New Operable Lung Cancer Algorhytms: Nothing is What it Used to Be!

Benny Weksler, MD, MBA, FACS, FACCP
Chief of Thoracic Surgery
Allegheny Health Network
Professor of Surgery
Drexel University Medical College

Allegheny Health Network
Allegheny General Hospital

Disclosures

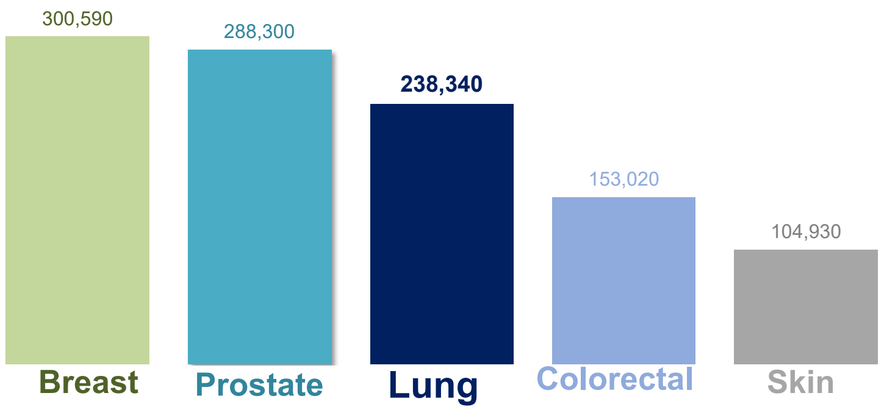
- AstraZeneca - Speaker and advisory board
- Merck - Speaker
- Intuitive - Proctor
- Atricure - Research grant

US Lung Cancer Incidence and Mortality

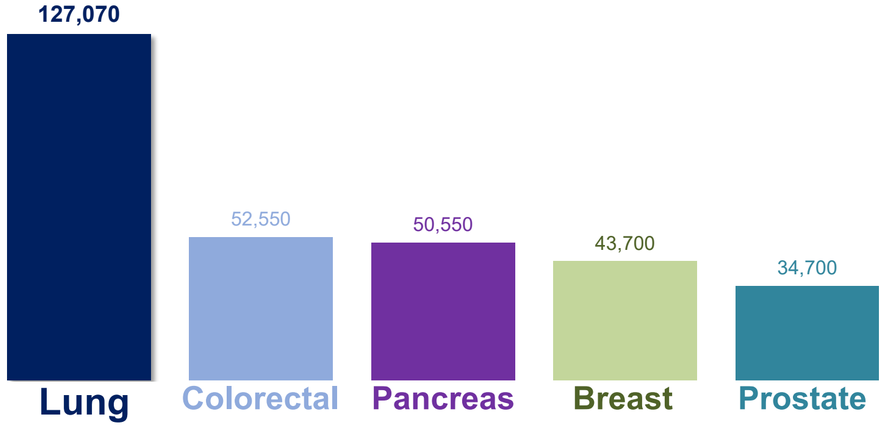
238,340 diagnosed with lung cancer in 2023

127,070 died from lung cancer in 2023

Estimated Cases by Tumor Type



Estimated Deaths by Tumor Type



1 of every 4 cancer deaths is a lung cancer death

ACS Facts & Figures 2023

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NICOTINE IS A WHY PEOPLE SMOKE CIGARETTES

After inhaling, nicotine reaches the brain in

7-10 seconds

- “euphoria” without being “stoned”
- immediate reinforcement of drug-taking behavior
- allow moment to moment titration of dose to achieve the desired effects

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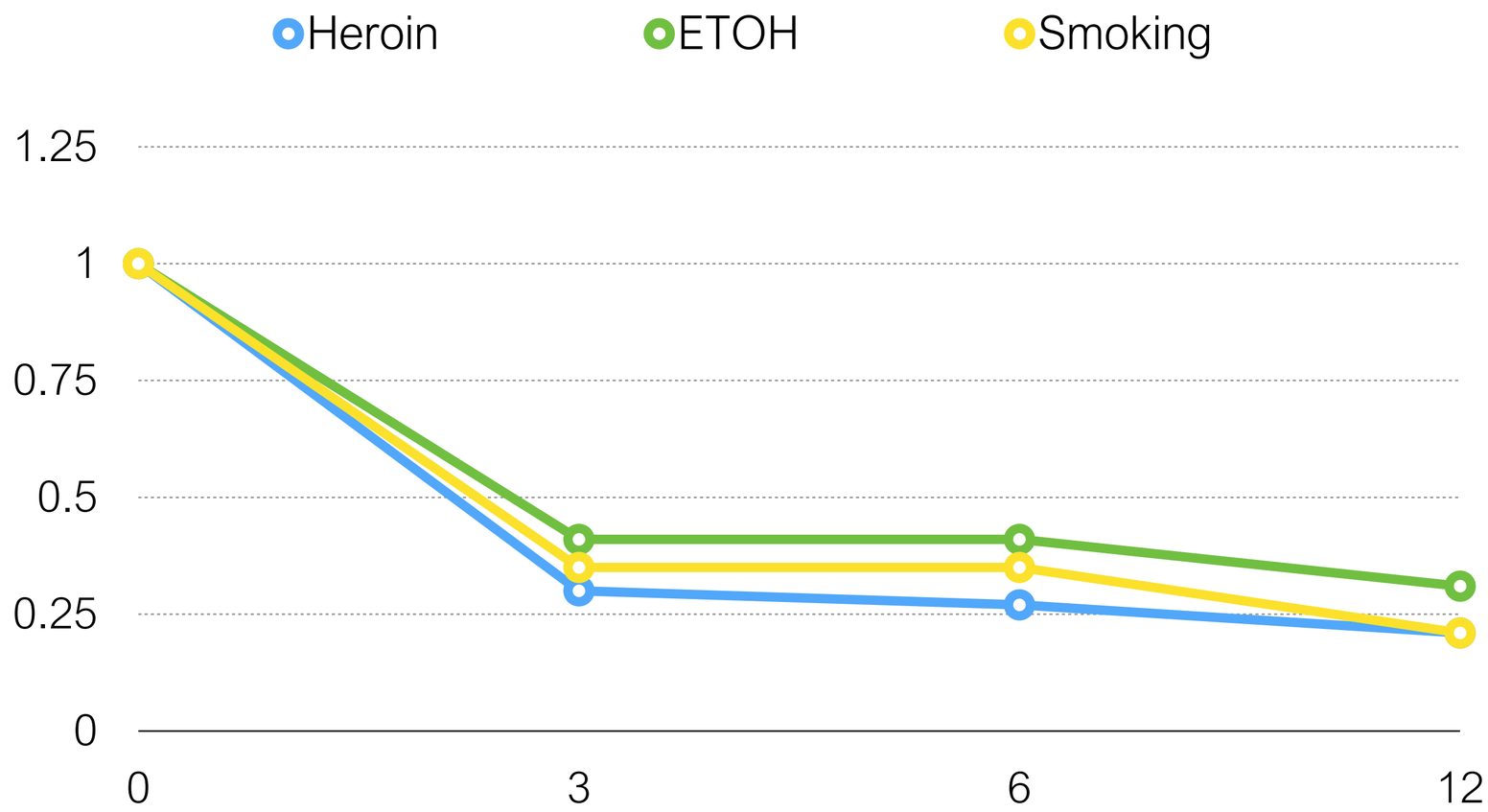
Rate of Relapse



Hunt et al., 1971

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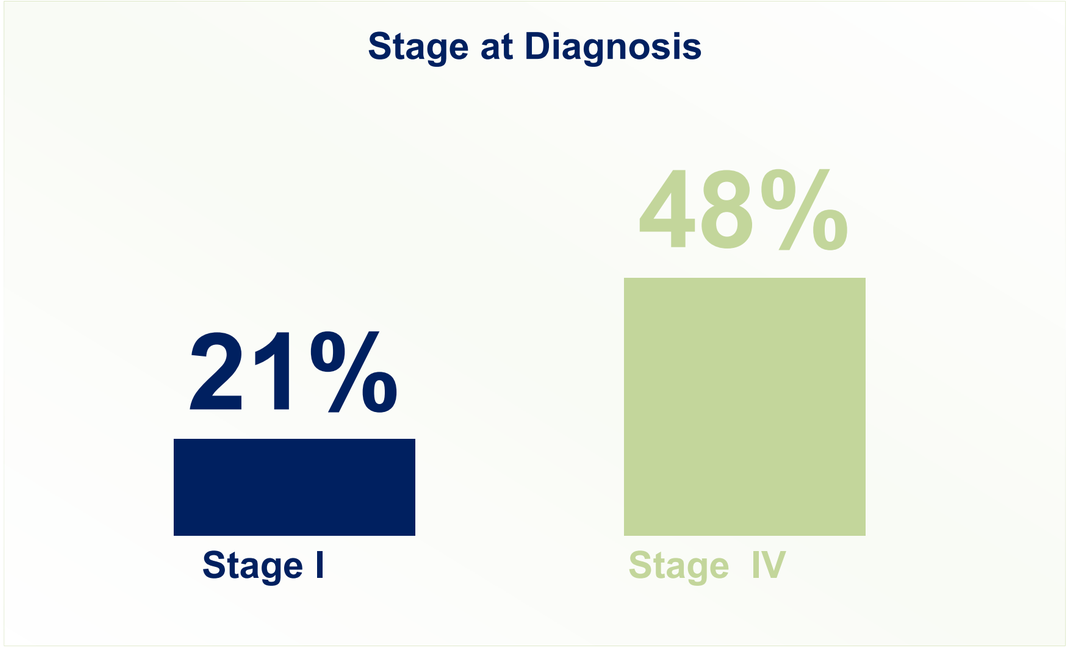
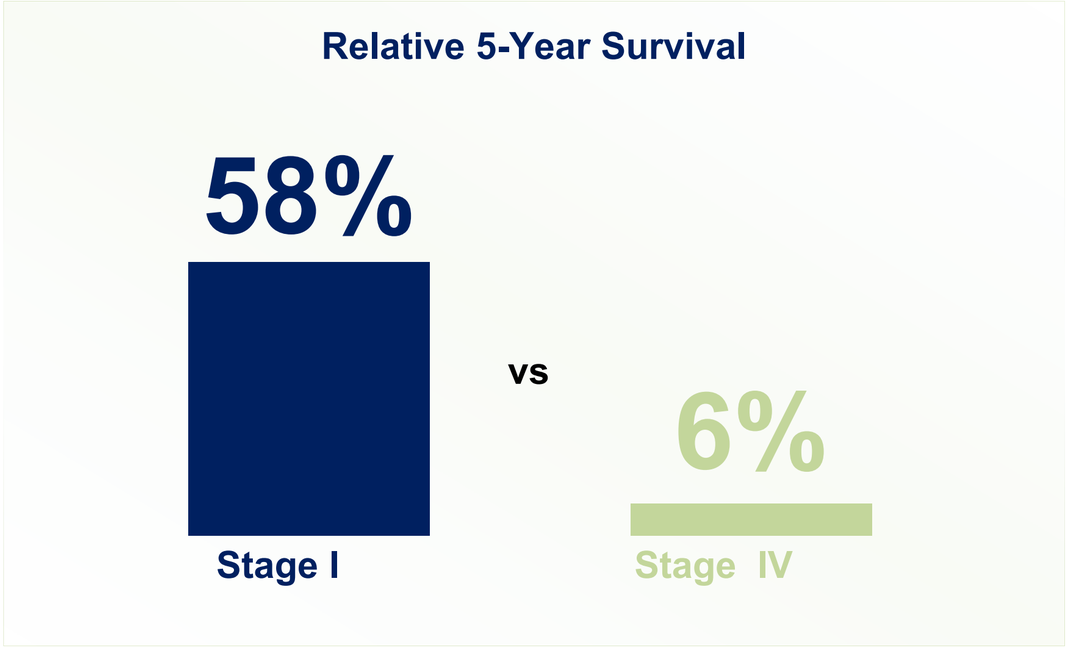
Clinical Reasons for Poor Lung Cancer Prognosis

Two-pronged problem:

We diagnose pts too late



Treatments are ineffective



Early detection and treatment are critical to improving clinical outcomes in patients with lung cancer

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The New York Times

Late Edit

Today, variably clou wers, high 54. Tonight, p udy, cooler, low 40. To sun mixed with clouds, cool, high 50. Weather o.

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Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

ABSTRACT

BACKGROUND

The aggressive and heterogeneous nature of lung cancer has thwarted efforts to reduce mortality from this cancer through the use of screening. The advent of low-dose helical computed tomography (CT) altered the landscape of lung-cancer screening, with studies indicating that low-dose CT detects many tumors at early stages. The National Lung Screening Trial (NLST) was conducted to determine whether screening with low-dose CT could reduce mortality from lung cancer.

METHODS

From August 2002 through April 2004, we enrolled 53,454 persons at high risk for lung cancer at 33 U.S. medical centers. Participants were randomly assigned to undergo three annual screenings with either low-dose CT (26,722 participants) or single-view posteroanterior chest radiography (26,732). Data were collected on cases of lung cancer and deaths from lung cancer that occurred through December 31, 2009.

RESULTS

The rate of adherence to screening was more than 90%. The rate of positive screening tests was 24.2% with low-dose CT and 6.9% with radiography over all three rounds. A total of 96.4% of the positive screening results in the low-dose CT group and 94.5% in the radiography group were false positive results. The incidence of

The members of the writing team (who are listed in the Appendix) assume responsibility for the integrity of the article. Address reprint requests to Dr. Christine D. Berg at the Early Detection Research Group, Division of Cancer Prevention, National Cancer Institute, 6130 Executive Blvd., Suite 3112, Bethesda, MD 20892-7346, or at bergc@mail.nih.gov.

*A complete list of members of the National Lung Screening Trial research team is provided in the Supplementary Appendix, available at NEJM.org.

This article (10.1056/NEJMoa1102873) was published on June 29, 2011, at NEJM.org.

N Engl J Med 2011;365:395-409.

A Quick Move From Tea Party To Flex Muscle

G.O.P. Is Pressed on a Post and a Strategy

By CARL HULSE and DAVID M. HERSZENHORN

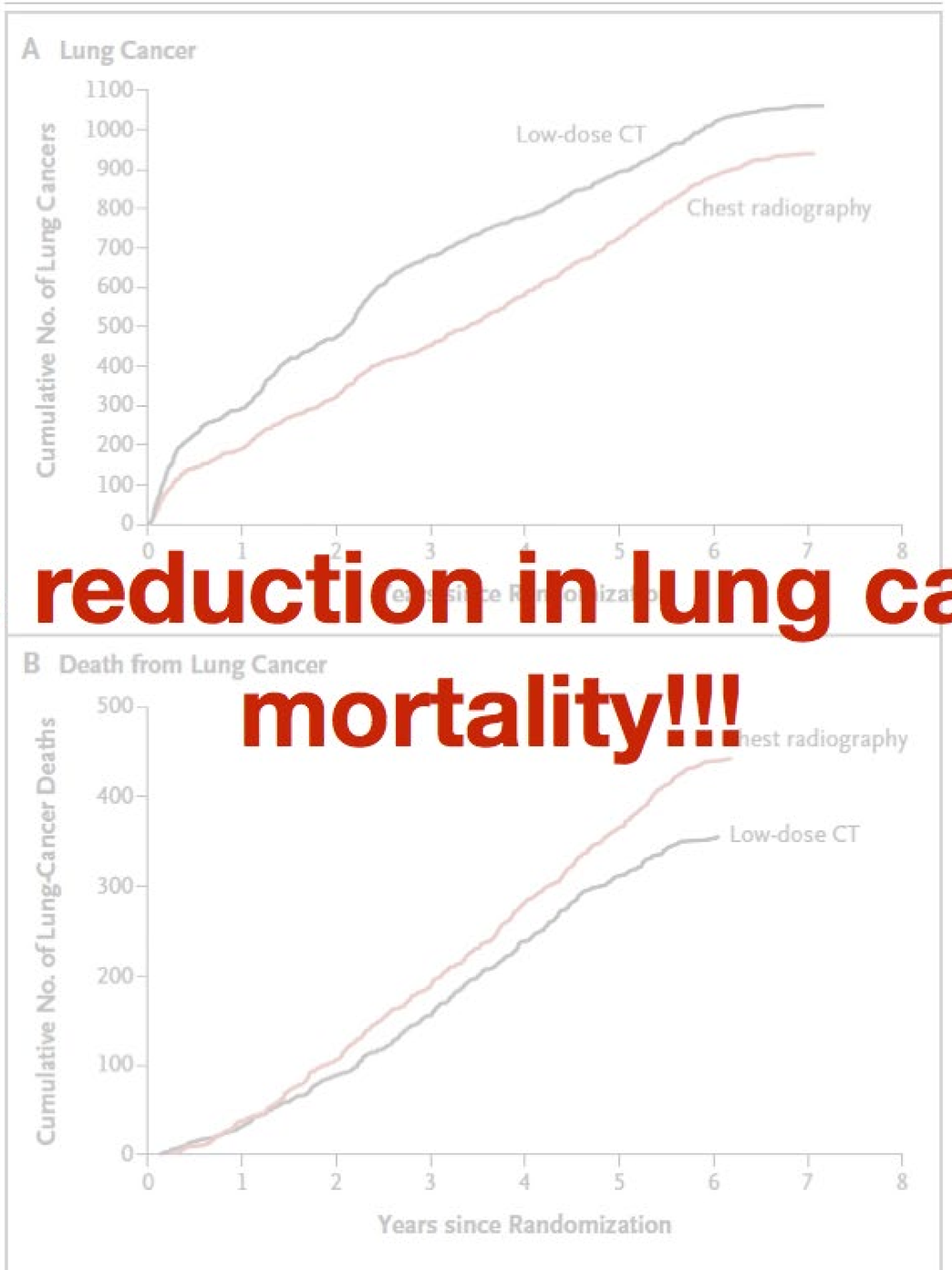
WASHINGTON — The incoming leadership of the new House Republican majority hardly had a chance to relish its dismantling of the Democrats before the Tea Party came calling in the form of

SCANS CUT DEATHS BY LUNG CANCER AMONG SMOKERS

BIG U.S.-FINANCED STUDY

20% Reduction Is Seen — Officials Debate Risks and Cost

By GARDINER HARRIS



20% reduction in lung cancer mortality!!!

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Out, damned spot! Out, I say!

Shakespeare in Lady Macbeth

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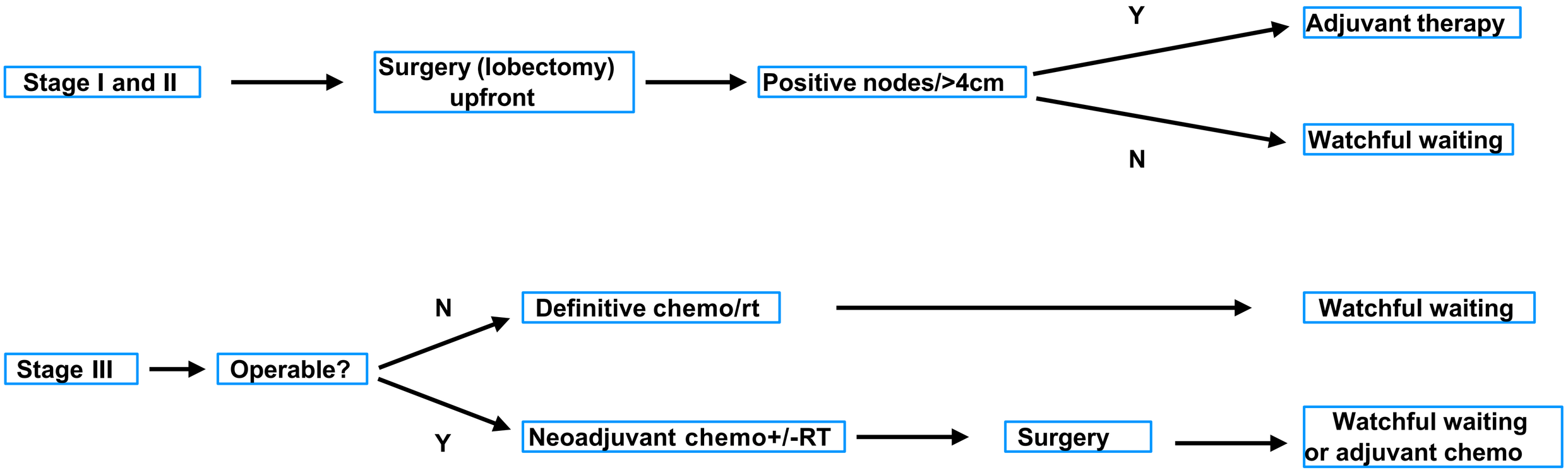
Old Paradigms



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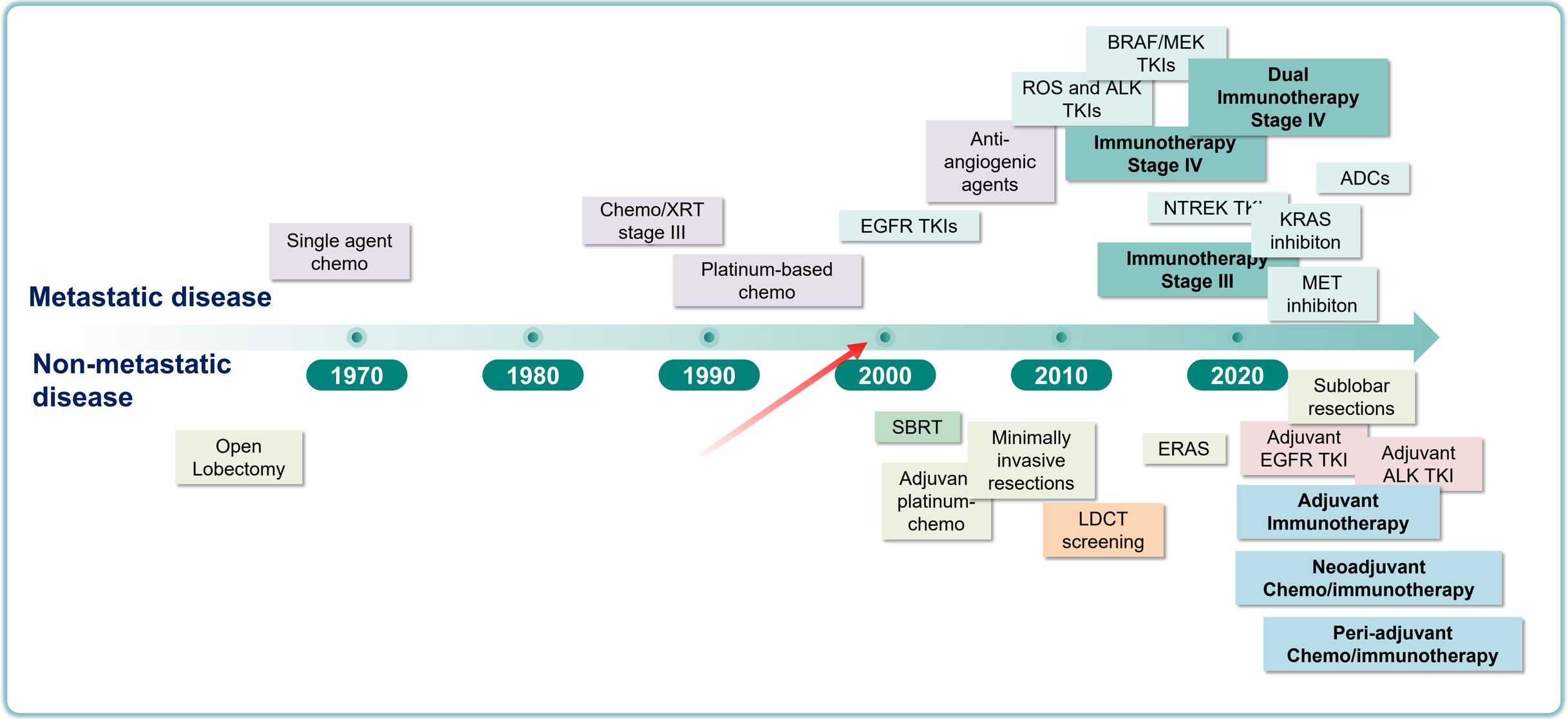
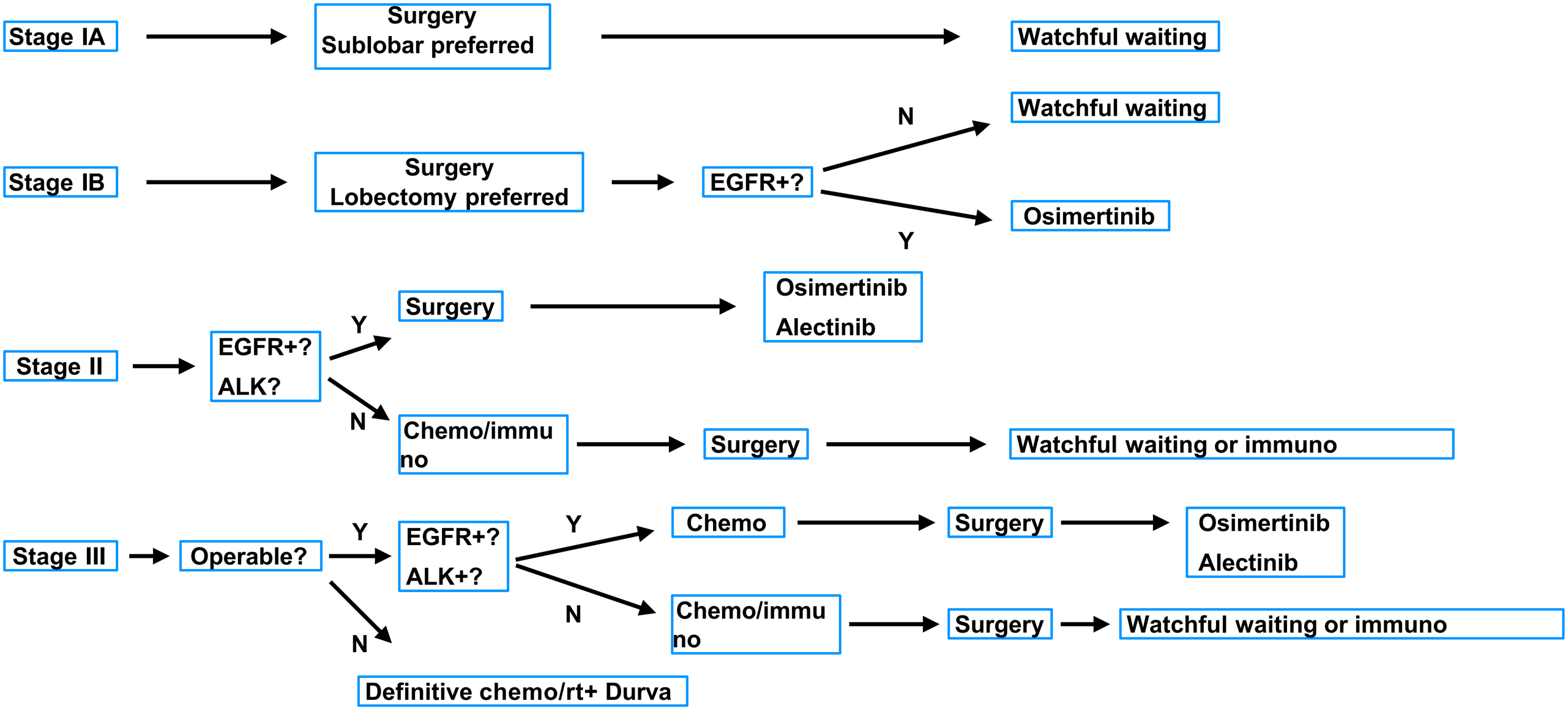
Milestones in NSCLC Treatment





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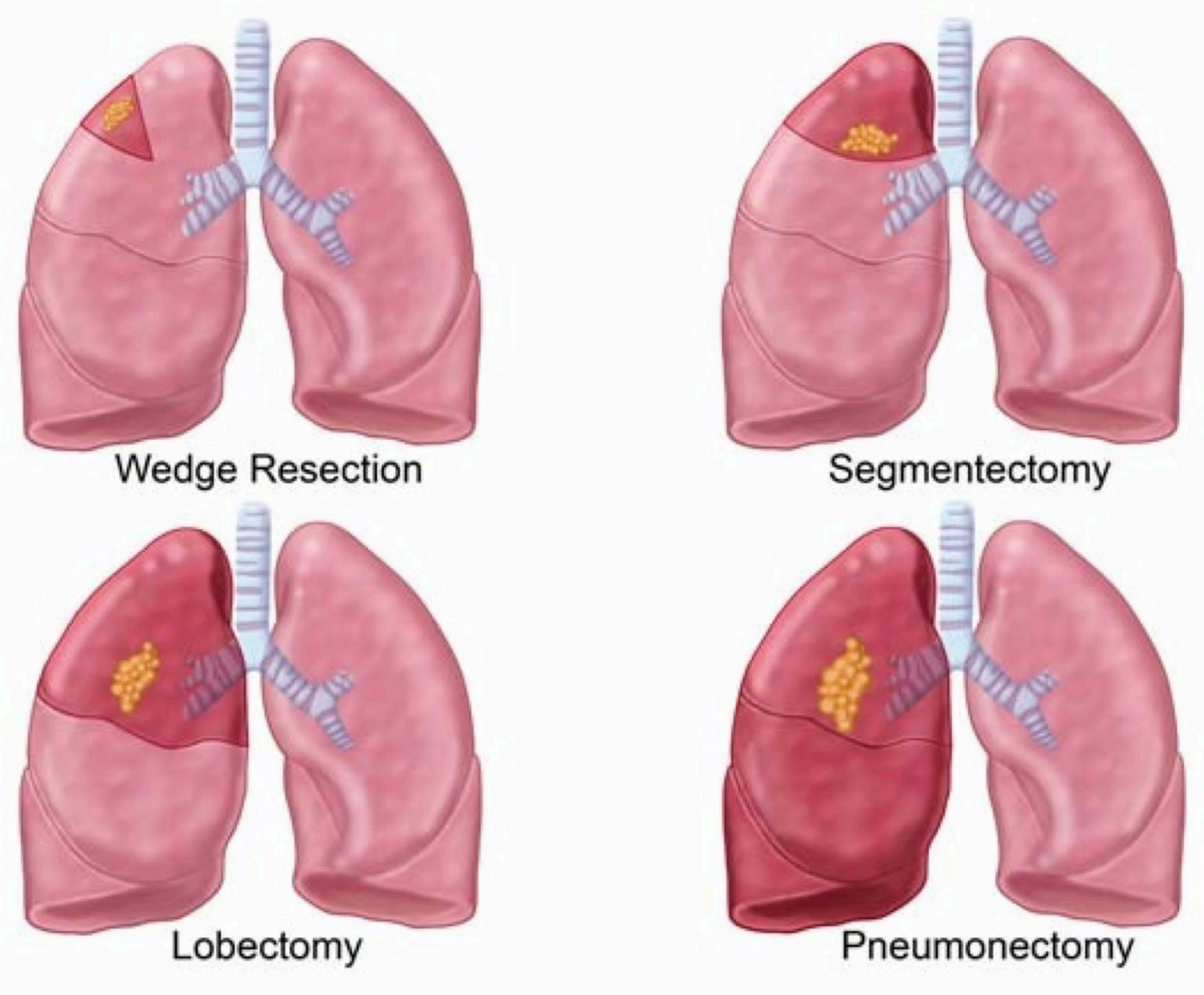

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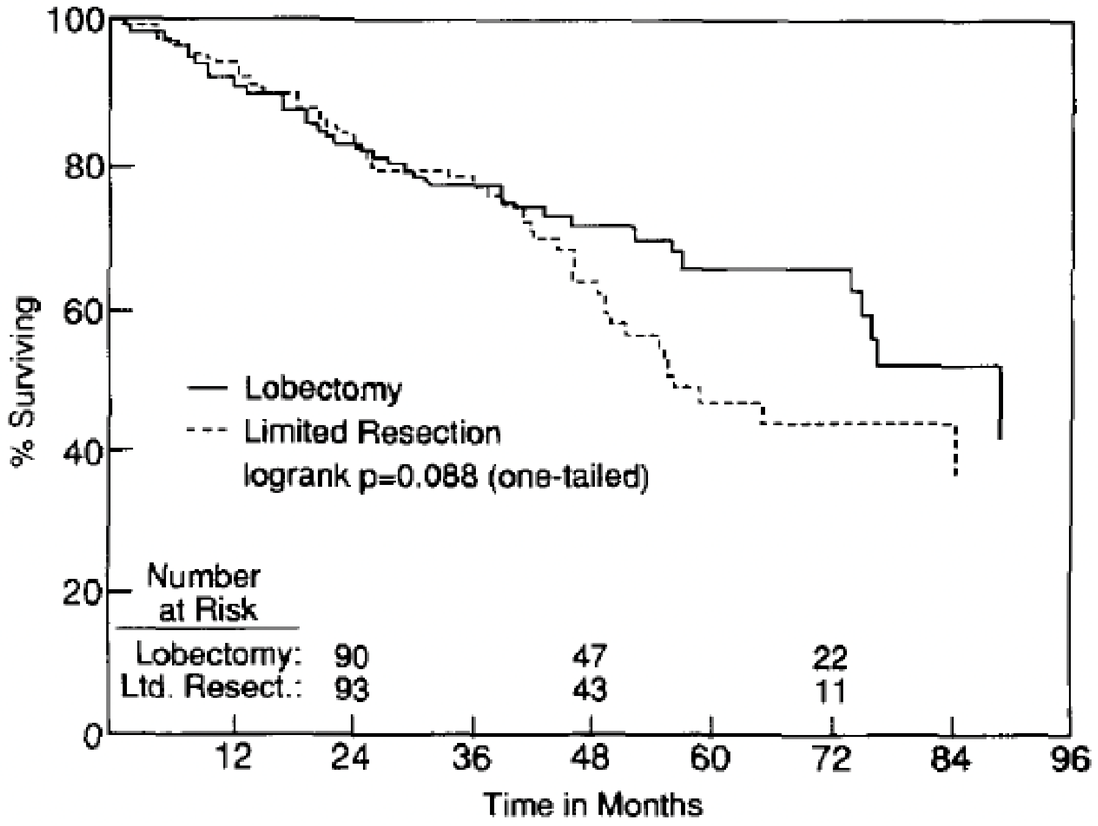
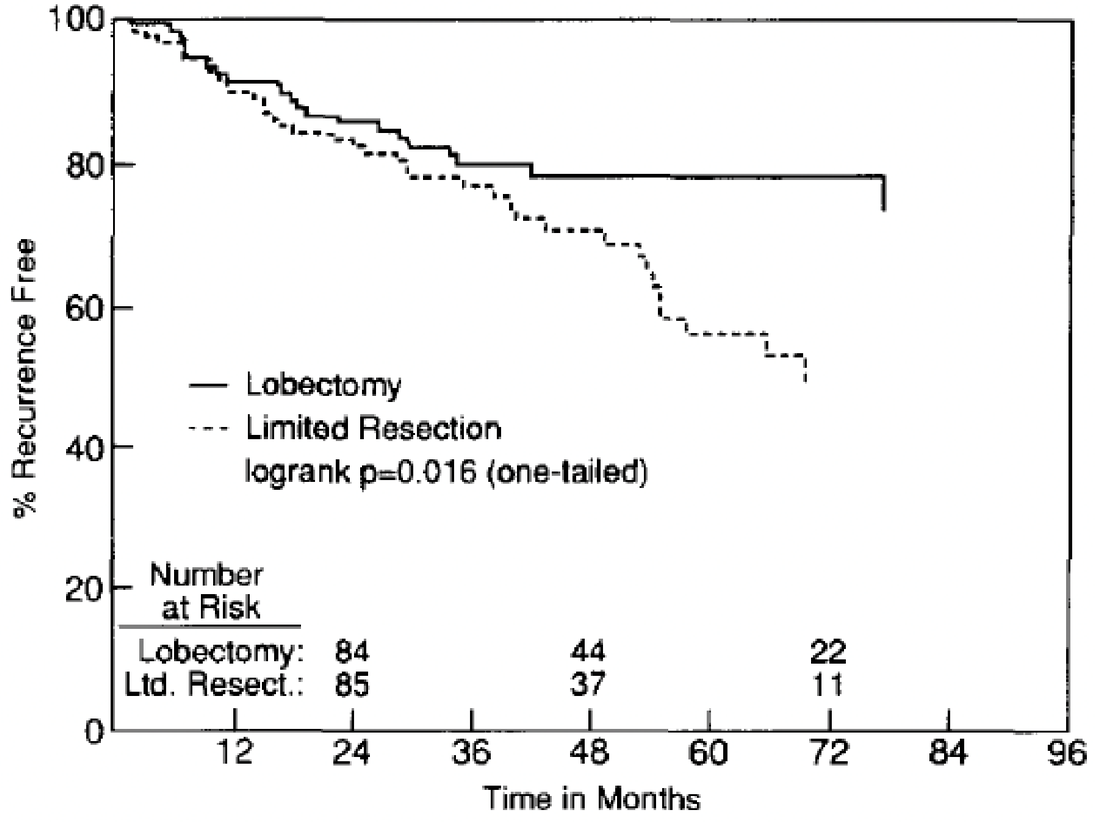
Stage IA

Randomized Trial of Lobectomy Versus Limited Resection for T1 N0 Non–Small Cell Lung Cancer

Lung Cancer Study Group (Prepared by Robert J. Ginsberg, MD, and Lawrence V. Rubinstein, PhD)





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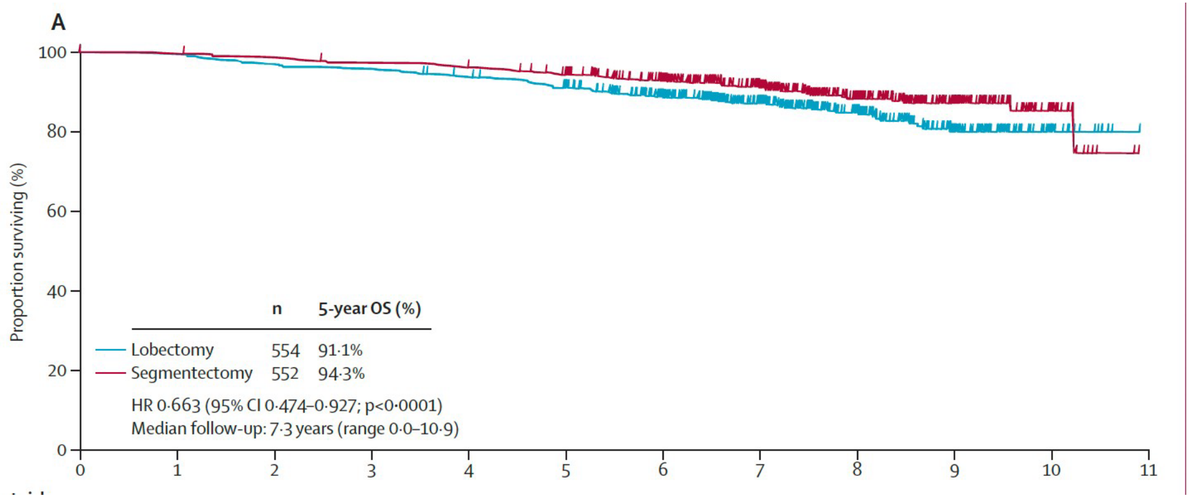
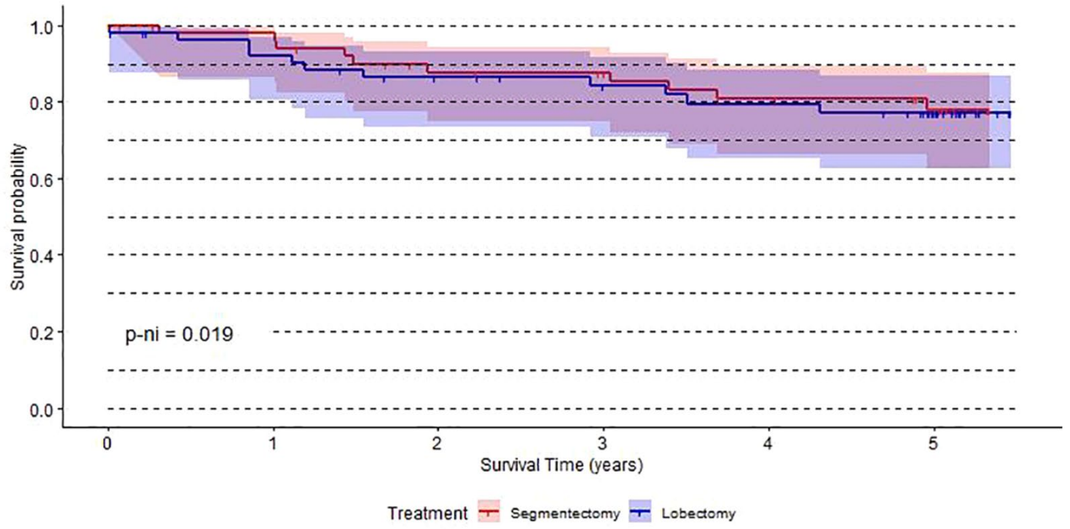
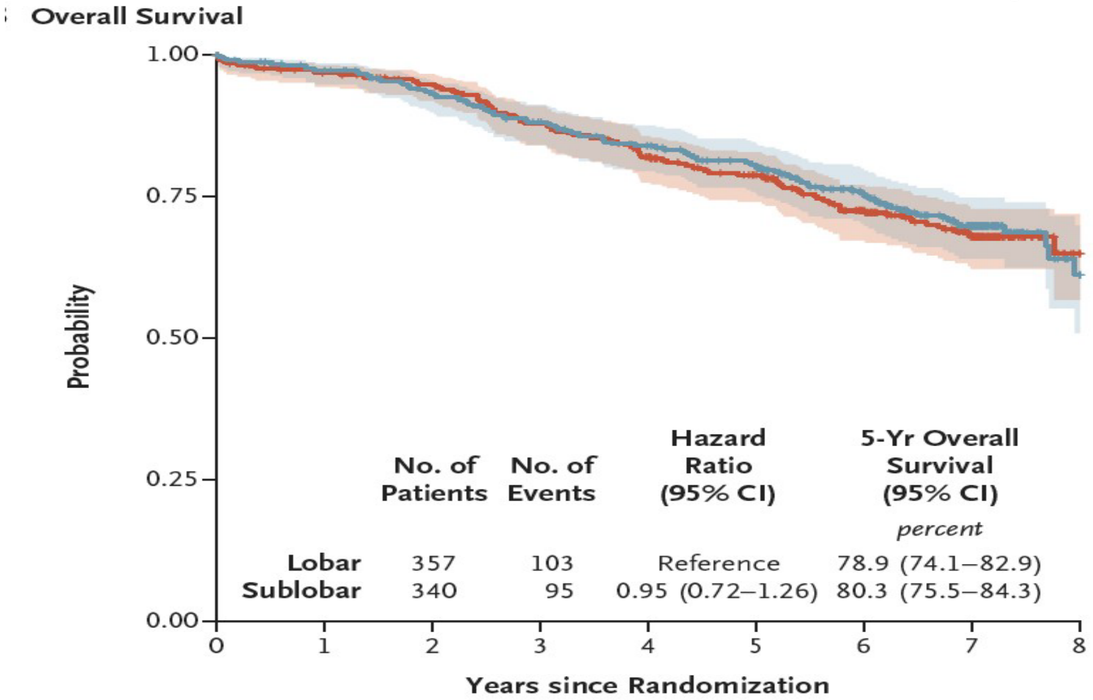


Saji et al, Lancet 2022, 399:1607-17



Stamatis et al, Lung Cancer 2022, 172:108-116



Altorki et al, NEJM 2023, 388:489-98

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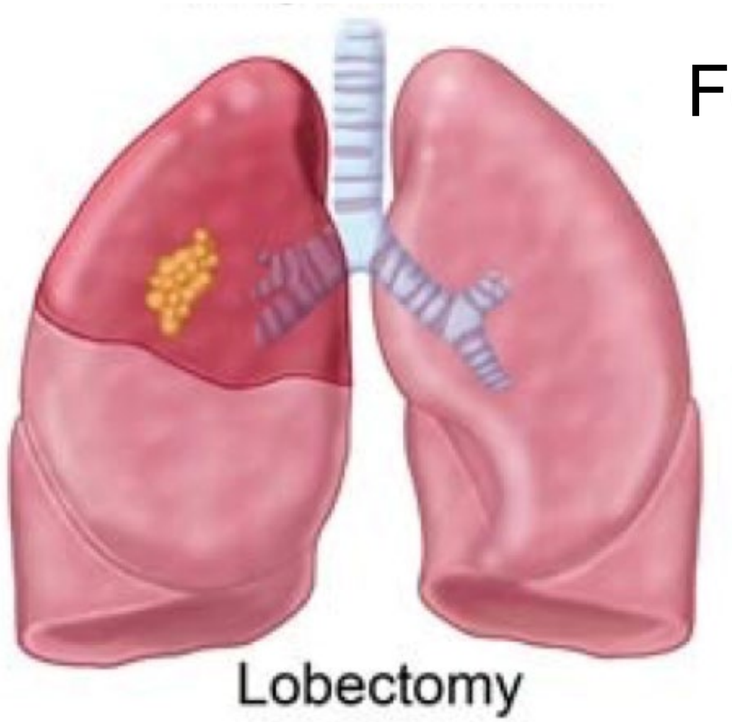
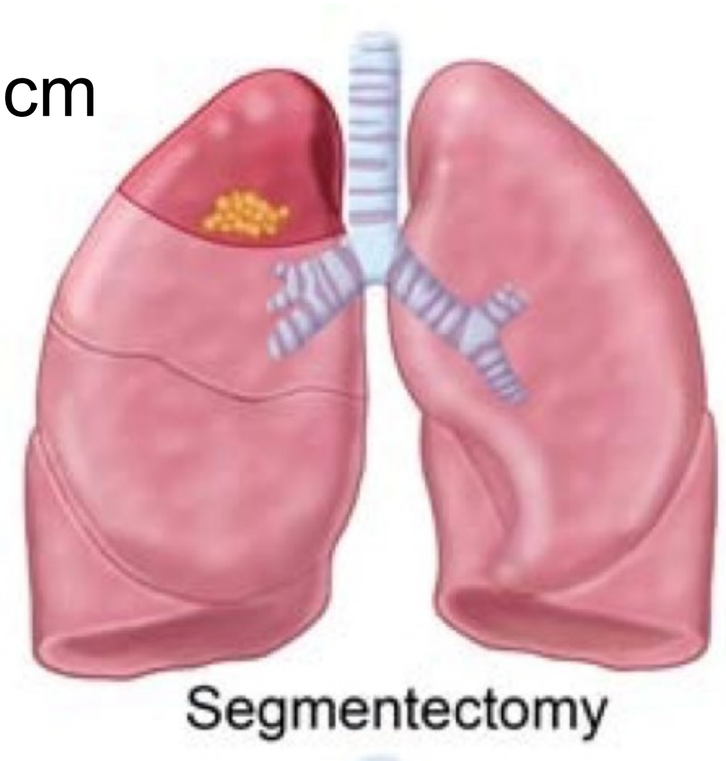
For Tumors smaller than 2 cm



Lobectomy



Segmentectomy

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Stage IB-III

Emerging Therapies in Resectable NSCLC

PD-1/PD-L1 inhibitors

Inhibit interactions between PD-1 and PD-L1 that activate T cells to recognize and eliminate

Does the tumor have a targetable mutation?

Atezolizumab (PD-1)
Durvalumab (PD-1)
Nivolumab (PD-L1)
Pembrolizumab (PD-L1)

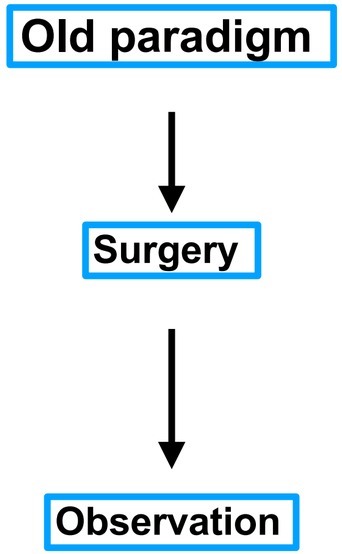
Biomarker-directed therapies

Inhibit oncogenic drivers, which are present in

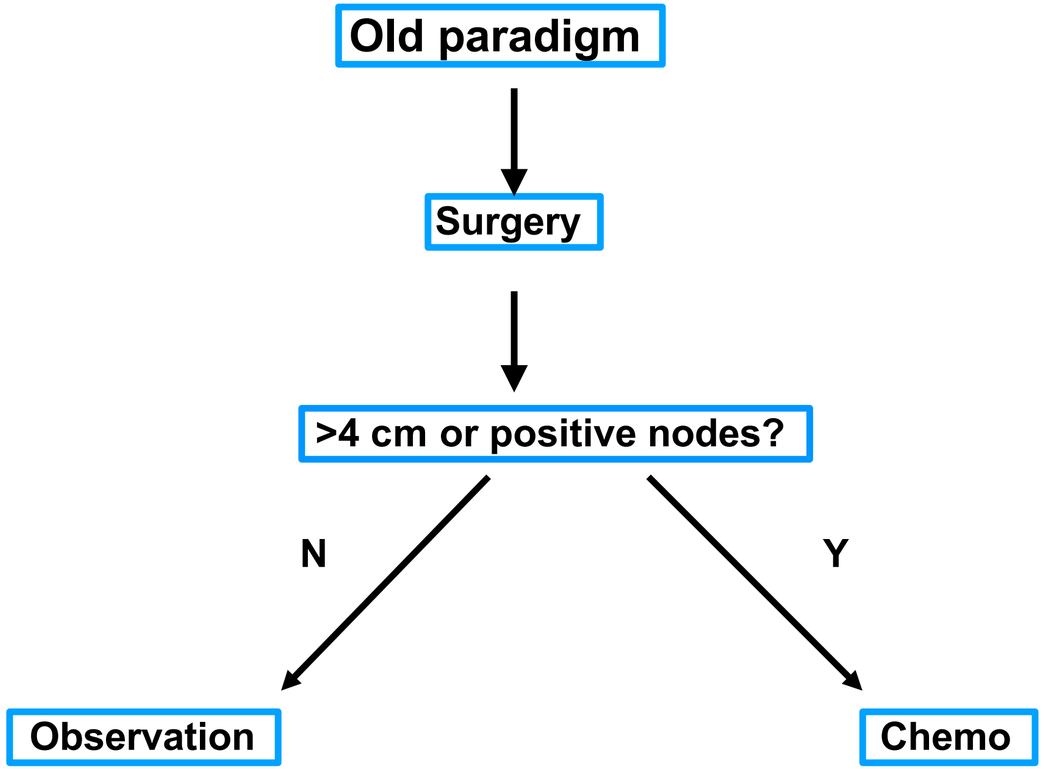
Osimertinib (EGFR)
Alectinib (ALK)

TOGA
Thoracic Oncology Group Australasia

Stage IB



Stage II



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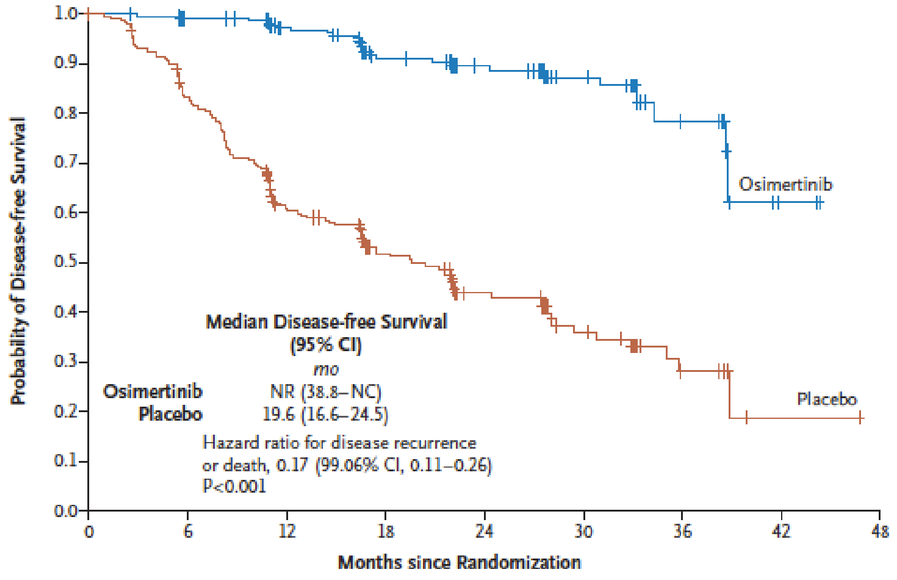
Osimertinib in Resected *EGFR*-Mutated Non–Small-Cell Lung Cancer

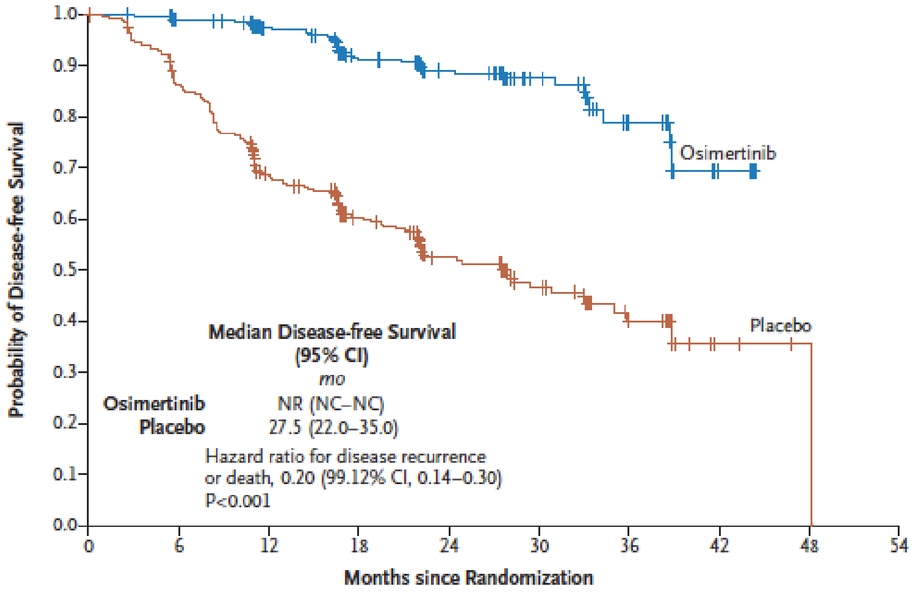
Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan Akewanlop, M.D., Chong-Jen Yu, M.D., Ph.D., Filippo de Marinis, M.D., Laura Bonanno, M.D., Manuel Domine, M.D., Ph.D., Frances A. Shepherd, M.D., Lingmin Zeng, Ph.D., Rachel Hodge, M.Sc., Ajlan Atasoy, M.D., Yuri Rukazenkov, M.D., Ph.D., and Roy S. Herbst, M.D., Ph.D., for the ADAURA Investigators*

NEJM 2020

A Patients with Stage II to IIIA Disease



B Patients with Stage IB to IIIA Disease



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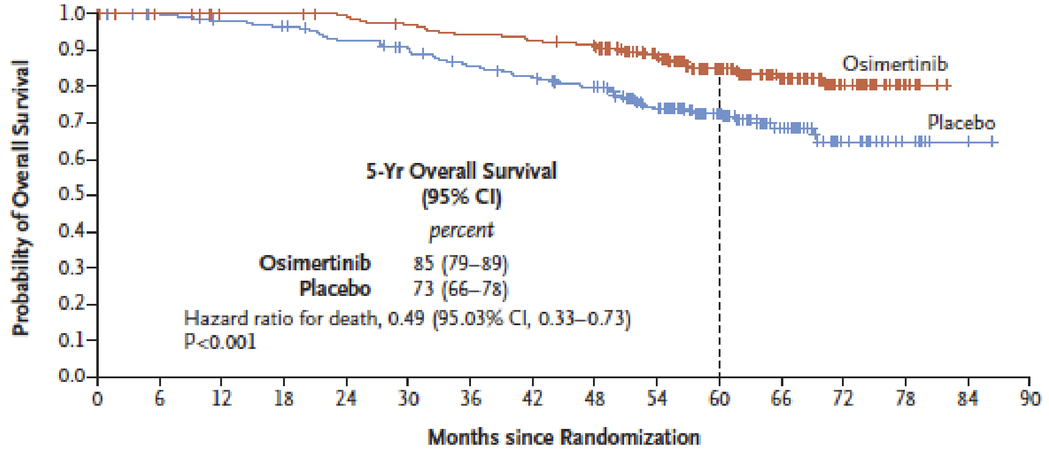
Overall Survival with Osimertinib in Resected *EGFR*-Mutated NSCLC

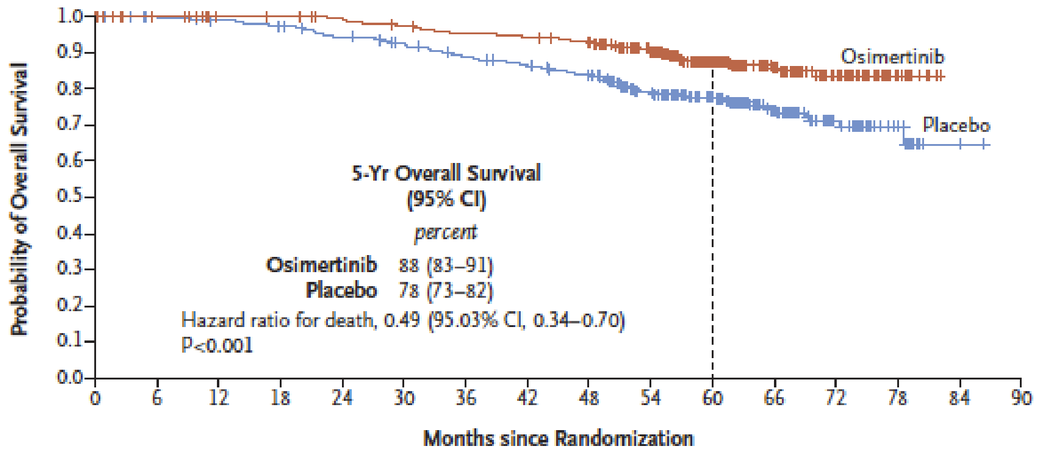
Masahiro Tsuboi, M.D., Roy S. Herbst, M.D., Ph.D.,
Thomas John, M.B., B.S., Ph.D., Terufumi Kato, M.D.,
Margarita Majem, M.D., Ph.D., Christian Grohé, M.D., Jie Wang, M.D., Ph.D.,
Jonathan W. Goldman, M.D., Shun Lu, M.D., Wu-Chou Su, M.D.,
Filippo de Marinis, M.D., Frances A. Shepherd, M.D., Ki Hyeong Lee, M.D., Ph.D.,
Nhieu Thi Le, M.D., Arunee Dechaphunkul, M.D., Dariusz Kowalski, M.D., Ph.D.,
Lynne Poole, M.Sc., Ana Bolanos, M.D., Yuri Rukazenkov, M.D., Ph.D.,
and Yi-Long Wu, M.D., for the ADAURA Investigators*

NEJM 2023

A Patients with Stage II to IIIA Disease



B Patients with Stage IB to IIIA Disease



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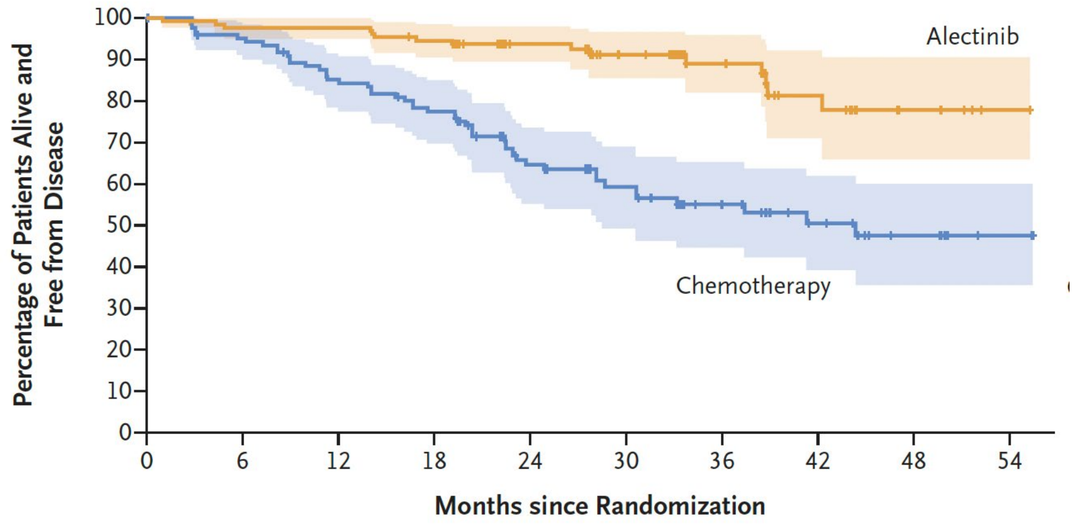
Alectinib in Resected *ALK*-Positive Non–Small-Cell Lung Cancer

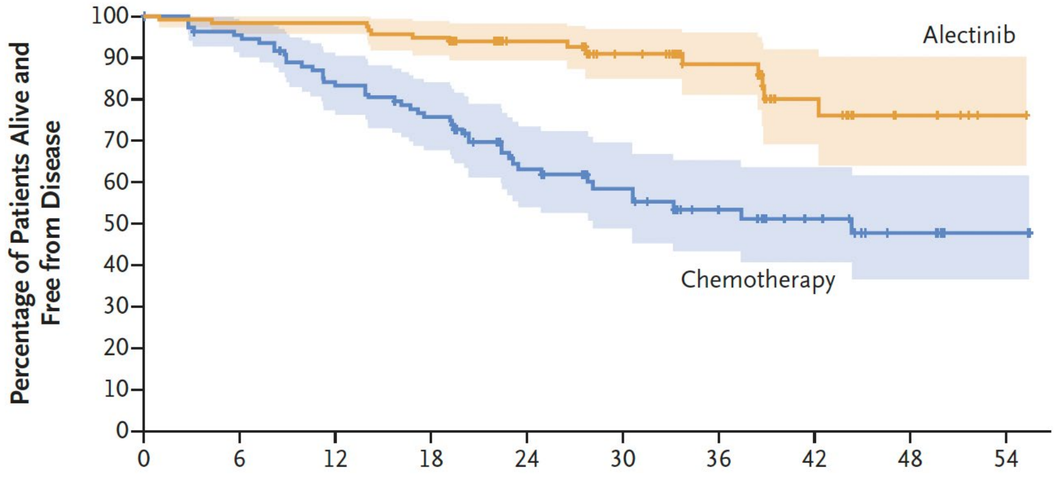
Yi-Long Wu, M.D., Rafal Dziadziuszko, M.D., Ph.D., Jin Seok Ahn, M.D., Ph.D., Fabrice Barlesi, M.D., Ph.D., Makoto Nishio, M.D., Ph.D., Dae Ho Lee, M.D., Ph.D., Jong-Seok Lee, M.D., Ph.D., Wenzhao Zhong, M.D., Ph.D., Hidehito Horinouchi, M.D., Ph.D., Weimin Mao, M.D., Ph.D., Maximilian Hochmair, M.D., Filippo de Marinis, M.D., M. Rita Migliorino, M.D., Igor Bondarenko, M.D., Ph.D., Shun Lu, M.D., Qun Wang, M.D., Tania Ochi Lohmann, Ph.D., Tingting Xu, M.D., Andres Cardona, M.Sc., Thorsten Ruf, M.D., Johannes Noe, Ph.D., and Benjamin J. Solomon, M.B., B.S., Ph.D., for the ALINA Investigators*

NEJM 2023

Intention-to-Treat Population



Patients with Stage II or IIIA Disease



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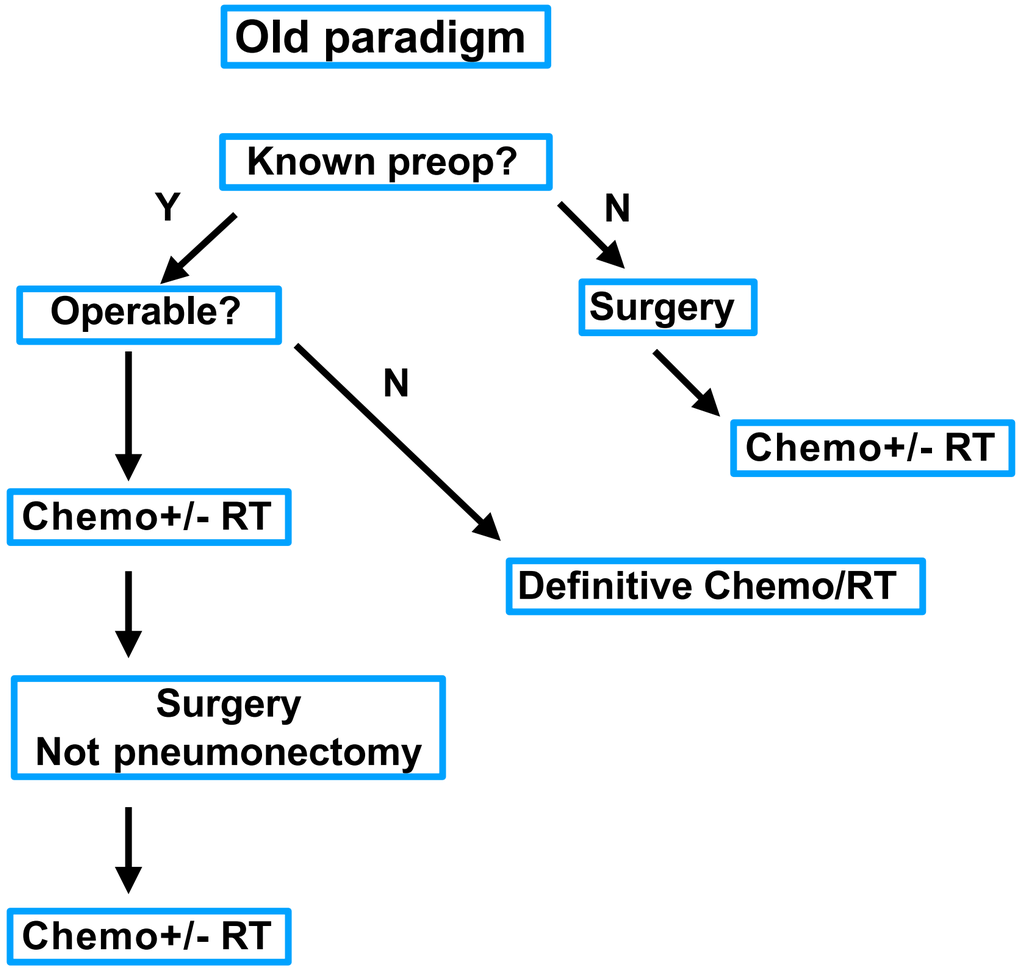
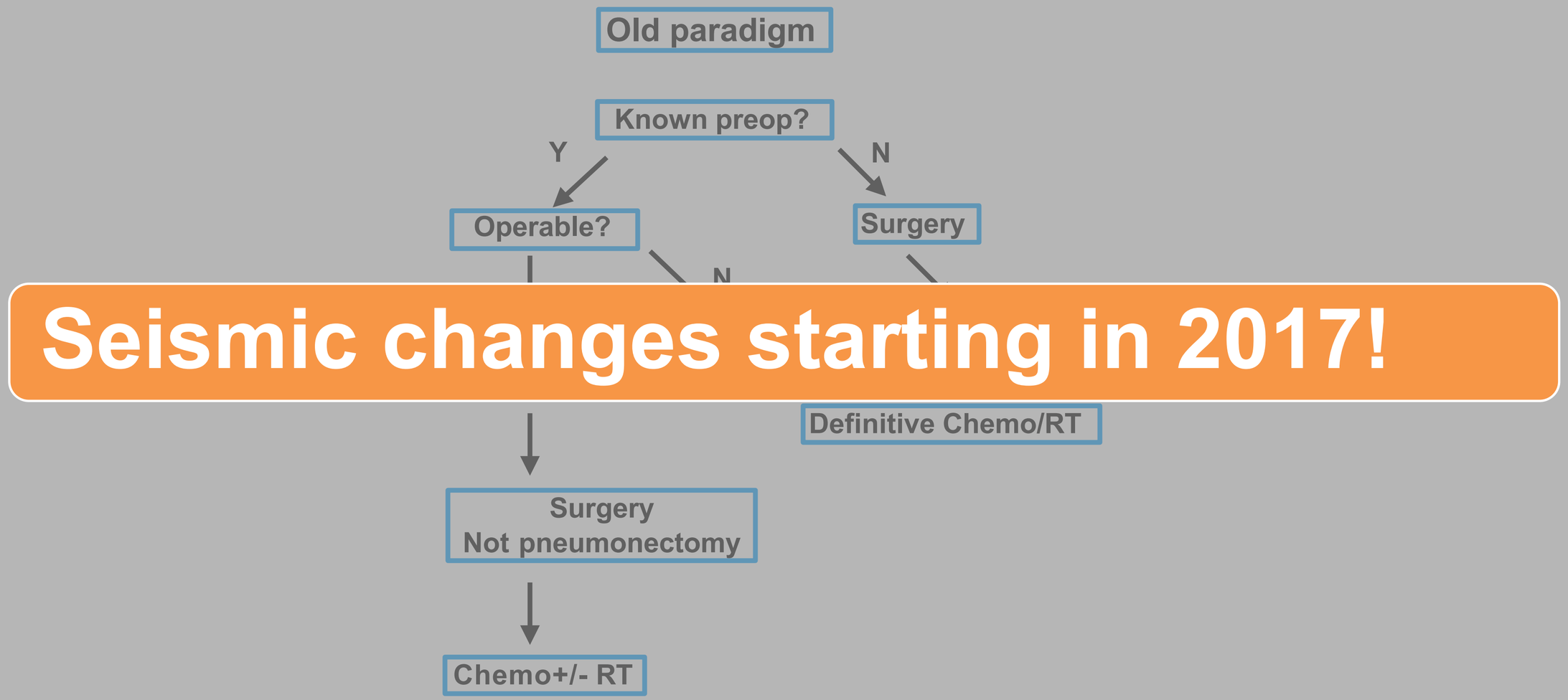
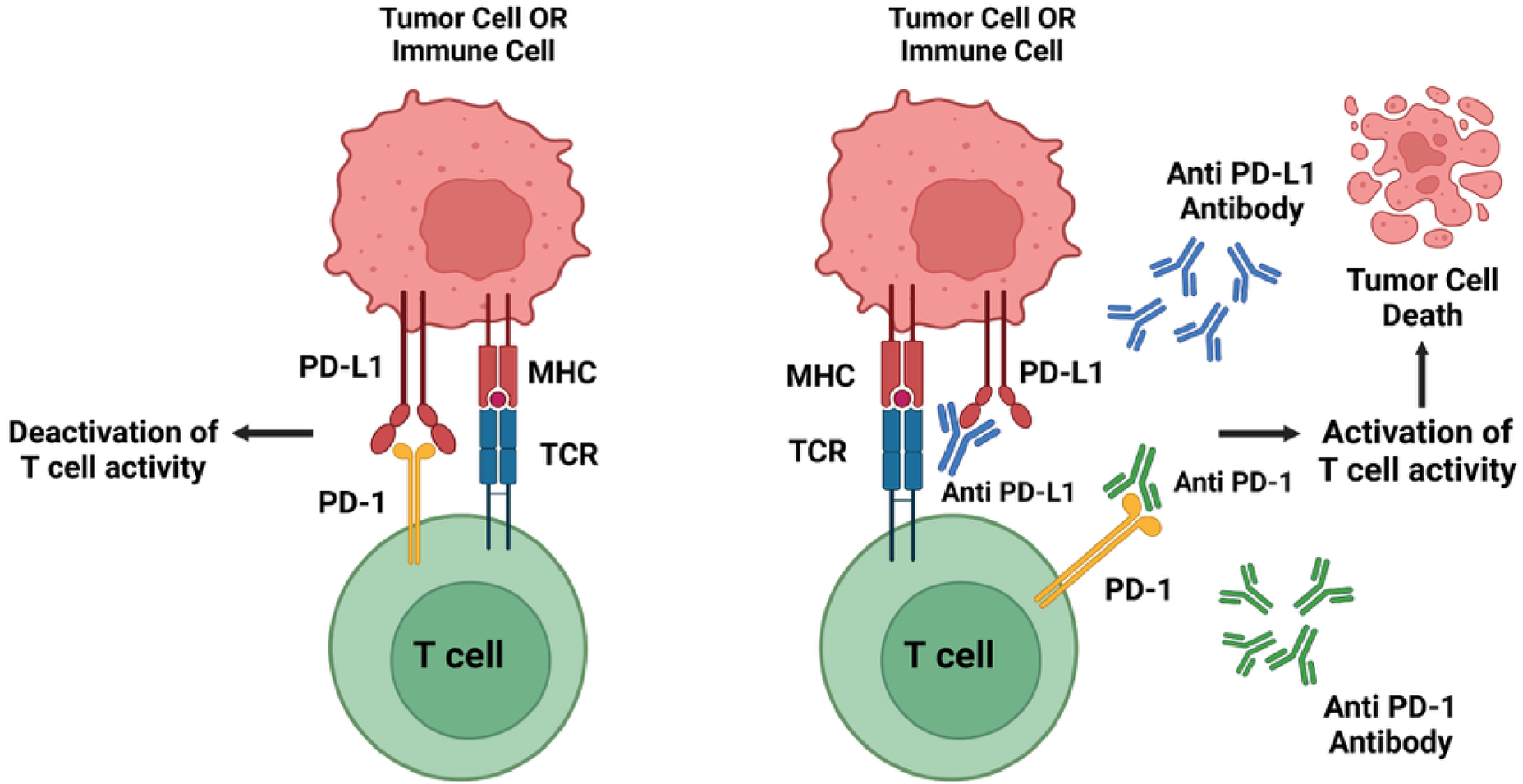
Stage III



Stage III



Seismic changes starting in 2017!



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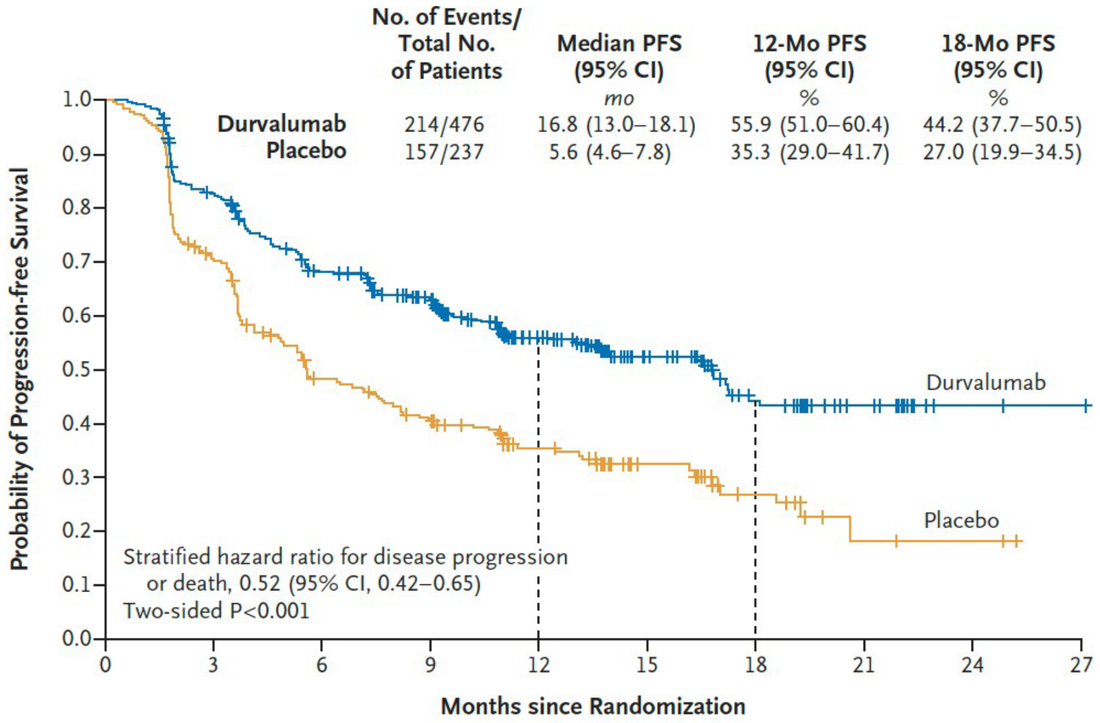
Hospital

ORIGINAL ARTICLE

Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

S.J. Antonia, A. Villegas, D. Daniel, D. Vicente, S. Murakami, R. Hui, T. Yokoi, A. Chiappori, K.H. Lee, M. de Wit, B.C. Cho, M. Bourhaba, X. Quantin, T. Tokito, T. Mekhail, D. Planchard, Y.-C. Kim, C.S. Karapetis, S. Hiret, G. Ostoros, K. Kubota, J.E. Gray, L. Paz-Ares, J. de Castro Carpeño, C. Wadsworth, G. Melillo, H. Jiang, Y. Huang, P.A. Dennis, and M. Özgüroğlu, for the PACIFIC Investigators*

NEJM 2017



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

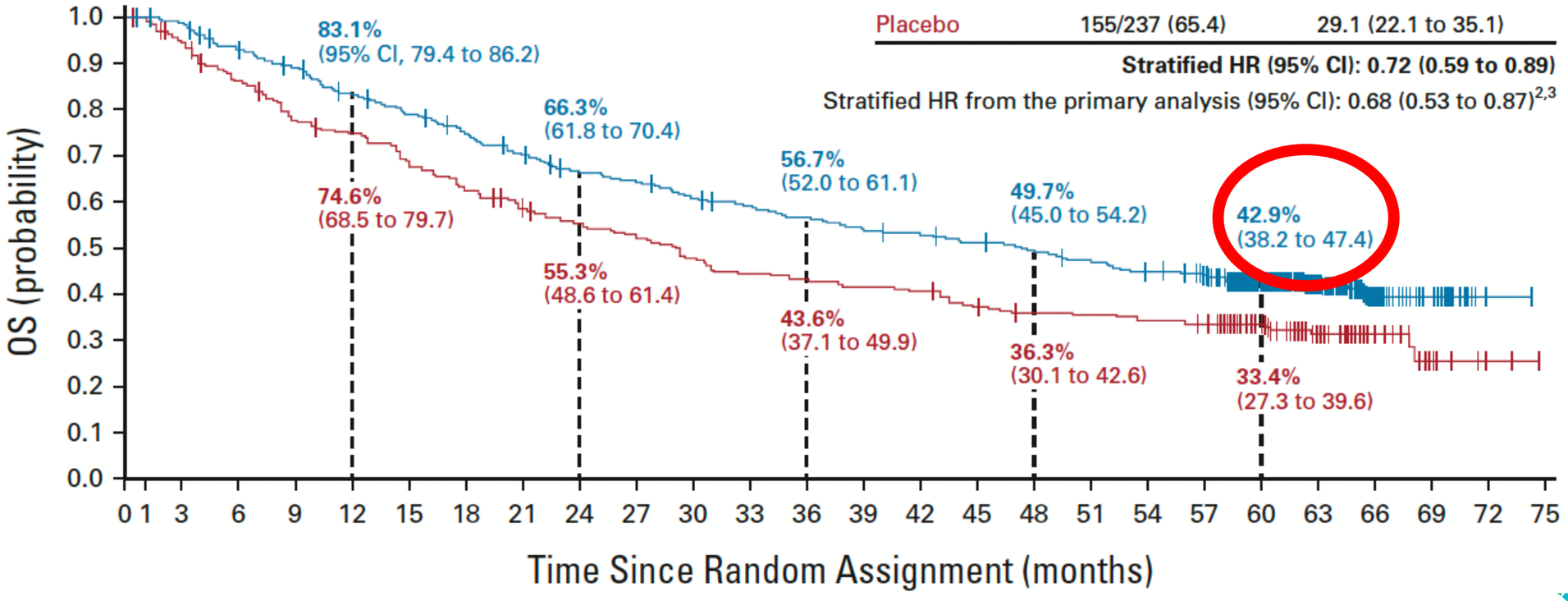
David R. Spigel, MD[1]; Corinne Faivre-Finn, MD, PhD[2]; Jhanelle E. Gray, MD[3]; David Vicente, MD[4]; David Planchard, MD, PhD[5]; Luis Paz-Ares, MD, PhD[6]; Johan F. Vansteenkiste, MD, PhD[7]; Marina C. Garassino, MD[8,9]; Rina Hui, PhD[10]; Xavier Quantin, MD, PhD[11]; Andreas Rimner, MD[12]; Yi-Long 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

J Clin Onc 2022

Arm	No. of Events/ Total No. of Patients (%)	Median OS (95% CI), Months
Durvalumab	264/476 (55.5)	47.5 (38.1 to 52.9)
Placebo	155/237 (65.4)	29.1 (22.1 to 35.1)

Stratified HR (95% CI): 0.72 (0.59 to 0.89)

Stratified HR from the primary analysis (95% CI): 0.68 (0.53 to 0.87)[2,3]



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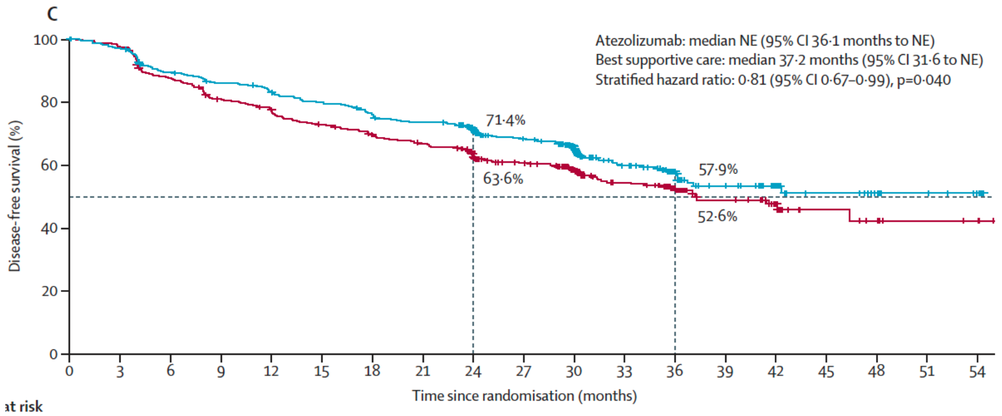
Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB–IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial

*Enriqueta Felip, Nasser Altorki, Caicun Zhou, Tibor Csőszi, Ihor Vynnychenko, Oleksandr Goloborodko, Alexander Luft, Andrey Akopov, Alex Martinez-Marti, Hirotsugu Kenmotsu, Yuh-Min Chen, Antonio Chella, Shunichi Sugawara, David Voong, Fan Wu, Jing Yi, Yu Deng, Mark McCleland, Elizabeth Bennett, Barbara Gitlitz, Heather Wakelee, for the IMpower010 Investigators**



Lancet 398:1344-57, 2021

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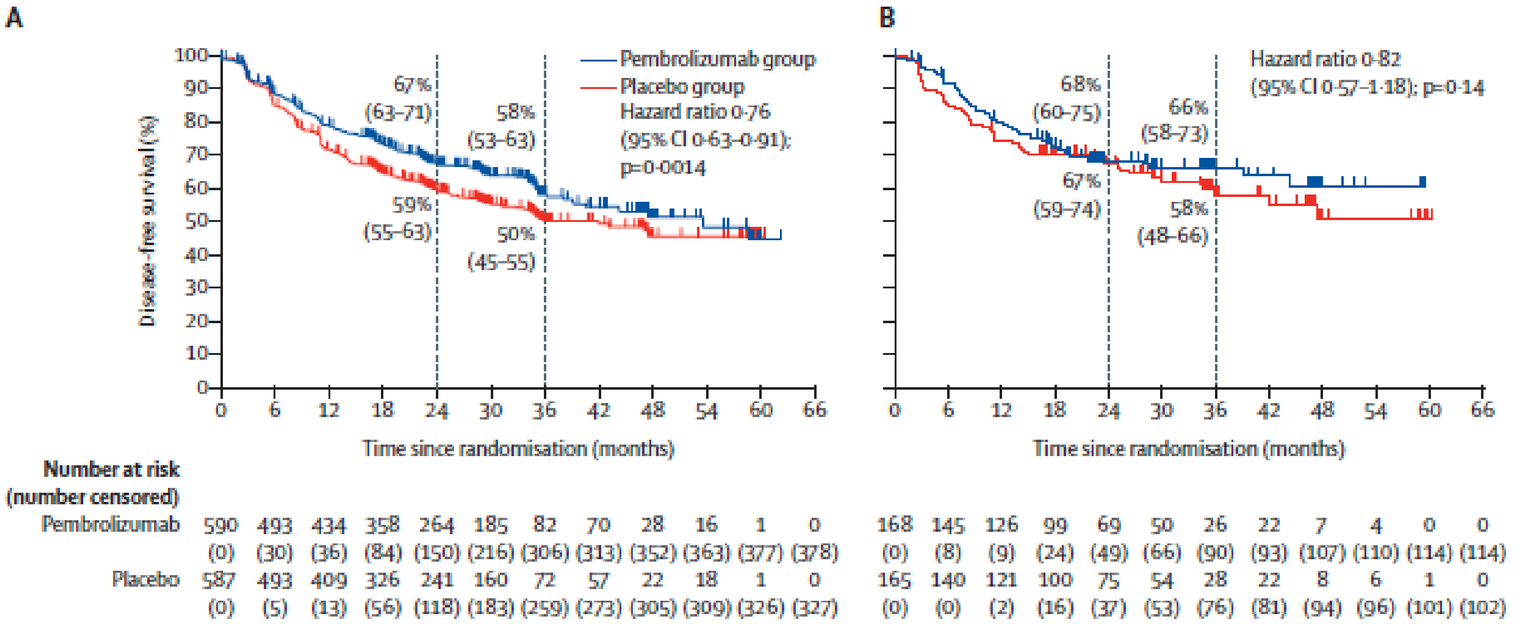
Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB–IIIA non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial

Mary O'Brien, Luis Paz-Ares*, Sandrine Marreaud, Urania Dafni, Kersti Oselin, Libor Havel, Emilio Esteban, Dolores Isla, Alex Martinez-Marti, Martin Faehling, Masahiro Tsuboi, Jong-Seok Lee, Kazuhiko Nakagawa, Jing Yang, Ayman Samkari, Steven M Keller, Murielle Mauer, Nitish Jha, Rolf Stahel, Benjamin Besse†, Solange Peters†, on behalf of the EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 Investigators‡*



Number at risk (number censored)												
Pembrolizumab	590 (0)	493 (30)	434 (36)	358 (84)	264 (150)	185 (216)	82 (306)	70 (313)	28 (352)	16 (363)	1 (377)	0 (378)
Placebo	587 (0)	493 (5)	409 (13)	326 (56)	241 (118)	160 (183)	72 (259)	57 (273)	22 (305)	18 (309)	1 (326)	0 (327)

Pembrolizumab	168 (0)	145 (8)	126 (9)	99 (24)	69 (49)	50 (66)	26 (90)	22 (93)	7 (107)	4 (110)	0 (114)	0 (114)
Placebo	165 (0)	140 (0)	121 (2)	100 (16)	75 (37)	54 (53)	28 (76)	22 (81)	8 (94)	6 (96)	1 (101)	0 (102)

Lancet Oncol 23:1274-1286, 2022

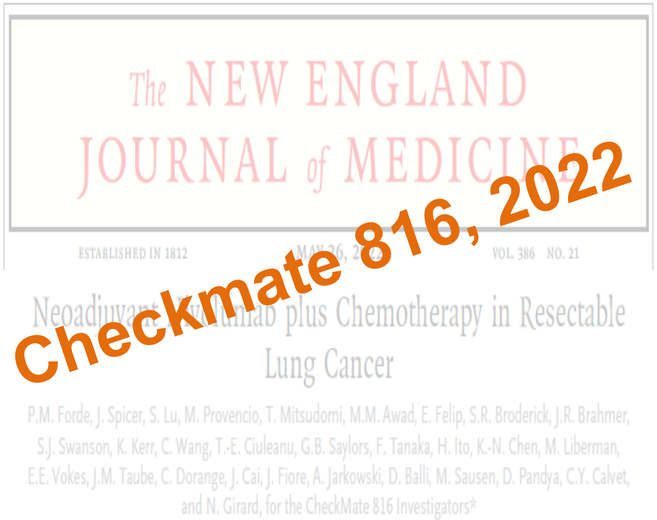
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 26, 2022 VOL. 386 NO. 21

Checkmate 816, 2022

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

P.M. Forde, J. Spicer, S. Lu, M. Provencio, T. Mitsudomi, M.M. Awad, E. Felip, S.R. Broderick, J.R. Brahmer, S.J. Swanson, K. Kerr, C. Wang, T.-E. Ciuleanu, G.B. Saylors, F. Tanaka, H. Ito, K.-N. Chen, M. Liberman, E.E. Vokes, J.M. Taube, C. Dorange, J. Cai, J. Fiore, A. Jarkowski, D. Balli, M. Sausen, D. Pandya, C.Y. Calvet, and N. Girard, for the CheckMate 816 Investigators*



Checkmate 816, 2022

ORIGINAL ARTICLE

Perioperative Durvalumab for Resectable Non–Small-Cell Lung Cancer

Aegean, 2023

J.V. Heymach, D. Harpole, T. Mitsudomi, J.M. Taube, G. Galffy, M. Hochmair, T. Winder, R. Zukov, G. Garbaos, S. Gao, H. Kuroda, G. Ostoros, T.V. Tran, J. You, K.-Y. Lee, L. Antonuzzo, Z. Papai-Szekely, H. Akamatsu, B. Biswas, A. Spira, J. Crawford, H.T. Le, M. Aperghis, G.J. Doherty, H. Mann, T.M. Fouad, and M. Reck, for the AEGEAN Investigators*

Allegheny Health Network
Allegheny General Hospital

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

Checkmate 816, 2022

Aegean, 2023

NADIM II, 2023

Allegheny Health Network
Allegheny General Hospital

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 10, 2023 VOL. 389 NO. 6

Checkmate 816, 2022

Aegean, 2023

NADIM II, 2023

Keynote 671, 2023

Perioperative Pembrolizumab for Early-Stage Non–Small-Cell Lung Cancer

H. Wakelee, M. Liberman, T. Kato, M. Tsuboi, S.-H. Lee, S. Gao, K.-N. Chen, C. Dooms, M. Majem, E. Eigendorff, G.L. Martinengo, O. Bylicki, D. Rodríguez-Abreu, J.E. Chaft, S. Novello, J. Yang, S.M. Keller, A. Samkari, and J.D. Spicer, for the KEYNOTE-671 Investigators*

Allegheny Health Network
Allegheny General Hospital

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 816, 2022

Aegean, 2023

NADIM II, 2023

Keynote 671, 2023

Checkmate 77T, 2024

Allegheny Health Network
Allegheny General Hospital

Chemotherapy + Immunotherapy

Adjuvant

IMPower010
Atezolizumab x 1Y
Resected II-IIIA PD-L1+
5Y DFS HR:0.70
FDA

Keynote 091
Pembrolizumab x 1Y
Resected IB-IIIA
1.5Y DFS HR:0.76
FDA

Neoadjuvant

Checkmate-816
Nivolumab x 3 cycles
Resectable IB-IIIA
4Y EFS HR:0.62
FDA

Sandwich

AEGEAN
Durvalumab 4c + 1Y
Resectable II-IIIA
2Y EFS HR:0.68
FDA

Keynote 671
Pembrolizumab 4c + 9M
Resectable II-IIIB
3Y OS HR:0.72
FDA

Neotorch
Torpalimab 3c + 10M
Resectable III
2Y EFS HR:0.40

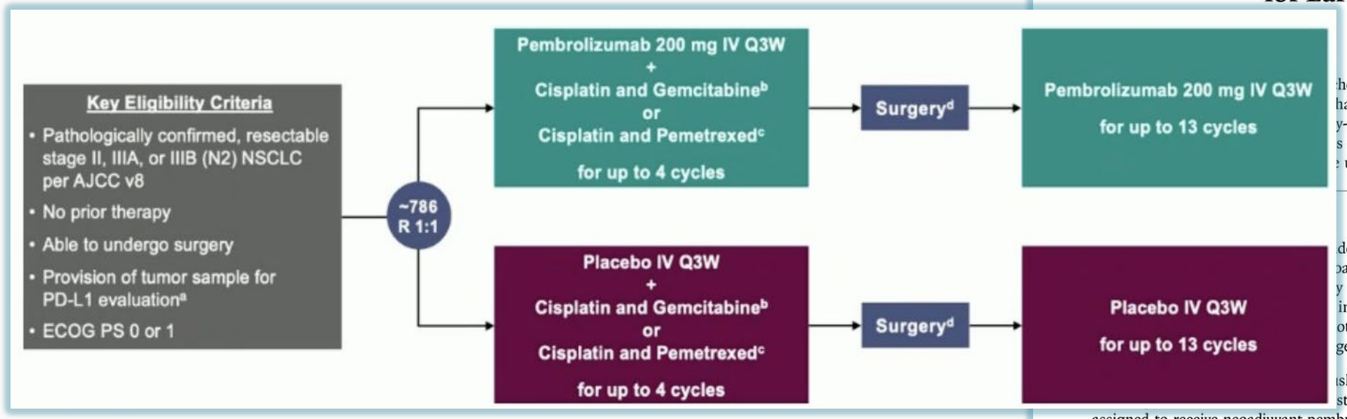
Checkmate-77T
Nivolumab x 4c + 1Y
Resectable II-IIIA
1.5 EFS HR:0.58

RATIONALE-315
Tislelizumab 3-4c + 10M
Resectable II-IIIA
MPR OR:7.5

Wakelee H, ASCO 2024; O'Brien M, Lancet Oncol 2022; Forde P, NEJM 2022; Spicer J, ASCO 2024; Heymach J, NEJM 2023; Wakelee H, NEJM 2023; Lu S, JAMA 2024; Cascone T, NEJM 2024: Yue DS, ESMO 2023.

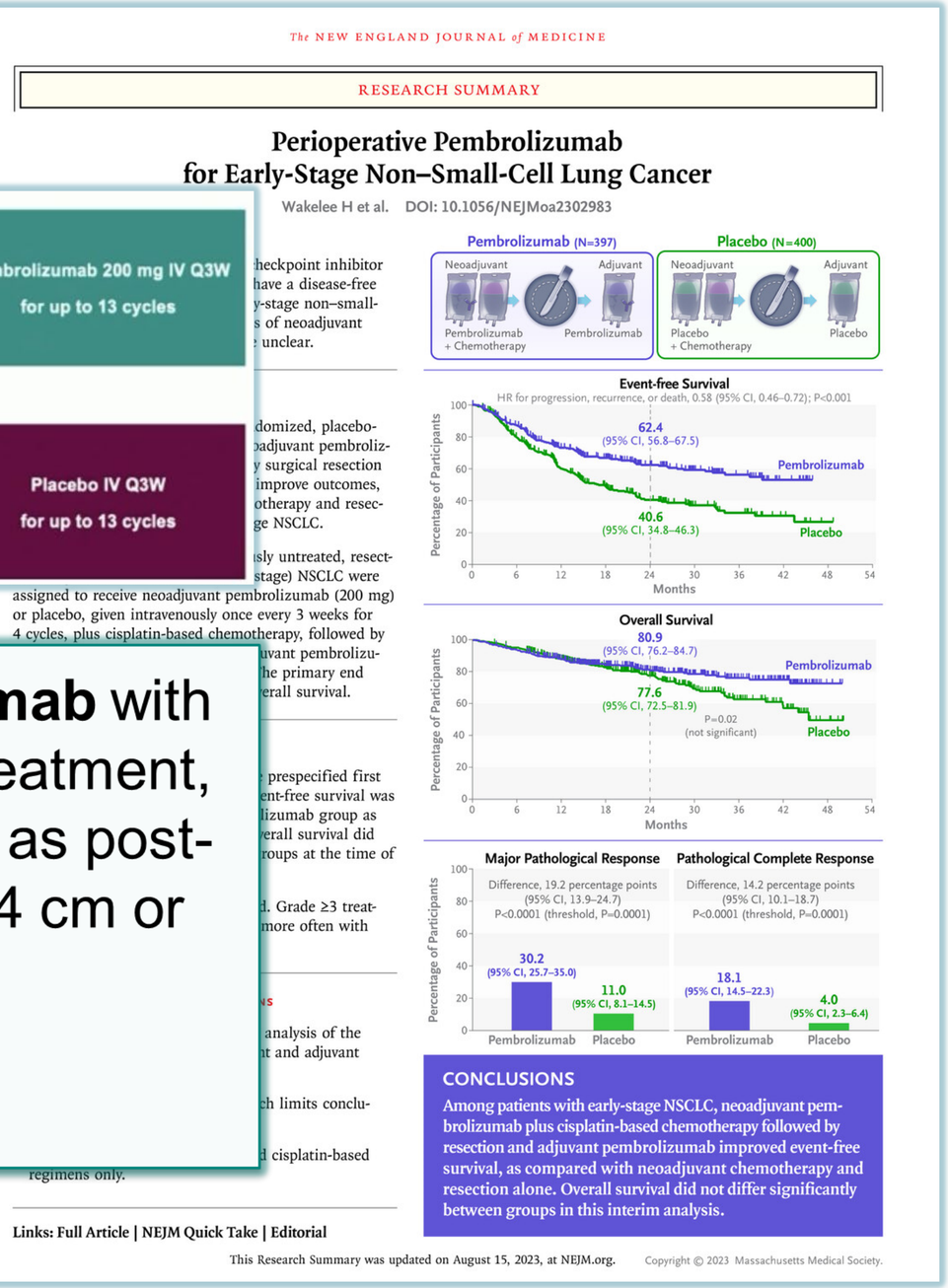
9th Edition TNM Descriptors and Stages						
				N2		
T/M	Categories and Descriptors	N0	N1	N2a	N2b	N3
T1	T1a ≤1 cm	IA1	IIA	IIB	IIIA	
	T1b >1 to ≤2 cm	IA2	IIA	IIB	IIIA	
	T1c >2 to ≤3 cm		IIA	IIB	IIIA	
T2	T2a Visceral pleura / central invasion	IB	IIB	IIIA	IIIB	
	T2a >3 to ≤4 cm	IB	IIB	IIIA	IIIB	
	T2b >4 to ≤5 cm	IIA	IIB	IIIA	IIIB	
T3	T3 >5 to ≤7 cm	IIB	IIIA	IIIA	IIIB	
	T3 Invasion	IIB	IIIA	IIIA	IIIB	
	T3 Same lobe separate tumor nodules	IIB	IIIA	IIIA	IIIB	
T4	T4 >7 cm	IIIA	IIIA	IIIB	IIIB	
	T4 Invasion	IIIA	IIIA	IIIB	IIIB	
	T4 Ipsilateral separate tumor nodules	IIIA	IIIA	IIIB	IIIB	

Keynote-671



In October 2023, the US FDA approved **pembrolizumab** with platinum-containing chemotherapy as neoadjuvant treatment, and with continuation of single-agent pembrolizumab as post-surgical adjuvant treatment for resectable (tumors ≥4 cm or node positive) NSCLC

NCCN designated a class I recommendation


The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Perioperative Pembrolizumab for Early-Stage Non–Small-Cell Lung Cancer

Wakelee H et al. DOI: 10.1056/NEJMoa2302983

heckpoint inhibitor have a disease-free y-stage non–small- s of neoadjuvant unclear.

domized, placebo- adjuvant pembroliz- y surgical resection improve outcomes, otherapy and resec- ge NSCLC.

sly untreated, resect- stage) NSCLC were assigned to receive neoadjuvant pembrolizumab (200 mg) or placebo, given intravenously once every 3 weeks for 4 cycles, plus cisplatin-based chemotherapy, followed by uvant pembrolizu- he primary end erall survival.

prespecified first ent-free survival was lizumab group as erall survival did roups at the time of

d. Grade ≥3 treat- more often with

analysis of the t and adjuvant

ch limits conclu-

d cisplatin-based regimens only.

Links: Full Article | NEJM Quick Take | Editorial

This Research Summary was updated on August 15, 2023, at NEJM.org.

CONCLUSIONS

Among patients with early-stage NSCLC, neoadjuvant pembrolizumab plus cisplatin-based chemotherapy followed by resection and adjuvant pembrolizumab improved event-free survival, as compared with neoadjuvant chemotherapy and resection alone. Overall survival did not differ significantly between groups in this interim analysis.

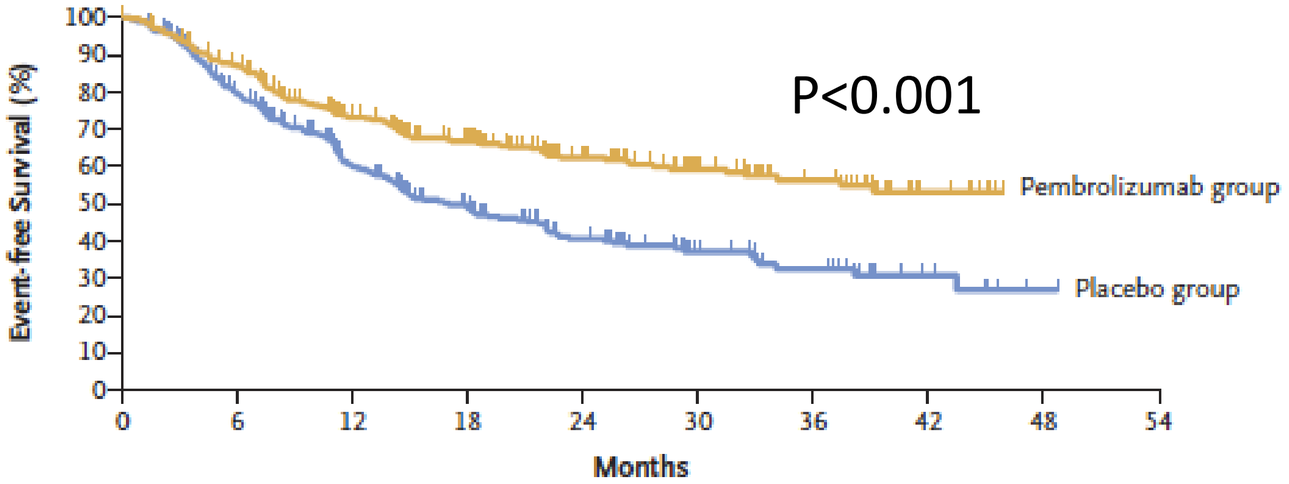
TOGA
Thoracic Oncology Group Australasia

Wakelee H, NEJM 2023

Perioperative Pembrolizumab for Early-Stage Non–Small-Cell Lung Cancer

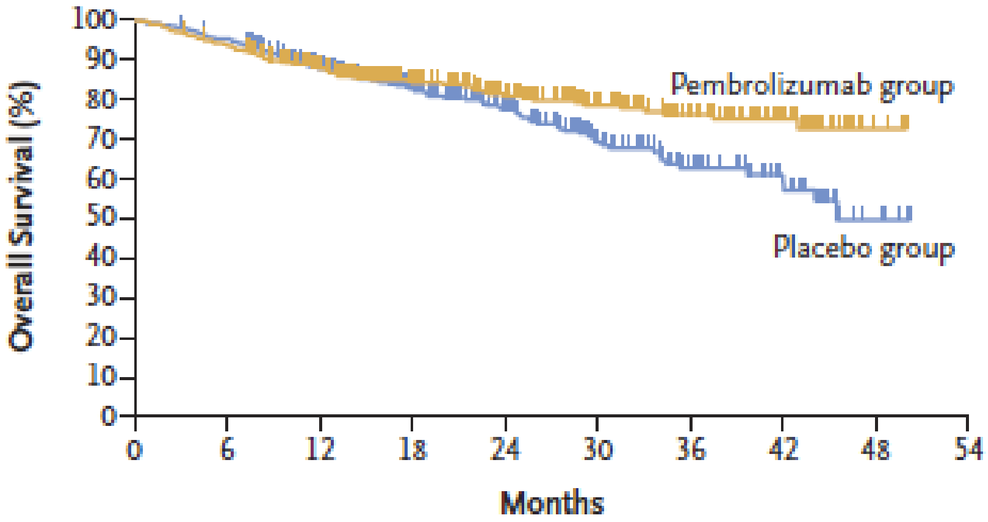
H. Wakelee, M. Liberman, T. Kato, M. Tsuboi, S.-H. Lee, S. Gao, K.-N. Chen, C. Dooms, M. Majem, E. Eigendorff, G.L. Martinengo, O. Bylicki, D. Rodríguez-Abreu, J.E. Chaft, S. Novello, J. Yang, S.M. Keller, A. Samkari, and J.D. Spicer, for the KEYNOTE-671 Investigators*

NEJM 2023



P<0.001

P=0.02



Pre specified threshold p=0.00462

Pathological stage at baseline — no. (%)		
II	118 (29.7)	121 (30.2)
III	279 (70.3)	279 (69.8)
IIIA	217 (54.7)	225 (56.2)
IIIB	62 (15.6)	54 (13.5)

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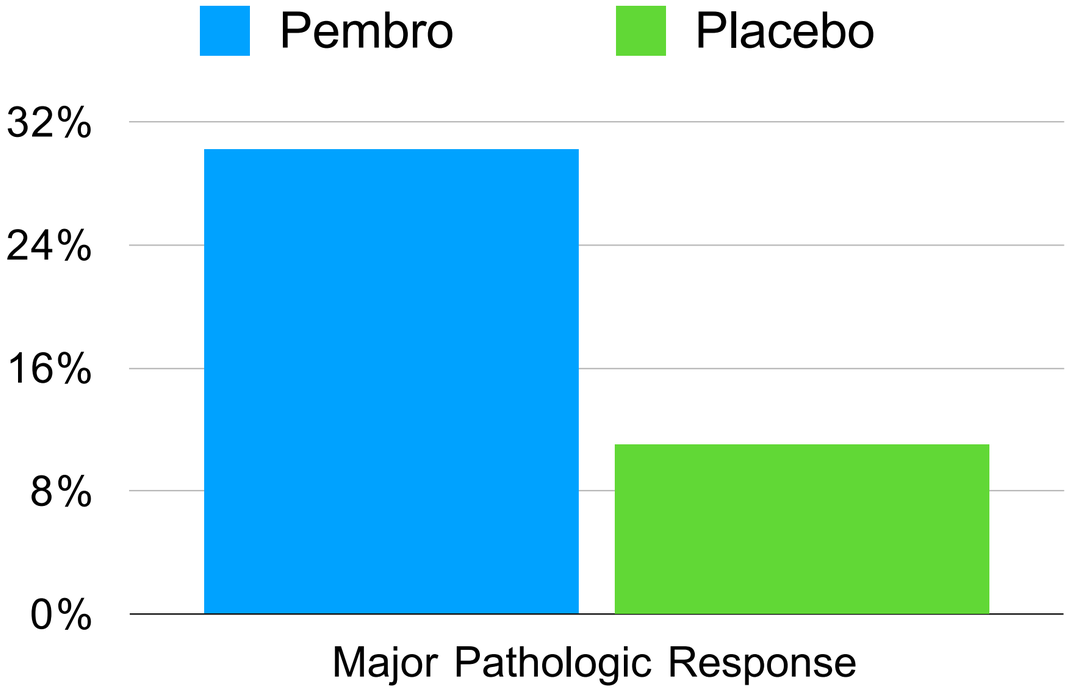
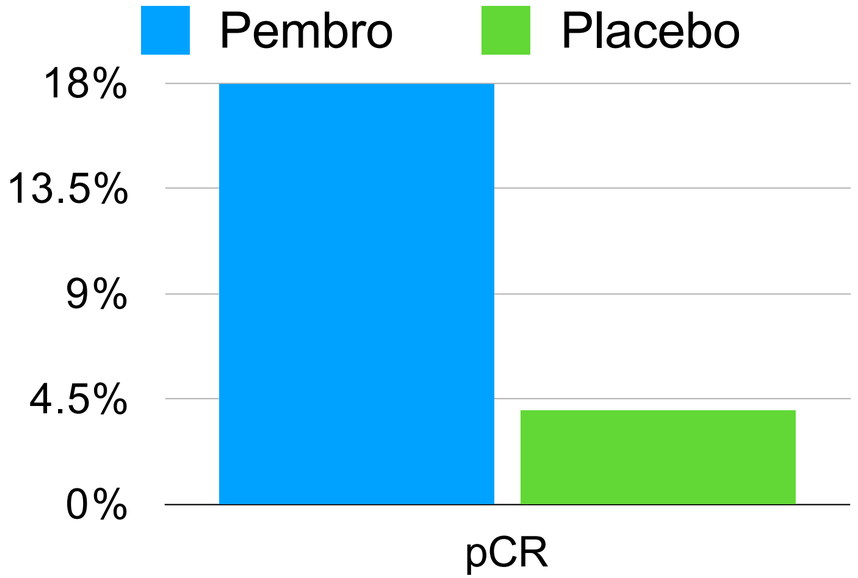
Pathologic Response

P<0.001



P<0.001



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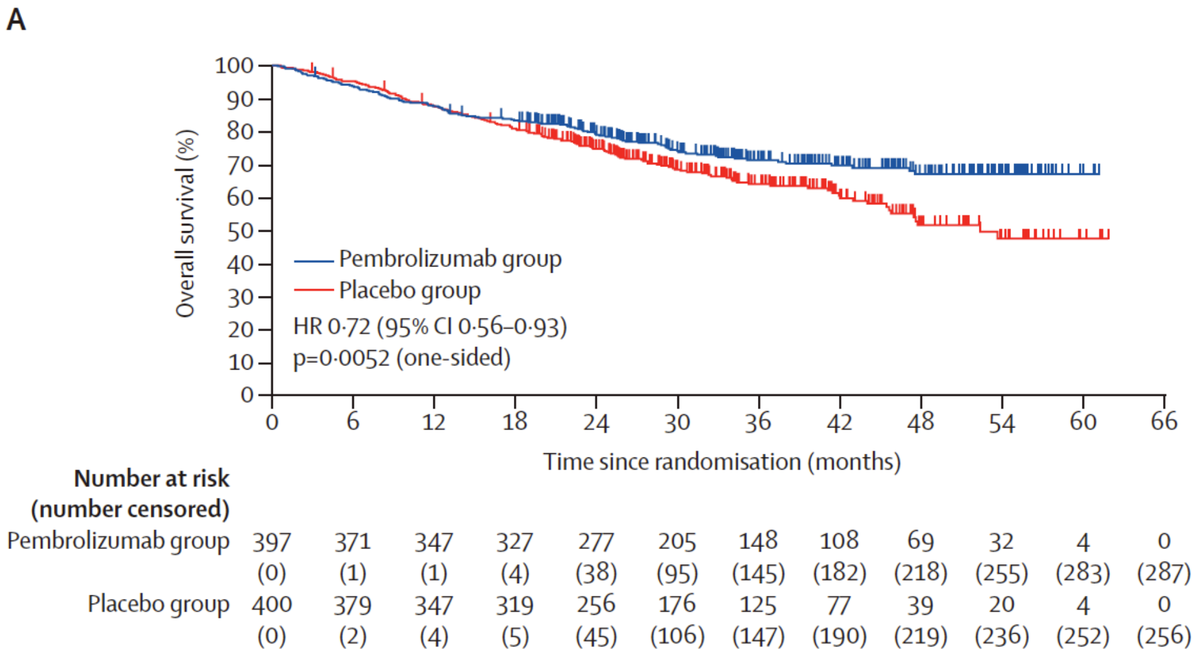
Neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab compared with neoadjuvant chemotherapy alone in patients with early-stage non-small-cell lung cancer (KEYNOTE-671): a randomised, double-blind, placebo-controlled, phase 3 trial

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†*

- Median survival
  - Pembro NR
  - Placebo 52.4 months
- P=0.005
- 71% vs 64% overall 36 months survival



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)

Lancet 404:1240-52, 2024

Allegheny Health Network
Allegheny General Hospital

Initial results of pulmonary resection after neoadjuvant nivolumab in patients with resectable non–small cell lung cancer

Matthew J. Bott, MD,[a] Stephen C. Yang, MD,[b] Bernard J. Park, MD,[a] Prasad S. Adusumilli, MD,[a] Valerie W. Rusch, MD,[a] James M. Isbell, MD,[a] Robert J. Downey, MD,[a] Julie R. Brahmer, MD,[c] Richard Battafarano, MD, PhD,[b] Errol Bush, MD,[b] Jamie Chaft, MD,[d] Patrick M. Forde, MD,[c] David R. Jones, MD,[a] and Stephen R. Broderick, MD, MPHS[b]

20 patients

54% conversion rate

50% complication

0 deaths

JTCVS 158:269-276, 2019

What about the Randomized Trials?

- Trials that did not report granular surgical data:
  - Aegean
  - Nadim II
  - Checkmate 77T

Trial	MIS (%)	Conversion (%)	Surgery cancelation (%)	Complications	30-day death	90-day death
816 control	52%	16.2%	20.3%	15.4% > grade 3	0*	NA
816 IO	49.2%	11.4%	15.6%	11.4% > grade 3	3.4%	NA
671 control	62.1%	16.6%	10%	21.5% > 3	0.6%	0.9%
671 IO	64.5%	15.6%	20%	25.8% > 3	1.8%	2.2%
Neostar	27%	17%	0%	35% all	0%	2.7%
LCMC3	54%	15%	6.6% excluded	6.9% grade 4/5	1.3%	1.3%

Roadmap to Successful MIS resection

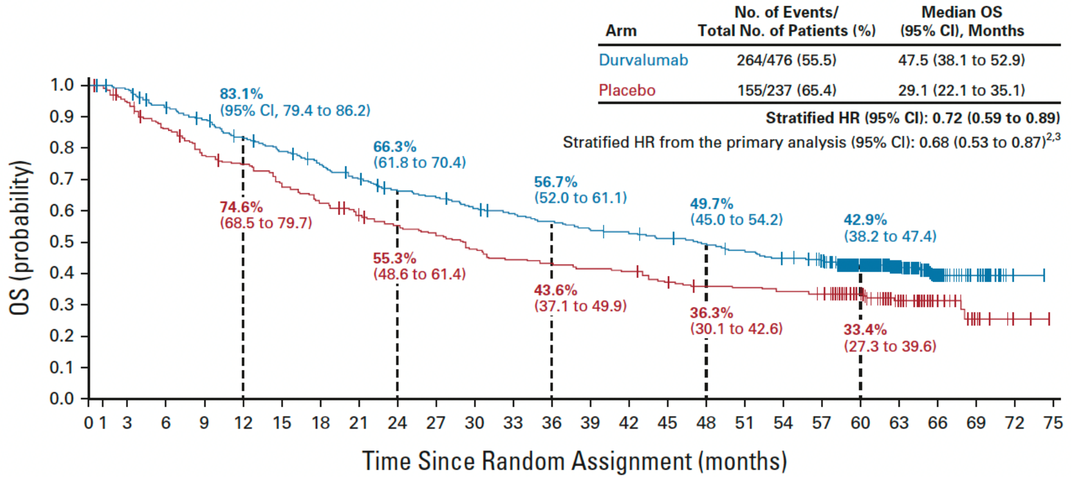
- Appropriate workup, CT with IV contrast, and MRI chest when indicated.
- Assess the resectability of invasive tumors
- Appropriate mediastinal staging to rule out N3 disease.
- Positive N1 nodes are more difficult than positive N2.
- Beware of the invasive lymph node!
- A SURGEON MUST SEE THE PATIENT BEFORE INITIATION OF TREATMENT!

In my practice

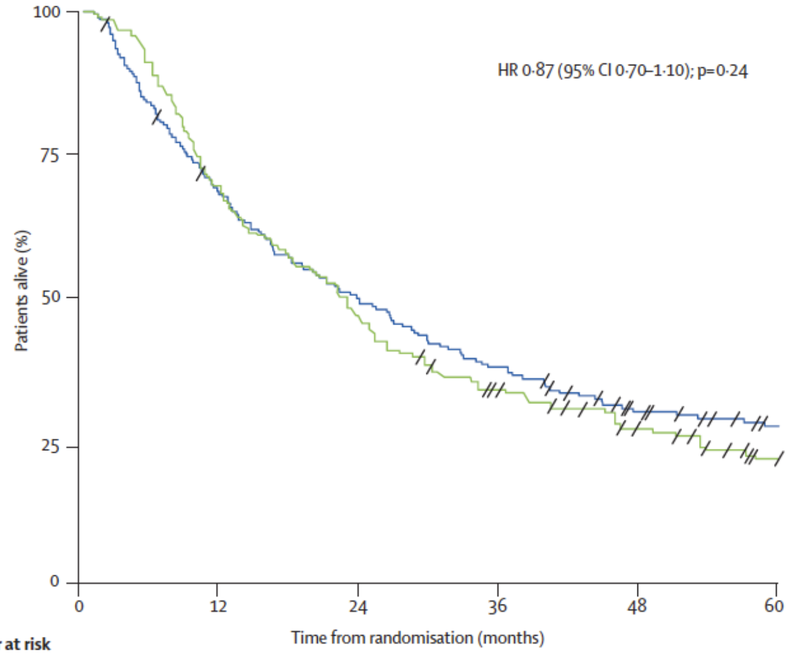
- I restage the mediastinum in all patients with N1 or N2 disease (mediastinoscopy)
- All cases start with robotics.
  - Plan elective conversion for arterial sleeve resections, vena cava resection, and vertebral body resection.
- Never in a hurry.

If you do not know what to do, take another lymph node!

RJ Ginsberg

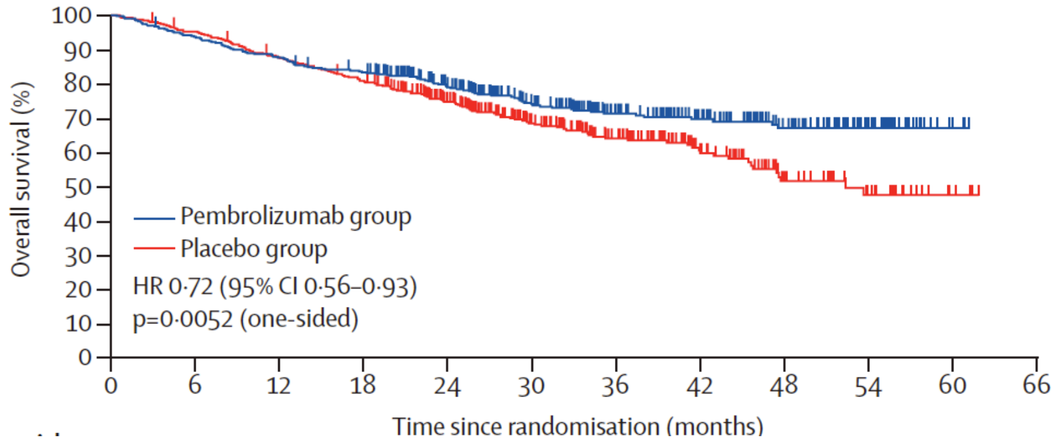


Median 47% - 2017



Median 23 months - 2009

A



71% alive 36 mo, MS not reached 2024

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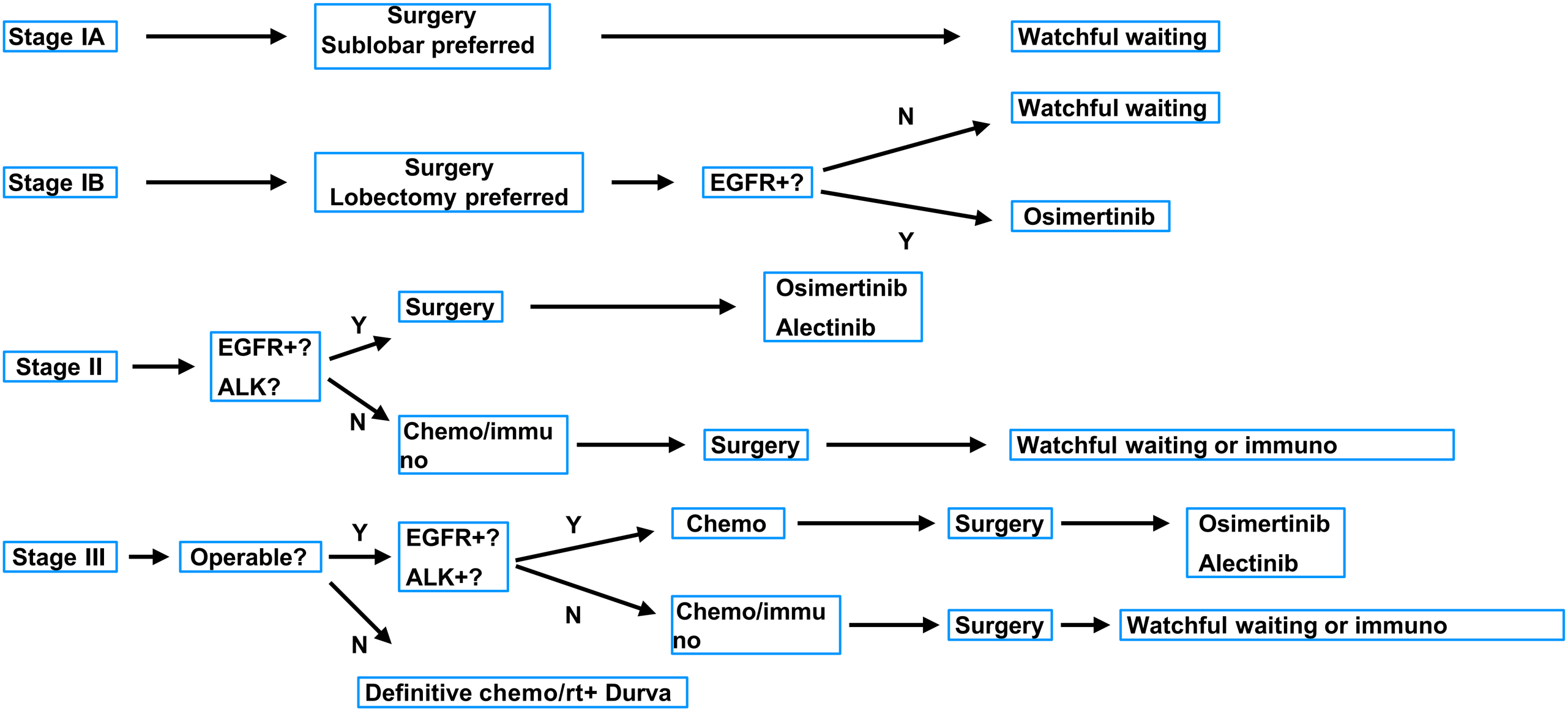
It’s funny how things change slowly, until we realized they’ve changed completely!

Nancy Gibbs



Allegheny Health Network
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Thank you!