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Multidisciplinary Perspectives on the Current and Emerging Treatment Landscape of Lung Cancer I: What Do Your Cross-Functional Colleagues Need to Know?

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Why Collaborate

1. Complex Problems Need Diverse Perspectives
Medical issues often involve biological, psychological, social, and environmental factors. A single-discipline approach may miss key pieces of the puzzle.

2. Innovation Happens at the Intersections
Breakthroughs often emerge when different fields overlap. For instance:
- **AI researchers + radiologists** = powerful diagnostic tools that detect disease faster and more accurately.
- **Engineers + surgeons** = development of robotic-assisted surgeries or advanced prosthetics.

3. Better Data, Better Decisions
Modern medical research often involves **huge datasets**—genomics, electronic health records, wearables, etc. Collaborations with **data scientists, statisticians, and informatics experts** are essential to analyze and interpret this data accurately

4. From Bench to Bedside
Translational research—the process of turning lab discoveries into clinical treatments—requires collaboration between scientists and varied clinicians

5. Better Patient Care

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MultiD Care in Lung Cancer

Lung cancer patients require multidisciplinary care

Regardless of stage

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Select Neoadjuvant/Periop IO Trials

Trial Name	Phase	Population	Treatment Regimen	Key Outcomes
NADIM	Phase 2	Stage IIIA NSCLC	Neoadjuvant paclitaxel, carboplatin, nivolumab; adjuvant nivolumab	5-year OS: 69.3%, PFS: 65.0%
NADIM II	Phase 2	Stage IIIA/IIIB NSCLC	Neoadjuvant nivolumab + chemotherapy; adjuvant nivolumab	Improved pCR, PFS, OS vs. chemotherapy alone
CheckMate 816	Phase 3	Stage IB-IIIA NSCLC	Neoadjuvant nivolumab + chemotherapy	Improved pCR, EFS
AEGEAN	Phase 3	Stage II-III NSCLC	Perioperative durvalumab + chemotherapy	Improved EFS, pCR
KEYNOTE-671	Phase 3	Stage IIA-IIIB NSCLC	Perioperative pembrolizumab + chemotherapy	Improved OS, EFS
CheckMate 77T	Phase 3	Stage IIA-IIIB NSCLC	Perioperative nivolumab + chemotherapy; adjuvant nivolumab	Improved EFS, pCR, OS

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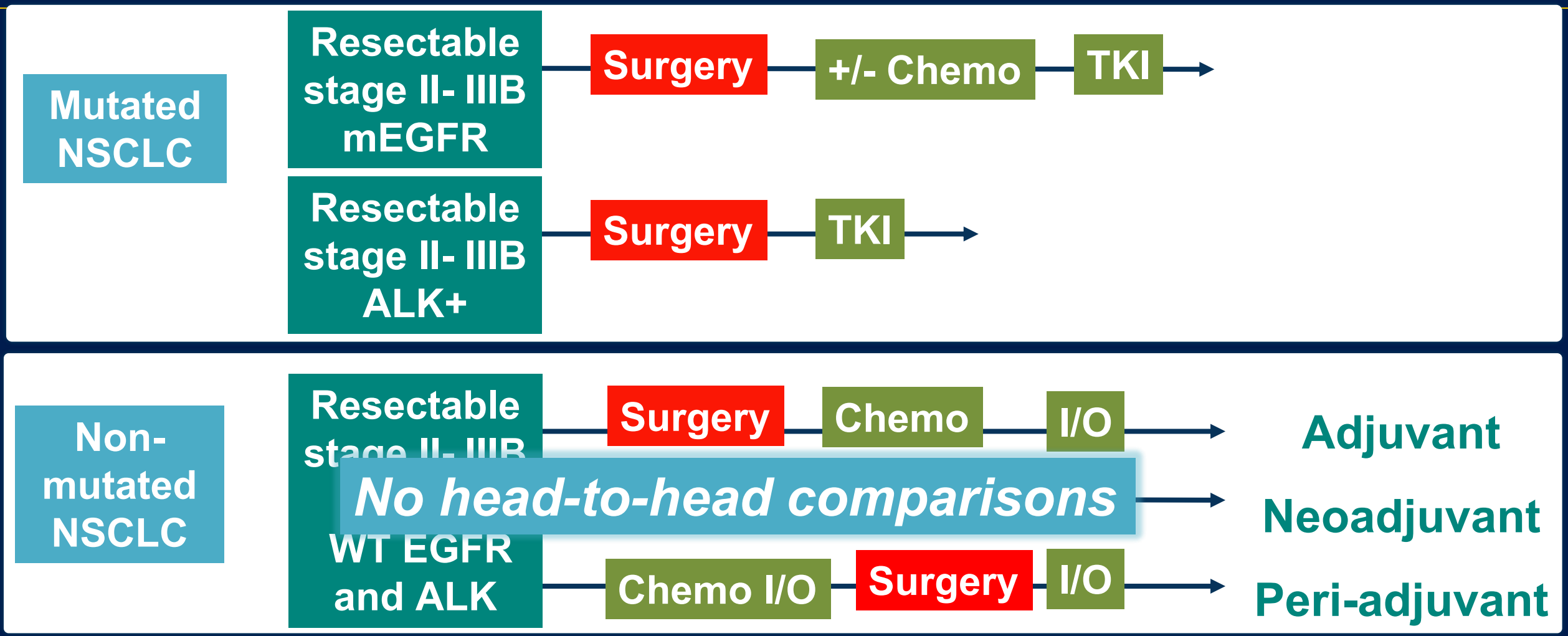
Approved Approaches for Resectable Stage II and III NSCLC



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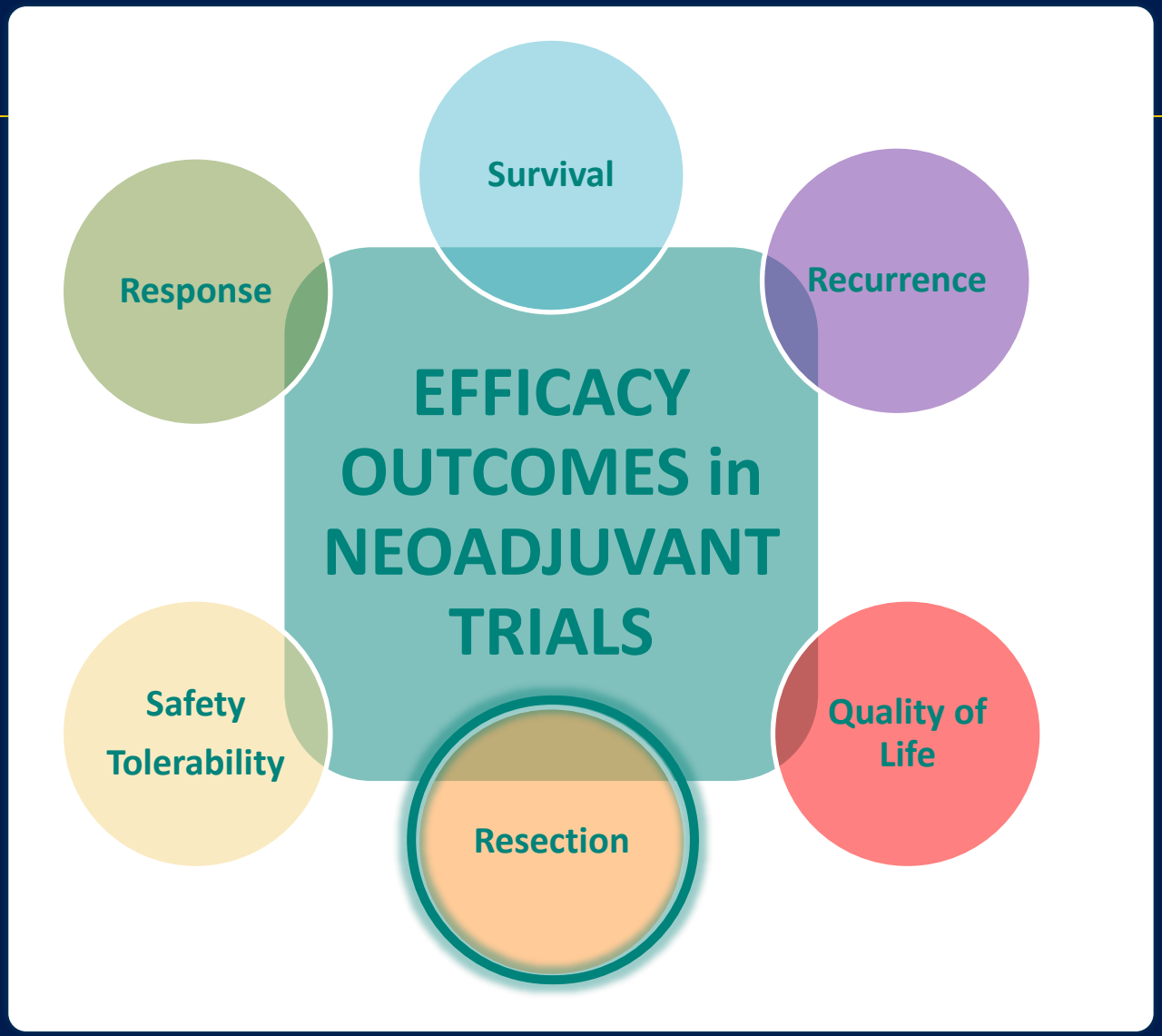

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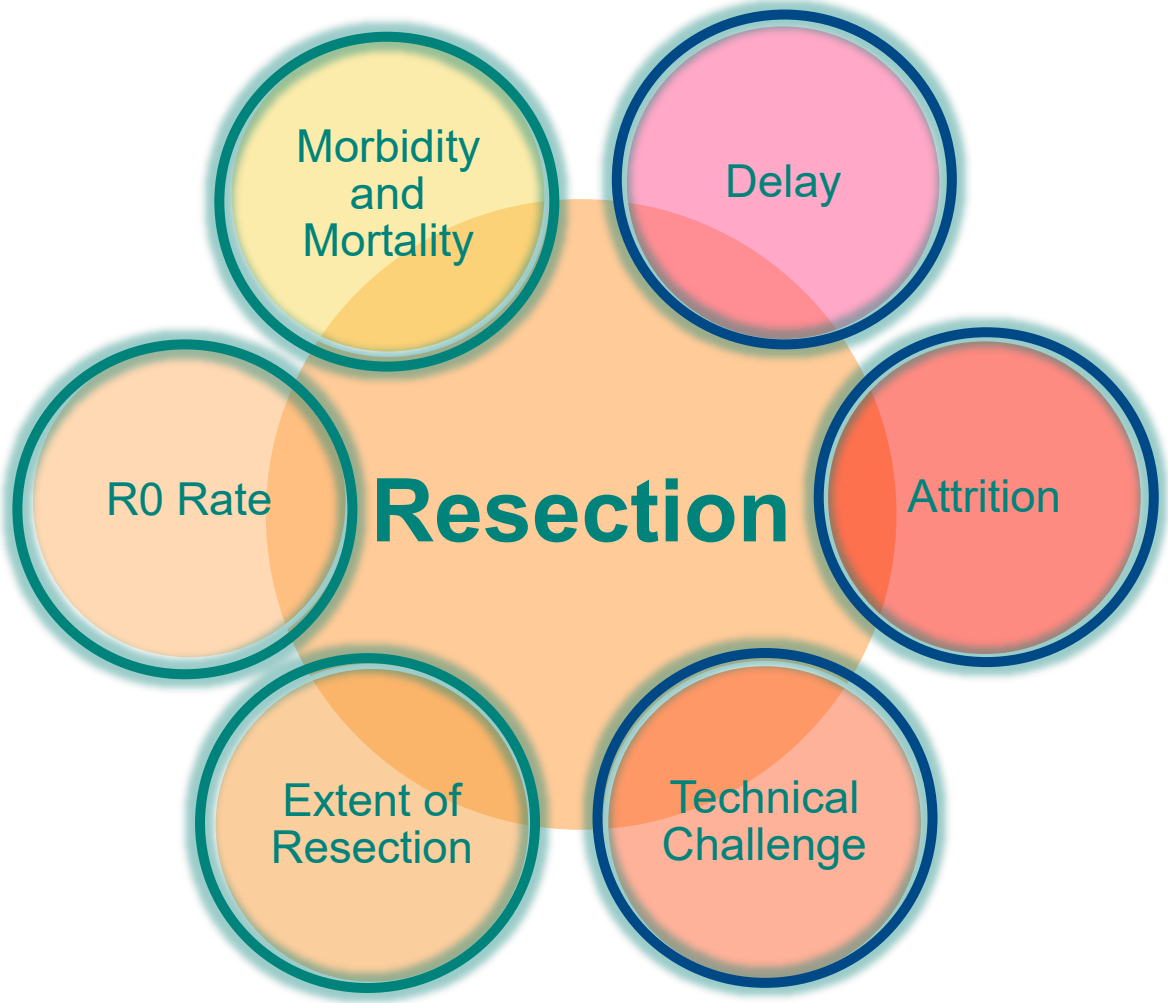
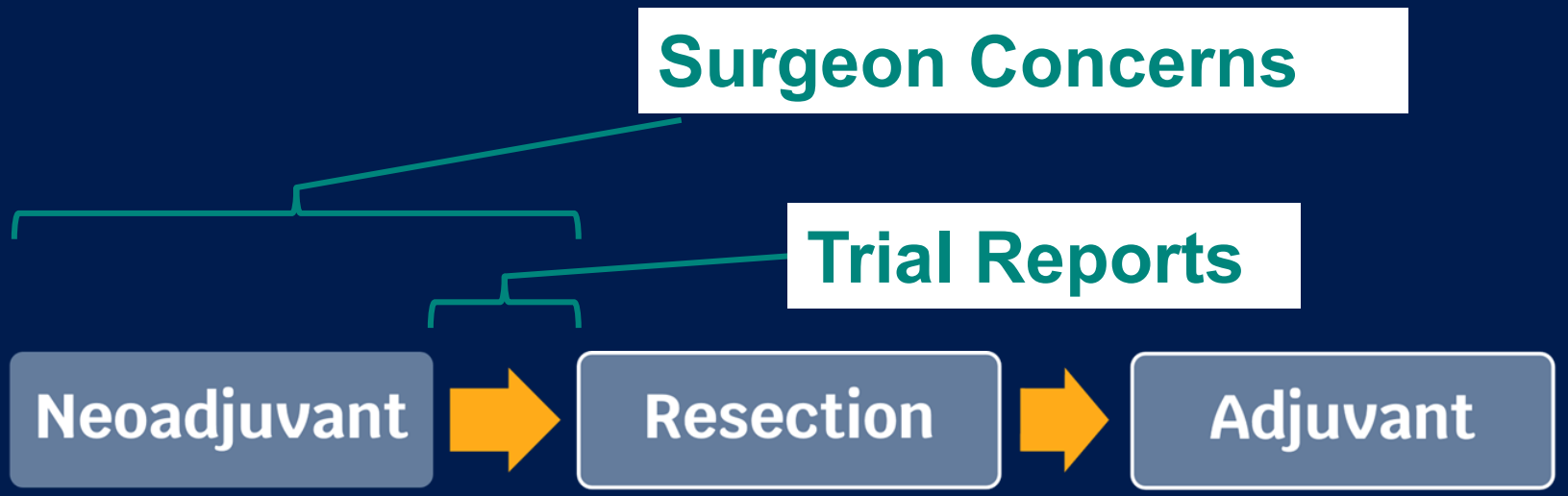


- Surgical attrition included in EFS endpoints
- Few other surgical endpoints consistently included as key pre-specified outcomes or reported at all
- Early data on M&M, R0 and extent resection encouraging others are troublesome

Delays



Neoadjuvant Therapy

- Balance between
  - •long enough to allow response
  - •not delaying control of local-regional disease

- 3-20% surgical delay across trials

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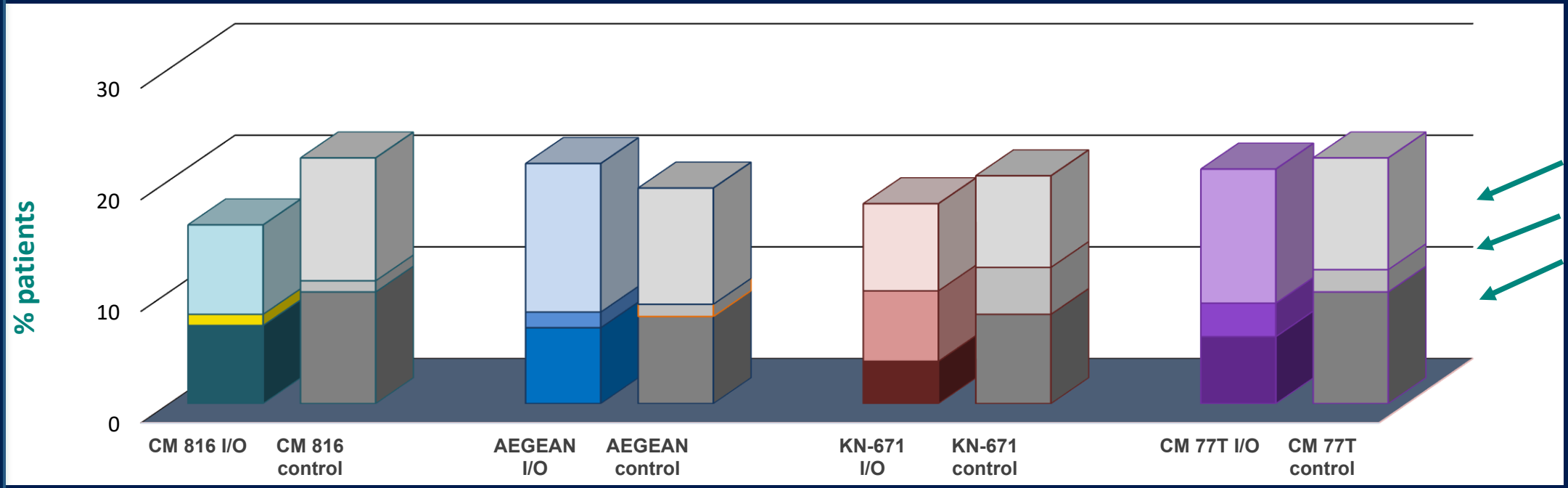
Reasons Trial Patients did NOT go to Surgery



Other?

Forde P, NEJM 2022; Heymach J, NEJM 2023: Wakelee H, NEJM 2023; Cascone T, NEJM 2024;

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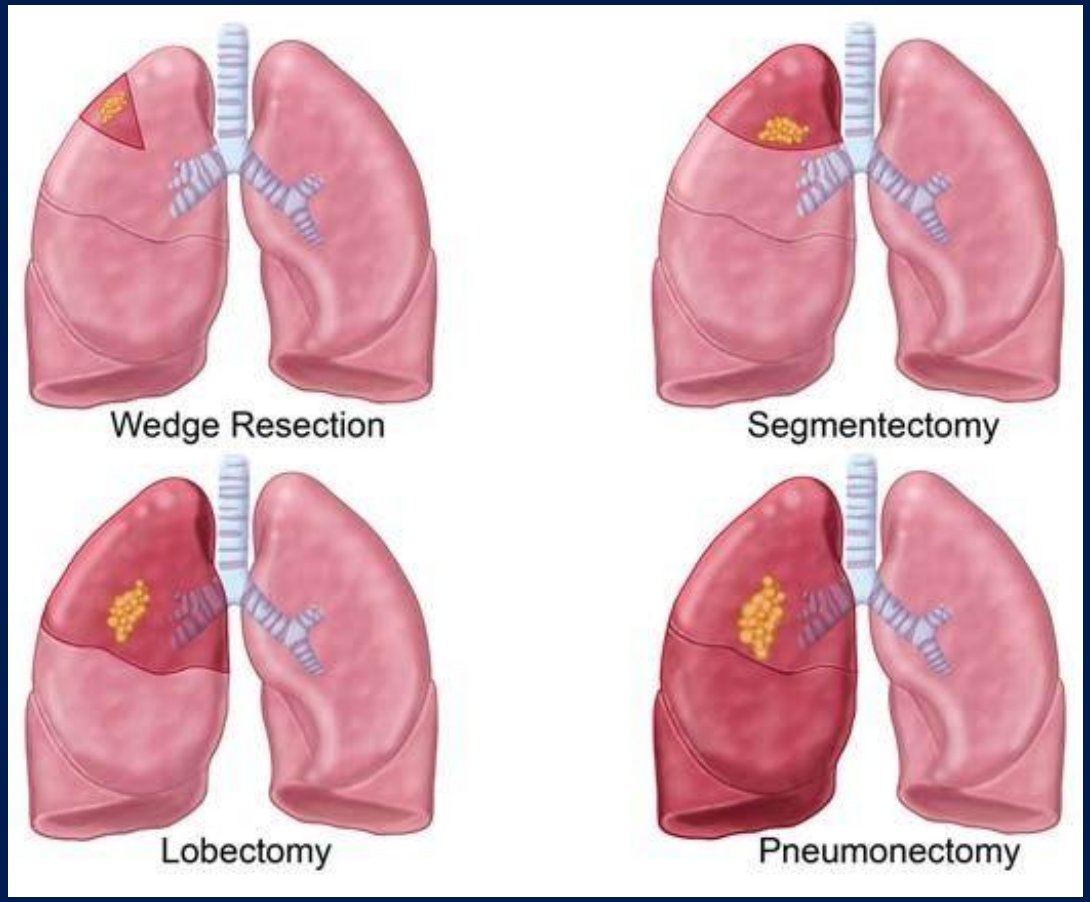
Surgical Options

- Minimally invasive surgery
  - Thoracoscopic lung resections
  - Robotic Lung Resections
- Anatomic Resections
  - Segmentectomy
  - Lobectomy
  - Pneumonectomy
- Non-anatomic resection
  - Wedge Resection



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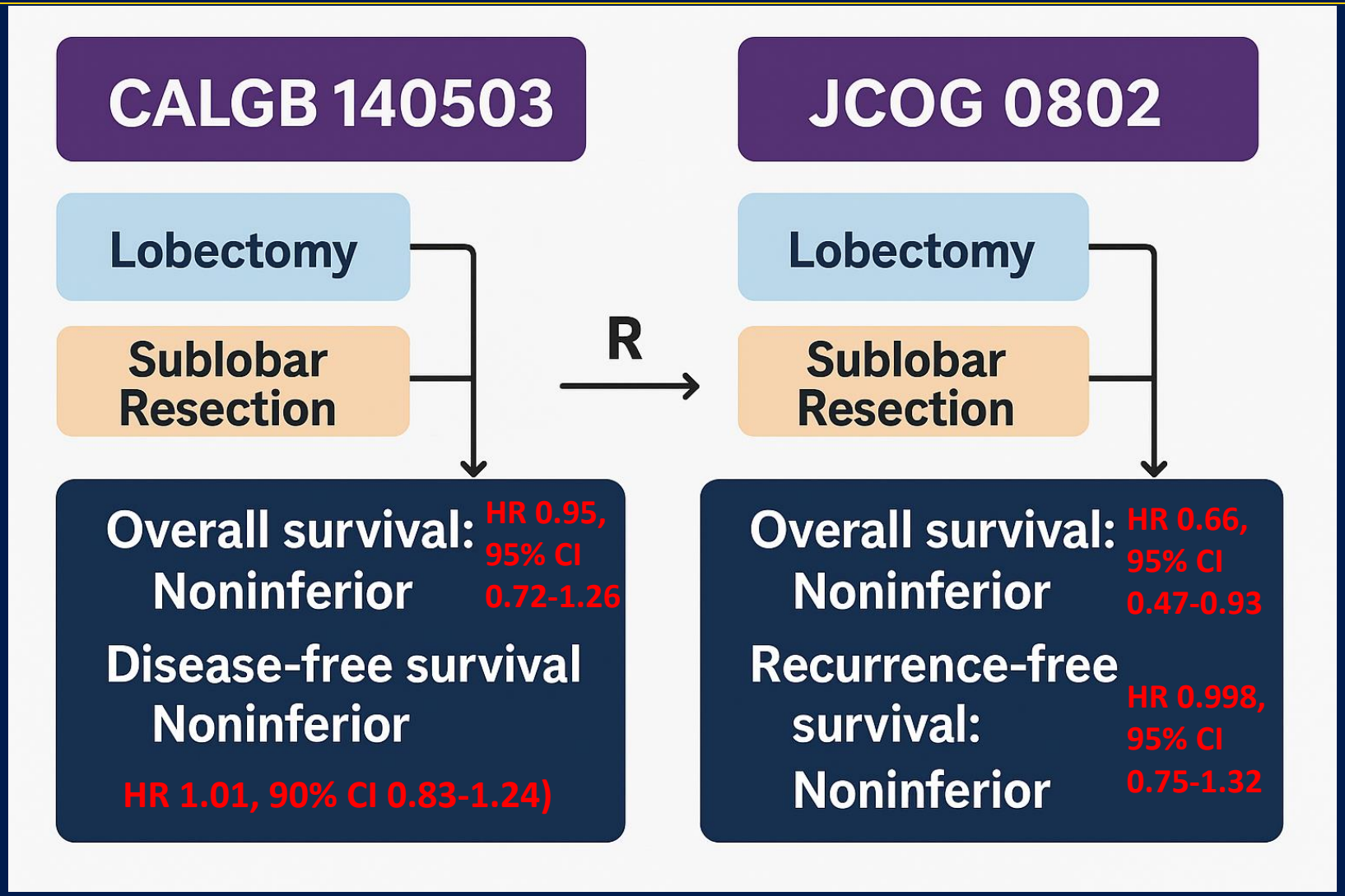
Sublobar Resection versus Lobectomy



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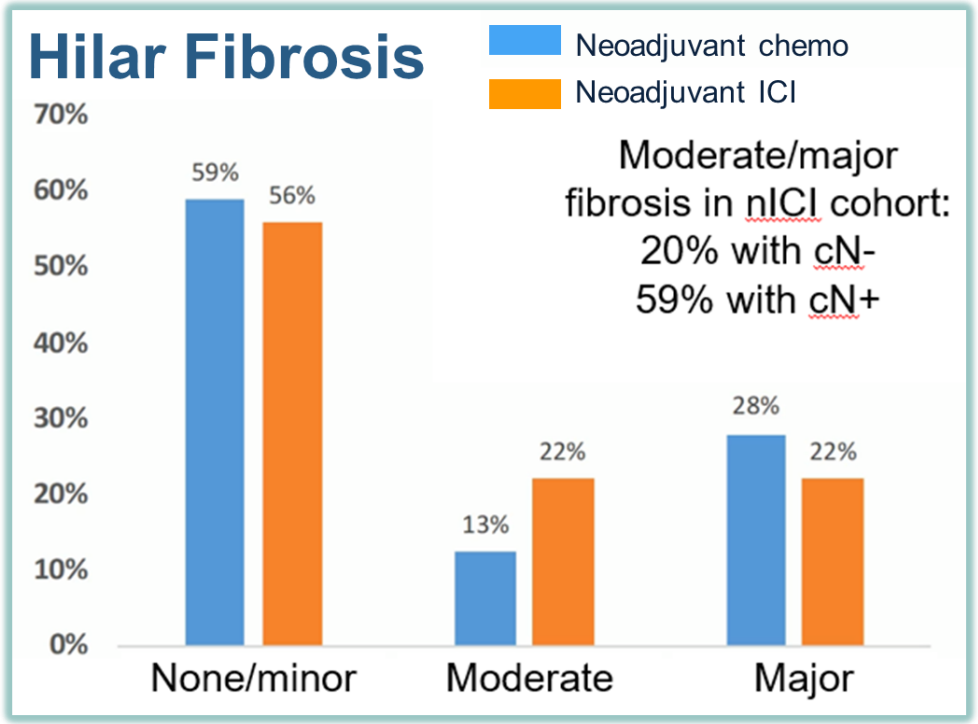
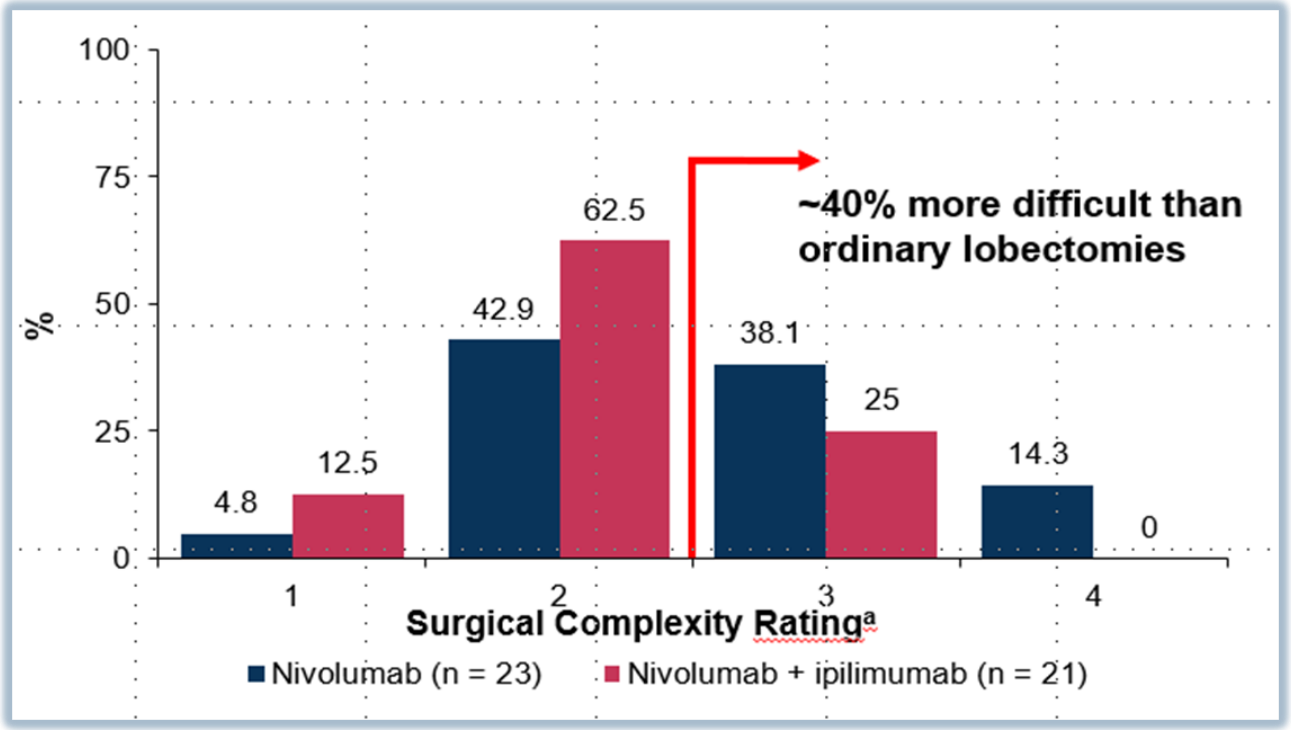
Technical Challenge Reported by Surgeons

Weill Cornell: 40% moderate-major fibrosis



MD Anderson: 40% more difficult than normal



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Surgical Outcomes: Checkmate 816

	Nivolumab plus Chemotherapy (N = 179)	Chemotherapy (N = 179)
Patients with definitive surgery* — no. (%)	149 (83.2)	135 (75.4)
Time from last neoadjuvant dose to definitive surgery — wk		
Median (IQR)	5.3 (4.6–6.0)	5.0 (4.6–5.9)
Patients with cancelled definitive surgery — no. (%)	28 (15.6)	37 (20.7)
Disease progression	12 (6.7)	17 (9.5)
Adverse event	2 (1.1)	1 (0.6)
Other†	14 (7.8)	19 (10.6)
Patients with delayed surgery‡,§ — no. (%)	31 (20.8)	24 (17.8)
Administrative reason	17 (11.4)	8 (5.9)
Adverse event	6 (4.0)	9 (6.7)
Other	8 (5.4)	7 (5.2)
Length of delay in surgery — wk		
Median (IQR)	2.0 (0.6–3.0)	2.4 (1.0–3.7)
Of patients with delayed surgery, proportion no. (%) with delay of¶		
≤2 wk	17 (54.8)	11 (45.8)
>2 and ≤4 wk	8 (25.8)	8 (33.3)
>4 and ≤6 wk	3 (9.7)	2 (8.3)
>6 wk	3 (9.7)	3 (12.5)

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Surgical Outcomes: Checkmate 816

Duration of surgery‖ — min		
Median (IQR)	185.0 (133.0–260.0)	213.5 (150.0–283.0)
Surgical approach§ — no. (%)		
Thoracotomy	88 (59.1)	85 (63.0)
Minimally invasive**	44 (29.5)	29 (21.5)
Minimally invasive to thoracotomy	17 (11.4)	21 (15.6)
Type of surgery§,†† — no. (%)		
Lobectomy	115 (77.2)	82 (60.7)
Sleeve lobectomy	2 (1.3)	10 (7.4)
Bilobectomy	3 (2.0)	4 (3.0)
Pneumonectomy	25 (16.8)	34 (25.2)
Other	24 (16.1)	21 (15.6)
Completeness of resection§ — no. (%)		
R0 (no residual tumor)	124 (83.2)	105 (77.8)
R1 (microscopic residual tumor)	16 (10.7)	21 (15.6)
R2 (macroscopic residual tumor)	5 (3.4)	4 (3.0)
Rx (unknown)	4 (2.7)	5 (3.7)
Sampled lymph nodes — median (IQR)	19 (12–25)	18.5 (10–26)
Median length of hospital stay — days (IQR)	10.0 (7.0–14.0)	10.0 (7.0–15.0)
Median length of hospital stay by surgery type — days (IQR)		
Lobectomy	10.0 (7.0–15.0)	9.0 (6.0–14.0)
Pneumonectomy	10.0 (8.0–13.0)	11.0 (9.0–16.0)
Other‡‡	8.5 (4.0–13.0)	9.0 (7.0–14.0)

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Surgical Outcomes: Checkmate 816

	Nivolumab + chemo	Chemo alone
Delayed Surgery due to treatment AE	3.4%	5.1%
Cancelled Surgery due to treatment AE	1.1%	0.6%
All Surgical Adverse Events	41.6%	46.7%
Grade Surgical 3-4 AEs	11.4%	14.8%
Grade Surgical 5 AEs	1.3%	0

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Minimally Invasive Lobectomy after Immunotherapy

Safety and feasibility of minimally invasive lobectomy after neoadjuvant immunotherapy for non–small cell lung cancer

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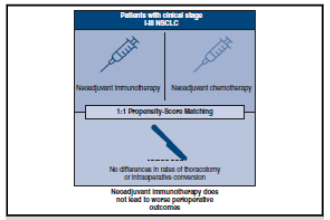
ABSTRACT

Objective: The objective of this study was to evaluate the feasibility of minimally invasive surgery (MIS) and perioperative outcomes following neoadjuvant immunotherapy for resectable non-small cell lung cancer (NSCLC).

Methods: Patients with stage I to III NSCLC treated with immunotherapy with or without chemotherapy or chemotherapy alone prior to lobectomy were identified in the National Cancer Database (2010-2018). The percentage of operations performed minimally invasively, conversion rates, and perioperative outcomes were evaluated using propensity-score matching. Propensity-score matching was also used to compare perioperative outcomes between patients who underwent an open lobectomy and those who underwent an MIS lobectomy after neoadjuvant immunotherapy.

Results: Of the 4229 patients identified, 218 (5%) received neoadjuvant immunotherapy and 4011 (95%) received neoadjuvant chemotherapy alone. There was no difference in the rate of MIS lobectomy among patients who received immunotherapy compared with those who received chemotherapy alone in propensity score–matched analysis (60.8% vs 51.6%; $P = .11$). There also were no significant differences in the rate of conversion from MIS to open lobectomy (14% vs 15%, $P = .83$; odds ratio, 1.1; 95% confidence interval, 0.51-2.24) or in nodal downstaging, margin positivity, 30-day readmission, and 30- and 90-day mortality between the 2 groups. In a subgroup analysis of only patients treated with neoadjuvant immunotherapy, there were no differences in pathologic or perioperative outcomes between patients who underwent open lobectomy and those who underwent MIS lobectomy.

Conclusions: In this national analysis, neoadjuvant immunotherapy for resectable NSCLC was not associated with an increased likelihood of the need for thoracotomy, conversion from MIS to open lobectomy, or inferior perioperative outcomes. (J Thorac Cardiovasc Surg 2023; ■:1-9)



Neoadjuvant immunotherapy does not lead to worse perioperative outcomes.

CENTRAL MESSAGE

Induction immunotherapy for stage I-III non–small cell lung cancer is not associated with increased rate of thoracotomy, increased rate of conversion, or worse perioperative outcomes.

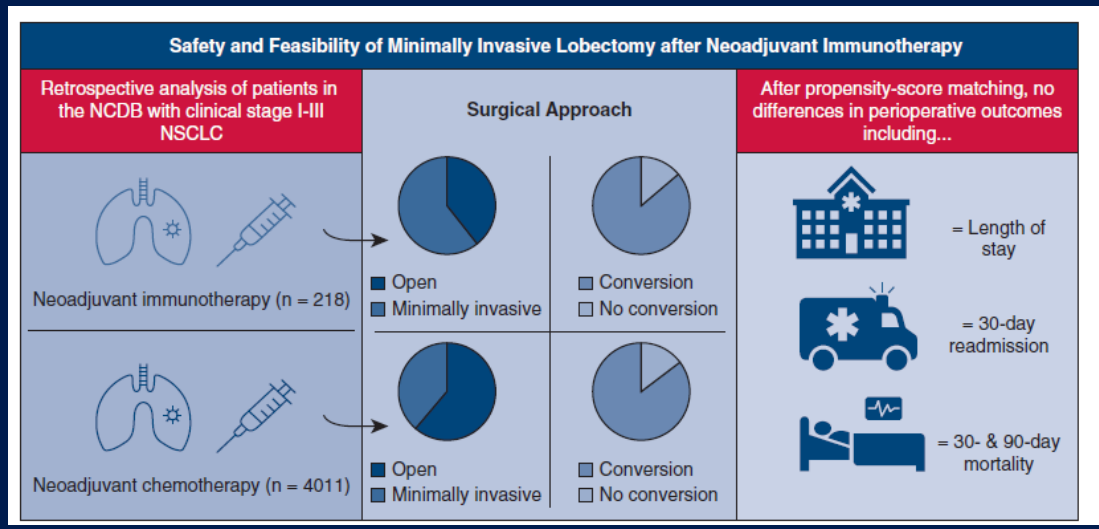
PERSPECTIVE

Although there is growing enthusiasm for induction immunotherapy in the treatment of resectable non-small cell lung cancer, some fear that this may increase the difficulty and morbidity of subsequent surgical resection. Here we report that induction immunotherapy is not associated with increased rates of thoracotomy, conversion, or worse perioperative outcomes relative to induction chemotherapy.

See Commentary on page XXX.

THOR

- NCDB analysis
- No difference in:
  - Use of MIS (60% vs 51%)
  - Conversion to open (14% vs 15%)
- No difference in:
  - Length of stay
  - Readmission
  - 30 and 90 day mortality



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In summary, multidisciplinary collaboration breaks down silos, accelerates innovation, and ensures that medical research is more comprehensive, accurate, and impactful.

Lung cancer care continues to innovate and evolve, becoming more multidisciplinary in the process.