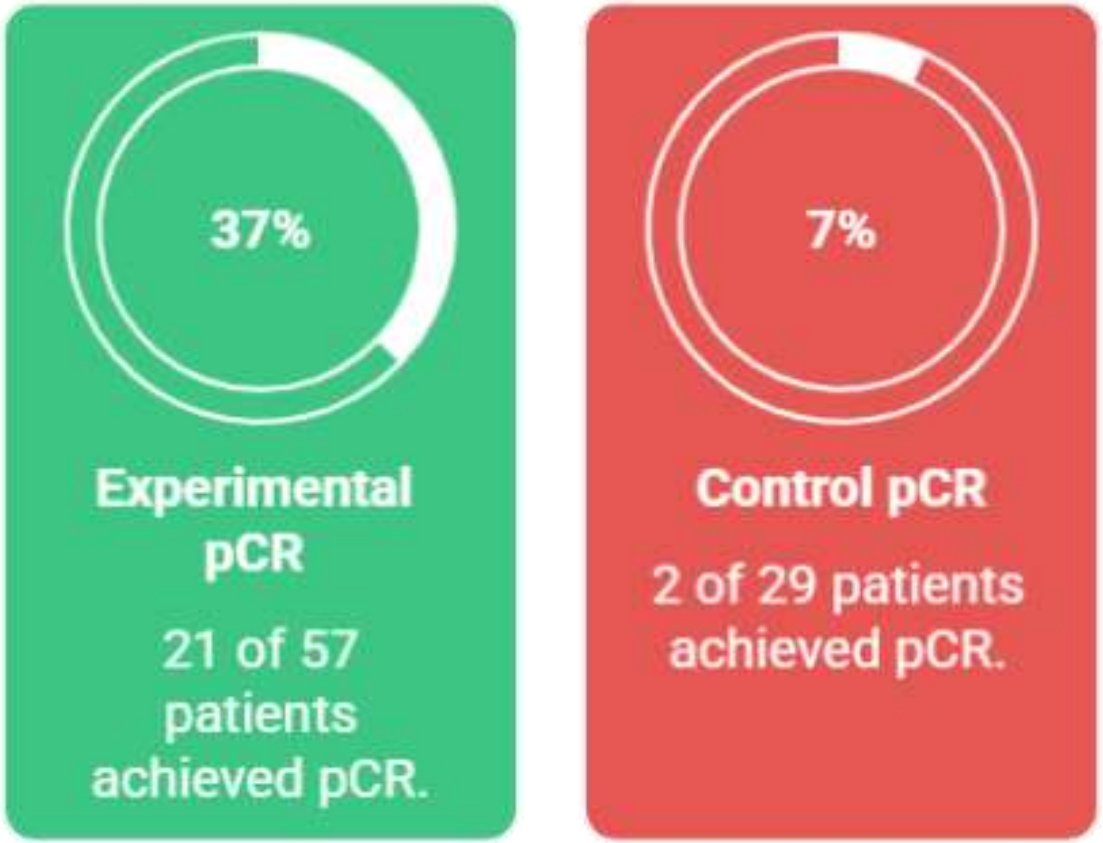
pCR (0% viable tumor):

- 37% in experimental
- 7% in control

P = 0.02

Major pathological response (≤10% viable tumor):

- 53% vs 14%



Pathological Outcomes II

Nodal downstaging

Experimental

38 patients experienced nodal downstaging.

72%

Control

8 patients experienced nodal downstaging.

40%

Tumor downstaging

Experimental

47 patients experienced T downstaging

88.7%

Control

13 patients experienced T downstaging

65%

cN2 to pN0

Experimental Clinical N2 to Pathological N0

26 of 38 patients achieved conversion

Control Clinical N2 to Pathological N0

6 of 13 patients achieved conversion

Pathological Outcomes III

Histological Changes in Lymph Nodes

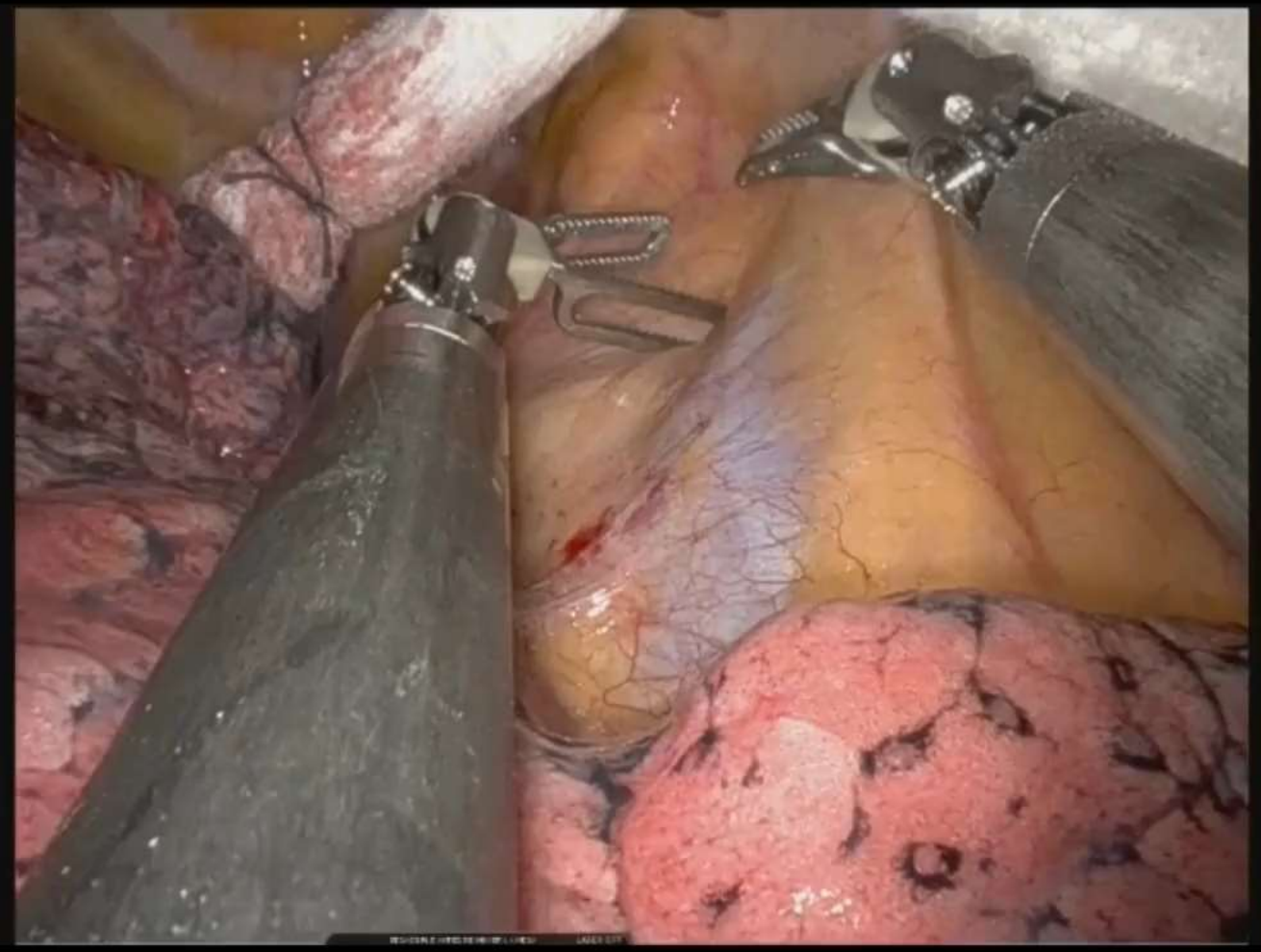
Characteristic	Control	Experimental
Yb Yes	5 (45 %)	21 (39.6 %)
No No	9 (25 %)	22 (41.5 %)
Na NA	6 (30 %)	10 (19%)

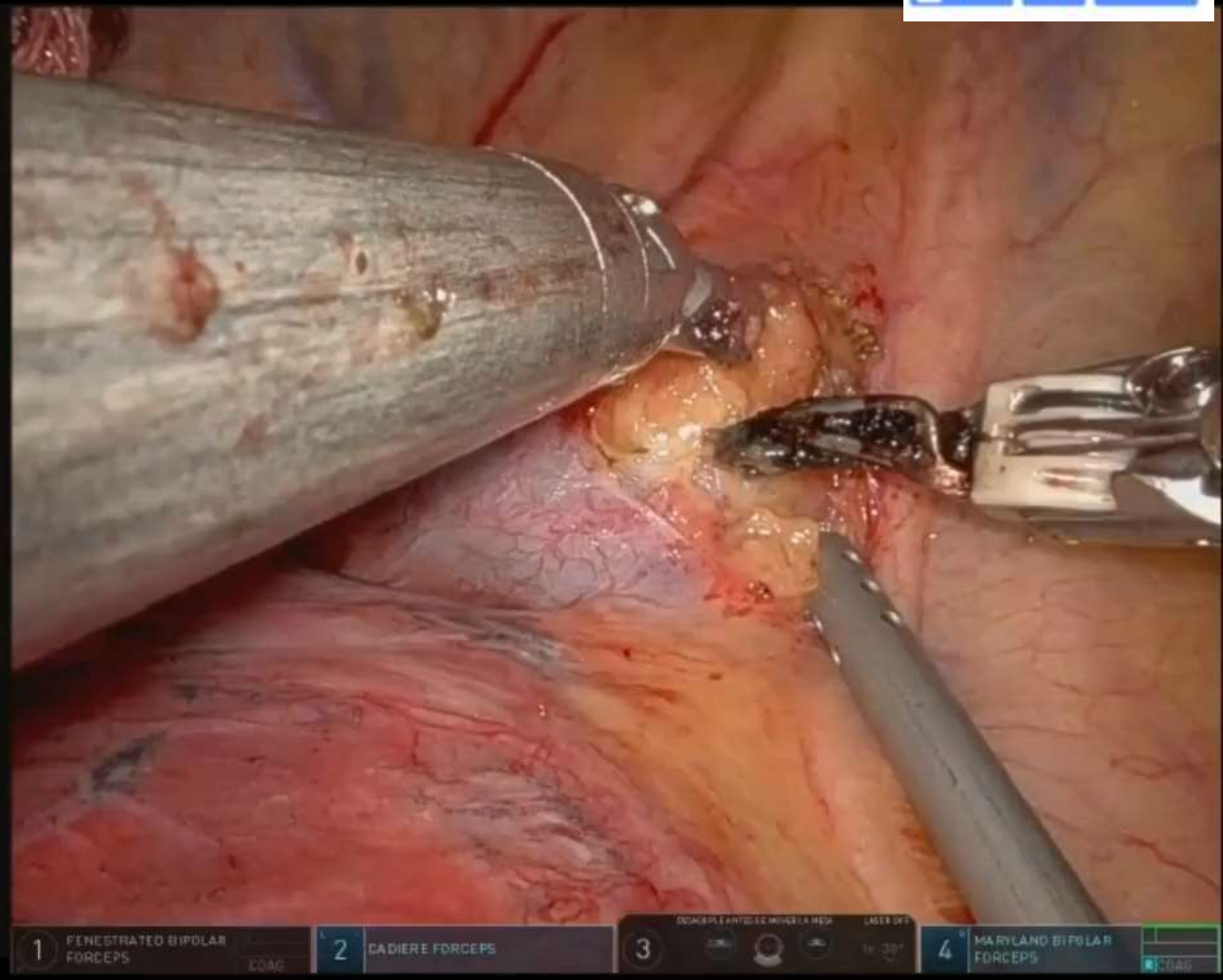
Periadventitial Fibrosis Comparison

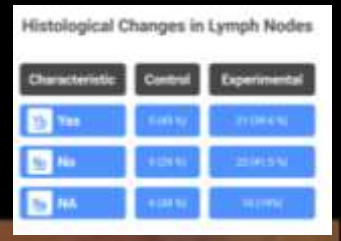
Characteristic	Control	Experimental
Yes	5 (25 %)	15 (28.3 %)
No	7 (35 %)	19 (35.8 %)
NA	8 (40 %)	19 (35.8 %)

What is the surgical viewpoint…?

Lymphadenectomy

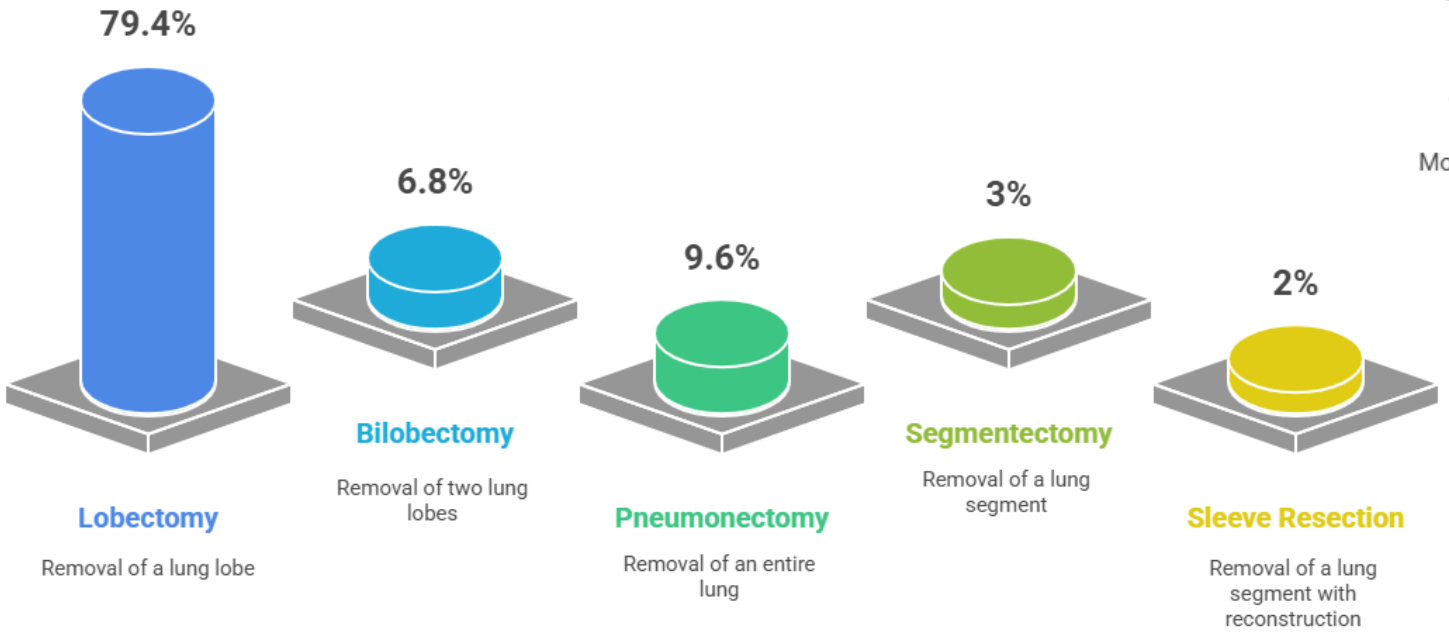


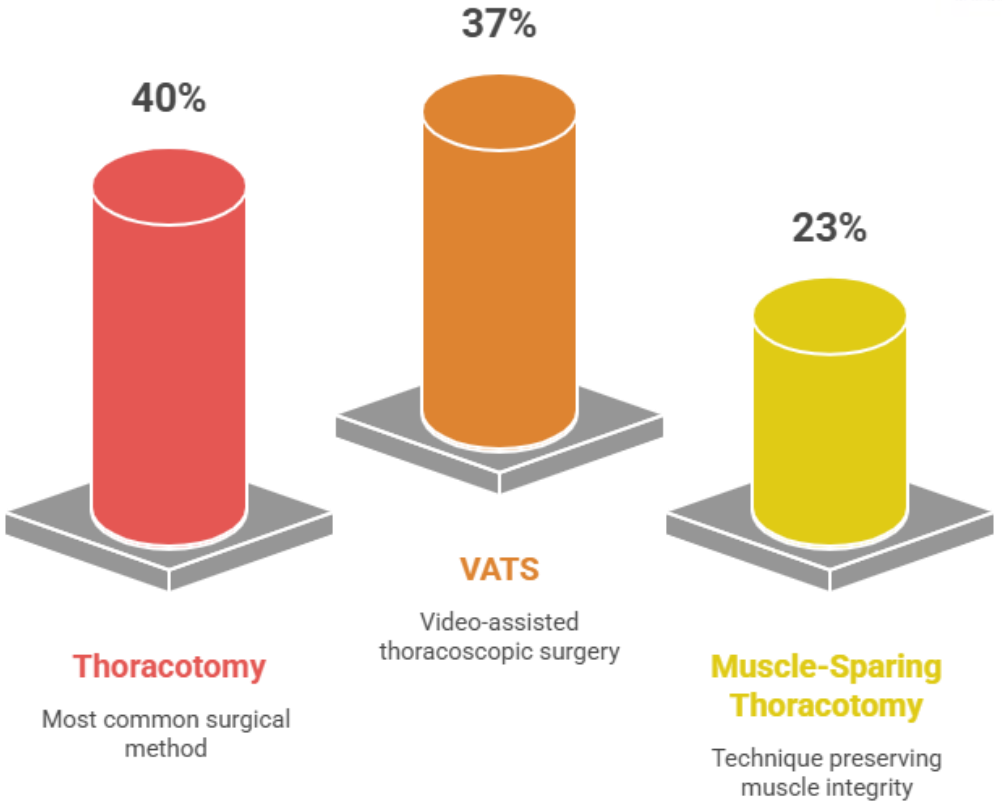




Surgical Outcomes

Comorbidity: No differences.
Pulmonary function (FEV1, DLCO): No changes after therapy.
Location: Upper lobes (64%), Right lung (73%).
Time surgery: mean 3h 37 min (90-255). Similar in both groups.





Surgical Complications

Complication	Experimental (n=53)	Control (n=20)
Chylothorax	1 (1.9%)	0 (0%)
Arrhythmia	1 (1.9%)	2 (10%)
Subcutaneous emphysema	1 (1.9%)	0 (0%)
Respiratory insufficiency	2 (3.8%)	0 (0%)
Air leakage (>5 days)	3 (5.7%)	2 (10%)
Atelectasis	1 (1.9%)	1 (5%)
Respiratory infection	3 (5.7%)	0 (0%)
Pulmonary thromboembolism	1 (1.9%)	0 (0%)
Post-surgery effusion	4 (7.5%)	0 (0%)
Pneumothorax	4 (7.5%)	0 (0%)
Other (anemia, vascular, etc.)	1 (1.9%)	2 (10%)

Characteristic	Experimental	Control	
Median Hospital Stay (Days)	7	9.16	p=0.1
Median Chest Tube Removal (Days)	5.8	10.5	
Comprehensive Complication Index	7.8	10.2	p=0.57
Mortality (30/90 Days)	1.9% pneumonectomy	0%	

Clavien–Dindo classification:

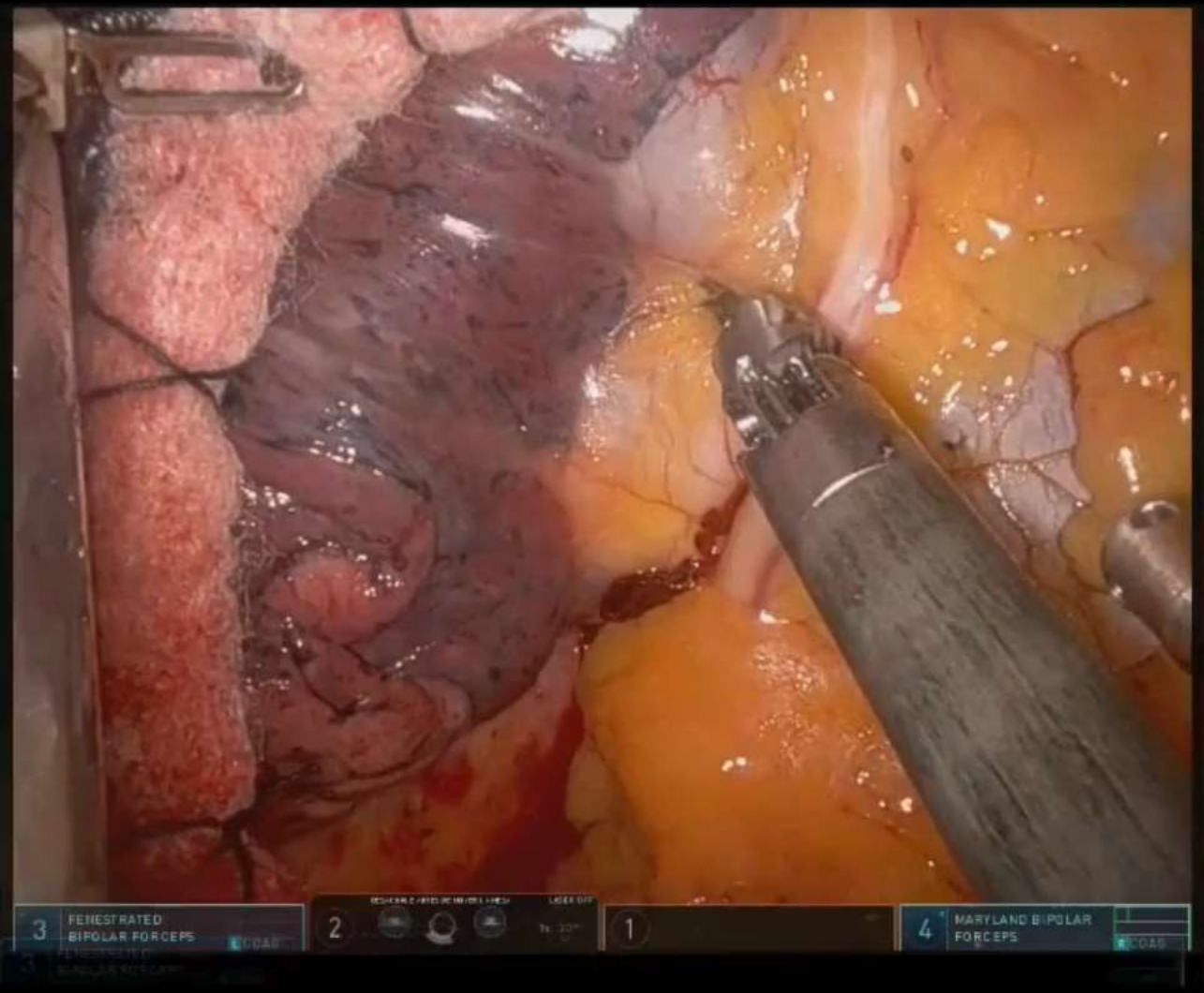
75.9% of complications were Grade I–II

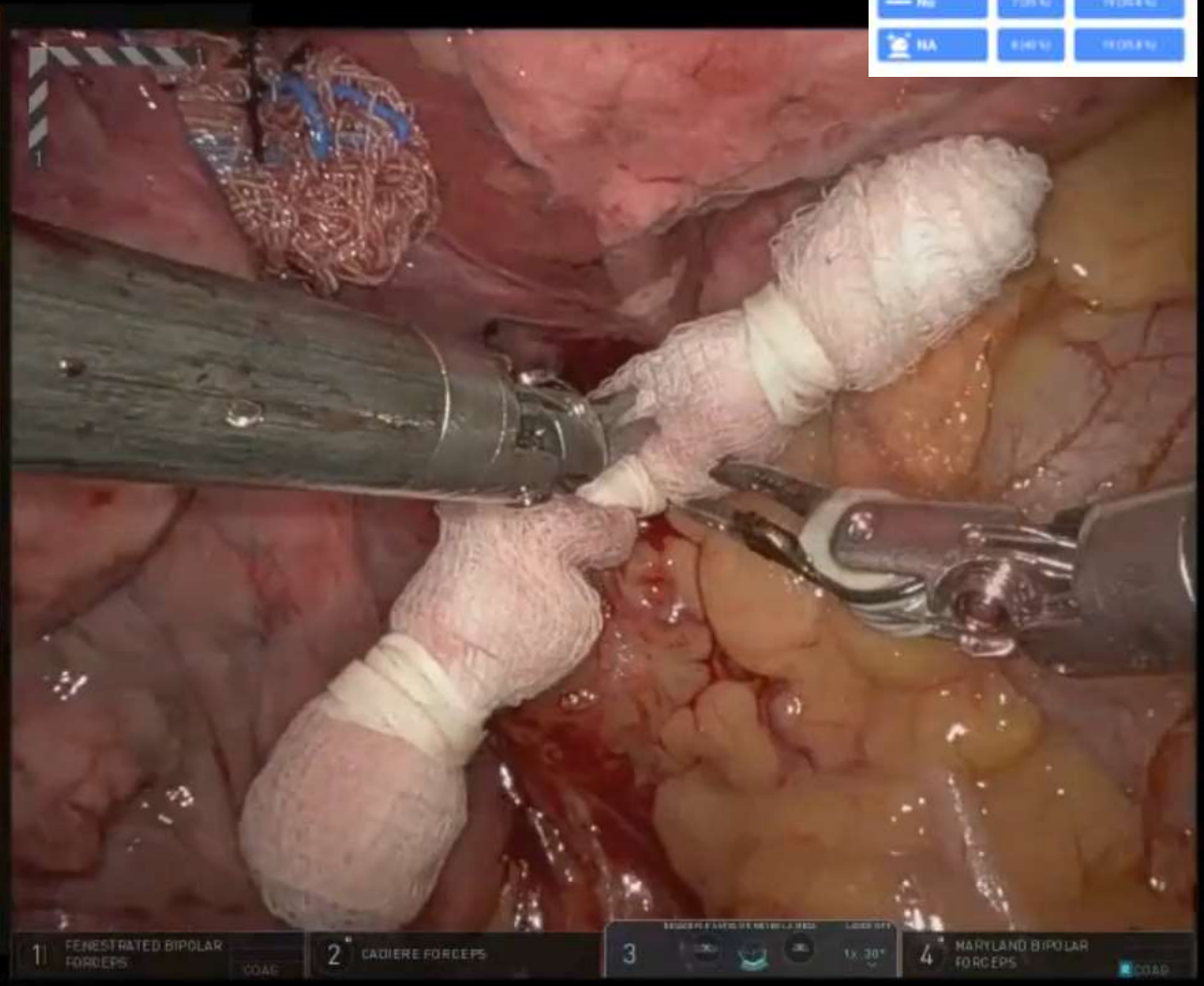
Severe cases:

- Grade IIIB: 1 case (required surgical intervention under general anesthesia).
- Grade IVB: 1 case (multi-organ dysfunction requiring ICU).

Both severe cases occurred in the experimental group.

Lobectomy





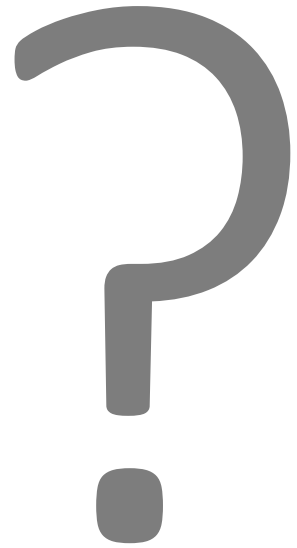
Oncological Quality of Surgery

Median time from the end of neoadjuvant treatment to surgery: **7 weeks (range, 2 to 9)**
No differences between trial groups

We performed a hilar and mediastinal lymphadenectomy according to the criteria of IASLC

≥6 lymph nodes

≥3 mediastinal including subcarinal and
≥3 hilar/intrapulmonary



Oncological Quality of Surgery II

Average N1 nodes resected: 5.1 (range 0–29)
Average N2 nodes resected: 9.6 (range 1–32)
Total nodes: 14.63 (range 2–48)

Lymph node counts are pathologist-dependent

Oncological Quality of Surgery II

Average N1 nodes resected: 5.1 (range 0–29)
Average N2 nodes resected: 9.6 (range 1–32)
Total nodes: 14.63 (range 2–48)

Lymph node counts are pathologist-dependent

73 p

- 42 p (58%): fullfill IASLC criteria
- 31 p (42%): Do not fullfill IASLC criteria
  - 22 p: < 3 LN
  - 2 p: No Biopsy N7
  - 3 p: No biopsy N7 + < 3 N1 + <3 N2
  - 3 p: No biopsy N7 + <3 N2
  - 1: No biopsy N7 + < 3 N1

Oncological Quality of Surgery III

Average N1 nodes resected: 5.1 (range 0–29)
Average N2 nodes resected: 9.6 (range 1–32)
Total nodes: 14.63 (range 2–48)

73 pacients

42 p (58%): fullfill IASLC criteria

31 p (42%): Do not fullfill IASLC criteria

Uncertain resection:
42%

Conclusions I

- **Surgical management** in patients included in the NADIM II trial was **safe and feasible**.

- **No significant differences in surgical complexity** or operative time were observed between treatment arms.

- **Hospital stay and chest tube duration** tended to be longer in the chemotherapy-only group.

- The incidence and severity of **postoperative complications were comparable** across both neoadjuvant strategies; most were Clavien–Dindo grade I–II.

Conclusions II

- 30-day and 90-day postoperative **mortality was 1.4%, confirming low early mortality**.

- According to IASLC lymph node assessment criteria, **42% of resections did not meet** the standard, highlighting room for improvement in mediastinal staging.

- **Combining immunotherapy with surgery** is essential for optimal outcomes, despite potentially **more complex procedures**.

- These findings support continuing along this therapeutic pathway, and **thoracic surgeons must ensure complete resection and a systematic lymphadenectomy** following IASLC oncological standards.

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THANK YOU

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