Key Papers of 2024

Linda W Martin, MD, MPH
University of Virginia

March 6, 2025

Folder with all slides, papers

@LindaMThoracic

Disclosures – Linda Martin

Commercial Interest	**Relationship(s)**
Astra Zeneca	Advisory Board; Principal Investigator MDT-Bridge
On Target Laboratories	Steering Committee for ELUCIDATE trial
Genentech	Speakers Bureau
Ethicon	Speakers Bureau
BMS	Advisory Board

Methodology

- Review of journal sites for top papers:
  - NEJM
  - Lancet
  - JCO
  - JTO
  - Annals of Surgery
  - JAMA Surgery
- Annals of Thoracic Surgery and JTCVS sent me top cited, read papers
- Twitter
- Podcasts

Last Year – 2024

- **Lung Cancer Papers**
  - Keynote 671 – podcast 1
  - AEGEAN
  - NADIM 2 – podcast 1
  - NeoTorch Interim Report
  - ADAURA Survival Data
  - ASCO stage 3 guidelines update
  - AATS 2023 Expert Consensus Document: Staging and multidisciplinary management of patients with early-stage non–small cell lung cancer
  - LCMC3 surgical outcomes
  - Virtual reality planning for segmentectomy
  - CEACAM5 molecular imaging
- **Thoracic Videos**
  - **Top 5 CTSnet thoracic videos of 2023**
- **Esophageal Cancer Papers**
  - Omental Flaps for Anastomosis Reinforcement
  - Comparison of Gastric Ischemic Preconditioning Techniques
  - ICG imaging in thoracic and esophageal surgery
  - DICE
  - Survival Impact Of Thoracic Duct Resection
- **Benign Esophagus Papers**
  - MUSOIC study – perforation outcomes
  - Heller technique comparison over 48 years
- **Professional Topics**
  - Effect of Smoke Evacuator on Reduction of Volatile Organic Compounds and Particles in Surgical Smoke: A Randomized Controlled Trial

Today's Review: 2024-2025

- **General:**
  - Cancer Statistics 2025
  - Radiation Toxicities Review
- **Top Annals and JTCVS papers**
- **Mesothelioma:**
  - MARS 2
  - 9th edition TNM –Dr. Rusch
- **Lung Cancer:**
  - Pack-Year Smoking History Revisited
  - All 140503 papers
  - CANOPY-A
  - NADIM(1) 5 year outcomes
  - EORTC Consensus on Resectability (and STS video)
  - CheckMate 77T
  - Keynote 671 Survival Outcomes
  - ALINA – June GTSC Podcast
  - 9th edition TNM – Dr. Rusch
  - NeoAdaura – NEXT YEAR
- **Esophageal Cancer**
  - ESOPEC trial
  - Esophageal Cancer Review
  - SANO –Dr. Ferri
  - Checkmate 577 survival NEXT YEAR
  - 9th edition TNM – Dr. Hofstetter
- **Benign Esophagus**
  - Gastropexy in PEH repair
- **Professional Matters**
  - Surgeon Shortage
  - Female vs Male Surgeon Outcomes
  - Divorce Rate For Surgeons vs Nonsurgeons
  - For The Love Of the Game - Academic "Tax"

General Cancer Topics

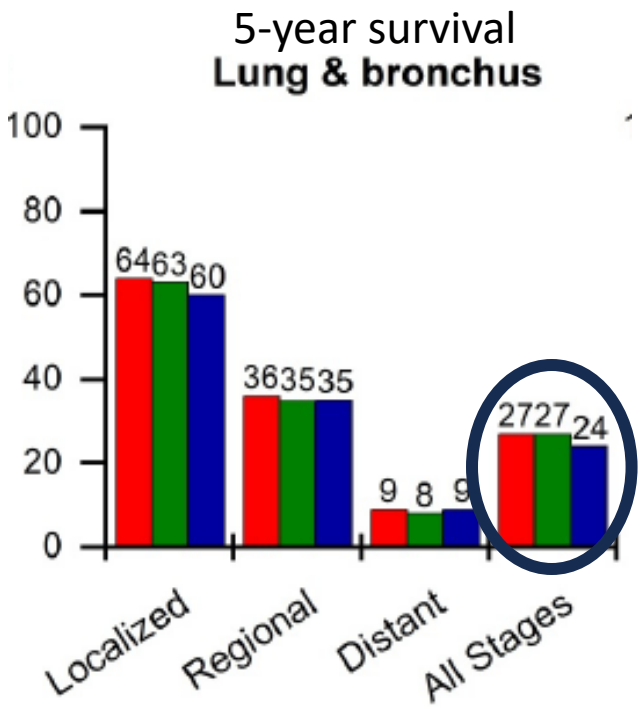
Cancer Statistics 2025

CA A Cancer Journal Jan 2025

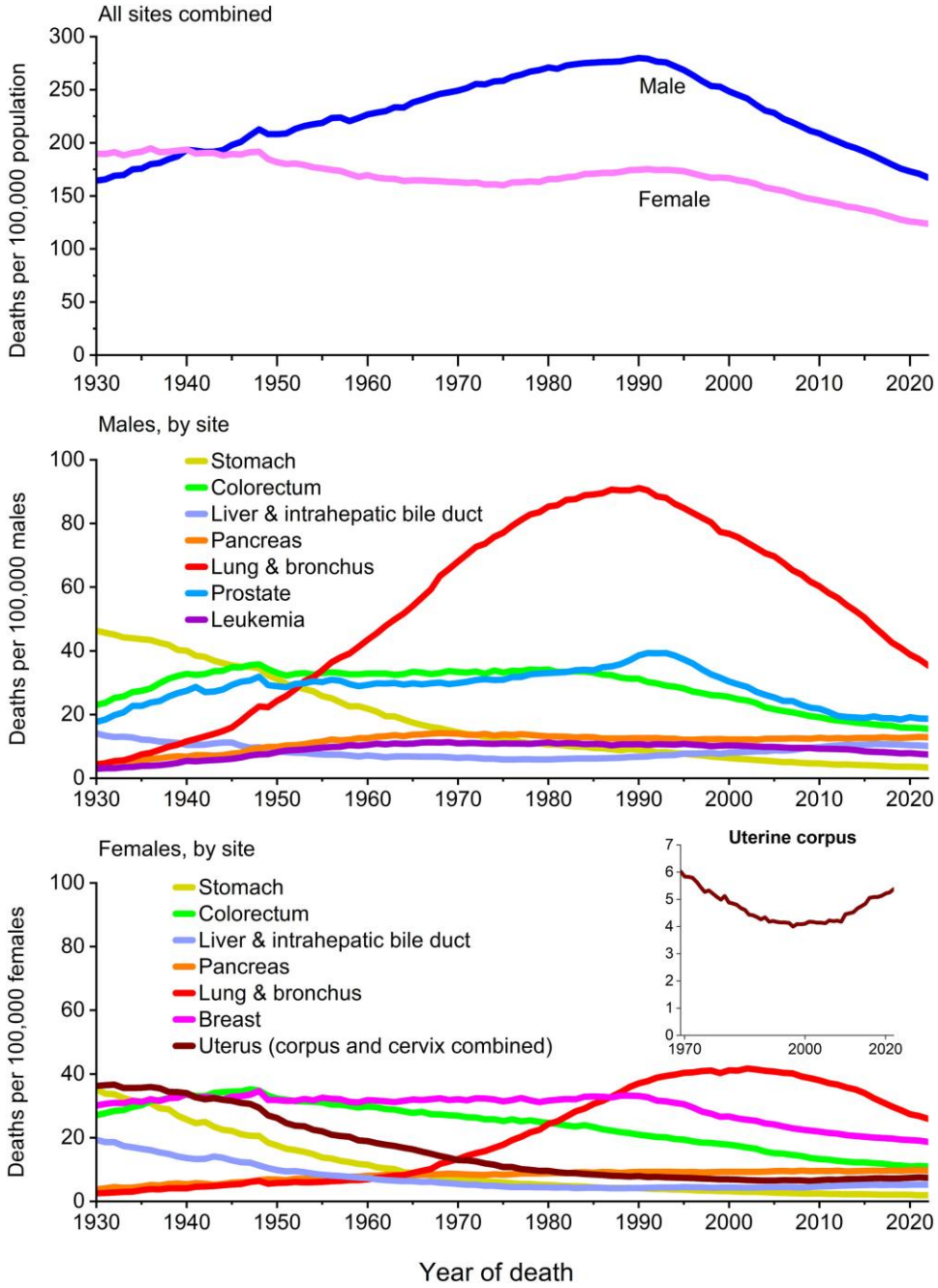
Cancer statistics, 2025

Rebecca L. Siegel MPH[1] | Tyler B. Kratzer MPH[1] | Angela N. Giaquinto MSPH[1]
Hyuna Sung PhD[1] | Ahmedin Jemal DVM, PhD[2]

- Cancer mortality down by **34%** 2022 compared to 1991
- More cancer in 50-64 age group
- More cancer in women than men
- Lung cancer incidence in women SURPASSED men:
  - 115,9870 vs. 110,680
- NO LONGER more lung cancer deaths than breast/prostate/colon combined!



15% when I started practice



CA Cancer J Clin. 2025;75:10–45.

Radiation Toxicities - Review

Lancet January 2025

Radiotherapy toxicities: mechanisms, management, and future directions

Ioannis I Verginadis, Deborah E Citrin, Bonnie Ky, Steven J Feigenberg, Alexandros G Georgakilas, Christine E Hill-Kayser, Constantinos Koumenis, Amit Maity, Jeffrey D Bradley, Alexander Lin

Lancet 2025; 405: 338–52
Published Online January 16, 2025
https://doi.org/10.1016/S0140-6736(24)02319-5

Department of Radiation Oncology (I I Verginadis PhD, Prof S J Feigenberg MD, Prof C Koumenis PhD, Prof J D Bradley MD, Prof A Lin MD,

For over a century, radiotherapy has revolutionised cancer treatment. Technological advancements aim to deliver high doses to tumours with increased precision while minimising off-target effects to organs at risk. Despite advancements such as image-guided, high-precision radiotherapy delivery, long-term toxic effects on healthy tissues remain a great clinical challenge. In this Review, we summarise common mechanisms driving acute and long-term side-effects and discuss monitoring strategies for radiotherapy survivors. We explore ways to mitigate toxic effects through novel technologies and proper patient selection and counselling. Additionally, we address policies and management strategies to minimise the severity and impact of toxicity during and after treatment. Finally, we examine the potential advantages of emerging technologies and innovative approaches to improve conformity, accuracy, and minimise off-target effects.

Part of being a cancer surgeon is understanding other modalities used in cancer treatment

-great review of evolution of radiation techniques, toxicities, how to minimize them

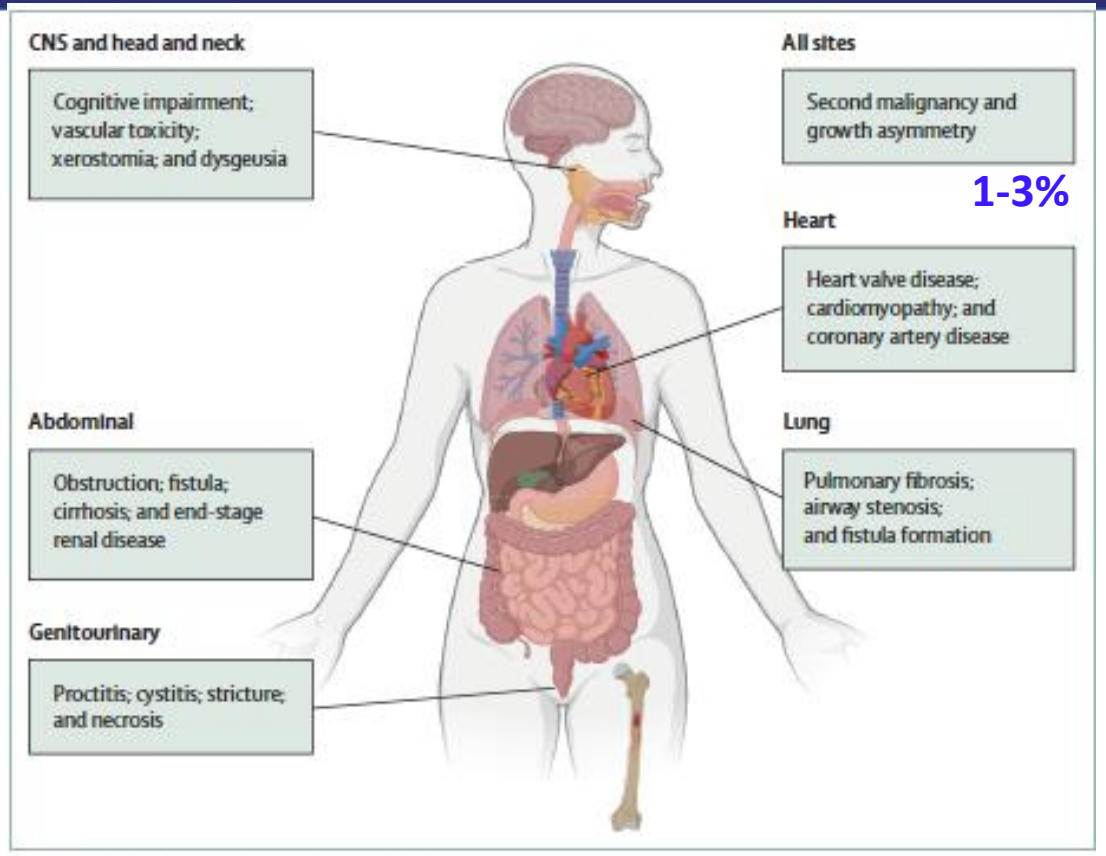


Figure 1: **Toxic effects of radiotherapy by site**
General overview of the most common long-term toxic effects of radiotherapy arising in different regions of the body. Figure created with BioRender.com.

Thorax			
Oesophagus	Fistula and stenosis	Fistula (with chemoradiation for non-small-cell lung cancer): <1% (grade 5);[35] stenosis: 2% (at 50·0 Gy or less) to 15% (at >60·0 Gy)[36]	Limit max dose to oesophagus to <50·0 Gy
Heart	Cardiovascular events (eg, coronary disease, valvular dysfunction, heart failure, pericardial disease, and arrythmia)	23–32% (with high-dose irradiation close to the organ)[37]	Limit mean dose to heart to <20·0 Gy;[38] limit volume of left anterior descending artery receiving 15·0 Gy to <10%[39] and volume of left ventricle receiving 15·0 Gy to <1%[39]
Lung	Pneumonitis	12% (grade 1–2); <1% (grade ≥3, with high-dose direct irradiation)[40]	With conventional radiotherapy, limit volume of lung receiving 20·0 Gy to ≤40% and mean lung dose to ≤20·0 Gy†[35]
Lung	Fibrosis	10% (grade 1–2, with high-dose direct irradiation)[40]	Limit dose to <30 Gy[41]

Top Cited/Downloaded: Annals of Thoracic Surgery

Top Annals of Thoracic Surgery Papers for 2024

Top Viewed/Cited

The Annals: Top Papers in GENERAL THORACIC SURGERY (2023-4 Articles)	Authors	2024 Cites	Total Usage
Segmentectomy vs. Lobectomy for Early Non-Small-Cell Lung Cancer with Visceral Pleural Invasion	Mathey-Andrews, Abrusso, Venkateswaran, Potter, Senthil, Beqari, Yang, Lanuti	11	1086
The Society of Thoracic Surgeons General Thoracic Surgery Database: 2023 Update on Outcomes and Research	Towe, Servais, Brown, Blasberg, Mitchell, Worrell, Seder, David	10	620
The Impact of Enhanced Recovery After Surgery on Persistent Opioid Use Following Pulmonary Resection	Turner, Delman, Griffith, Wima, Wallen, Starnes, Budde, Van Haren	10	701
Enhanced Recovery Protocol Associated with Decreased 3-Month Opioid Use Following Thoracic Surgery	Strobel, Krebs, Cunningham, Chaudry, Mehaffey, Sarosiek, Durieux, Dunn, Naik, Blank, Martin	7	549
Importance Of Lymph Node Evaluation In 2-centimeter Or Less Pure Solid Non-small Cell Lung Cancer	Choi, Yoon, Shin, Kim, Choi, Kim, Shim, Cho	8	693
Impact of Operation on Disease Progression and Survival of Patients with Pleural Mesothelioma	Nakamura, Hashimoto, Kuroda, Matsumoto, Kondo, Kitajima, Minami, Kuribayashi, Kijima, Hasegawa	6	583
5-year Sustained Impact of a Thoracic Enhanced Recovery after Surgery Program	Young, Viktorsson, Strobel, Rotar, Cramer, Scott, Carrott, Blank, Martin	6	484

Top Cited/Downloaded: JTCVS

Top Cited JTCVS papers for 2023-2024

Title	Authors	date	Citations
Lobectomy, segmentectomy, or wedge resection for peripheral clinical T1aN0 non–small cell lung cancer: A post hoc analysis of CALGB 140503 (Alliance)	Altorki, N.; Wang, X.; Damman, B.; Mentlick, J.; Landreneau, R.; Wigle, D.; Jones, D.; Conti, M.; Ashrafi, A.; Liberman, M.; de Perrot, M.; Mitchell, J.; Keenan, R.; Bauer, T.; Miller, D.; Stinchcombe, T.	7/23	34
Neoadjuvant therapy does not increase postoperative morbidity of sleeve lobectomy in locally advanced non–small cell lung cancer	Li, X.; Li, Q.; Yang, F.; Gao, E.; Lin, L.; Li, Y.; Song, X.; Duan, L.	3/23	14
Long-term outcome of patients with peripheral ground-glass opacity–dominant lung cancer after sublobar resections	Yoshino, I.; Moriya, Y.; Suzuki, K.; Wakabayashi, M.; Saji, H.; Aokage, K.; Suzuki, M.; Ito, H.; Matsumoto, I.; Kobayashi, M.; Okamoto, T.; Okada, M.; Yamashita, M.; Ikeda, N.; Nakamura, S.; Kataoka, T.; Tsuboi, M.; Watanabe, S.	1/23	14
Extent of surgical resection for radiologically subsolid T1N0 invasive lung adenocarcinoma: When is a wedge resection acceptable?	Zhang, C.; Pan, Y.; Li, H.; Zhang, Y.; Li, B.; Zhang, Y.; Luo, X.; Miao, L.; Ma, L.; Chen, S.; Hu, H.; Sun, Y.; Zhang, Y.; Xiang, J.; Wang, S.; Gu, Y.; Li, Y.; Shen, X.; Wang, Z.; Ye, T.; Chen, H.	6/23	11
Two-year outcomes of clinical N2-3 esophageal squamous cell carcinoma after neoadjuvant chemotherapy and immunotherapy from the phase 2 NICE study	Yang, Y.; Liu, J.; Liu, Z.; Zhu, L.; Chen, H.; Yu, B.; Zhang, R.; Shao, J.; Zhang, M.; Li, C.; Li, Z.	9/23	11

Top Viewed JTCVS papers for 2023-2024

Title	Authors	Date	Total Usage
The 2023 American Association for Thoracic Surgery (AATS) Expert Consensus Document: Management of subsolid lung nodules	Chen, H.; Kim, A.; Hsin, M.; Shrager, J.; Prosper, A.; Wahidi, M.; Wigle, D.; Wu, C.; Huang, J.; Yasufuku, K.; Henschke, C.; Suzuki, K.; Tailor, T.; Jones, D.; Yanagawa, J.	6/24	7,201
The American Association for Thoracic Surgery (AATS) 2023 Expert Consensus Document: Staging and multidisciplinary management of patients with early-stage non–small cell lung cancer	Kidane, B.; Bott, M.; Spicer, J.; Backhus, L.; Chaft, J.; Chudgar, N.; Colson, Y.; D'Amico, T.; David, E.; Lee, J.; Najmeh, S.; Sepesi, B.; Shu, C.; Yang, J.; Swanson, S.; Stiles, B.	6/23	6,811
Long-term outcome of patients with peripheral ground-glass opacity–dominant lung cancer after sublobar resections	Yoshino, I.; Moriya, Y.; Suzuki, K.; Wakabayashi, M.; Saji, H.; Aokage, K.; Suzuki, M.; Ito, H.; Matsumoto, I.; Kobayashi, M.; Okamoto, T.; Okada, M.; Yamashita, M.; Ikeda, N.; Nakamura, S.; Kataoka, T.; Tsuboi, M.; Watanabe, S.	1/23	5,381
Surgery for oligometastatic non–small cell lung cancer	Antonoff, M.; Deboever, N.; Werner, R.; Altan, M.; Gomez, D.; Opitz, I.	9/23	3,882
Surgical outcomes after chemotherapy plus nivolumab and chemotherapy plus nivolumab and ipilimumab in patients with non–small cell lung cancer	Feldman, H.; Sepesi, B.; Leung, C.; Lin, H.; Weissferdt, A.; Pataer, A.; William, W.; Walsh, G.; Rice, D.; Roth, J.; Mehran, R.; Hofstetter, W.; Antonoff, M.; Rajaram, R.; Gibbons, D.; Lee, J.; Heymach, J.; Vaporciyan, A.; Swisher, S.; Cascone, T.	10/23	3,627
Surgical management of non–small cell lung cancer with limited metastatic disease involving only the brain	Kumar, A.; Kumar, S.; Potter, A.; Raman, V.; Kozono, D.; Lanuti, M.; Jeffrey Yang, C.	4/23	2,233

Mesothelioma

MARS 2

Lancet Respiratory Medicine May 2024

(Bryan Burt reviewed last year)

MARS 2

Extended pleurectomy decortication and chemotherapy versus chemotherapy alone for pleural mesothelioma (MARS 2): a phase 3 randomised controlled trial

Eric Lim, David Waller, Kelvin Lau, Jeremy Steele, Anthony Pope, Clinton Ali, Rocco Bilancia, Manjusha Keni, Sanjay Popat, Mary O'Brien, Nadza Tokaca, Nick Maskell, Louise Stadon, Dean Fennell, Louise Nelson, John Edwards, Sara Tenconi, Laura Socci, Robert C Rintoul, Kelly Wood, Amanda Stone, Dakshinamoorthy Muthukumar, Charlotte Ingle, Paul Taylor, Laura Cove-Smith, Raffaele Califano, Yvonne Summers, Zacharias Tasigiannopoulos, Andrea Bille, Riyaz Shah, Elizabeth Fuller, Andrew Macnair, Jonathan Shamash, Talal Mansy, Richard Milton, Pek Koh, Andreea Alina Ionescu, Sarah Treece, Amy Roy, Gary Middleton, Alan Kirk, Rosie A Harris, Kate Ashton, Barbara Warnes, Emma Bridgeman, Katherine Joyce, Nicola Mills, Daisy Elliott, Nicola Farrar, Elizabeth Stokes, Vikki Hughes, Andrew G Nicholson, Chris A Rogers, on behalf of the MARS 2 Investigators*

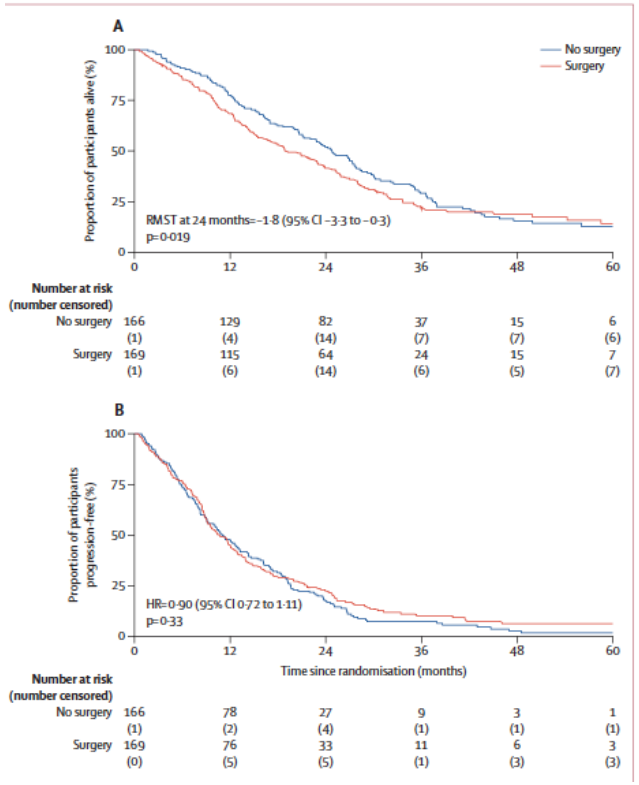
Lancet Respir Med 2024; 12: 457–66

Published Online May 10, 2024 https://doi.org/10.1016/S2213-2600(24)00119-X

Summary

Background Extended pleurectomy decortication for complete macroscopic resection for pleural mesothelioma has never been evaluated in a randomised trial. The aim of this study was to compare outcomes after extended pleurectomy

Lancet Respir Med 2024; 12: 457–66

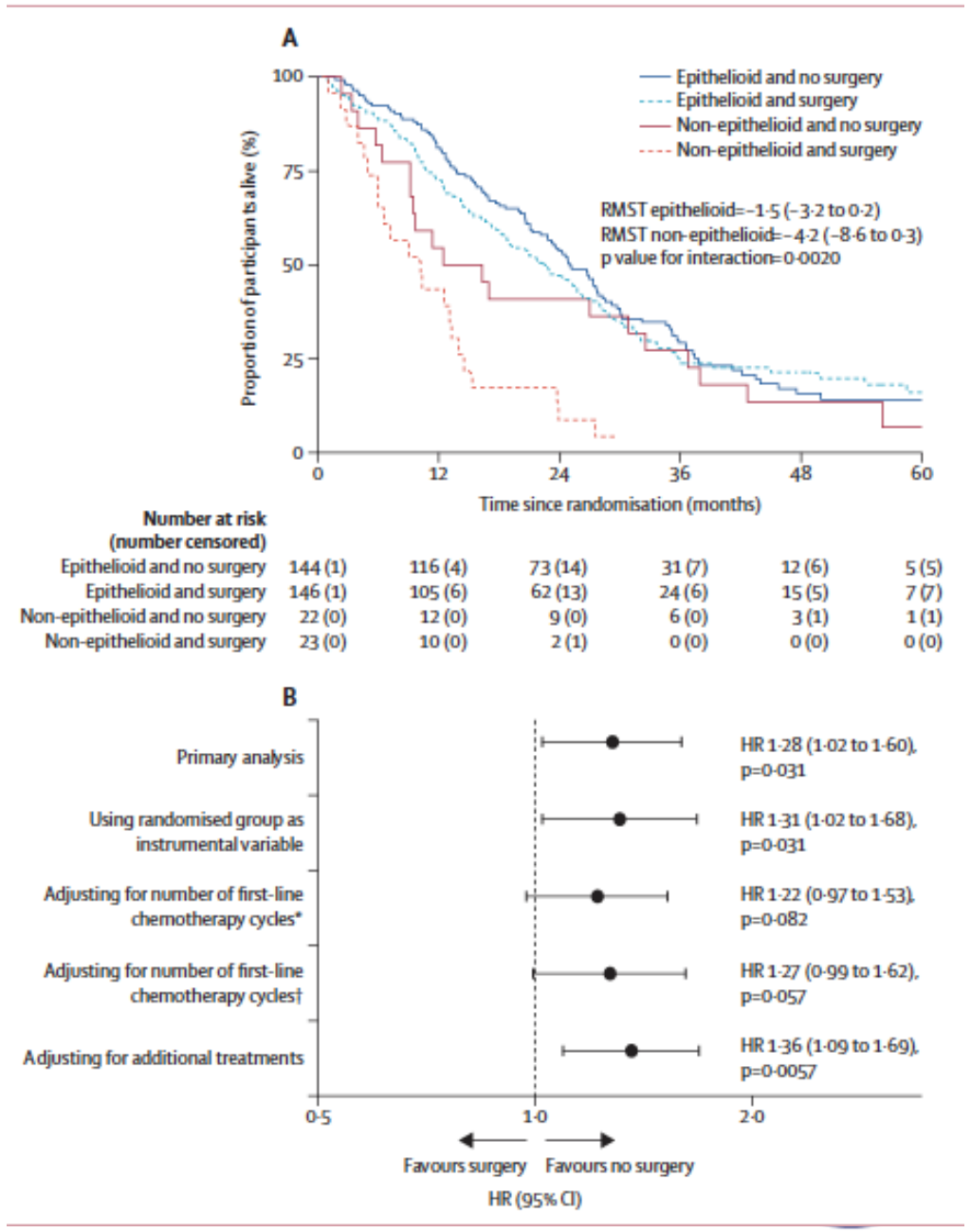


Chemo alone vs. Surgery + chemo

P/D or extended P/D

12% were not epithelioid

2 year survival WORSE with surgery, more AE's



Lung Cancer Papers

Pack-Year Smoking History: An Inadequate and Biased Measure to Determine Lung Cancer Screening Eligibility

JCO March 2024

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Original Reports | Cancer Prevention and Control

Pack-Year Smoking History: An Inadequate and Biased Measure to Determine Lung Cancer Screening Eligibility

Alexandra L. Potter, BS[1]; Nuo N. Xu, MSPH[2]; Priyanka Senthil[1]; Deepti Srinivasan, BS[1]; Hang Lee, PhD[3]; G. Scott Gazelle, MD, MPH, PhD[4,5]; Lydia Chelala, MD[6]; Wei Zheng, MD, MPH, PhD[7,8]; Florian J. Fintelmann, MD[4]; Lecia V. Sequist, MD, MPH[9]; Jessica Donington, MD[10]; Julie R. Palmer, ScD[2]; and Chi-Fu Jeffrey Yang, MD[1]

DOI https://doi.org/10.1200/JCO.23.01780

Of people diagnosed with lung cancer, how many met USPSTF criteria in Southern Community Cohort?

Changing Screening Criteria from 20 *pack-years* to 20 *years* increases eligibility in:

Black lung cancer patients from 57.6% to 85.3%

White lung cancer patients from 74% to 82%

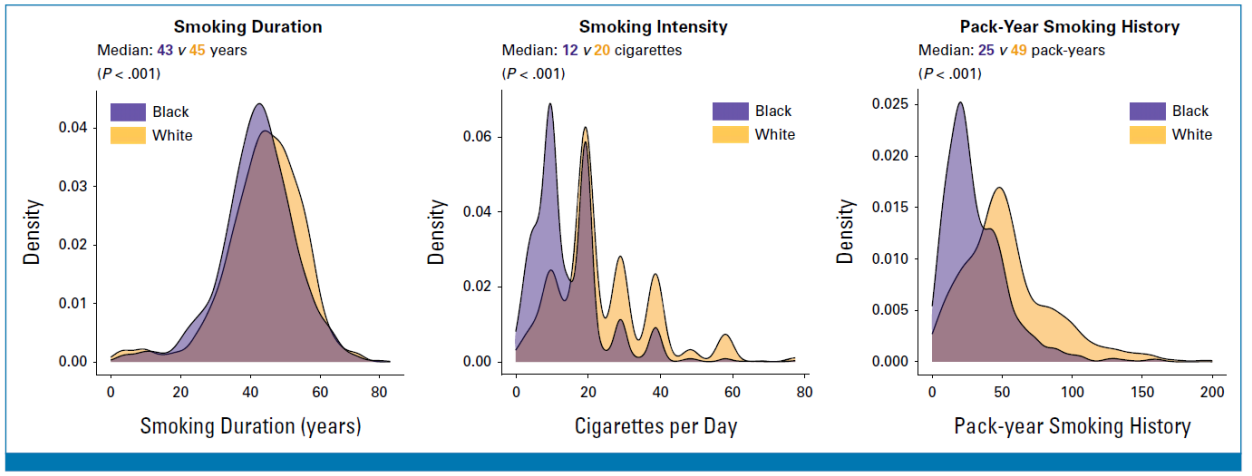


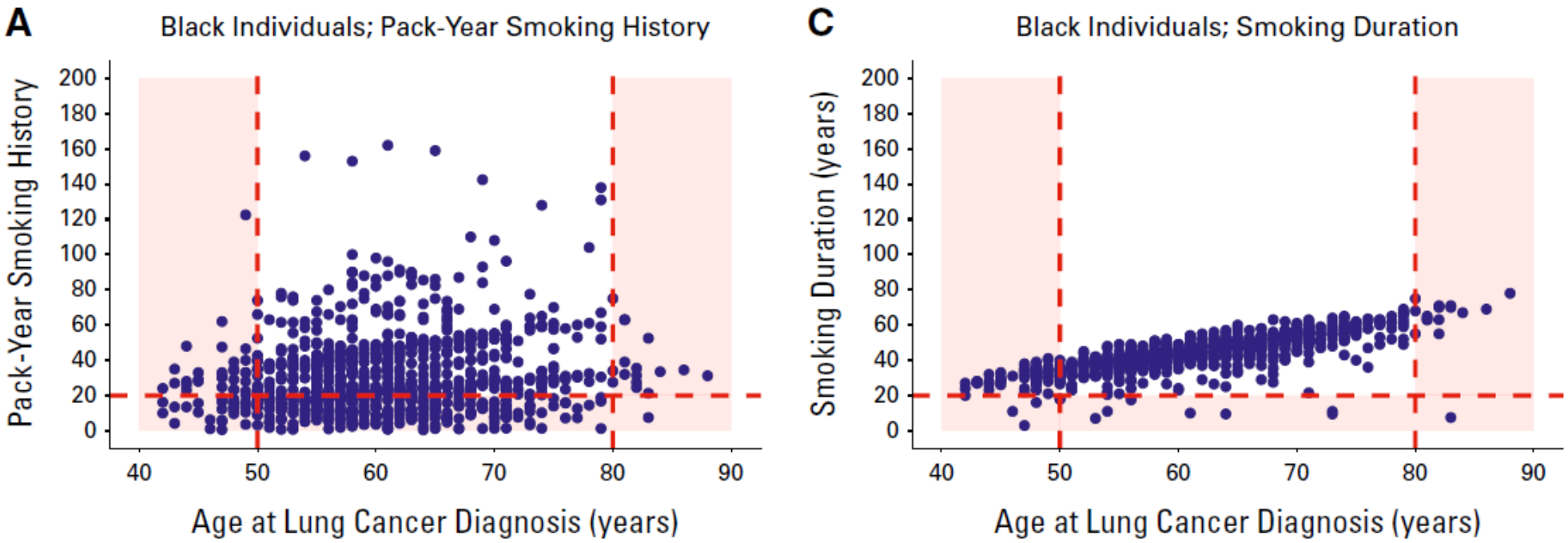
FIG 1. Distribution of smoking duration (years), smoking intensity (cigarettes per day), and pack-year smoking history among SCCS participants diagnosed with lung cancer. SCCS, Southern Community Cohort Study.

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

Original Reports | Cancer Prevention and Control

Check for updates

Pack-Year Smoking History: An Inadequate and Biased Measure to Determine Lung Cancer Screening Eligibility



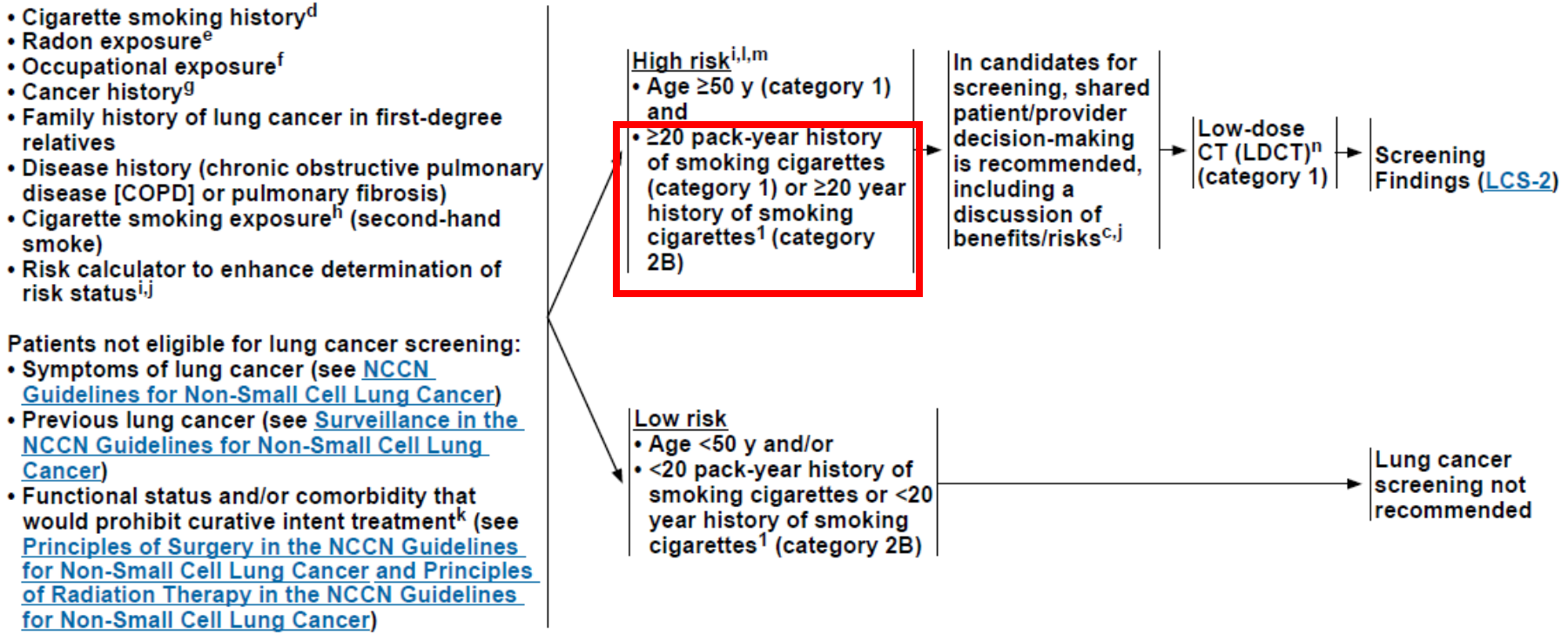
Key Finding: Revising the USPSTF lung cancer screening guideline to include a 20-year smoking duration cutoff increased the proportion of individuals with lung cancer who would have qualified for screening and eliminated the racial disparity in screening eligibility between Black and White individuals.

Alexandra L. Potter, Chi-Fu Jeffrey Yang et al, *Journal of Clinical Oncology*. 2024 42(17):2026-2037

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Lung Cancer Screening

NCCN Guidelines Index
Table of Contents
Discussion



[1] Potter AL, Xu NN, Senthil P, et al. Pack-year smoking history: An inadequate and biased measure to determine lung cancer screening eligibility. J Clin Oncol 2024;42:2026-2037.

The "Potter Criteria" is born...

CALGB 140503 publications

Published to Date – CALGB 140503

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 9, 2023 VOL. 388 NO. 6

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D., David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. , Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, M.D., John D. M ian, M.D., Thomas Bauer, M.D., Daniel Miller, M.D., Leslie D., and Everett Vokes, M.D.

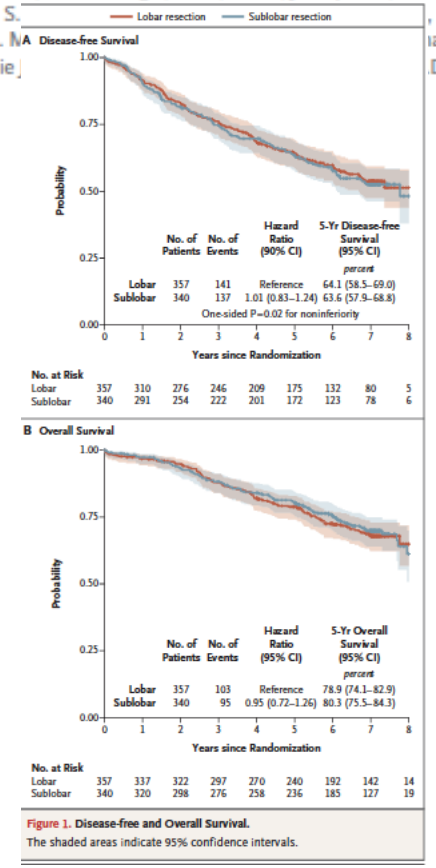
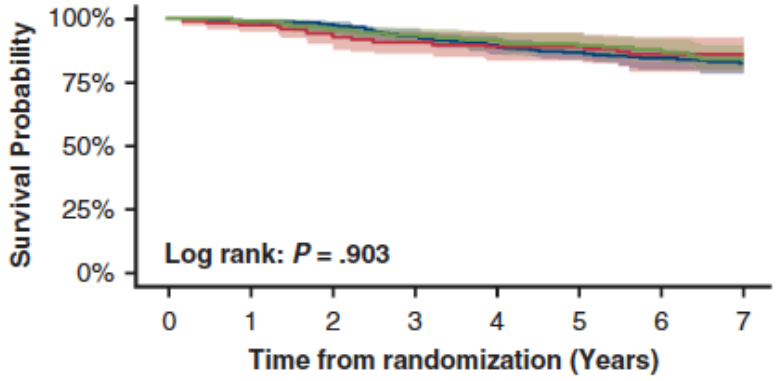


Figure 1. Disease-free and Overall Survival.
The shaded areas indicate 95% confidence intervals.

Sublobar not inferior to lobar resection for DFS

Lobectomy, segmentectomy, or wedge resection for peripheral clinical T1aN0 non–small cell lung cancer: A post hoc analysis of CALGB 140503 (Alliance)

Nasser Altorki, MD,[a] Xiaofei Wang, MD,[b] Bryce Damman, MD,[c] Jennifer Mentlick, MD,[c] Rodney Landreneau, MD,[d] Dennis Wigle, MD,[e] David R. Jones, MD,[f] Massimo Conti, MD,[g] Ahmad S. Ashrafi, MD,[h] Moishe Liberman, MD,[i] Marc de Perrot, MD,[j] John D. Mitchell, MD,[k] Robert Keenan, MD,[l] Thomas Bauer, MD,[m] Daniel Miller, MD,[n] and Thomas E. Stinchcombe, MD[o]



No. at risk

Lobectomy	362	339	325	299	271	242	193	141
Segment	131	123	114	101	97	93	75	49
Wedge	204	195	181	173	160	141	109	79

	n	nEvents	HR (95% CI)	5-year LCFS (95% CI)
Lobectomy	362	54	reference	86.8 (83.2 - 90.6%)
Segment	131	19	0.94 (0.55 - 1.61)	89.2 (83.8 - 94.9%)
Wedge	204	28	0.90 (0.57 - 1.43)	89.7 (85.4 - 94.2%)

C

Procedure Lobectomy Segment Wedge

Lung cancer specific survival at 5 years all 87-89% for lobe, wedge, segment

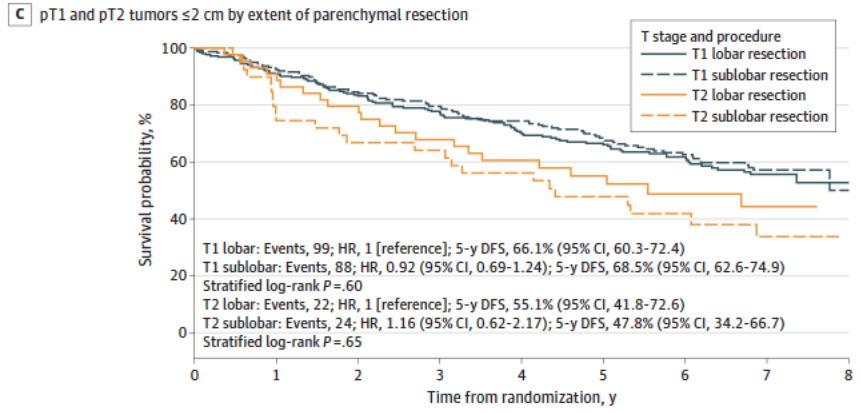
Published to Date – CALGB 140503

JAMA Oncology | Original Investigation

Recurrence of Non–Small Cell Lung Cancer With Visceral Pleural Invasion
A Seconday Analysis of a Randomized Clinical Trial

Nasser Altorki, MD; Xiaofei Wang, PhD; Bryce Damman, MS; David R. Jones, MD; Dennis Wigle, MD, PhD; Jeffrey Port, MD; Massimo Conti, MD; Ahmad S. Ashrafi, MD; Moishe Lieberman, MD, PhD; Rodney Landreneau, MD; Kazuhiro Yasufuku, MD, PhD; Stephen Yang, MD; John D. Mitchell, MD; Robert Keenan, MD; Thomas Bauer, MD; Daniel Miller, MD; David Kozono, MD, PhD; Jennifer Mentlick; Everett Vokes, MD; Thomas E. Stinchcombe, MD

CONCLUSIONS AND RELEVANCE The results of this secondary analysis suggest that compared with patients with tumors without VPI, patients who had tumors with VPI had worse disease-free and recurrence-free survival and a higher rate of local and distant disease recurrence. These high rates of recurrence were independent of the extent of parenchymal resection, and these data support the inclusion of these patients in adjuvant therapy trials.



*Visceral Pleural Invasion impacts **systemic** but not local recurrence*

Secondary Analysis of the Rate of Second Primary Lung Cancer From Cancer and Leukemia Group B 140503 (Alliance) Trial of Lobar Versus Sublobar Resection for T1aN0 Non–Small-Cell Lung Cancer

Thomas E. Stinchcombe, MD[1]; Xiaofei Wang, PhD[2]; Bryce Damman, MS[3]; Jennifer Mentlick, HS[3]; Rodney Landreneau, MD[4]; Dennis Wigle, MD, PhD[5]; David R. Jones, MD[6]; Massimo Conti, MD[7]; Ahmad S. Ashrafi, MD[8]; Moishe Liberman, MD, PhD[9]; Marc de Perrot, MD[10]; John D. Mitchell, MD[11]; Robert Keenan, MD[12]; Thomas Bauer, MD[13]; Daniel Miller, MD[14]; and Nasser Altorki, MD[15]

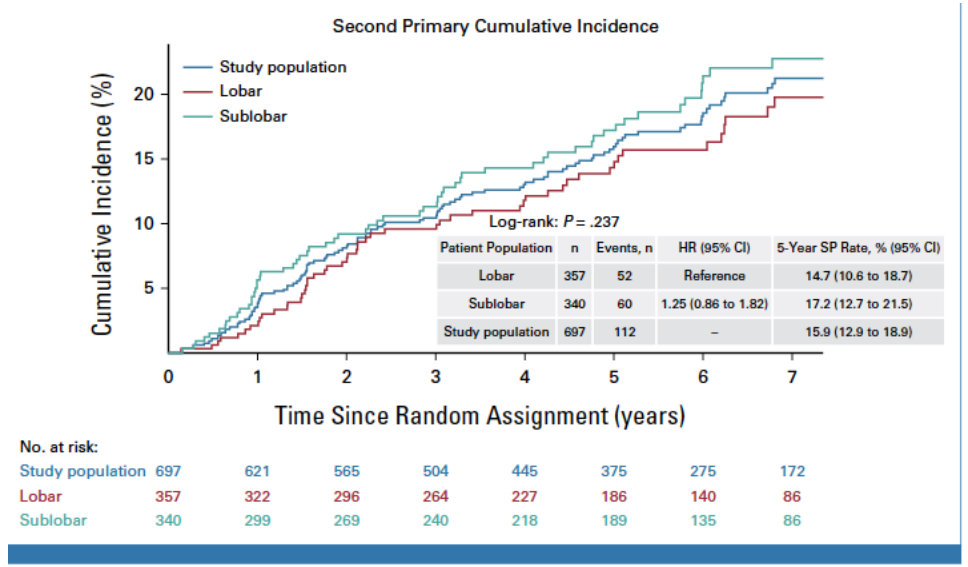


FIG 1. Cumulative incidence of second primary lung cancer in the study population, sublobar arm, and obar arm. HR, hazard ratio.

Second primary lung cancer:
Risk about 3.5% per year
Cumulative 15-17% at 5 years
Not significant between resection types

Recent Abstracts – CALGB 140503

2024 World Conference on Lung Cancer | SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA | #WCLC24 wclc2024.iaslc.org

Postoperative Complications Compromised Disease-Free and Recurrence-Free Survival in CALGB 140503 (Alliance) Trial Patients

Daniel Miller[1], Xiaofei Wang[2], Bryce Damman[3], Thomas Stinchcombe[4], Jennifer Mentlick[3], Rodney Landreneau[5], Dennis Wigle[3], David Jones[6], Massimo Conti[7], Ahmad Ashrafi[8], Moishe Liberman[9], Marc de Perrot[10], John Mitchell[11], Robert Keenan[12], Thomas Bauer[13], Nasser Altorki[14]

[1]Emory University School of Medicine, Atlanta, GA, [2]Alliance Statistics/Data Management Center, Duke University, Durham, NC, [3]Mayo Clinic, Rochester, MN [4]Biostatistics and Bioinformatics, Duke University, Durham, NC, of Pittsburgh Medical Center, Pittsburgh, PA,, [6]Memorial Sloan Kettering Cancer Center, New York, NY, Universitaire de Cardiologie et Pneumologie de Québec, Québec, QC, [8]Surrey Memorial Hospital, Fraser Val Authority, BC, [9]Centre Hospitalier de l'Université de Montréal, Montreal, QC, [10]Thoracic Surgery, Toronto, ON of Colorado Hospital School of Medicine, Aurora, CO, [12]Moffitt Cancer Center, Tampa, FL, [13]Hackensack Mer System, Edison, NJ, [14]Weill Cornell Medicine/New York-Presbyterian, New York, NY.

2024 World Conference on Lung Cancer | SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA | #WCLC24 wclc2024.iaslc.org

Conclusions

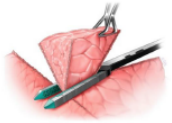
In this large, prospective randomized trial, High Grade AEs negatively influenced Disease-Free and Recurrence-Free survival, but not overall survival. LRR and DR survivals were also affected, but not significantly.

This analysis shows that even in patients who undergo resection for the smallest (≤ 2 cm) of NSCLCs, postoperative High-Grade AEs can decrease cancer-specific survivals.

Prevention (ERAS protocols) of postoperative High-Grade AEs is mandatory in patients undergoing surgical treatment for early-stage NSCLC to reduce recurrence and maximize survival. Less than 10% of sites had Fast track or ERAS protocols during trial time period.

Recent Abstracts – CALGB 140503

Association of Surgical Margin Distance, Locoregional Recurrence, and Survival Among Patients Undergoing Sublobar Resection in CALGB 140503



September 9, 2024

L.W. Martin, C.F. Yang, X. Wang, B. Damman, T. Stinchcombe, J.Mentlick, R. Landreneau, D. Wigle, D.R. Jones, M. Conti, A.S. Ashrafi, M.Liberman, M. dePerrot, J.D. Mitchell, R. Keenan, N. Altorki.

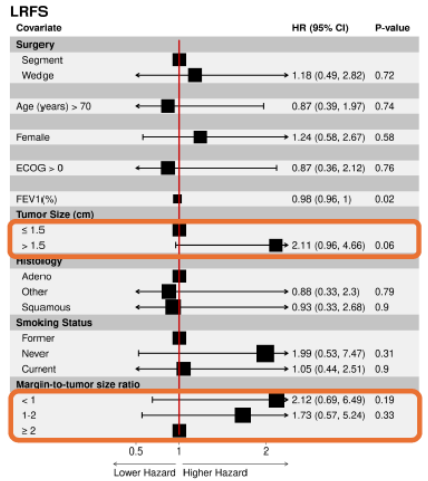
ALLIANCE FOUNDATION TRIALS

NCT

2024 World Conference on Lung Cancer | SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA | #WCLC24 wclc2024.iaslc.org

Results – Locoregional Recurrence Free Survival

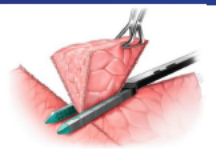
- Tumor size >1.5 cm (P=0.06) and margin-to-tumor size ratio<1 (*P*=0.19) trended towards but did not achieve statistical significance.



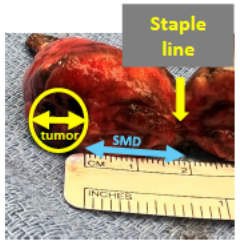
ALLIANCE

2024 World Conference on Lung Cancer | SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA | #WCLC24 wclc2024.iaslc.org

Conclusions



- ✓In this analysis of the sublobar resection cohort in CALGB 140503, **13.9% experienced locoregional recurrence**.
- ✓Margin to tumor size ratio <1 trended towards more locoregional recurrence
- ✓Study likely underpowered to detect clinically important differences
- ✓***We highly recommend that you get the widest margin you can!***



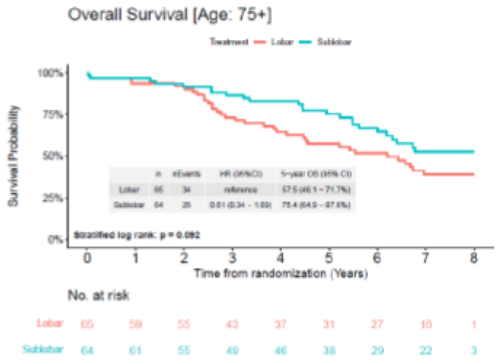
ALLIANCE FOUNDATION TRIALS

Recent Abstracts – CALGB 140503

Outcomes of Older Patients in CALGB 140503 (Alliance): Lobar vs Sublobar Resection for Peripheral Stage IA Non-Small Cell Lung Cancer

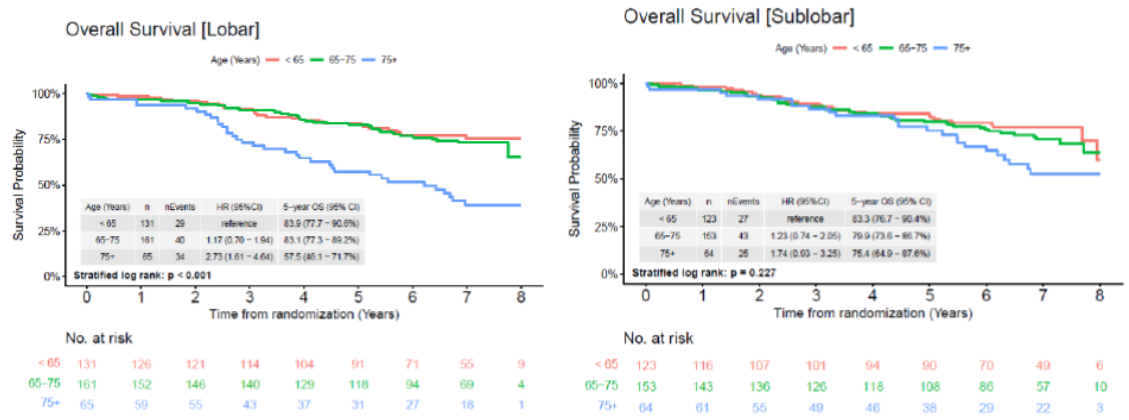
Apar Kishor Ganti, Bryce Damman, Xiaofei Wang, Thomas E. Stinchcombe, Nasser Altorki

VA Nebraska Western Iowa Healthcare System and University of Nebraska Medical Center, Omaha, NE; Mayo Clinic, Rochester, MN; Duke University, Durham, NC; Weill Cornell Medicine, New York, NY USA



P=NS

Results - OS



Conclusions

- Older patients tolerated surgical resection in CALGB 140503 well,
  - Similar adverse events and 90-day mortality as younger patients
- The reasons for a lower DFS and OS in patients >75 who underwent a lobectomy need to be studied further
- Surgical resection for early-stage NSCLC should be offered to all appropriate patients regardless of age

CANOPY-A Trial

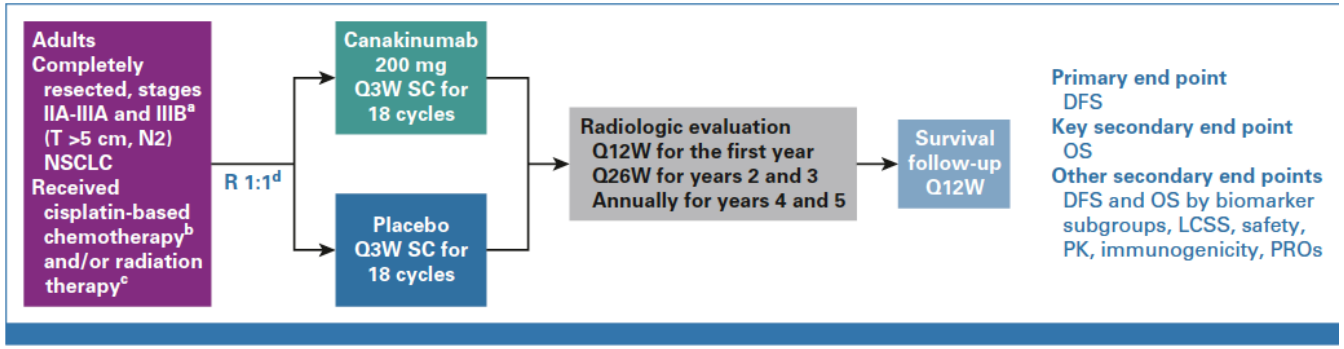
JCO Oct 2023

Canakinumab as Adjuvant Therapy in Patients With Completely Resected Non–Small-Cell Lung Cancer: Results From the CANOPY-A Double-Blind, Randomized Clinical Trial

Edward B. Garon, MD[1]; Shun Lu, MD[2]; Yasushi Goto, MD, PhD[3]; Pedro De Marchi, MD, PhD[4]; Luis Paz-Ares, MD, PhD[5]; David R. Spigel, MD[6]; Michael Thomas, MD[7]; James Chih-Hsin Yang, MD, PhD[8]; Andrea Ardizzoni, MD[9]; Fabrice Barlesi, MD, PhD[10,11]; Sergey Orlov, MD, PhD[12]; Hiroshige Yoshioka, MD, PhD[13]; Giannis Mountzios, MD, PhD[14]; Sadhvi Khanna, MS[15]; Claudia Bossen, PhD[16]; Mariana Carbini, MD[16]; Sabine Turri, MS[15]; Andrea Myers, MD, PhD[17]; and Byoung Chul Cho, MD, PhD[18]

- Inflammation assoc. with cancer development
- IL-1β drives inflammation
- Block IL-1β, should block cancer growth
- Canakinumab blocks IL-1β
- CANTOS trial for cardiovasc. disease – unexpected reduction in lung cancer incidence and mortality

Phase 3 RCT
1382 patients
Stage II-IIIB NSCLC

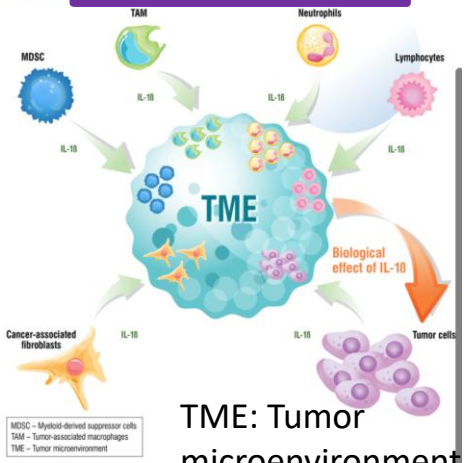


(Colchicine was considered instead of canakinumab but not used)

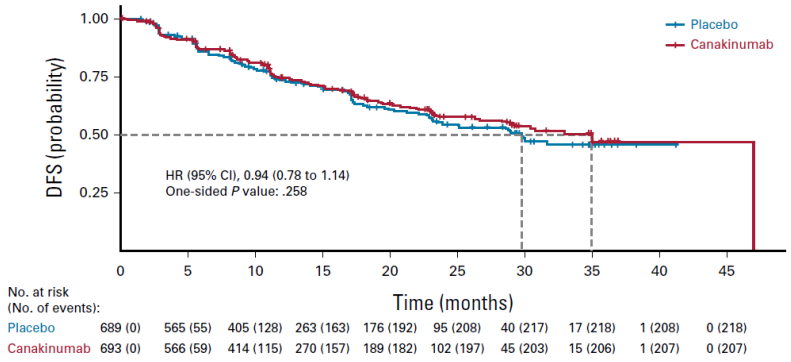
Targeting IL-1β:

- induces cytokine production
- angiogenesis
- tumor epithelial-to-mesenchymal transition,
- Growth
- Invasion
- Adhesion

Inflammasome



TME: Tumor microenvironment



Conclusions:
Negative trial; not helpful in adjuvant setting
Ongoing prevention trial for high-risk people

NCT03447769 JCO Oct 2023

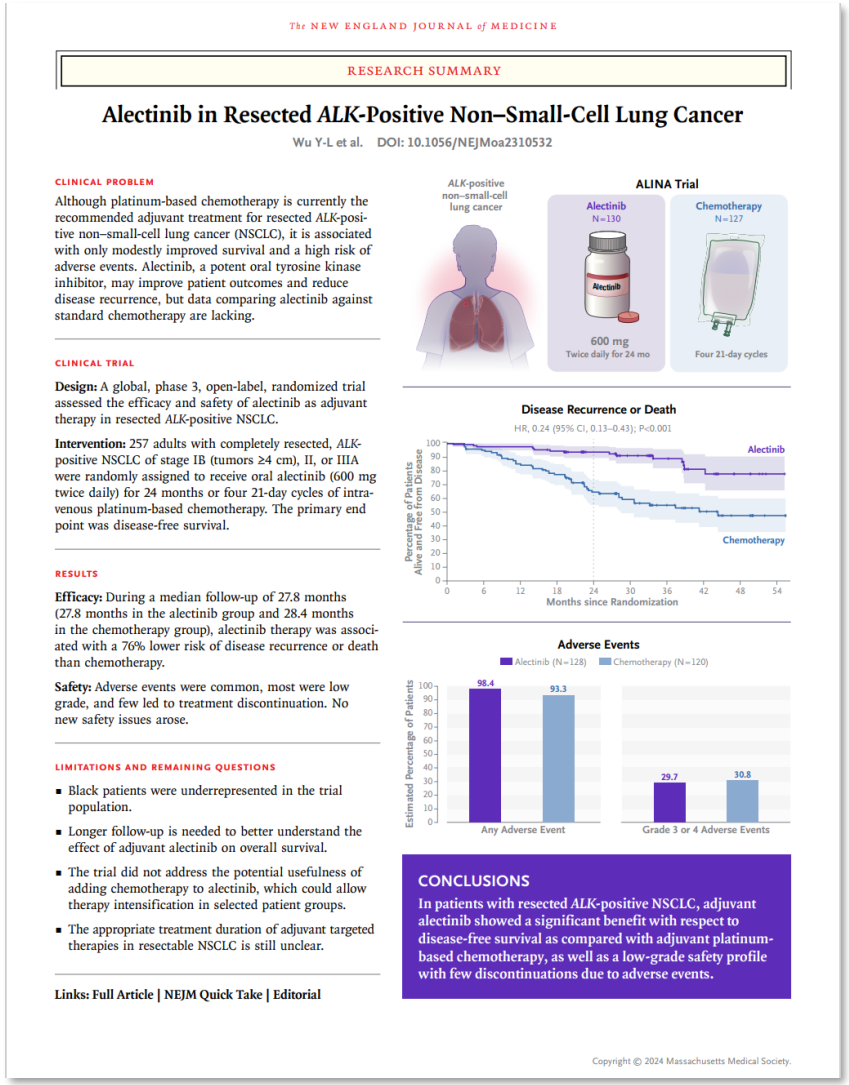
ALINA Trial

NEJM April 2024

(see also GTSC Podcast)

Adjuvant Therapy for ALK + Lung Cancer

STS2025
January 24-26, 2025
Los Angeles, California



The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Alectinib in Resected *ALK*-Positive Non–Small-Cell Lung Cancer

Wu Y-L et al. DOI: 10.1056/NEJMoa2310532

CLINICAL PROBLEM

Although platinum-based chemotherapy is currently the recommended adjuvant treatment for resected *ALK*-positive non–small-cell lung cancer (NSCLC), it is associated with only modestly improved survival and a high risk of adverse events. Alectinib, a potent oral tyrosine kinase inhibitor, may improve patient outcomes and reduce disease recurrence, but data comparing alectinib against standard chemotherapy are lacking.

CLINICAL TRIAL

Design: A global, phase 3, open-label, randomized trial assessed the efficacy and safety of alectinib as adjuvant therapy in resected *ALK*-positive NSCLC.

Intervention: 257 adults with completely resected, *ALK*-positive NSCLC of stage IB (tumors ≥4 cm), II, or IIIA were randomly assigned to receive oral alectinib (600 mg twice daily) for 24 months or four 21-day cycles of intravenous platinum-based chemotherapy. The primary end point was disease-free survival.

RESULTS

Efficacy: During a median follow-up of 27.8 months (27.8 months in the alectinib group and 28.4 months in the chemotherapy group), alectinib therapy was associated with a 76% lower risk of disease recurrence or death than chemotherapy.

Safety: Adverse events were common, most were low grade, and few led to treatment discontinuation. No new safety issues arose.

LIMITATIONS AND REMAINING QUESTIONS

- Black patients were underrepresented in the trial population.
- Longer follow-up is needed to better understand the effect of adjuvant alectinib on overall survival.
- The trial did not address the potential usefulness of adding chemotherapy to alectinib, which could allow therapy intensification in selected patient groups.
- The appropriate treatment duration of adjuvant targeted therapies in resectable NSCLC is still unclear.

Links: Full Article | NEJM Quick Take | Editorial

CONCLUSIONS

In patients with resected *ALK*-positive NSCLC, adjuvant alectinib showed a significant benefit with respect to disease-free survival as compared with adjuvant platinum-based chemotherapy, as well as a low-grade safety profile with few discontinuations due to adverse events.

ALINA

alectinib

Recurrence in brain: HR 0.22

Wu Y NEJM April 2024

5-7% of adenocarcinoma patients are ALK +

Postoperative treatment with targeted therapy, ***NO CHEMO***

Recurrence HR 0.24!!!

Survival data NR yet

#STS2025

NADIM (1)
Lancet Oncology 2024

Perioperative chemotherapy and nivolumab in non-small-cell lung cancer (NADIM): 5-year clinical outcomes from a multicentre, single-arm, phase 2 trial

Mariano Provencio, Ernest Nadal, Amelia Insa, Rosario García Campelo, Joaquín Casal, Manuel Dómine, Bartomeu Massuti, Margarita Majem, Delvys Rodríguez-Abreu, Alex Martínez-Martí, Javier de Castro, David Gómez de Antonio, Iván Macía, Santiago Figueroa, Luís Fernández Vago, Virginia Calvo, Ramón Palmero, Belén Sierra-Rodero, Cristina Martínez-Toledo, Marta Molina-Alejandre, Roberto Serna-Blasco, Atocha Romero, Alberto Cruz-Bermúdez

Summary

Background Perioperative immunotherapy improves short-term outcomes in resectable non-small-cell lung cancer (NSCLC). We now report 5-year survival from the NADIM trial to assess its long-term benefit.

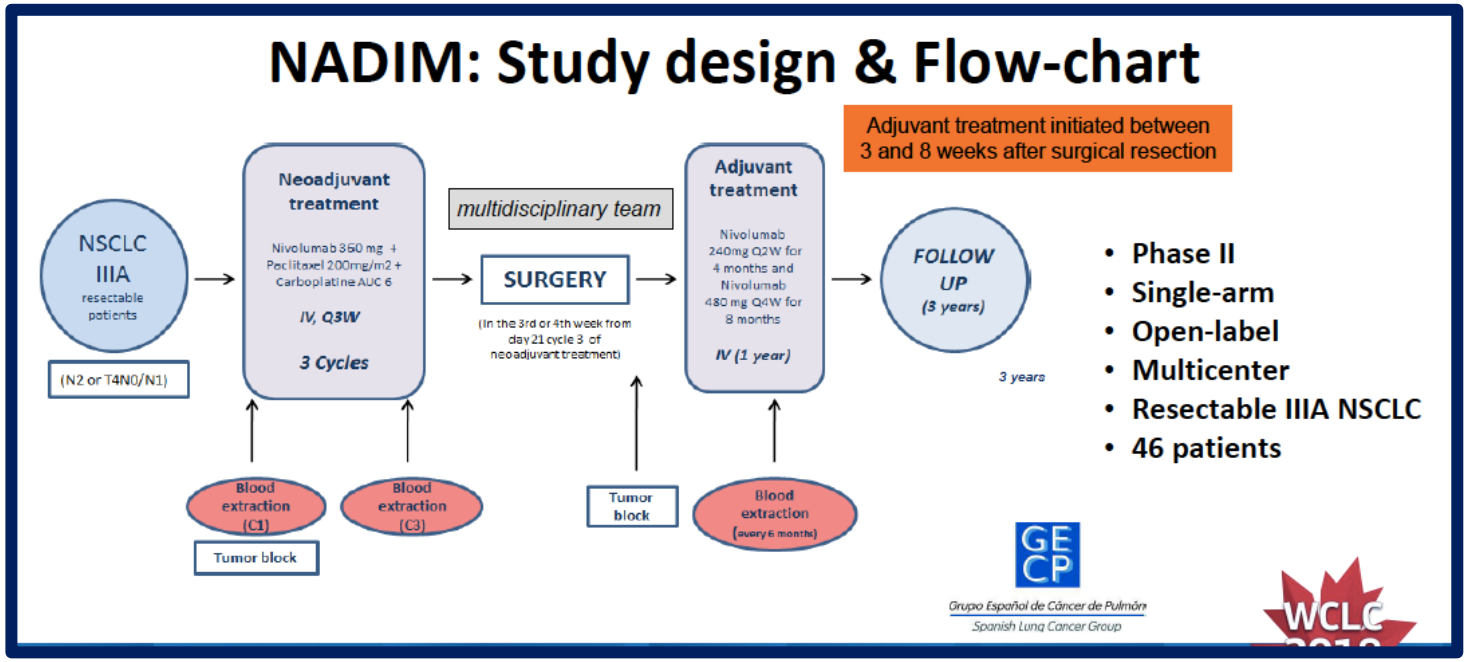
Methods NADIM was a multicentre, single-arm, phase 2 trial conducted across 18 hospitals in Spain. Patients were aged 18 years or older, had an Eastern Cooperative Oncology Group performance status of 0 or 1, and had histologically

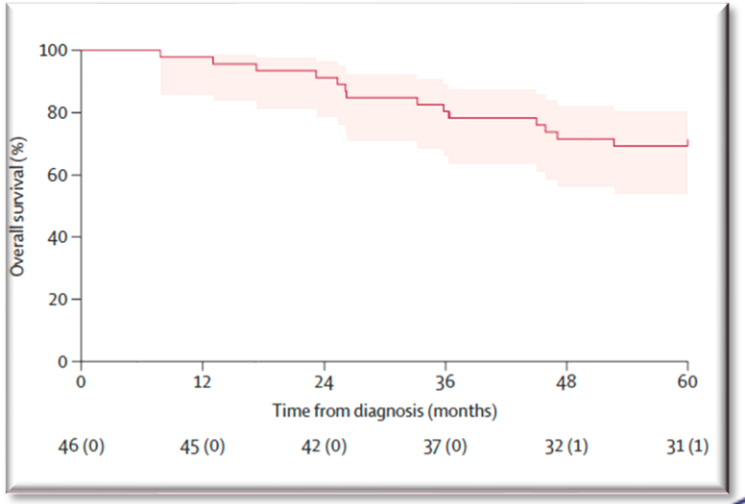
Lancet Oncol 2024; 25: 1453-64
Published Online October 14, 2024
https://doi.org/10.1016/S1470-2045(24)00498-4

NADIM (1)

Phase 2 trial, 18 centers
46 patients
5 years of follow up

Overall 5 year survival 69%



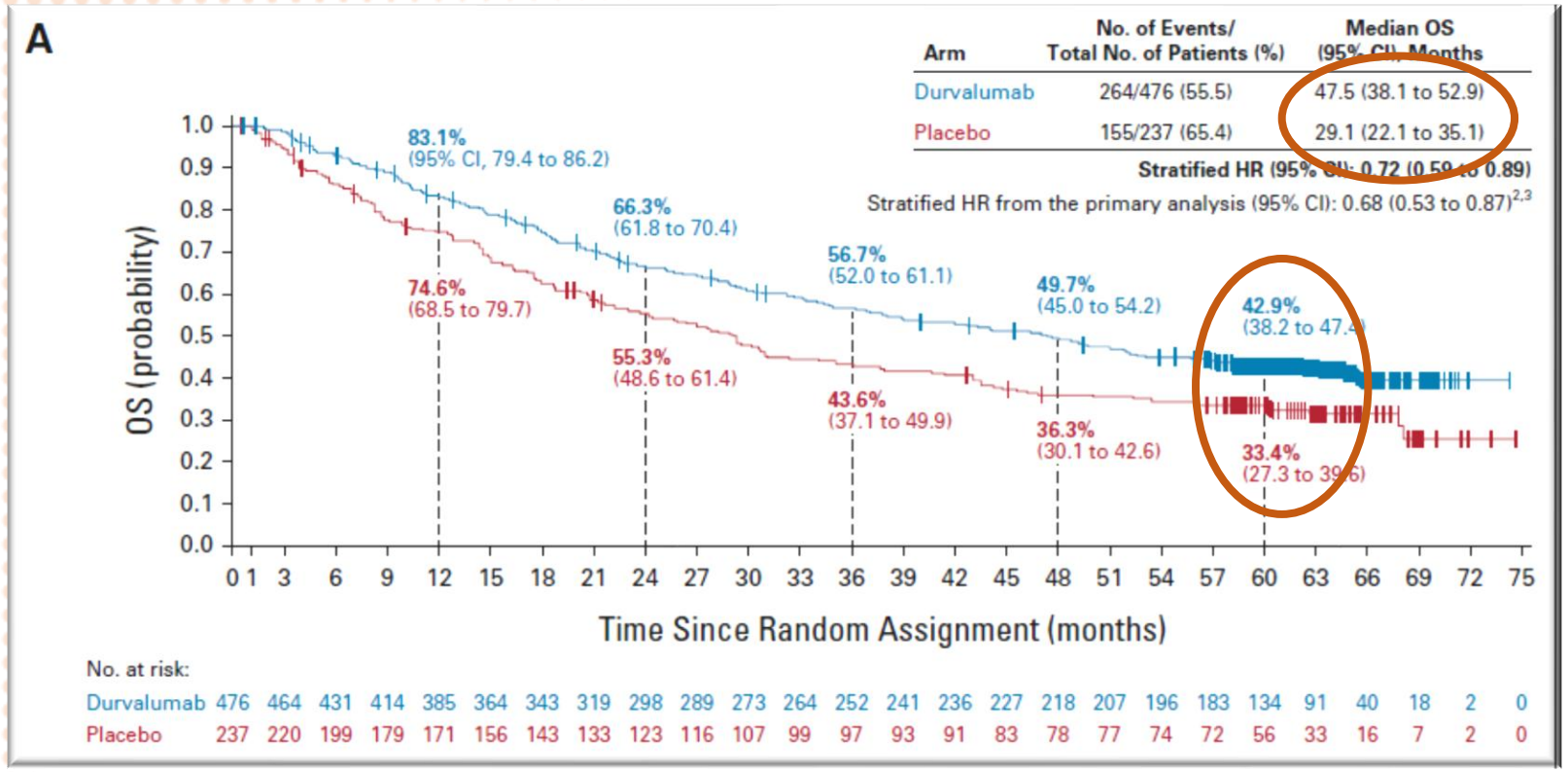


Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

David R. Spigel, MD[1]; Corinne Faivre-Finn, MD, PhD[2]; Jhanelle E. Gray, MD[3]; David Vicente, MD[4]; David Planchard, MD, PhD[5]; Luis Paz-Ares, MD, PhD[6]; Johan F. Vansteenkiste, MD, PhD[7]; Marina C. Garassino, MD[8,9]; Rina Hui, PhD[10]; Xavier Quantin, MD, PhD[11]; Andreas Rimner, MD[12]; Yi-Long Wu, MD[13]; Mustafa Özgüroğlu, MD[14]; Ki H. Lee, MD[15]; Terufumi Kato, MD[16]; Maike de Wit, MD, PhD[17]; Takayasu Kurata, MD[18]; Martin Reck, MD, PhD[19]; Byoung C. Cho, MD, PhD[20]; Suresh Senan, PhD[21]; Jarushka Naidoo, MBBCH, MHS[22]; Helen Mann, MSc[23]; Michael Newton, PharmD[24]; Piruntha Thiyagarajah, MD[23]; and Scott J. Antonia, MD, PhD[3]; on behalf of the PACIFIC Investigators

Pacific

Journal of Clinical Oncology Feb 2022



Overall 5 year survival 43%

University of Virginia Health System | UVA Cancer Center
An NCI-Designated Cancer Center

Cross trial comparison – yep, “illegal”

- 5 year survival **Nadim 1** vs **PACIFIC**:
- **69% vs 42%**
- PACIFIC methods never described how patients were deemed unresectable – just ask Harvey Pass
- I am sure many PACIFIC patients could have been NADIM patients

EORTC Resectability Guidelines

Lung Cancer Jan 2025

An international and multidisciplinary EORTC survey on resectability of stage III non-small cell lung cancer

Ilias Houda[a], Idris Bahce[a], Chris Dickhoff[b], Tiuri E. Kroese[c], Stephanie G.C. Kroeze[d], Alessio V. Mariolo[e], Marco Tagliamento[f,g], Laura Moliner[h], Mariana Brandão[i], Yassin Pretzenbacher[j], John Edwards[k], Isabelle Opitz[l], Alessandro Brunelli[m], Matthias Guckenberger[n], Paul E. van Schil[o], Sanjay Popat[p], Torsten Blum[q,r], Corinne Faivre-Finn[s,t], Dirk de Ruysscher[u,v], Jordi Remon[f], Thierry Berghmans[i], Anne-Marie C. Dingemans[w], Benjamin Besse[f], Lizza E.L. Hendriks[x,*]

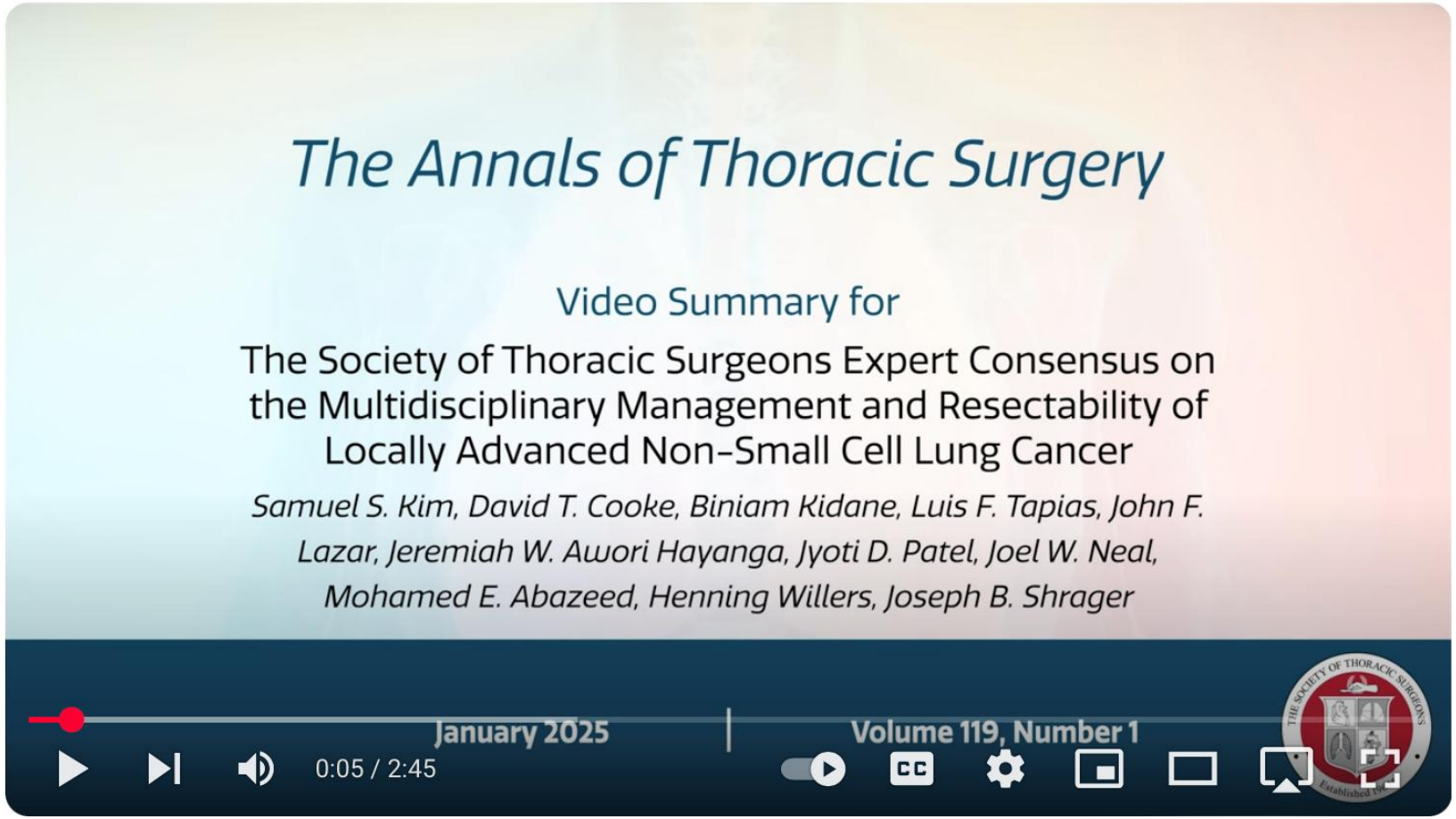
Lung Cancer 199 (2025) 108061

Dec 2024 online

When the respondents were asked "Would you recommend surgery after downstaging with neoadjuvant chemoimmunotherapy, assuming available in your country, in cases that were answered with maybe" (assessed by the respondent in the resectability assessment of the TNM-subsets in stage III NSCLC), the respondents agreed on recommending surgery (83%, n=463). A similar question with unresectable cases showed no agreement between the respondents (49%, n=275).

	N0	N1	N2 SINGLE	N2 MULTI	N2 BULKY	N2 INVASIVE
T1-2	N/A	N/A	POTENTIALLY RESECTABLE (95%)	NO AGREEMENT (50%)	UNRESECTABLE (75%)	UNRESECTABLE (84%)
T3 SIZE	N/A	RESECTABLE (83%)[a]	POTENTIALLY RESECTABLE (87%)	NO AGREEMENT (39%)	UNRESECTABLE (80%)	UNRESECTABLE (88%)
T3 SATELLITE	N/A	POTENTIALLY RESECTABLE (94%)	POTENTIALLY RESECTABLE (79%)	NO AGREEMENT (34%)	UNRESECTABLE (84%)	UNRESECTABLE (91%)
T3 INVASION	N/A	POTENTIALLY RESECTABLE (89%)	NO AGREEMENT (71%)[b]	NO AGREEMENT (28%)[c]	UNRESECTABLE (87%)	UNRESECTABLE (92%)
T4 SIZE	POTENTIALLY RESECTABLE (94%)	POTENTIALLY RESECTABLE (90%)	NO AGREEMENT (66%)	UNRESECTABLE (77%)	UNRESECTABLE (88%)	UNRESECTABLE (93%)
T4 SATELLITE	POTENTIALLY RESECTABLE (78%)	NO AGREEMENT (71%)[b]	NO AGREEMENT (44%)	UNRESECTABLE (85%)	UNRESECTABLE (92%)	UNRESECTABLE (94%)
T4 INVASION	NO AGREEMENT (62%)[b]	NO AGREEMENT (57%)[b]	NO AGREEMENT (34%)[c]	UNRESECTABLE (90%)	UNRESECTABLE (95%)	UNRESECTABLE (94%)

STS Summary Video on Resectability



CheckMate 77T

NEJM May 2024

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Nivolumab in Resectable Lung Cancer

T. Cascone, M.M. Awad, J.D. Spicer, J. He, S. Lu, B. Sepesi, F. Tanaka, J.M. Taube, R. Cornelissen, L. Havel,* N. Karaseva, J. Kuzdzal, L.B. Petruzelka, L. Wu, J.-L. Pujol, H. Ito, T.-E. Ciuleanu, L. de Oliveira Muniz Koch, A. Janssens, A. Alexandru, S. Bohnet, F.V. Moiseyenko, Y. Gao, Y. Watanabe, C. Coronado Erdmann, P. Sathyanarayana, S. Meadows-Shropshire, S.I. Blum, and M. Provencio Pulla, for the CheckMate 77T Investigators†

CheckMate 77T

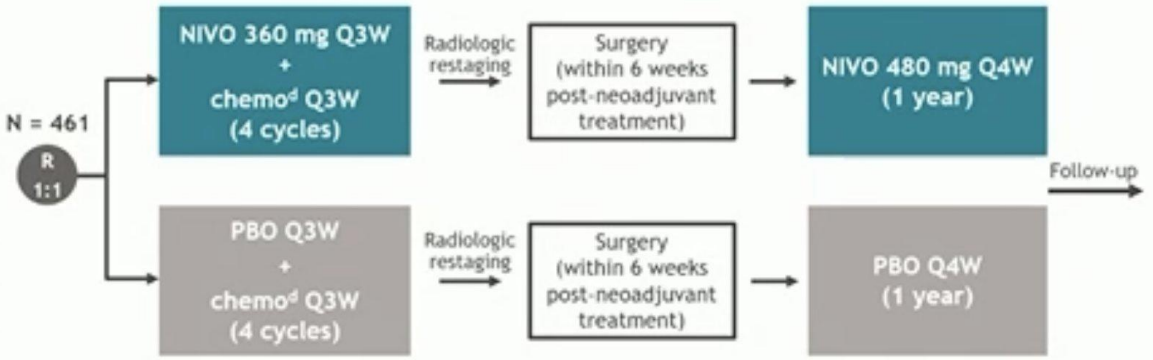
Stage 2A-3B
EGFR/Alk wild type
461 patients randomized

Primary endpoint:
Event free survival

CheckMate 77T[a] study design

Key eligibility criteria
- Resectable, stage IIA (> 4 cm)-IIIB (N2) NSCLC (per AJCC 8th edition)
- No prior systemic anti-cancer treatment
- ECOG PS 0-1
- No *EGFR* mutation/known *ALK* alterations[b]

Stratified by histology (NSQ vs SQ) disease stage (II vs III), and tumor PD-L1[c] (≥ 1% vs < 1% vs not evaluable/indeterminate)



Follow-up, median (range): 25.4 (15.7-44.2) months

Primary endpoint	Secondary endpoints	Exploratory analyses
• EFS by BICR	• pCR[e] by BIPR • MPR[e] by BIPR • OS • Safety	• EFS by pCR/MPR • EFS by adjuvant treatment

Database lock date: September 6, 2023.

[a]NCT04025879. [b]*EGFR* testing was mandatory in all patients with NSQ histology. *ALK* testing was done in patients with a history of *ALK* alterations. *EGFR*/*ALK* testing done using US FDA/local health authority-approved assays. [c]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako). [d]NSQ: cisplatin + pemetrexed, carboplatin + pemetrexed, or carboplatin + paclitaxel; SQ: cisplatin + docetaxel or carboplatin + paclitaxel. [e]Assessed per immune-related pathologic response criteria.[1] BICR, blinded independent central review; BIPR, blinded independent pathological review. 1. Cottrell TR, et al. *Ann Oncol* 2018;29:1853-1860.

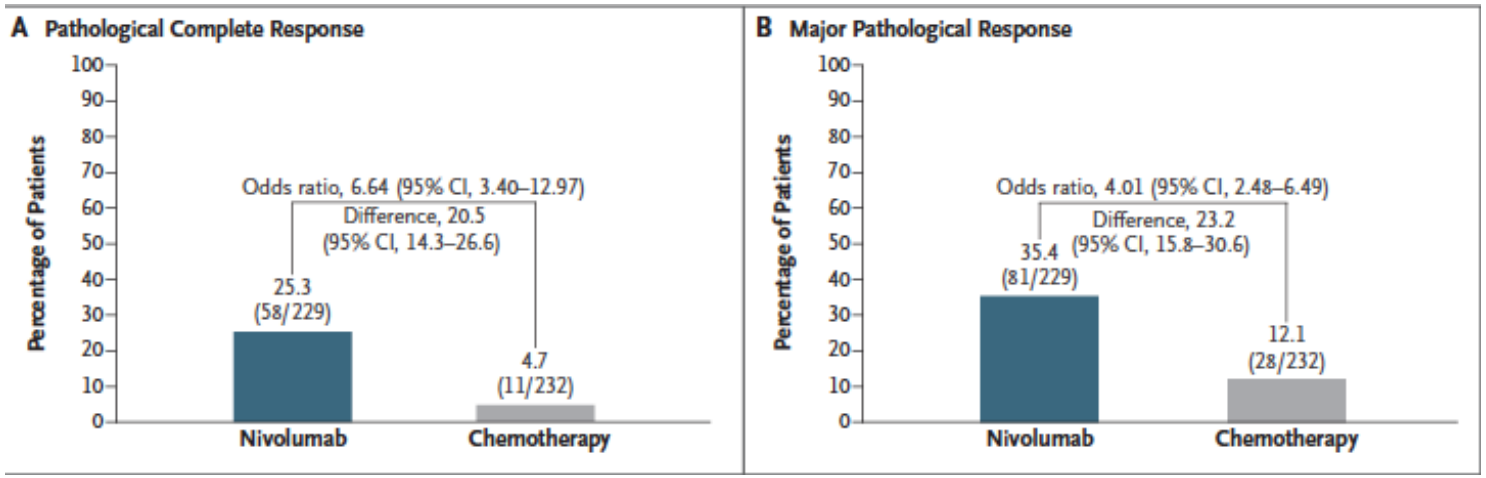
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Nivolumab in Resectable Lung Cancer

T. Cascone, M.M. Awad, J.D. Spicer, J. He, S. Lu, B. Sepesi, F. Tanaka, J.M. Taube, R. Cornelissen, L. Havel,* N. Karaseva, J. Kuzdzal, L.B. Petruzelka, L. Wu, J.-L. Pujol, H. Ito, T.-E. Ciuleanu, L. de Oliveira Muniz Koch, A. Janssens, A. Alexandru, S. Bohnet, F.V. Moiseyenko, Y. Gao, Y. Watanabe, C. Coronado Erdmann, P. Sathyanarayana, S. Meadows-Shropshire, S.I. Blum, and M. Provencio Pulla, for the CheckMate 77T Investigators†

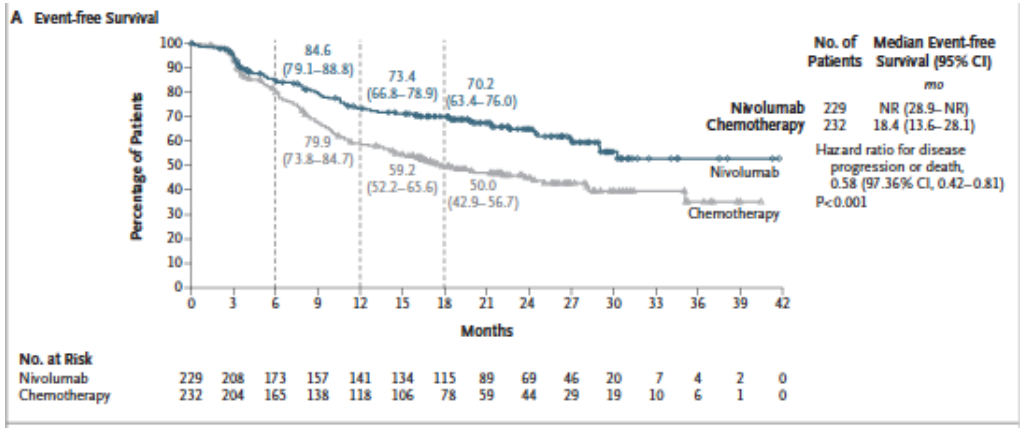
CheckMate 77T

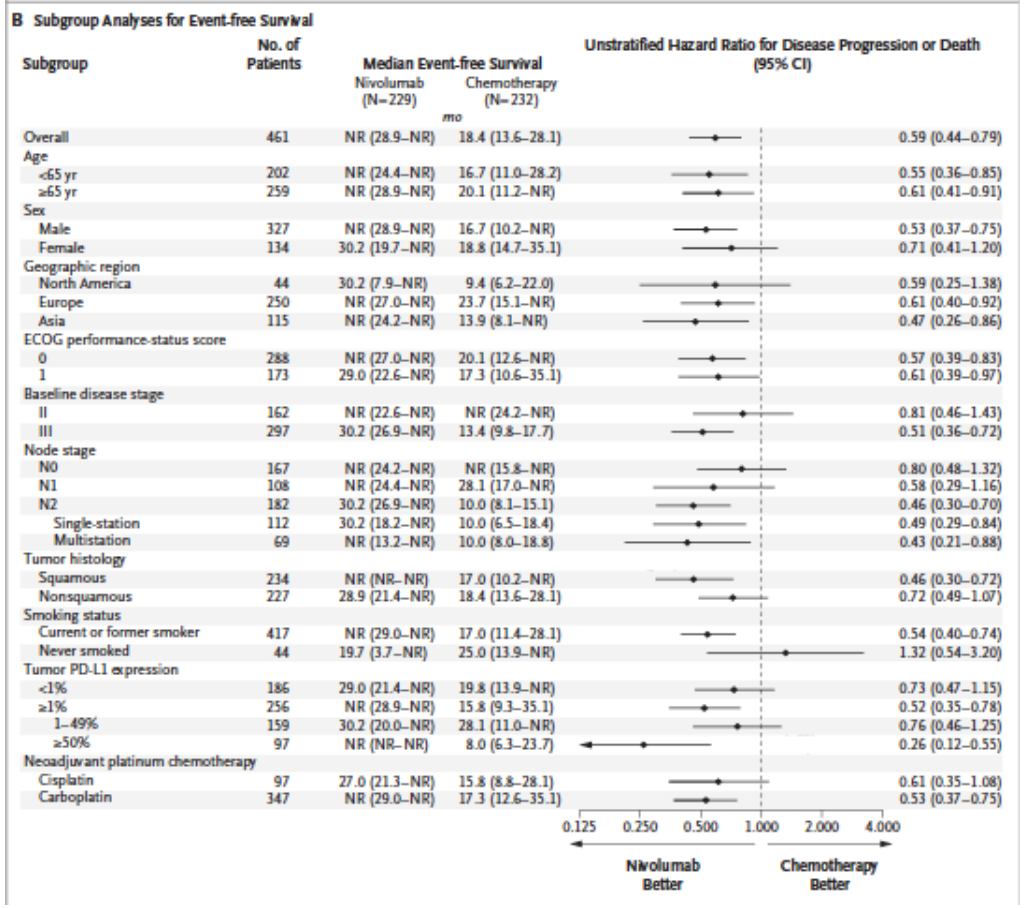


Path CR 25%, mPR 35%

EFS 70% vs 50% at 18 months

Higher PDL1 and higher stage benefit most





Keynote 671 Survival Outcomes

Lancet Sept 2024

Keynote 671: Survival Results

Neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab compared with neoadjuvant chemotherapy alone in patients with early-stage non-small-cell lung cancer (KEYNOTE-671): a randomised, double-blind, placebo-controlled, phase 3 trial

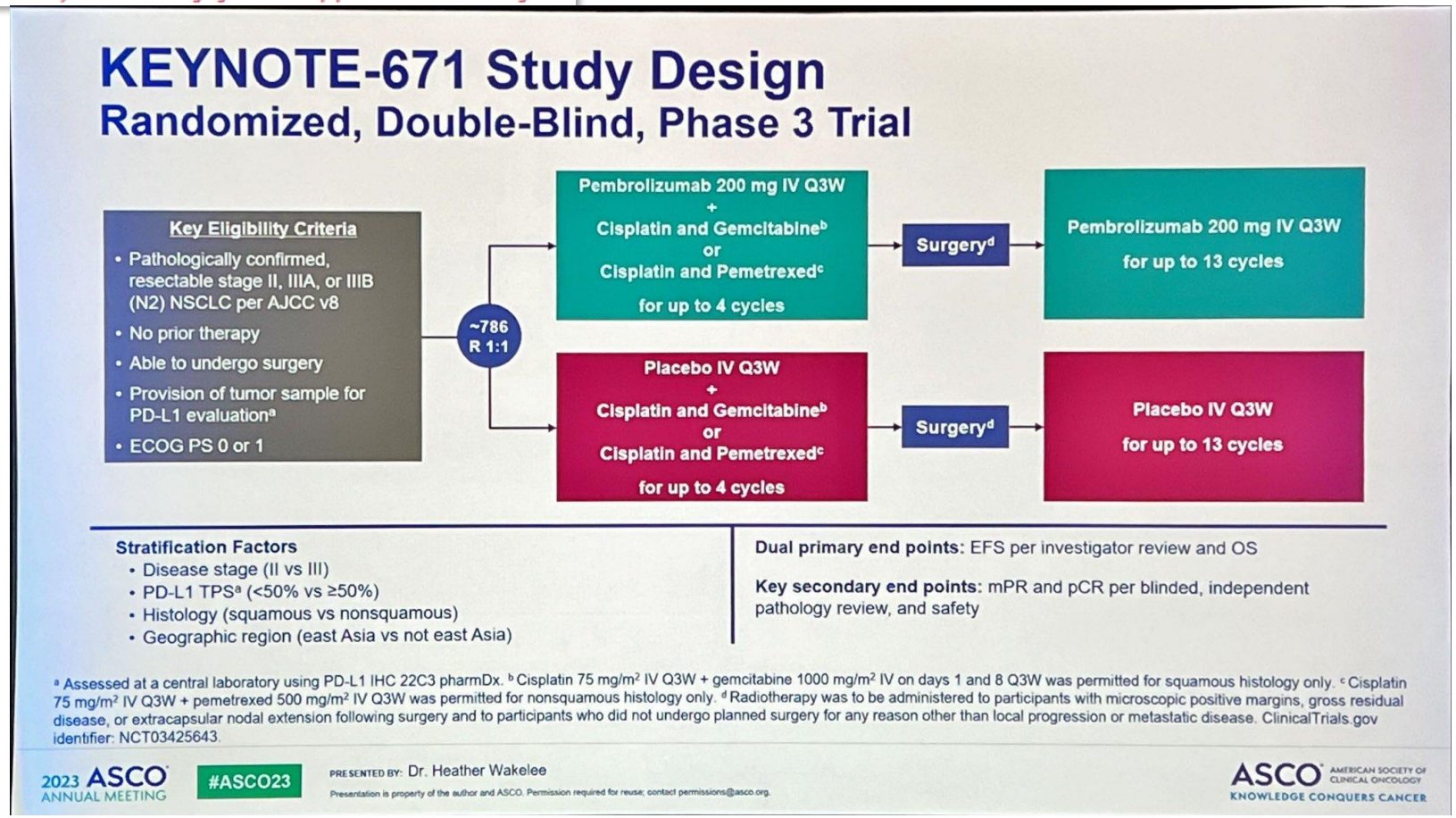
Jonathan D Spicer*, Marina C Garassino*, Heather Wakelee, Moishe Liberman, Terufumi Kato, Masahiro Tsuboi, Se-Hoon Lee, Ke-Neng Chen, Christophe Dooms, Margarita Majem, Ekkehard Eigendorff, Gastón L Martinengo, Olivier Bylicki, Delvys Rodríguez-Abreu, Jamie E Chaft, Silvia Novello, Jing Yang, Ashwini Arunachalam, Steven M Keller, Ayman Samkari, Shugeng Gao, on behalf of the KEYNOTE-671 Investigators†

www.thelancet.com Vol 404 September 28, 2024

Stage 2A-3B
(no egfr/alk rules)

797 patients randomized

Endpoints:
OS and EFS



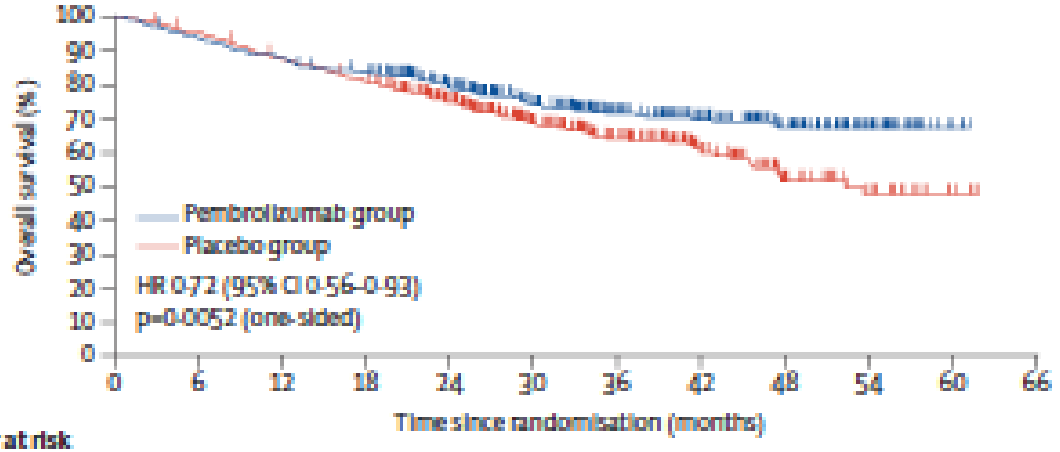
Neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab compared with neoadjuvant chemotherapy alone in patients with early-stage non-small-cell lung cancer (KEYNOTE-671): a randomised, double-blind, placebo-controlled, phase 3 trial

Jonathan D Spicer*, Marina C Garassino*, Heather Wakelee, Moishe Liberman, Terufumi Kato, Masahiro Tsuboi, Se-Hoon Lee, Ke-Neng Chen, Christophe Dooms, Margarita Majem, Ekkehard Eigendorff, Gastón L Martinengo, Olivier Bylicki, Delvys Rodríguez-Abreu, Jamie E Chaft, Silvia Novello, Jing Yang, Ashwini Arunachalam, Steven M Keller, Ayman Samkari, Shugeng Gao, on behalf of the KEYNOTE-671 Investigators†

at 3 years:
OS 71% vs 64%
HR 0.72

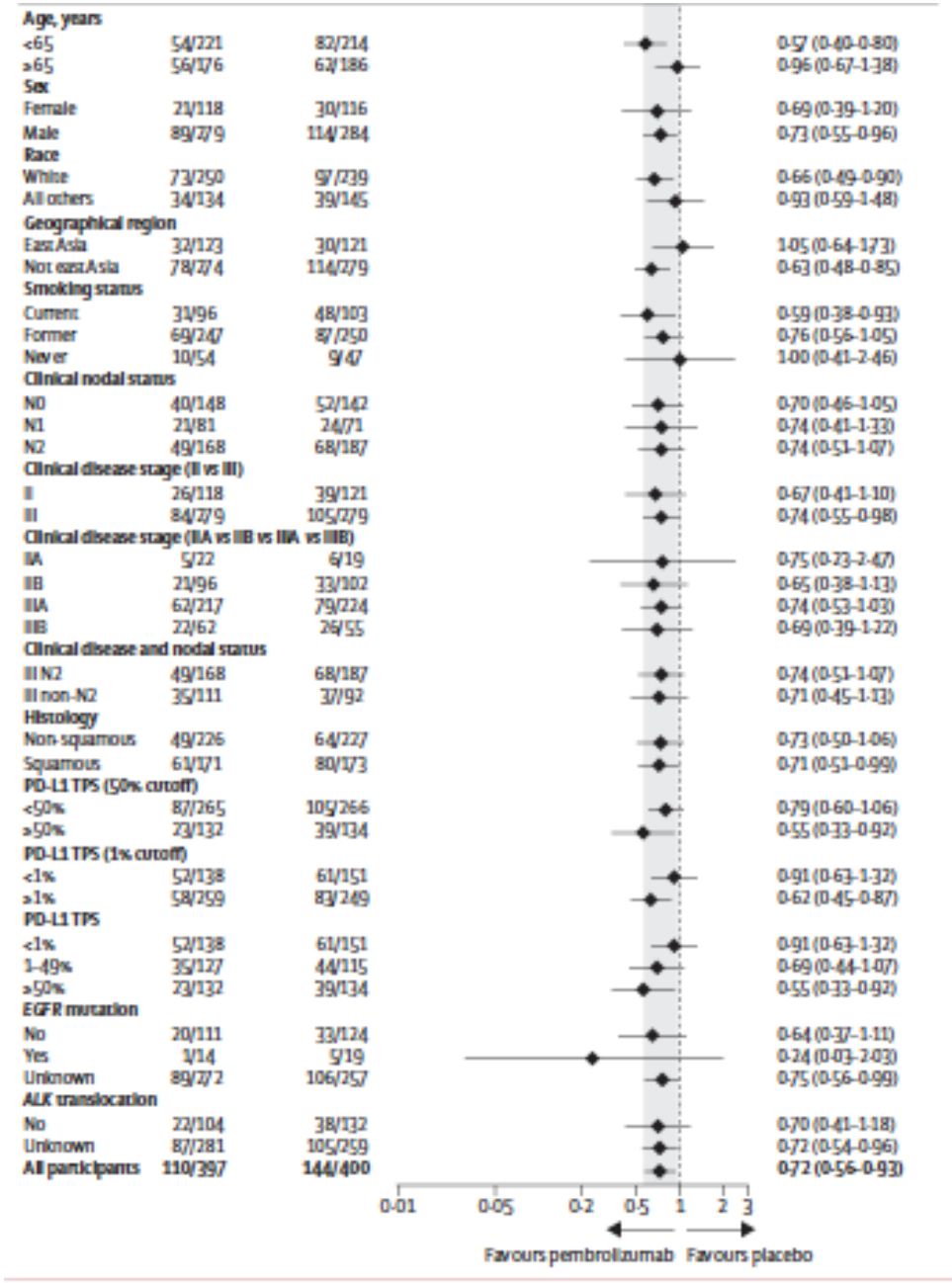
EFS 54% vs 35%
HR 0.59

A



Number at risk (number censored)												
Pembrolizumab group	397 (0)	371 (1)	347 (1)	327 (4)	277 (38)	205 (95)	148 (145)	108 (182)	69 (218)	32 (255)	4 (283)	0 (287)
Placebo group	400 (0)	379 (2)	347 (4)	319 (5)	256 (45)	176 (106)	125 (147)	77 (190)	39 (219)	20 (236)	4 (252)	0 (256)

B



Key Esophageal Papers

Esophageal Cancer

ESOPEC Trial

NEJM Jan 2025

(see also GTSC podcast)

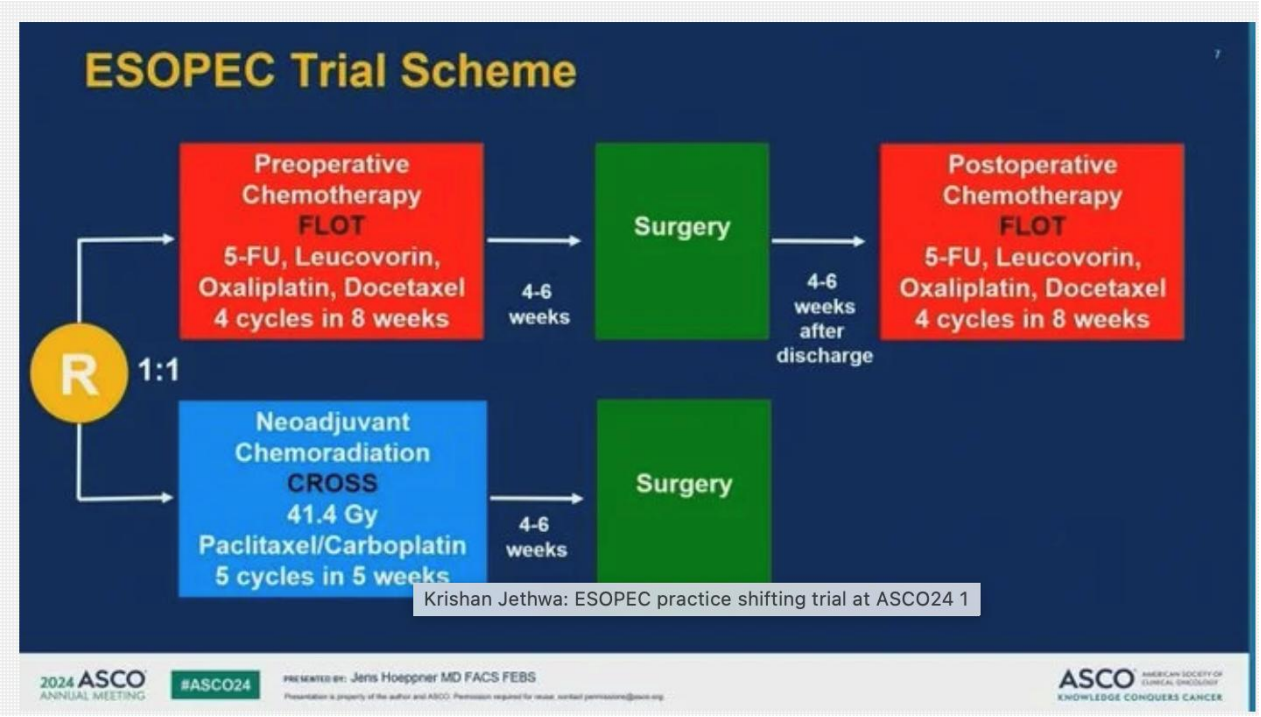
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 23, 2025 VOL. 392 NO. 4

Perioperative Chemotherapy or Preoperative Chemoradiotherapy in Esophageal Cancer

J. Hoeppner, T. Brunner, C. Schmoor, P. Bronsert, B. Kulemann, R. Claus, S. Utzolino, J.R. Izbicki, I. Gockel, B. Gerdes, M. Ghadimi, B. Reichert, J.F. Lock, C. Bruns, E. Reitsamer, M. Schmeding, F. Benedix, T. Keck, G. Folprecht, P. Thuss-Patience, U.P. Neumann, A. Pascher, D. Imhof, S. Daum, T. Strieder, C. Krautz, S. Zimmermann, J. Werner, R. Mahlberg, G. Illerhaus, P. Grimminger, and F. Lordick

ESOPEC Trial – Adenocarcinoma
cT2-4a cN0
CT1-4a cN+
438 patients randomized
all but 2% were Siewert 1 or 2



The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 23, 2025 VOL. 392 NO. 4

ESOPEC

Perioperative Chemotherapy or Preoperative Chemoradiotherapy in Esophageal Cancer

J. Hoeppner, T. Brunner, C. Schmoor, P. Bronsert, B. Kulemann, R. Claus, S. Utzolino, J.R. Izbicki, I. Gockel, B. Gerdes, M. Ghadimi, B. Reichert, J.F. Lock, C. Bruns, E. Reitsamer, M. Schmeding, F. Benedix, T. Keck, G. Folprecht, P. Thuss-Patience, U.P. Neumann, A. Pascher, D. Imhof, S. Daum, T. Strieder, C. Krautz, S. Zimmermann, J. Werner, R. Mahlberg, G. Illerhaus, P. Grimminger, and F. Lordick

Summary of Trial Results

	ESOPEC Trial				
	FLOT Group	CROSS Group	CROSS Trial (CRT Group - AC)	Neo-AEGIS Trial (CRT Group)	FLOT-4 (FLOT Group)
Completed **pre-op** treatment	87.3%	**67.7%**	92%	87% (RT - 99%)	90%
Completed **post-op** treatment	52.5%				46%
pCR	16.8%	**10%**	23%	12%	16%
Median OS	66 mos	**39 mos**	43 mos	49 mos	50 mos
3-year OS	57.4%	50.7%	54%	57%	57%

2024 ASCO ANNUAL MEETING #ASCO24 Karyn A. Goodman, MD, MS ASCO

HR for survival: 0.70
HR for PFS: 0.66
3 year 57% vs 50%
5 year 50% vs 38%

Median survival 66 mo
vs 37 mo

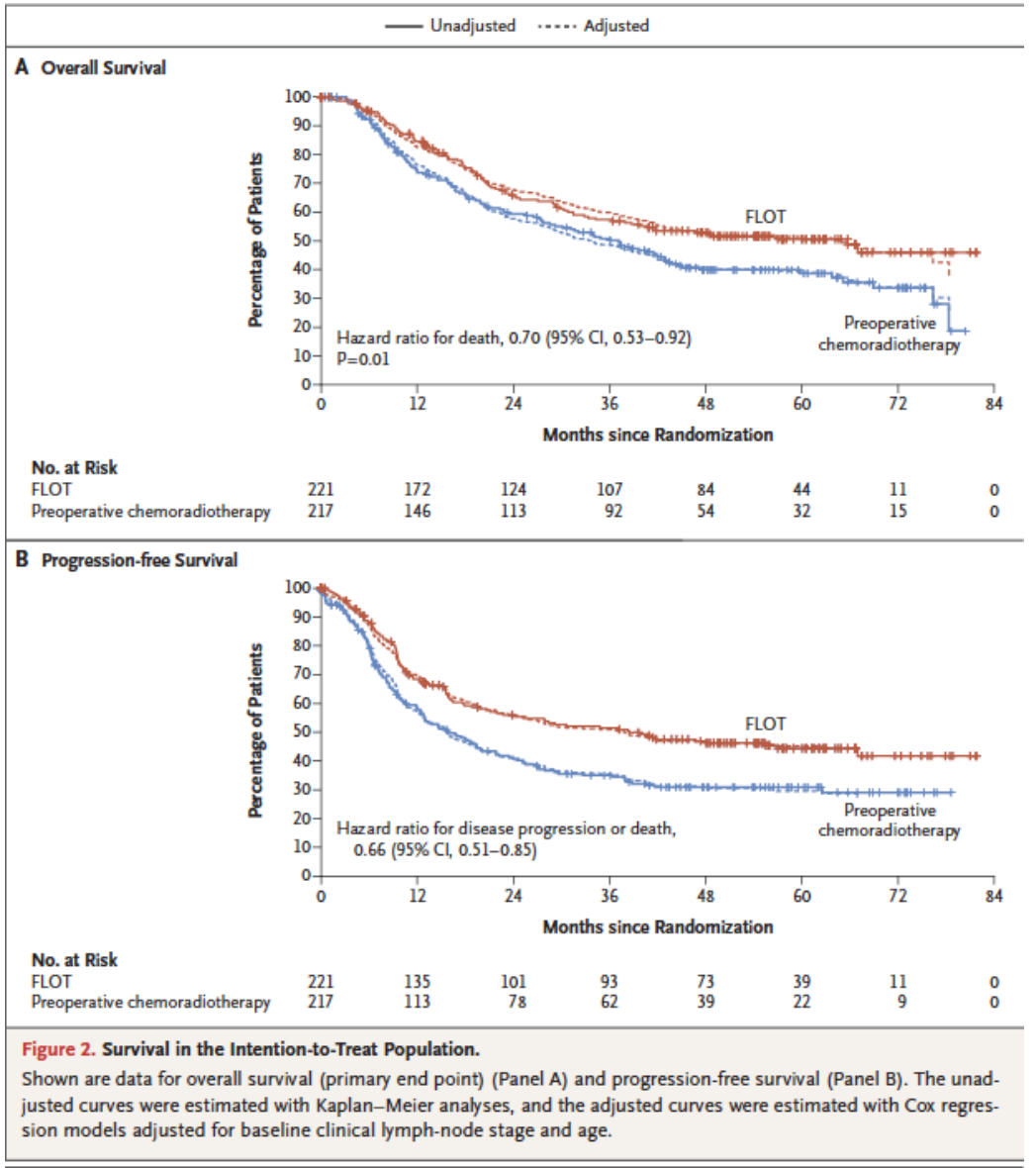
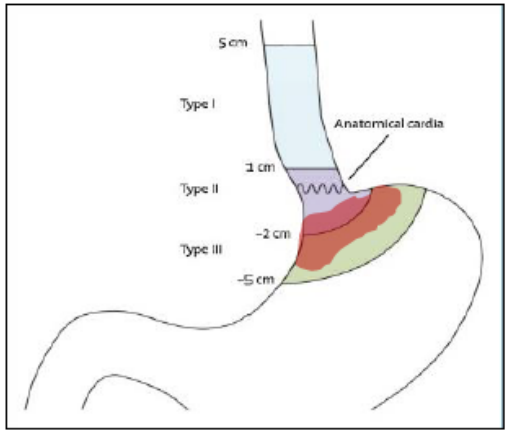


Figure 2. Survival in the Intention-to-Treat Population.
Shown are data for overall survival (primary end point) (Panel A) and progression-free survival (Panel B). The unadjusted curves were estimated with Kaplan–Meier analyses, and the adjusted curves were estimated with Cox regression models adjusted for baseline clinical lymph-node stage and age.

Neo-AEGIS: Phase 3 RCT CROSS vs FLOT NCT01726452 Reported ASCO 2021

377 patients Adeno of Eso/GEJ

- Carbo Taxol + 41 GY (CROSS) vs. Docetaxel, 5FU, Leucovorin, Oxaliplatin (FLOT) or MAGIC
- 3 year survival 56% and 57%
- NONINFERIORITY of periop chemo vs. CROSS
- *Useful for GEJ when not sure if Siewert 2 vs 3*



	Arm A (Magic/FLOT)	Arm B CROSS
R0 (negative margins)	82%	95%
ypN0	44.5%	60.1%
Tumor regression grade 1 & 2	12.1%	41.7%
Pathologic complete response	5%	16%
Neutropenia (Gr 3/4)	14.1%	2.8%
Neutropenic sepsis	2.7%	0.6%
Postoperative in-hospital deaths	3%	3%
Postoperative Pneumonia/ARDS	20%/0.6%	16%/4.3%
Anastomotic Leak	12%	11.7%
Clavien-Dindo > III<V	23.6%	22%

(Abstract Only)

DOI:10.1200/JCO.2021.39.15_suppl.4004 *Journal of Clinical Oncology* 39, no. 15_suppl (May 20, 2021) 4004-4004.

https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.15_suppl.4004

Esophageal Cancer Review

Lancet Nov 2024

www.thelancet.com Vol 404 November 16, 2024

Oesophageal cancer

Hong Yang, Feng Wang, Christopher L Hallemeier, Toni Lerut, Jianhua Fu

Oesophageal cancer is the seventh leading cause of cancer mortality worldwide. Two major pathological subtypes exist: oesophageal squamous cell carcinoma and oesophageal adenocarcinoma. Epidemiological studies in the last decade have shown a gradual increase in the incidence of oesophageal adenocarcinoma worldwide. The prognosis of oesophageal cancer has greatly improved due to breakthroughs in screening, surgical procedures, and novel treatment modalities. The success achieved with combined modality therapies, including surgery, chemotherapy, and radiotherapy, to treat locally advanced oesophageal cancer is particularly notable. Immunotherapy has become a crucial treatment for oesophageal cancer, with immune checkpoint inhibitor-based therapies now established as the standard of care in adjuvant and metastatic first-line settings. This Seminar provides an overview of advances in the screening, diagnosis, and treatment of oesophageal squamous cell carcinoma and oesophageal adenocarcinoma, with a particular focus on neoadjuvant therapies for locally advanced oesophageal cancer and immune checkpoint inhibitor-based therapies.

Lancet 2024; 404: 1991–2005

Department of Thoracic Surgery (Prof H Yang MD PhD, Prof J Fu MD PhD) and Department of Medical Oncology (Prof F Wang MD PhD), Sun Ya University Cancer Center, Guangzhou, China; Guangdong Provincial Clinical Research Center for Cancer, State Key Laboratory of Oncology in South China, Collaborative Innovation Centre for Cancer Medicine

	Number of participants	Tumour histology	Treatment	Overall survival rate (%);* HR (95% CI)	Progression-free survival or disease-free survival rate (%);* HR (95% CI)
Neoadjuvant chemotherapy					
OE02[20]	802	Oesophageal squamous cell carcinoma (247), oesophageal adenocarcinoma (533), undifferentiated or unknown cancer (22)	Neoadjuvant chemotherapy (fluorouracil and platinum) vs surgery	17% vs 23%; 0·84 (0·72–0·98)	NR; NR
JCOG9907[40]	330	Oesophageal squamous cell carcinoma	Neoadjuvant chemotherapy (fluorouracil and platinum) vs adjuvant chemotherapy (fluorouracil and platinum)	55% vs 43%; 0·73 (0·54–0·99)†	Progression-free survival 44% vs 39%; 0·84 (0·63–1·11)†
Perioperative chemotherapy					
MAGIC[18]	503	Gastro-oesophageal junction (131), gastric cancer (372)	Perioperative chemotherapy (fluorouracil and platinum) vs surgery	36% vs 23%; 0·66 (0·53–0·81)	Progression-free survival NR; 0·75 (0·60–0·93)
FNCLCC-FFCD[19]	224	Oesophageal adenocarcinoma (25), gastro-oesophageal junction (144), gastric cancer (55)	Perioperative chemotherapy (fluorouracil and platinum) vs surgery	38% vs 24%; 0·69 (0·50–0·95)	Disease-free survival 34% vs 19%; 0·65 (0·48–0·89)
FLOT4[41]	716	Gastro-oesophageal junction (398), gastric cancer (318)	Fluorouracil, leucovorin, oxaliplatin, and docetaxel vs epirubicin, cisplatin, and either fluorouracil or capecitabine	45% vs 36%; 0·77 (0·63–0·94)	Disease-free survival NR; 0·75 (0·62–0·91)
Preoperative chemoradiotherapy					
CROSS[42,43]	366	Oesophageal squamous cell carcinoma (84), oesophageal adenocarcinoma (275), undifferentiated cancer (7)	Neoadjuvant chemoradiotherapy (paclitaxel and platinum) vs surgery	38% vs 25%; 0·70 (0·55–0·89)†	Progression-free survival 44% vs 27%; 0·69 (0·52–0·92)
NEOCRTEC5010[44]	451	Oesophageal squamous cell carcinoma	Neoadjuvant chemoradiotherapy (vinorelbine and platinum) vs surgery	60% vs 49%; 0·73 (0·55–0·97)	Disease-free survival 64% vs 43%; 0·55 (0·40–0·74)
Chemotherapy vs chemoradiotherapy					
Neo-AEGIS[45]	362	Low oesophagus or type I gastro-oesophageal junction (249), type II gastro-oesophageal junction (84), type III gastro-oesophageal junction (29)	Perioperative chemotherapy‡ vs neoadjuvant chemoradiotherapy (paclitaxel and platinum)	55% vs 57%; 1·03 (0·77–1·38)§	Disease-free survival NR; 0·89 (0·68–1·17)
NeoRes[46]¶	181	Squamous cell carcinoma (50), adenocarcinoma (131)	Neoadjuvant chemoradiotherapy vs chemotherapy (fluorouracil and platinum)	49% vs 47%; NR§	Progression-free survival 44% vs 44%; NR§
CMISG1701[47]	264	Oesophageal squamous cell carcinoma	Neoadjuvant chemoradiotherapy vs chemotherapy (paclitaxel and platinum)	64% vs 55%; 0·82 (0·58–1·18)	Progression-free survival 54·3% vs 49·8%; 0·83 (0·59–1·16)
JCOG1109[48]	601	Oesophageal squamous cell carcinoma (591), basal cell cancer (8), oesophageal adenocarcinoma (2)	Neoadjuvant chemoradiotherapy vs chemotherapy (fluorouracil and platinum)	68% vs 63%; 0·84 (0·63–1·12)§	Progression-free survival 62% vs 48%; 0·77 (0·59–1·01)
JCOG1109[48]	601	Oesophageal squamous cell carcinoma (591), basal cell cancer (8), oesophageal adenocarcinoma (2)	Neoadjuvant chemotherapy (fluorouracil, platinum, and docetaxel) vs chemotherapy (fluorouracil and platinum)	72% vs 63%; 0·68 (0·50–0·92)§	Progression-free survival 59% vs 48%; 0·67 (0·51–0·88)

HR=hazard ratio. NR=not reported. *5-year survival rate unless specified otherwise. †10-year survival. ‡Oxaliplatin and fluorouracil or capecitabine before 2018; and fluorouracil, leucovorin, oxaliplatin, and docetaxel regimen after 2018. §3-year survival. ¶NeoRes trial is a phase 2 trial.

Table 2: **Key randomised clinical trials of preoperative or perioperative therapy for resectable oesophageal cancer**

Reviews advances in screening, diagnosis, treatment

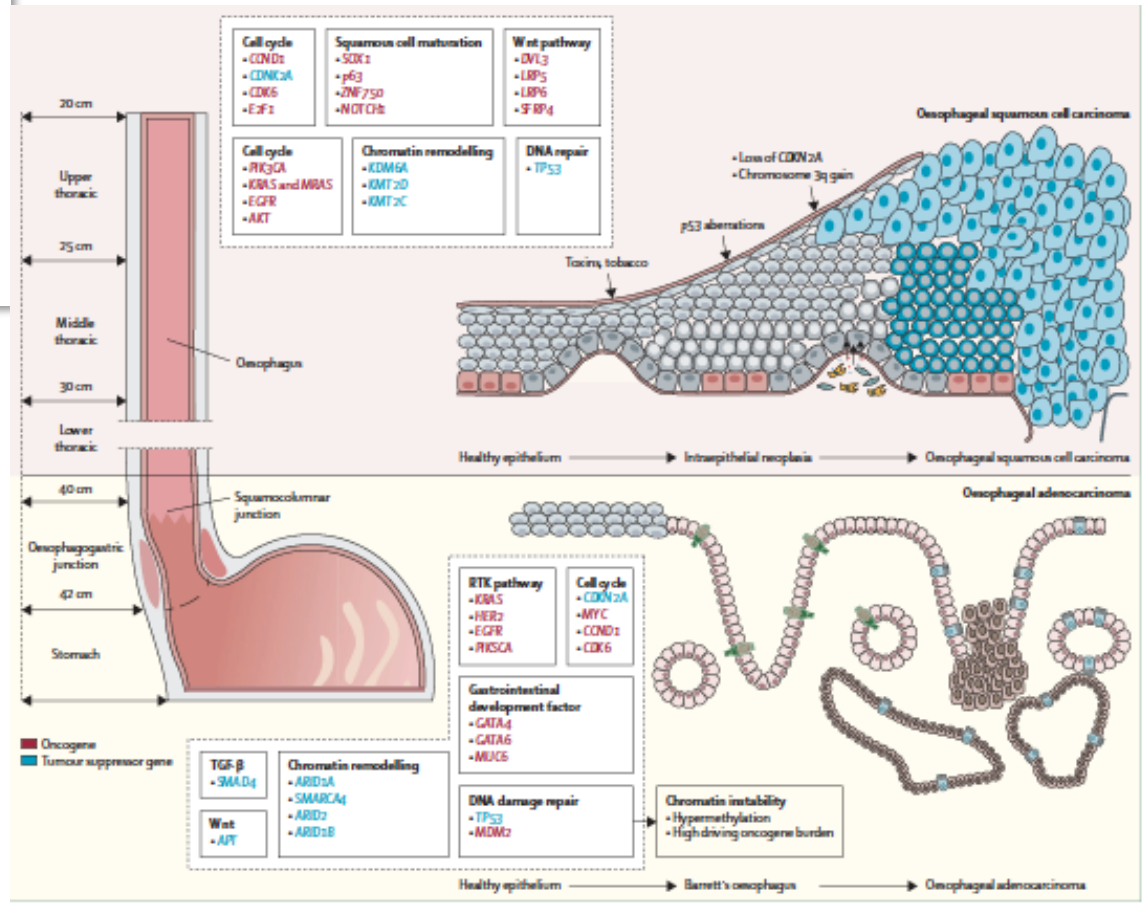


Figure: Genomic changes during the development of oesophageal cancer
Oesophageal squamous cell carcinoma and oesophageal adenocarcinoma are the two major histological types of oesophageal cancer. Oesophageal squamous cell carcinoma typically arises in the upper and middle oesophagus, whereas oesophageal adenocarcinoma predominates near the oesophagogastric junction. Oesophageal squamous cell carcinoma develops from malignant transformation of the squamous epithelium due to chronic exposure to tobacco and alcohol, with environmental carcinogens inducing DNA damage and somatic mutations. Key drivers include *TP53* mutations, somatic copy number alterations, and inactivation of cell cycle regulators, such as *CDKN2A*, leading to intraepithelial neoplasia. Genomic instability in intraepithelial neoplasia disrupts key pathways, such as RTK signalling, squamous cell maturation, and Wnt signalling, and causes chromatin remodelling, which can progress to oesophageal squamous cell carcinoma. In contrast, oesophageal adenocarcinoma arises from intestinal metaplasia at the squamocolumnar junction due to chronic gastric acid reflux, forming Barrett's oesophagus. Dysplasia of gland cells, driven by *TP53* mutations and oncogene alterations (eg, *HER2*), leads to oesophageal adenocarcinoma. Oncogene activation and tumour suppressor gene inactivation result in the malignant transformation from Barrett's oesophagus to oesophageal adenocarcinoma, through dysregulation of the RTK, TGF-β, and Wnt signalling pathways and chromatin remodelling. Genomically, oesophageal adenocarcinoma shares similarities with gastro-oesophageal adenocarcinoma of the chromatin instability type. RTK=receptor tyrosine kinase.

Benign Esophagus Papers

JAMA Surgery | Original Investigation

Anterior Gastropexy for Paraesophageal Hernia Repair
A Randomized Clinical Trial

Clayton C. Petro, MD; Ryan C. Ellis, MD; Sara M. Maskal, MD; Sam J. Zolin, MD; Chao Tu, MS; Adele Costanzo, RN; Lucas R. A. Beffa, MD; David M. Krpata, MD; Diya Alaedeen, MD; Ajita S. Prabhu, MD; Benjamin T. Miller, MD; Kevin F. Baier, MD; Alisan Fathalizadeh, MD; John Rodriguez, MD; Michael J. Rosen, MD

240 patients randomized
Imaging at 30d and 1y
Recurrence at 1 year:
15% with pexy vs 36% without

POPULATION
39 Males, 201 Females

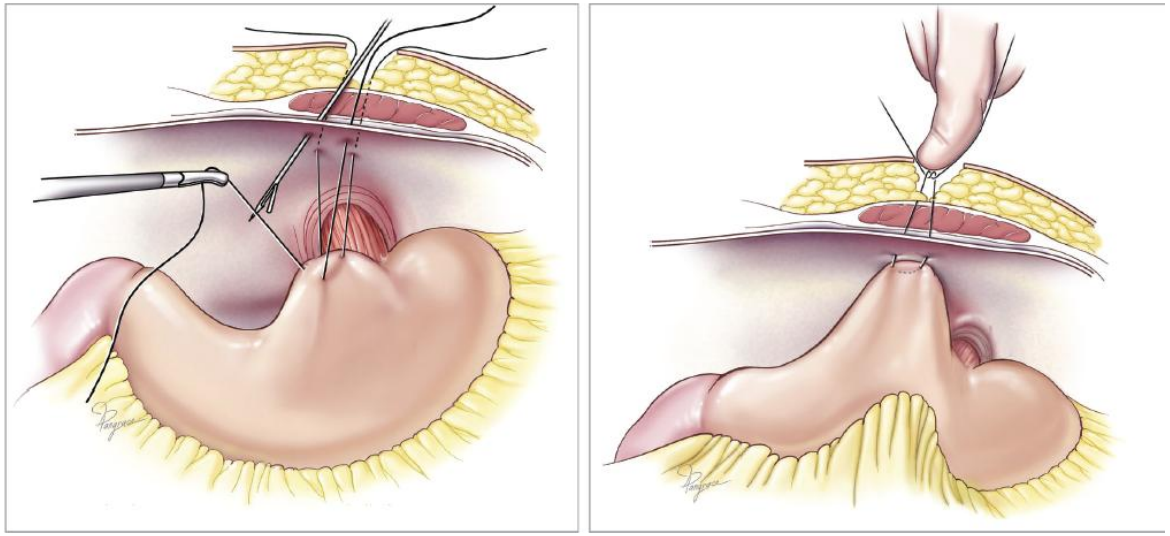
Adults with symptomatic paraesophageal hernias >5 cm
Mean age, 69 y

SETTINGS / LOCATIONS
3 Academic hospitals

Figure 1. Transfascial Anterior Gastropexy Suture Placement

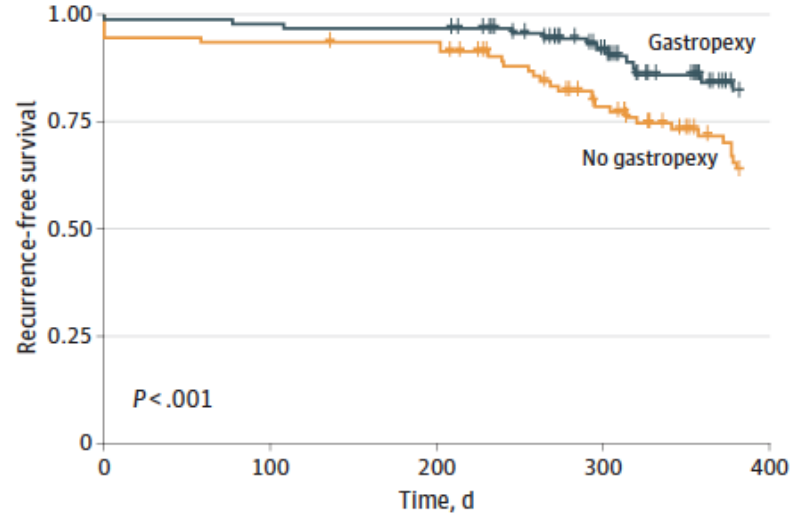
A Suture placement during anterior gastropexy

B Fixation of the anterior body of the stomach to the abdominal wall



transfascial fixation of the anterior body of the stomach near the greater curve to the left upper quadrant of the abdominal wall (using a suture passer) with 2 2-0 polypropylene sutures

Figure 3. Kaplan-Meier Plot for Paraoesophageal Hernia Recurrence



No. at risk				
Gastropexy	94	92	91	68
No gastropexy	94	88	87	64

JAMA Surgery Published online December 23, 2024 NCT04007952

Surgical Professional Issues

Thoracic Surgeon Shortage

JTCVS

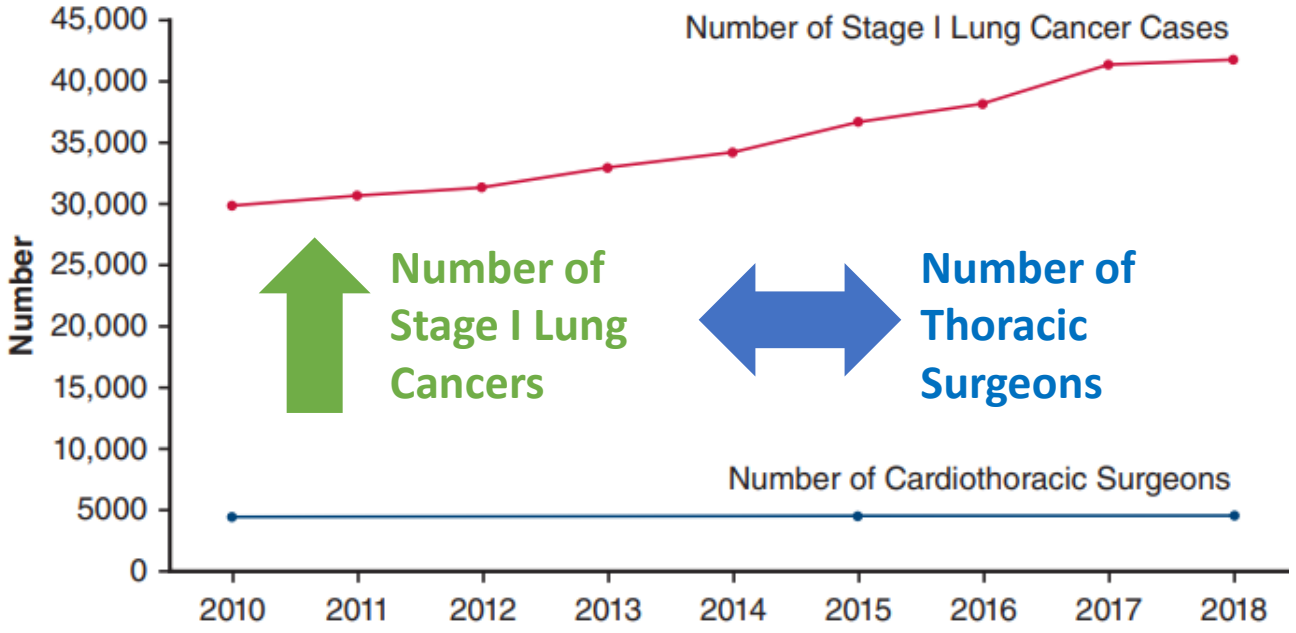
Shortage of thoracic surgeons in the United States: Implications for treatment and survival for stage I lung cancer patients

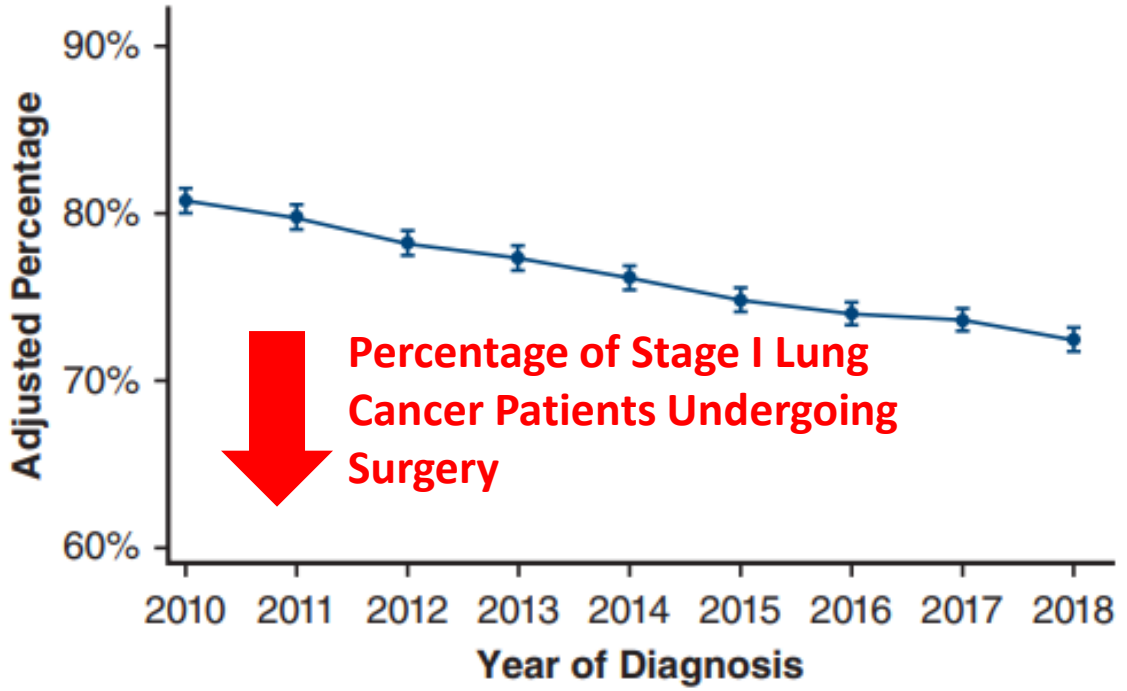
Alexandra L. Potter, BS,[a] Allison L. Rosenstein, BA,[a] Keervani Kandala, BSc,[a] Shivaek Venkateswaran,[a] Mathew V. Kiang, ScD,[b] Olugbenga T. Okusanya, MD,[c] Hugh G. Auchincloss, MD,[a] Linda W. Martin, MD,[d] Yolonda L. Colson, MD, PhD,[a] and Chi-Fu Jeffrey Yang, MD[a]

#surgeons per 100K population
#lung cancers between 2010-2018

Even fewer patients in underserved/rural areas had surgery for stage 1 lung cancer

Perhaps we need to increase training spots in thoracic surgery.....!





Potter et al, *Journal of Thoracic and Cardiovascular Surgery*, 2023

Comparison of Postoperative Outcomes Among Patients Treated by Male Versus Female Surgeons

Ann Surgery Jan 2025

Comparison of Postoperative Outcomes Among Patients Treated by Male Versus Female Surgeons

A Systematic Review and Meta-analysis

Natsumi Saka, MD, MSc, PhD,† Norio Yamamoto, MD,†‡ Jun Watanabe, MD, PhD,†§‖ Christopher Wallis, MD, PhD,¶#** Angela Jerath, MSc, MD, BSc,†† Hidehiro Someko, MD,†‡‡ Minoru Hayashi, MD,†§§ Kyosuke Kamijo, MD,†‖‖ Takashi Ariie, MSc, PhD,†¶¶ Toshiki Kuno, MD, PhD,## Hirotaka Kato, PhD,*** Hodan Mohamud, BSc,¶ Ashton Chang, MD,†† Raj Satkunasivam, MD, MS,†††‡‡‡§§§ and Yusuke Tsugawa, MD, MPH, PhD‖‖‖¶¶¶✉*

Ann Surg • Volume 280, Number 6, December 2024

Meta-analysis of 15 studies evaluating:
Mortality
Complications
readmissions

Given that female surgeons are compensated less and less likely to be promoted than male surgeons,[17–24] a better understanding of the performance of female surgeons has important clinical and policy implications. In this context, we performed a systematic review and meta-analysis of available evidence comparing patients' postoperative outcomes (mortality, readmission, and complication rates) between female and male surgeons.

TABLE 1. Summary of Findings Table on Postoperative Outcomes

	Anticipated absolute effects				
Outcomes	**Risk with male surgeons***	**Risk with female surgeons (95% CI)†**	**Relative effect (95% CI)**	**No. participants (studies)**	**Certainty of the evidence‡**
Mortality	10 per 1000	9 per 1000 (9–10)	OR 0.93 (0.88–0.97)	5,390,762 (8 studies)	Moderate§
Readmission	66 per 1000	78 per 1000 (55 –109)	OR 1.20 (0.83–1.74)	1,179,107 (3 studies)	Very low‖
Complication	94 per 1000	89 per 1000 (84–95)	OR 0.94 (0.88–1.01)	1,306,128 (8 studies)	Very Low¶

Mortality difference most pronounced for

- GENERAL surgeons vs specialty
- Nonelective cases

Divorce Among Surgeons and Other Physicians in the US

Ann Surgery Dec 2024

Divorce Among Surgeons and Other Physicians in the United States

Stephen A. Stearns, MD,† Alexander R. Farid, MD,*† and Anupam B. Jena, MD, PhD*†‡✉*

Ann Surg • Volume 281, Number 1, January 2025

US Census data
Included sex, race, income, hours worked/week, #children in household, controlling for age group

3171 surgeons
51660 nonsurgeons

TABLE 2. Prevalence of Divorce by Profession

	Physicians (n = 51,660)	Surgeons (n = 3171)	US adults (n = 12,174,210)
Ever divorced, no. (%)	9252 (17.9)	676 (21.3)	3,259,426 (26.8)
Relative risk of divorce, unadjusted (95% CI)	Reference	1.19 (1.11–1.28)	1.49 (1.47–1.52)
Times married, no. (%)			
Never	6824 (13.2)	278 (8.8)	3,142,348 (25.8)
1	38,094 (73.7)	2366 (74.6)	6,734,642 (55.3)
2	5600 (10.8)	451 (14.2)	1,778,278 (14.6)
3	1142 (2.2)	76 (2.4)	518,942 (4.3)
Relative risk of more than one marriage, unadjusted (95% CI)	Reference	1.27 (1.17–1.38)	1.45 (1.41–1.48)
Age at time of most recent marriage, y (mean)	28.6 (8.7)	29.3 (8.9)	27.6 (10.6)

TABLE 4. Adjusted Odds of Divorce Among Surgeons Compared With Nonsurgeon Physicians, by Sex and Race Subgroups

Subgroup	Adjusted odds ratio of divorce among surgeons compared with nonsurgeon physicians (95% CI)
Sex	
Male	1.26 (1.11–1.42)
Female	1.18 (0.91–1.53)
Race (%)	
White	1.22 (1.09–1.38)
Black	1.00 (0.49–2.06)
Asian	1.55 (1.06–2.26)
Other	0.81 (0.49–1.33)

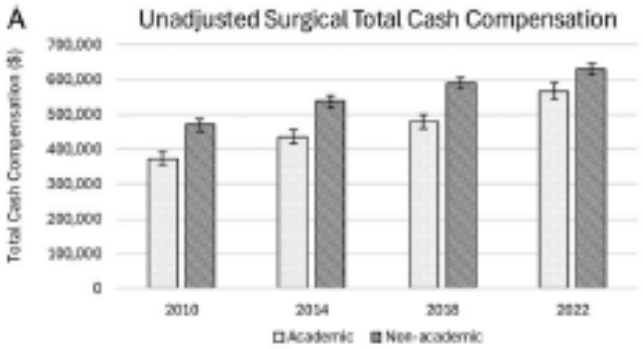
The table presents the odds ratio of divorce among surgeons compared with nonsurgeon physicians by sex and race subgroups, adjusting for age, age at the time of most recent marriage, income, hours worked per week, and the number of children in the household. In subgroup analysis by physician sex, race was additionally adjusted for and similarly, in subgroup analysis by physician race, sex was additionally adjusted for.

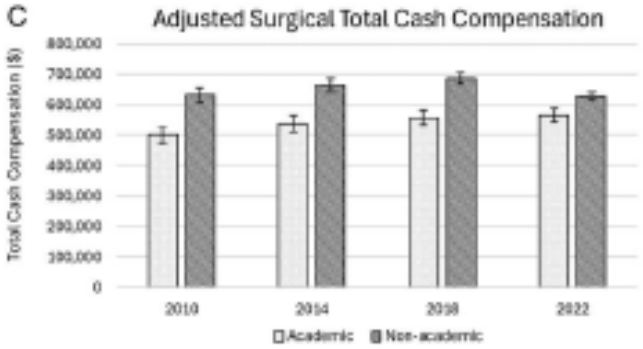
Conclusions: Both surgeons and physicians have lower divorce prevalence than the general population. Surgeons exhibit higher prevalence of divorce compared with nonsurgeon physicians, with measured demographic and work characteristics insufficient to explain this difference.

For the Love of the Game

Ann Surgery Dec 2024

Ann Surg • Volume 280, Number 4, October 2024





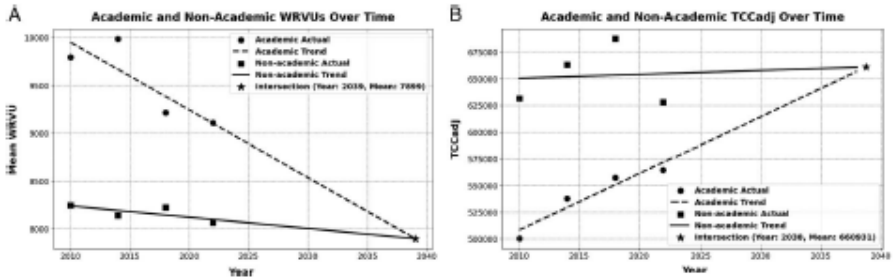


FIGURE 6. Trend analysis for academic and nonacademic surgeons over time. A, Work relative value units. B, Consumer Price Index-adjusted total cash compensation.

Academic vs Private RVU and pay should converge by 2038

ASA PAPER

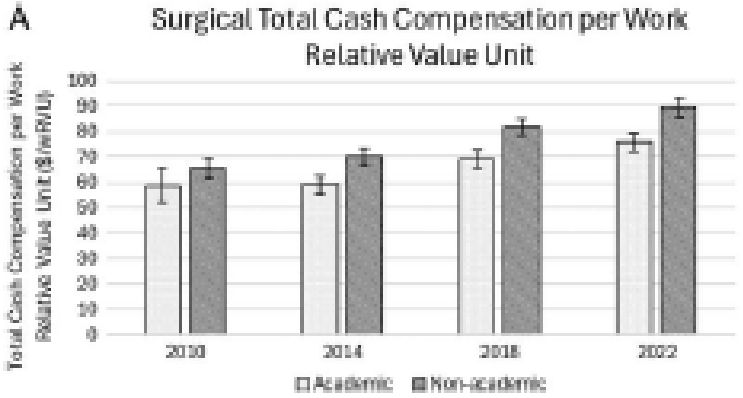
For the Love of the Game

Calculating the Premium Associated With Academic Surgical Practice

Emily A. Grimsley, MD, David O. Anderson, MBA, MHA,† Melissa A. Kendall, MD,* Tyler Zander, MD,* Rajavi Parikh, DO,* Ronald J. Weigel, MD, PhD, MBA,‡ and Paul C. Kuo, MD, MS, MBA*✉*

MGMA provider compensation data from 2010, 2014, 2018, 2022

TCC=total cash compensation
Collections
wRVU



Academic "premium" = 16%

"We can't eat prestige"

Conclusions: In 2022, academic surgeons had more clinical activity and superior organizational revenue capture, despite less total and normalized clinical compensation. On the basis of TCC/wRVUs, academia charges a premium of 16% over nonacademic surgery. However, trend analysis suggests that TCC will converge within the next 20 years.


ONCODAILY 100
Top 100 Xfluencers in Lung Cancer : Key Opinion Leaders to Follow on X (Twitter) in 2024

Folder with all slides, papers

Enjoy the meeting!
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linda.martin@uvahealth.org