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

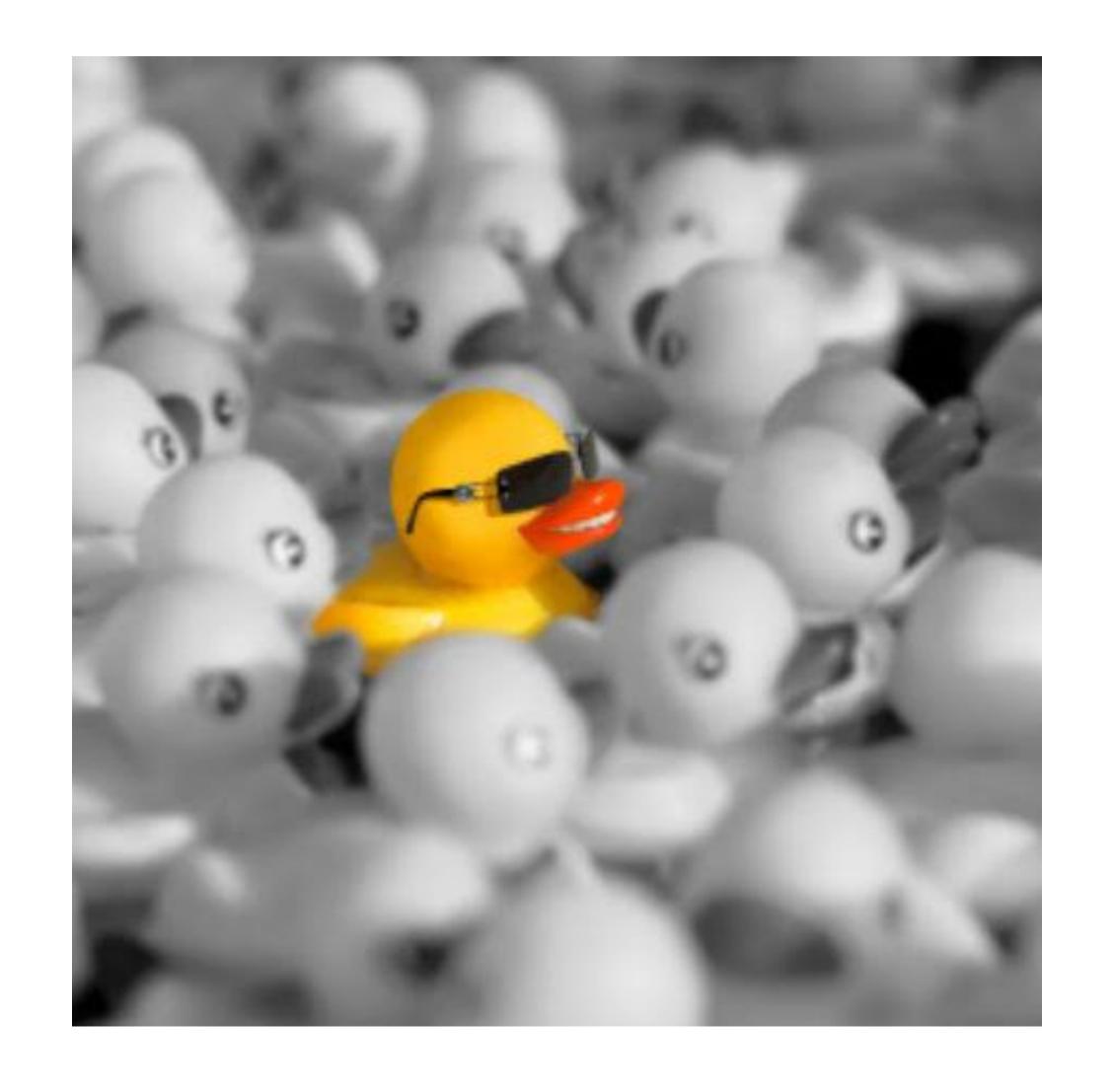
Benny Weksler, MD, MBA, FACS, FACCP Chief of Thoracic Surgery Allegheny Health Network Professor of Surgery Drexel University Medical College



Disclosures

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



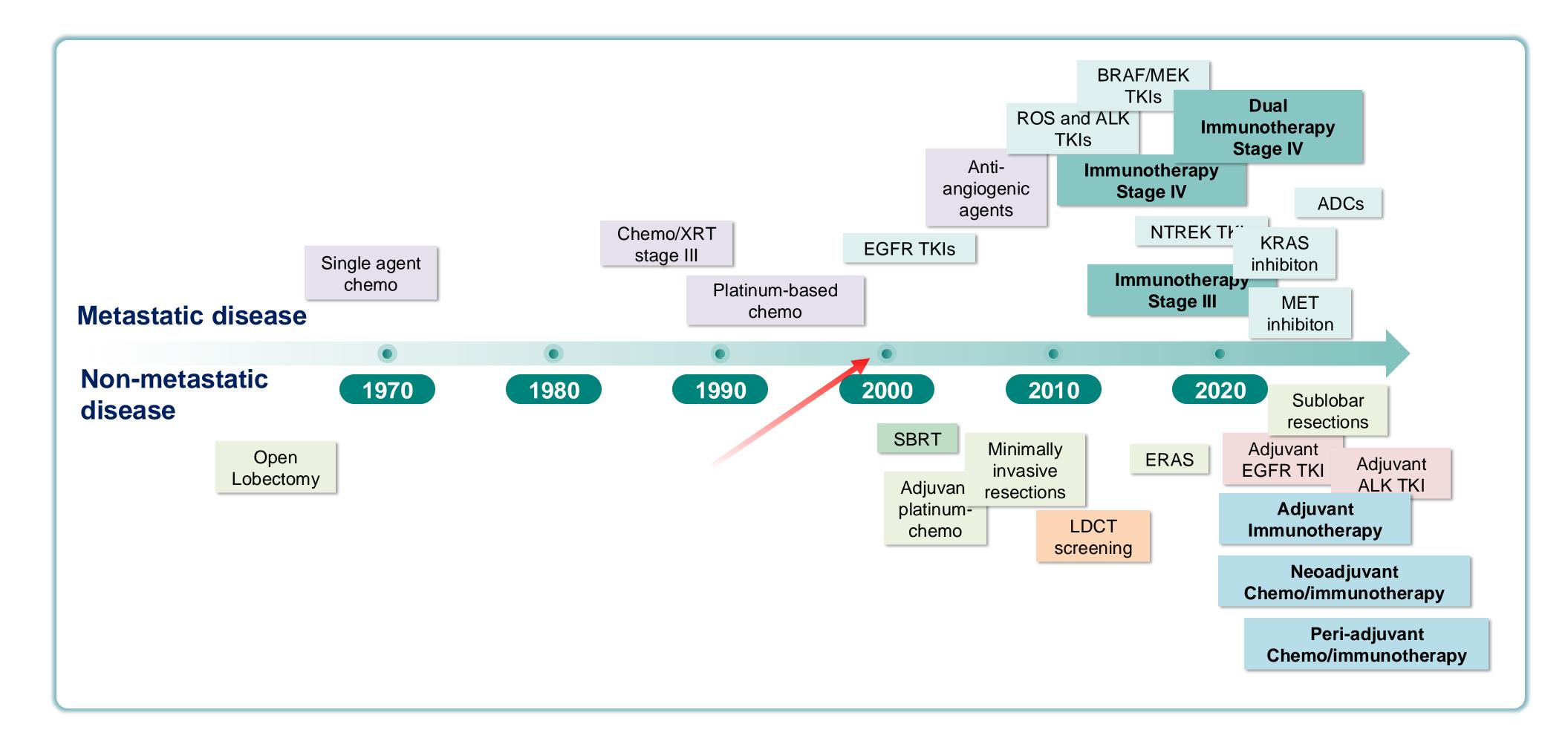








Milestones in NSCLC Treatment



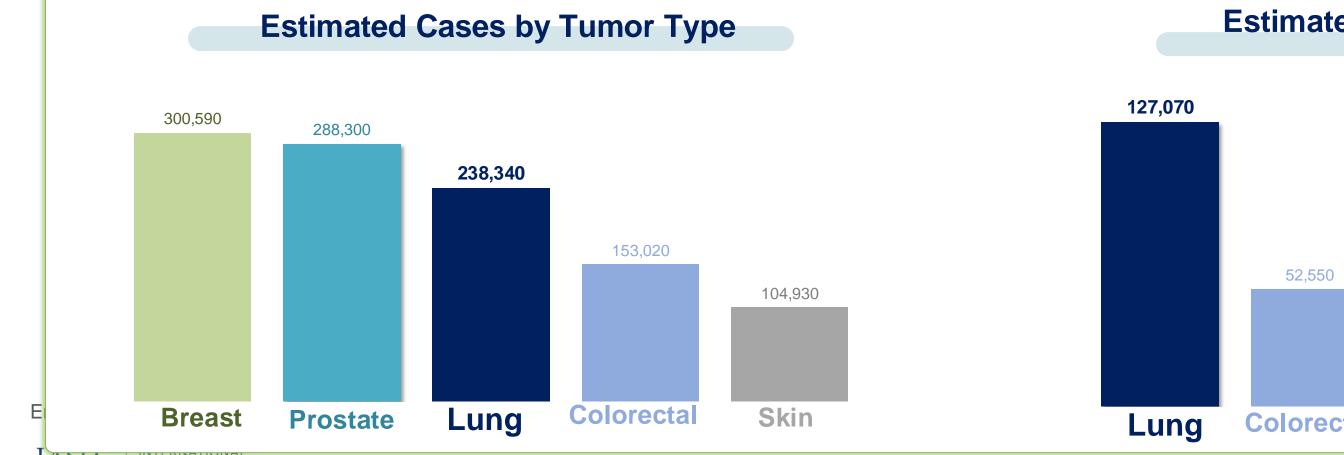
US Lung Cancer Incidence and Mortality

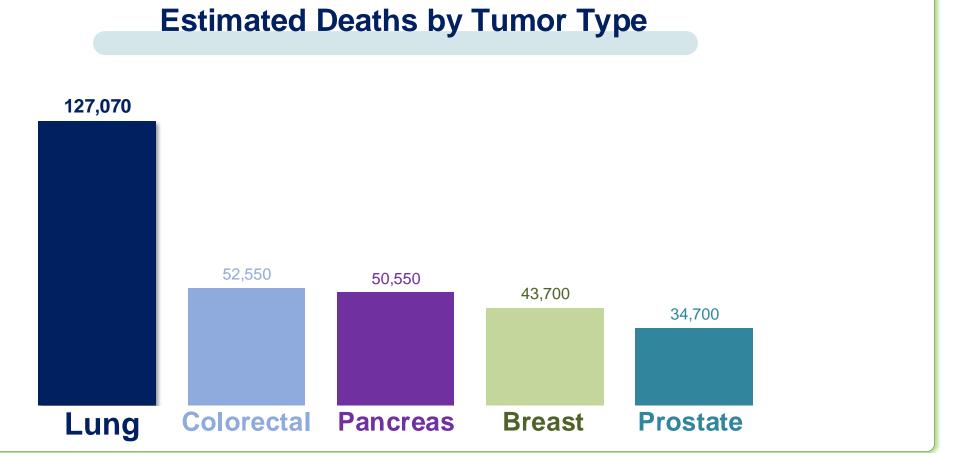


diagnosed with lung cancer in 2023



died from lung cancer in 2023





ASSOCIATION
FOR THE STUDY
OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

1 of every 4 cancer deaths is a lung cancer death

Cancer Mortality in the US

Cancer facts and figures estimated 2024

• Site

Deaths

• 1. Lung

125,070

• 2. Colon/Rectum

53,010

• 3. Pancreas

51,750

• 4. Breast

42,780

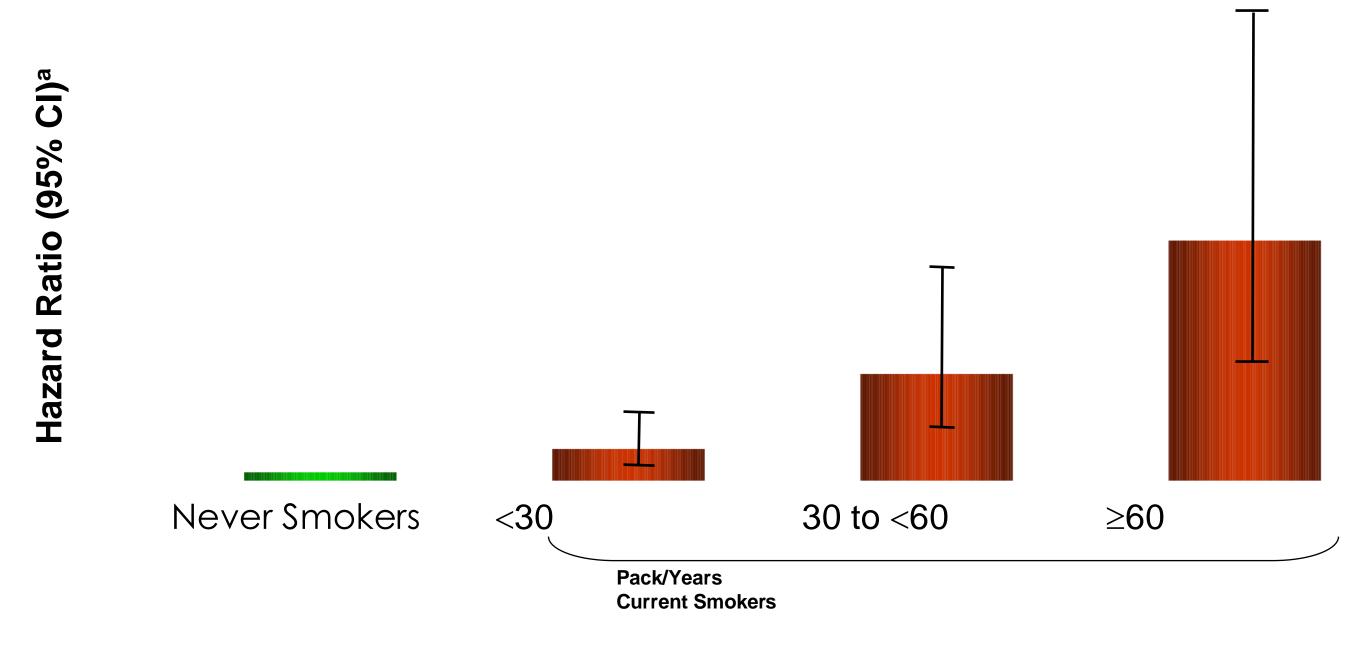
• 5. Prostate

35,250



RISK OF LUNG CANCER

 The risk of developing lung cancer is directly related to the amount smoked

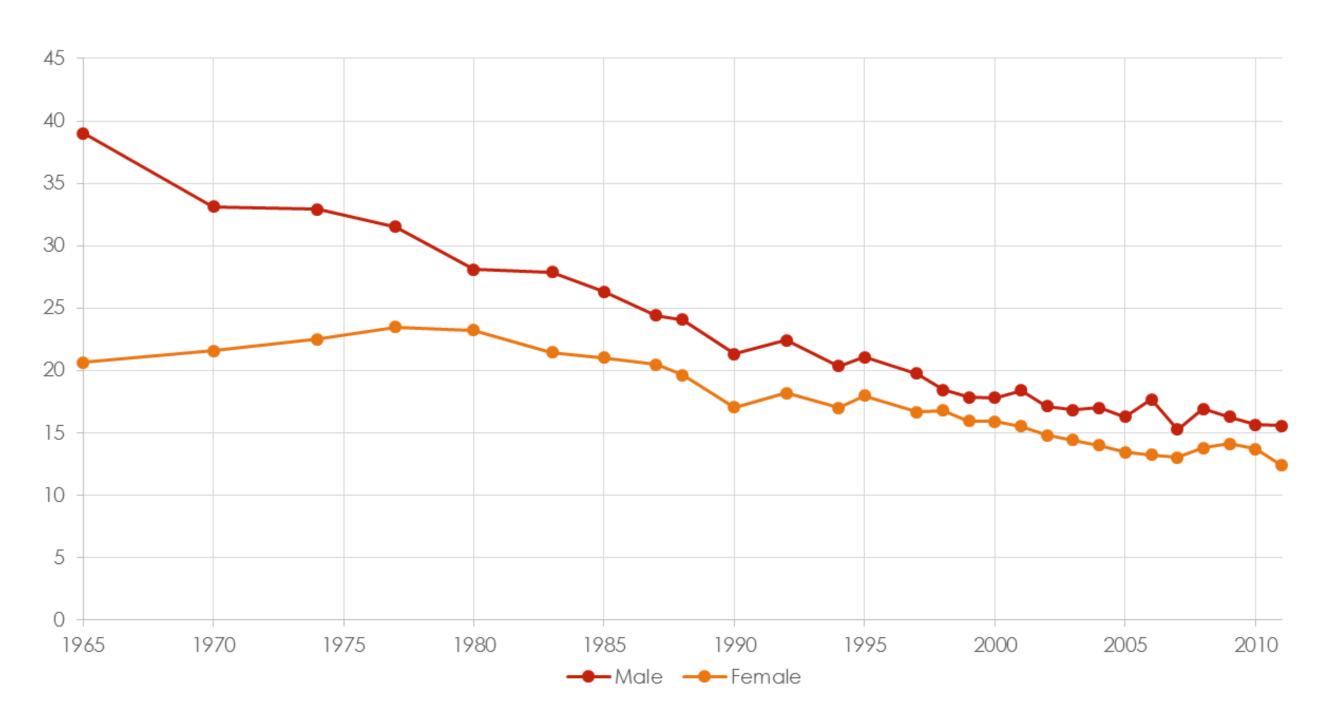


Pack/year was calculated by multiplying the average number of cigarettes smoked daily by the number of years smoked and dividing the product by 20.

^aThe relative likelihood of experiencing a particular event or the effect of an explanatory variable on the hazard or risk of an event. Mannino et al. *Arch Intern Med.* 2003;163:1475-1480.

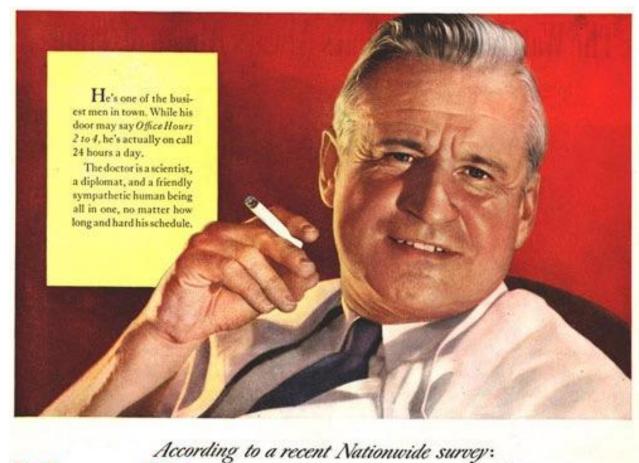


ANNUAL PREVALENCE OF CURRENT SMOKING AMONG ADULTS ≥35 IN THE US, 1965-2011



U.S. Department of Health and Human Services (2014). The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.





MORE DOCTORS SMOKE CAMELS THAN ANY OTHER CIGARETTE

DOCTORS in every branch of medicine—113,597 in all—were queried in this nationwide study of cigarette preference. Three leading research organizations made the survey. The gist of the query was—What cigarette do you smoke, Doctor?

The brand named most was Came!!

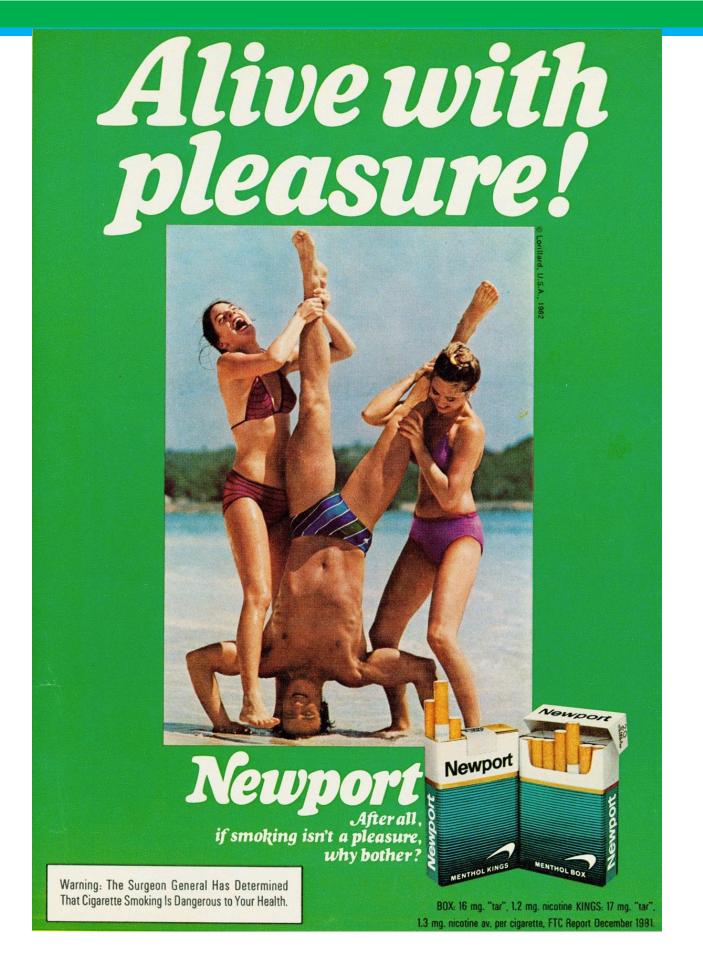
The rich, full flavor and cool mildness of Camel's superb blend of costsier tobaccos seem to have the same appeal to the smoking tastes of doctors as to millions of other smokers. If you are a Camel smoker, this preference among doctors will hardly surprise you. If you're not—well, try Camels now.















NICOTINE IS A WHY PEOPLE SMOKE CIGARETTES

After inhaling, nicotine reaches the brain in

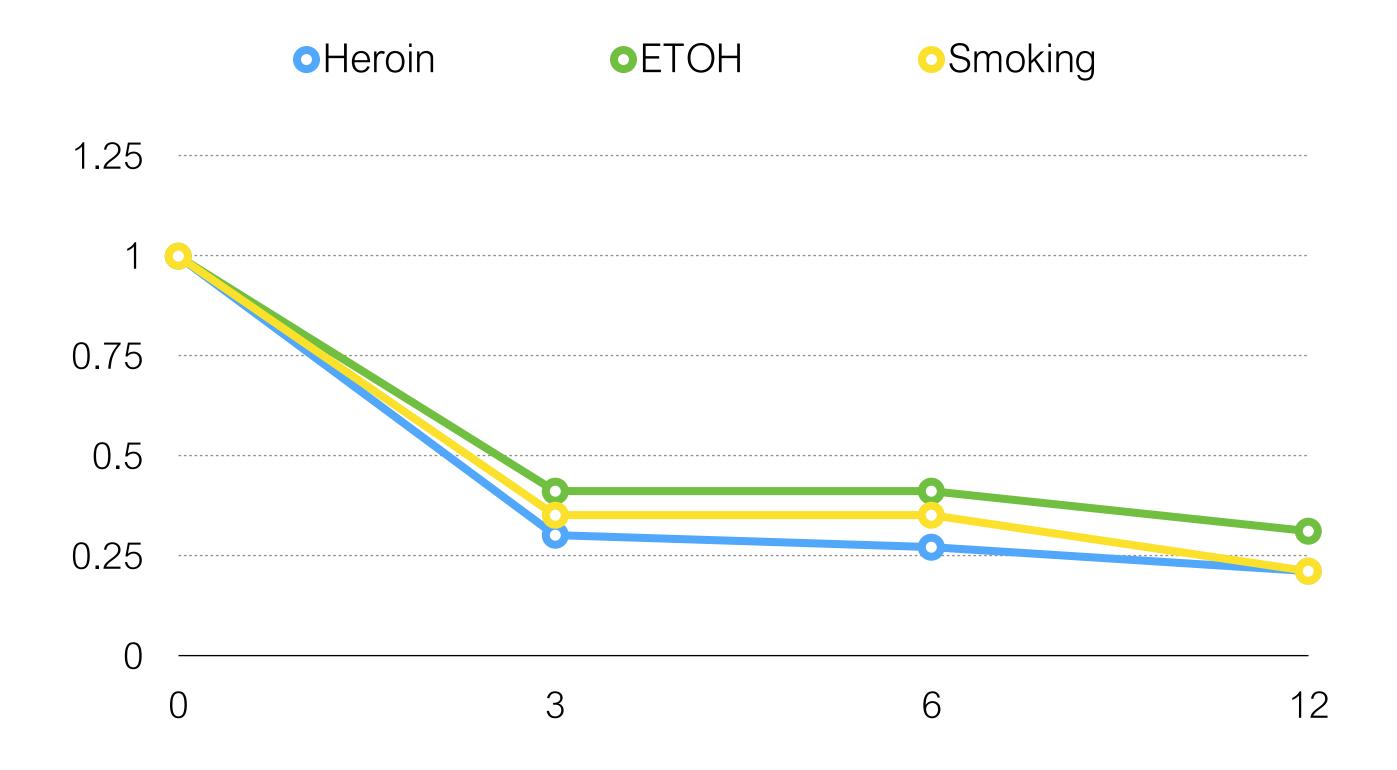
7-10 seconds



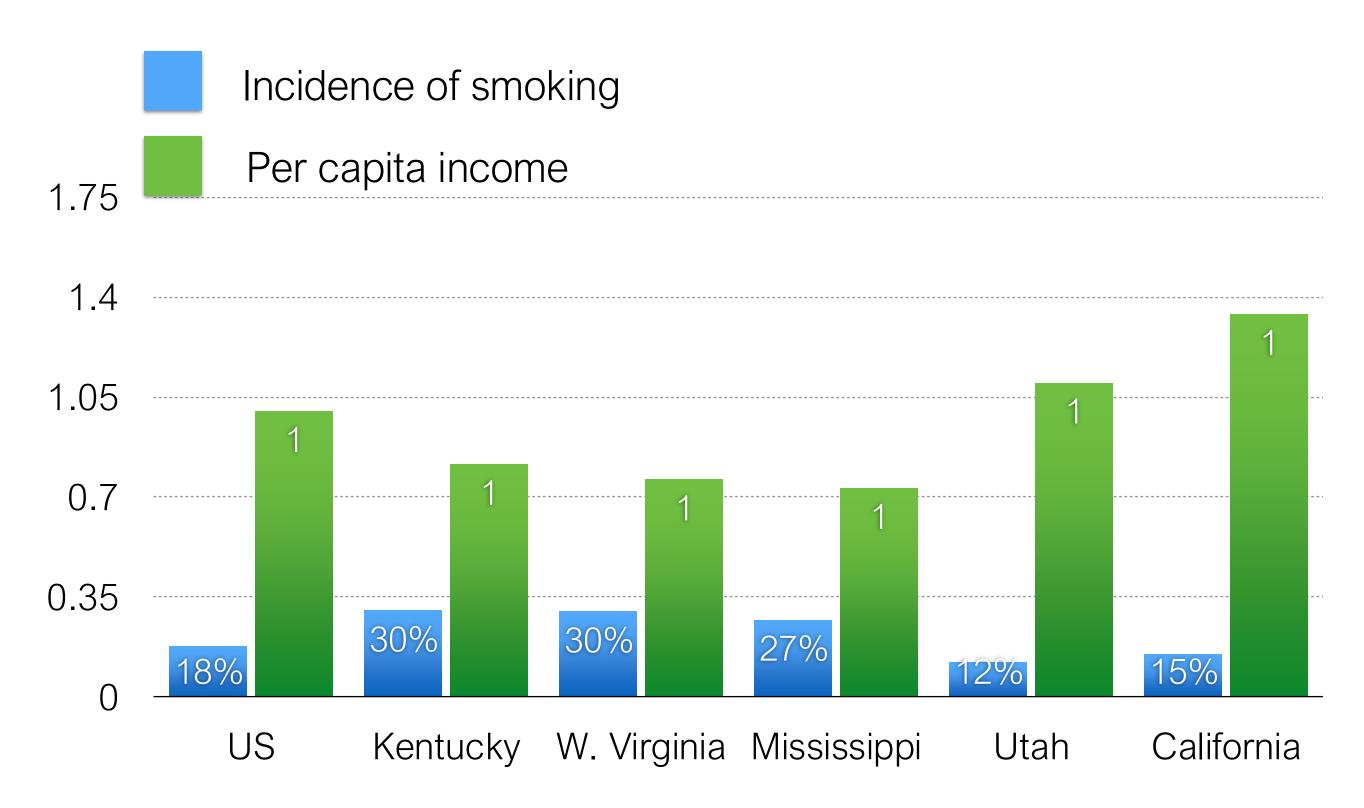
legheny General

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

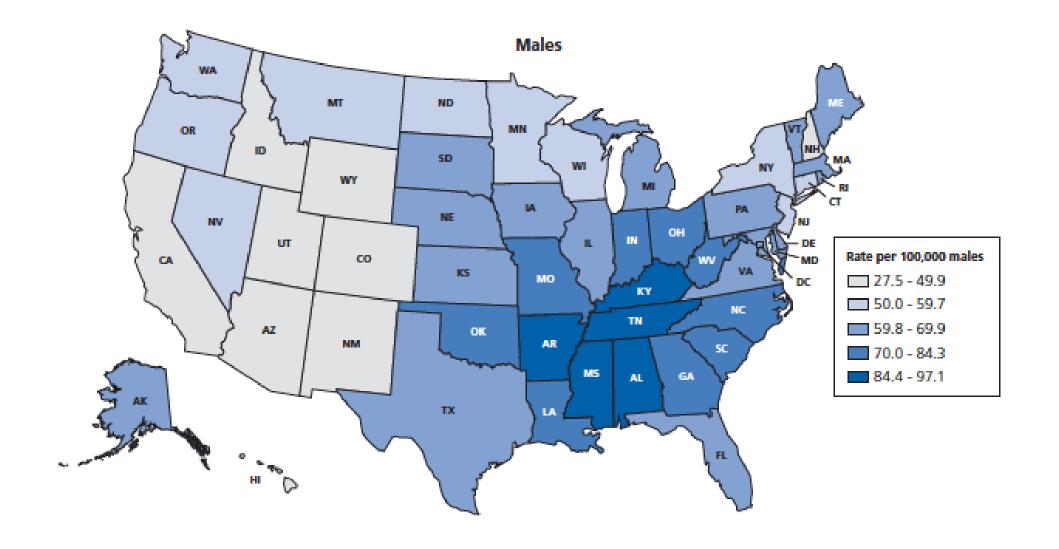
Rate of Relapse

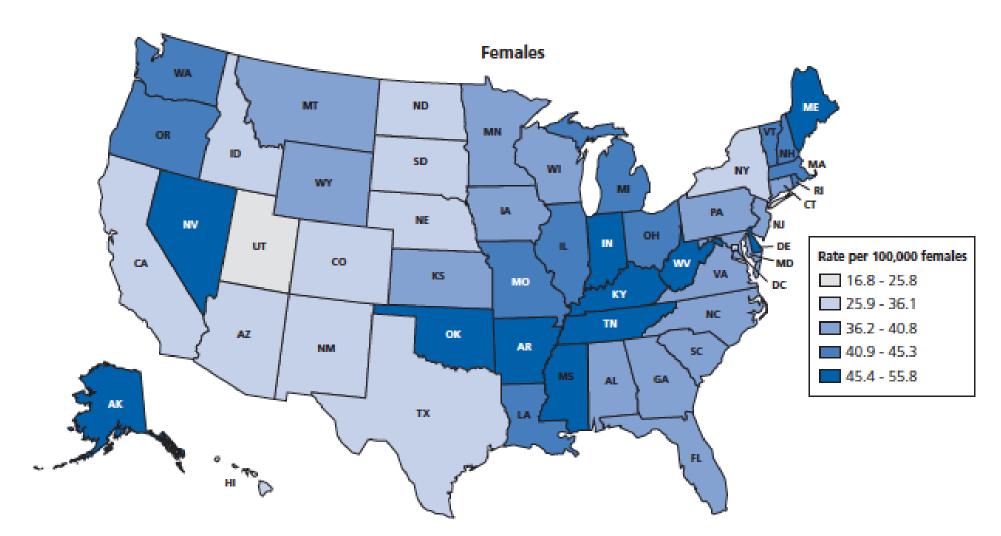


Incidence of Smoking vs Income



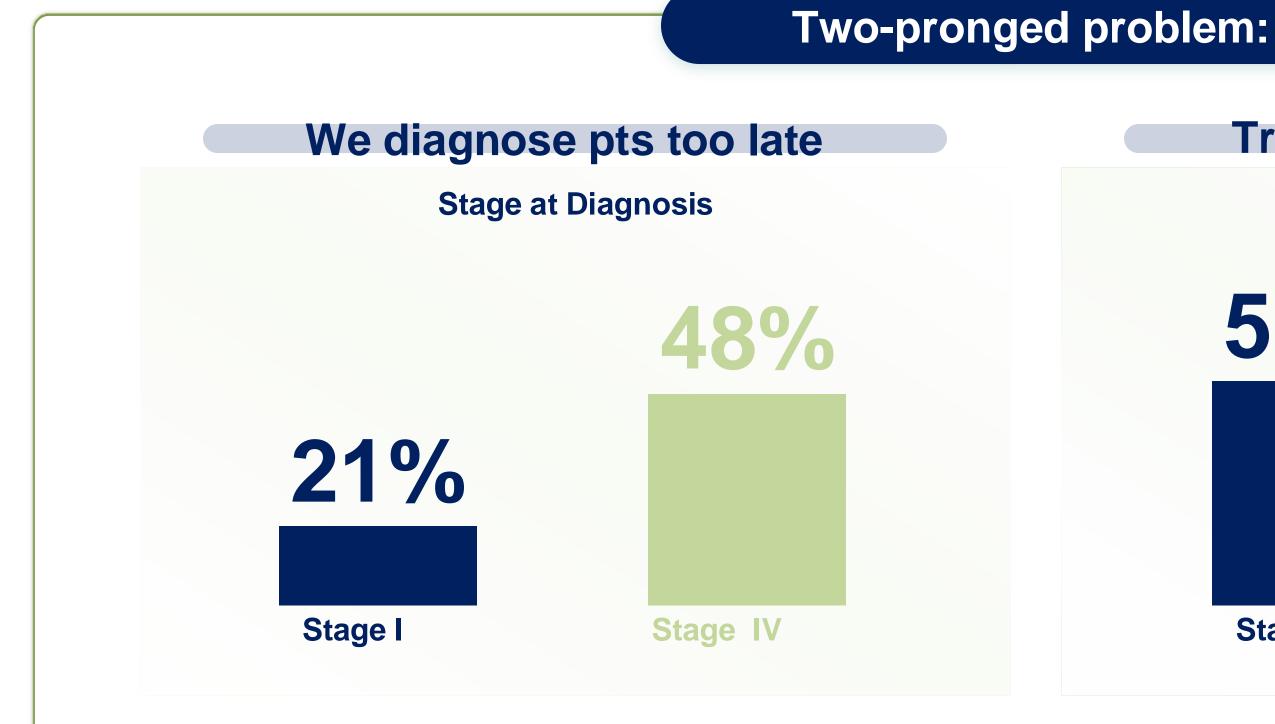


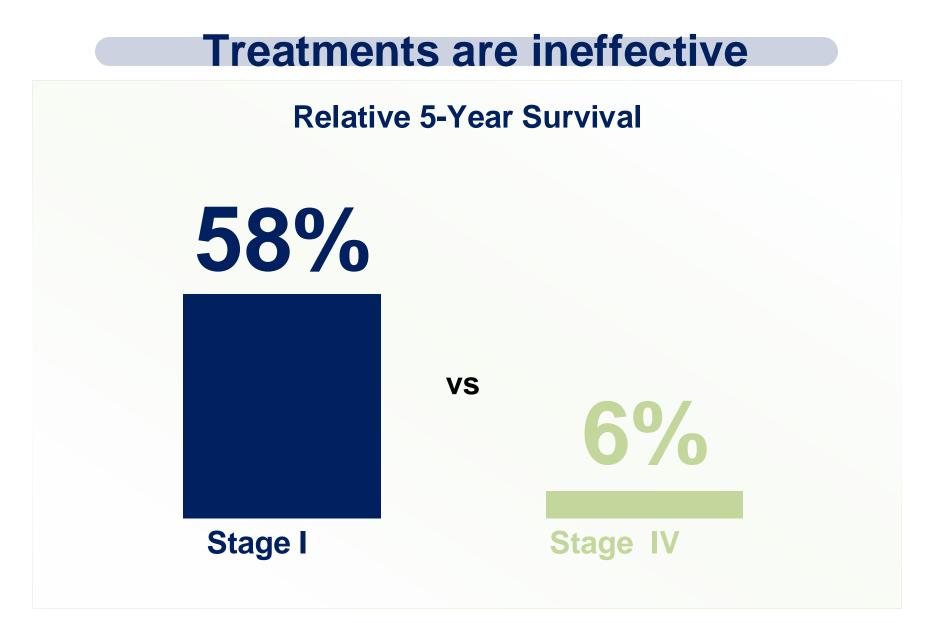






Clinical Reasons for Poor Lung Cancer Prognosis





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



he New Hork Eimes

Late Edit

Today, variably clou high 54. Tonight, p mixed with clouds, high 50. Weather

vers, oudy, sun cool,

© 2010 The New York Times

NEW YORK, FRIDAY, NOVEMBER 5, 2010

\$2.00

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 4, 2011

VOL. 365 NO. 5

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 The members of the writing team (who reduce mortality from this cancer through the use of screening. The advent of lowdose 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.

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

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. Copyright © 2011 Massachusetts Medical Society.

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

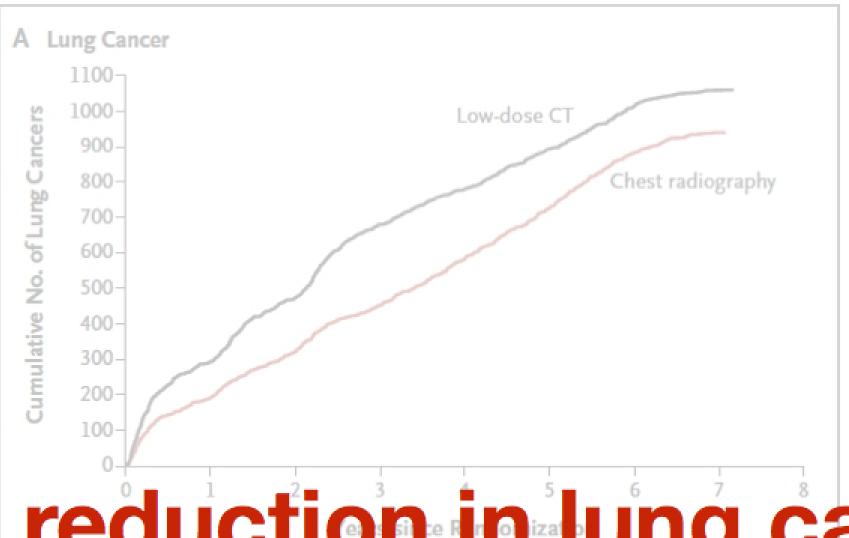
BIG U.S.-FINANCED STUDY

20% Reduction Is Seen — Officials Debate Risks and Cost

By GARDINER HARRIS

Allegheny Health Network





20% reduction in lung cancer





NCCN Guidelines Version 1.2025 Lung Cancer Screening

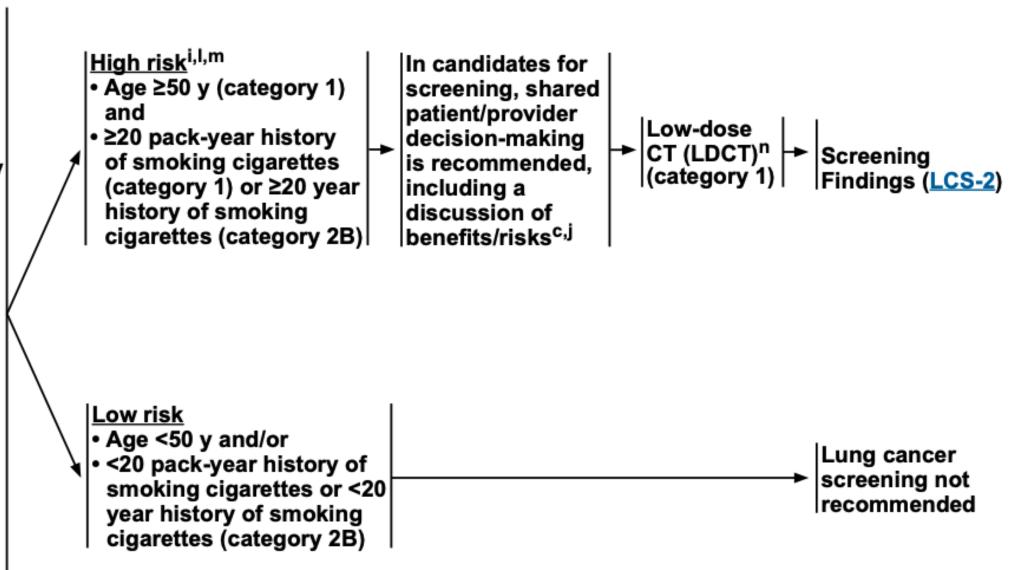
NCCN Guidelines Index
Table of Contents
Discussion

RISK ASSESSMENT^{a,b,c} RISK STATUS SCREENING

- Cigarette smoking history^d
- Radon exposure
- Occupational exposure^f
- Cancer history^g
- Family history of lung cancer in first-degree relatives
- Disease history (chronic obstructive pulmonary disease [COPD] or pulmonary fibrosis)
- Cigarette smoking exposure^h (second-hand smoke)
- Risk calculator to enhance determination of risk status^{i,j}

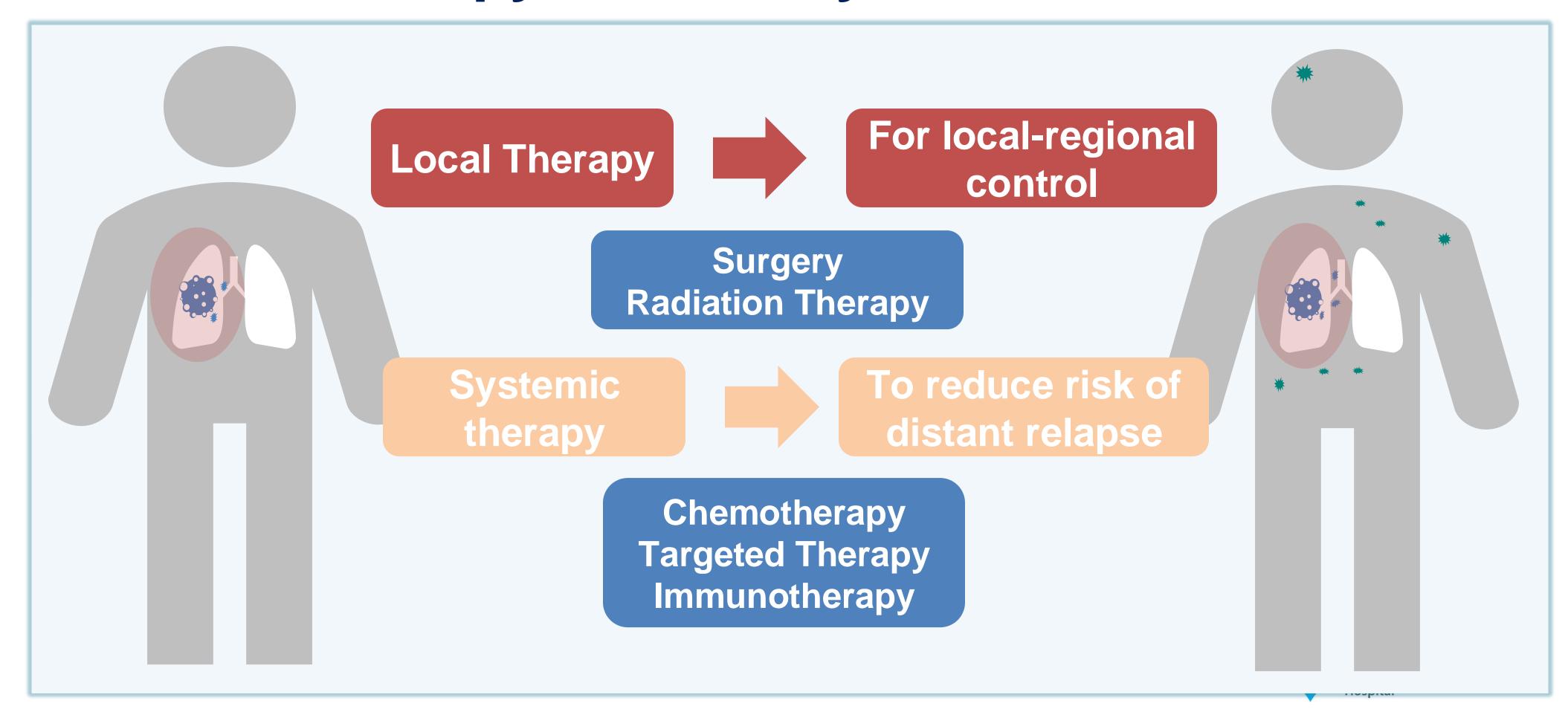
Patients not eligible for lung cancer screening:

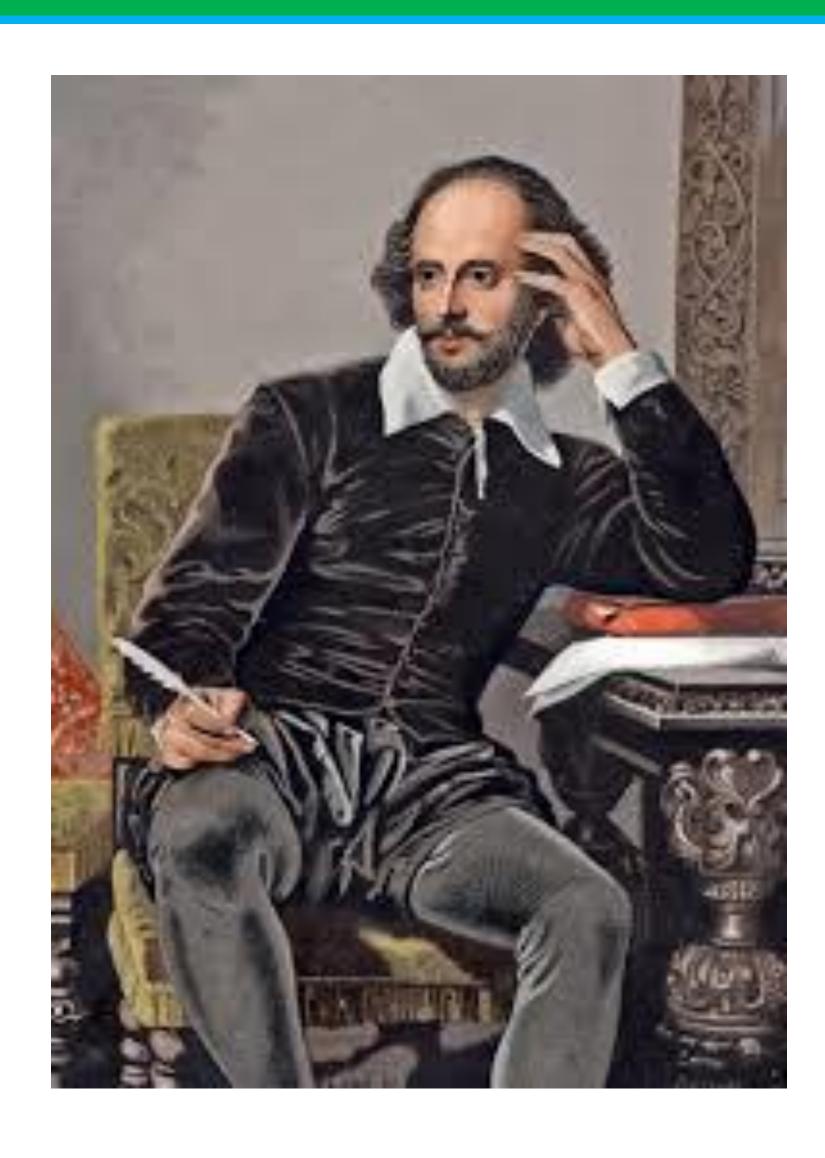
- Symptoms of lung cancer (see NCCN Guidelines for Non-Small Cell Lung Cancer)
- Previous lung cancer (see <u>Surveillance in the NCCN Guidelines for Non-Small Cell Lung Cancer</u>)
- Functional status and/or comorbidity that would prohibit curative intent treatment^k (see Principles of Surgery in the NCCN Guidelines for Non-Small Cell Lung Cancer and Principles of Radiation Therapy in the NCCN Guidelines for Non-Small Cell Lung Cancer)





Curative Therapy for Locally Advanced NSCLC

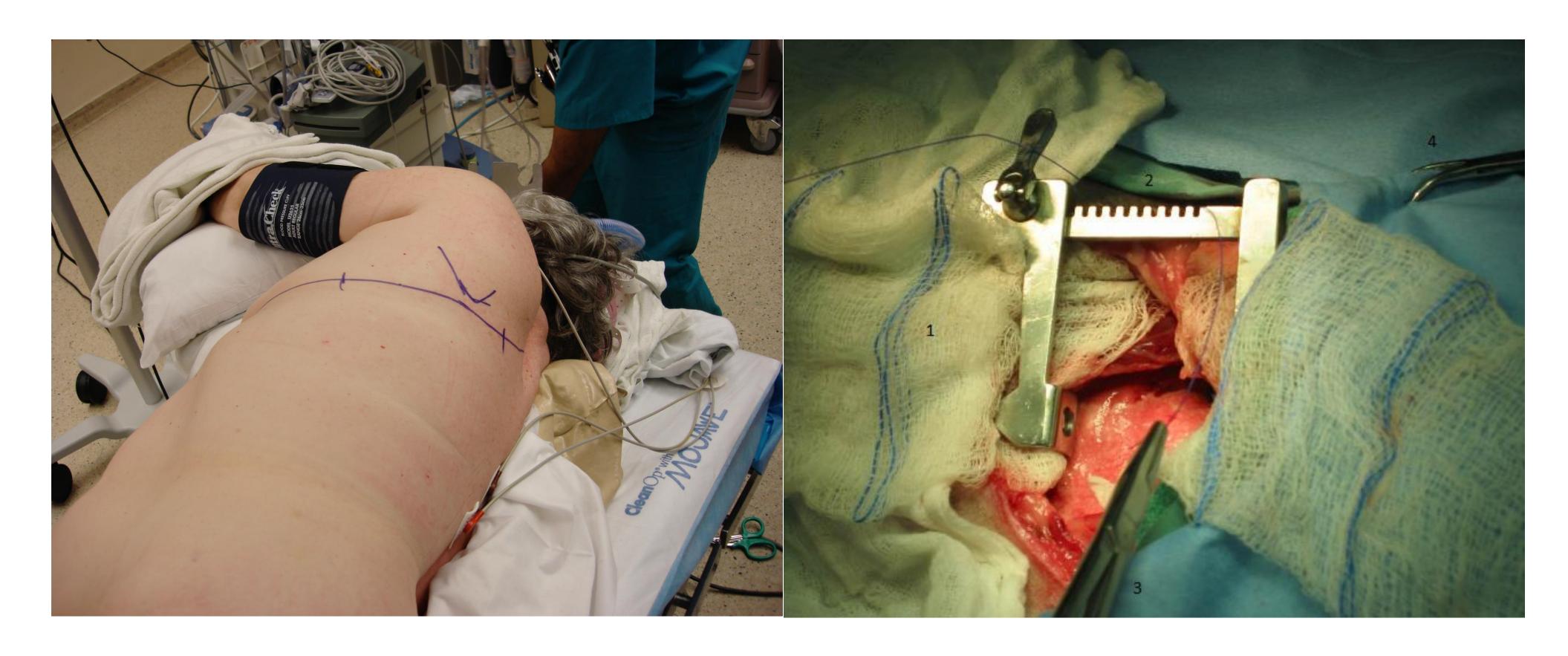




Out, damned spot! Out, I say!

Shakespeare in Lady Macbeth









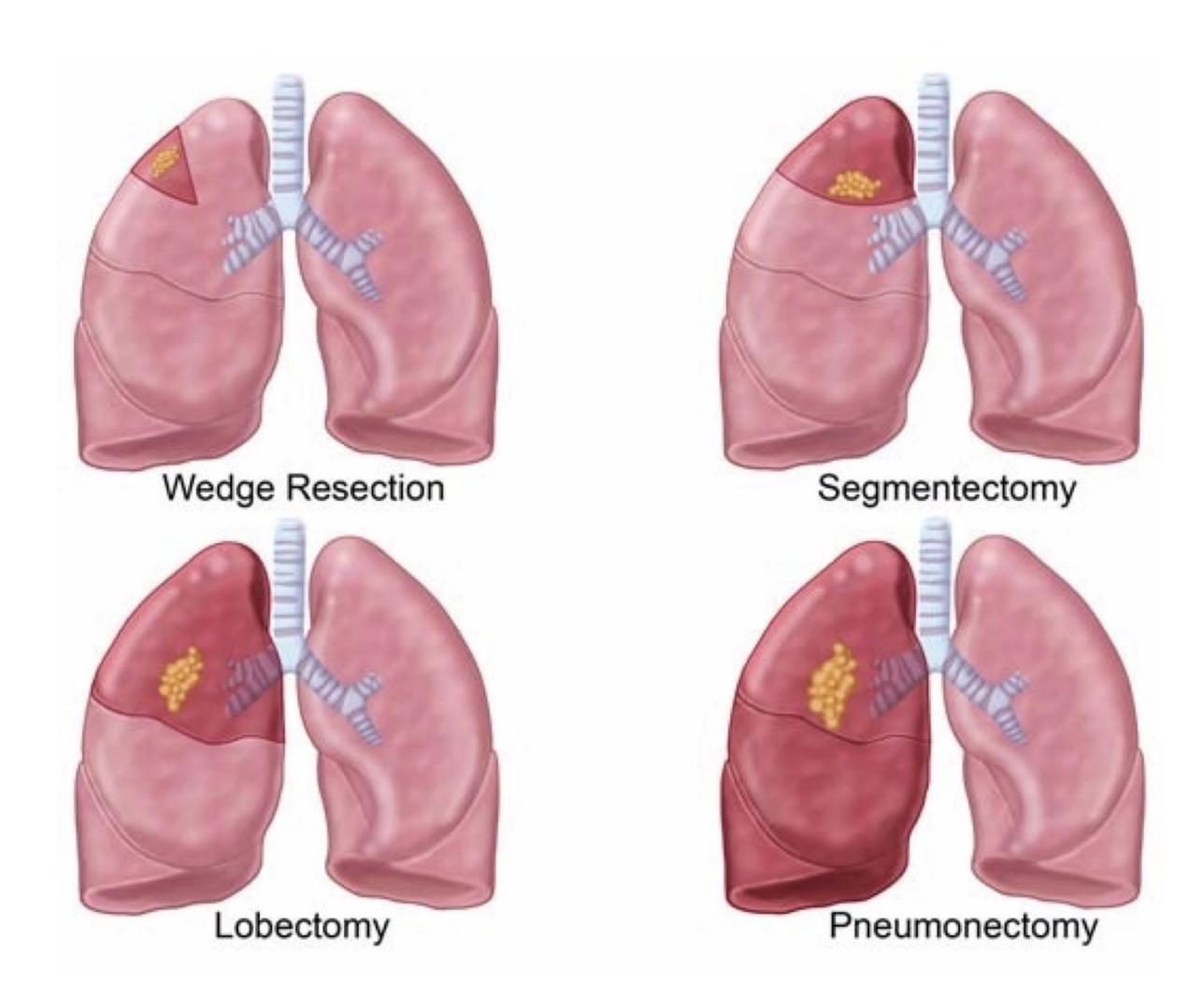




Advantages to Patients

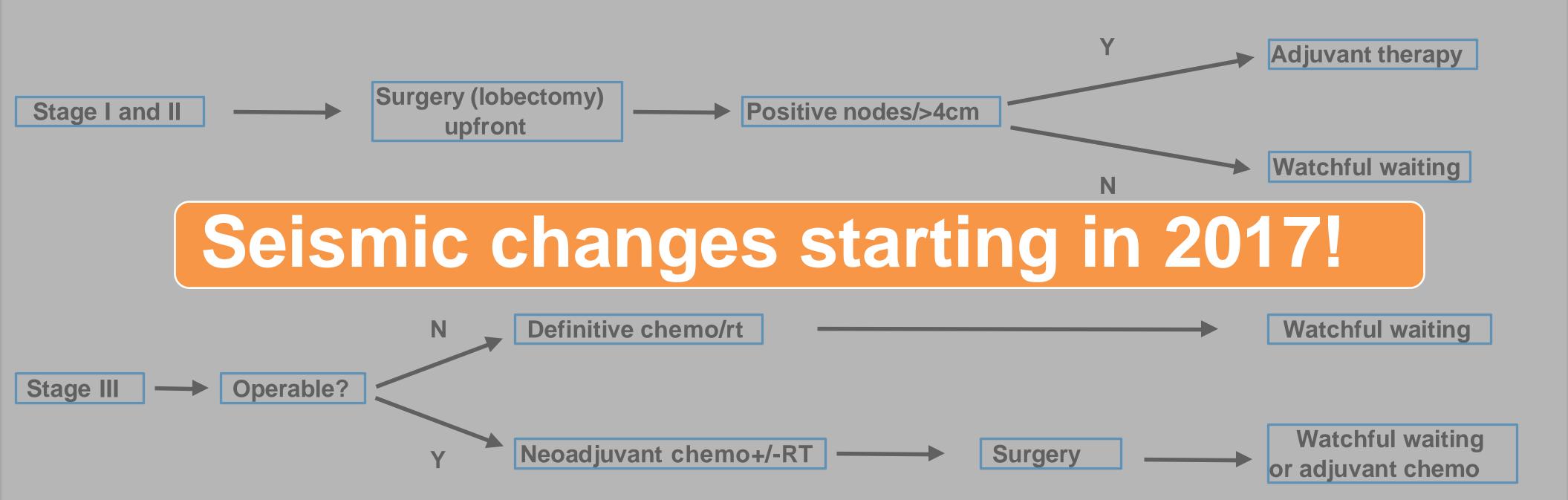
- Less pain
- Less narcotics usage
- Earlier discharge
- Earlier return to usual activities
- Improved quality of life
- Better tolerance of other treatments after surgery



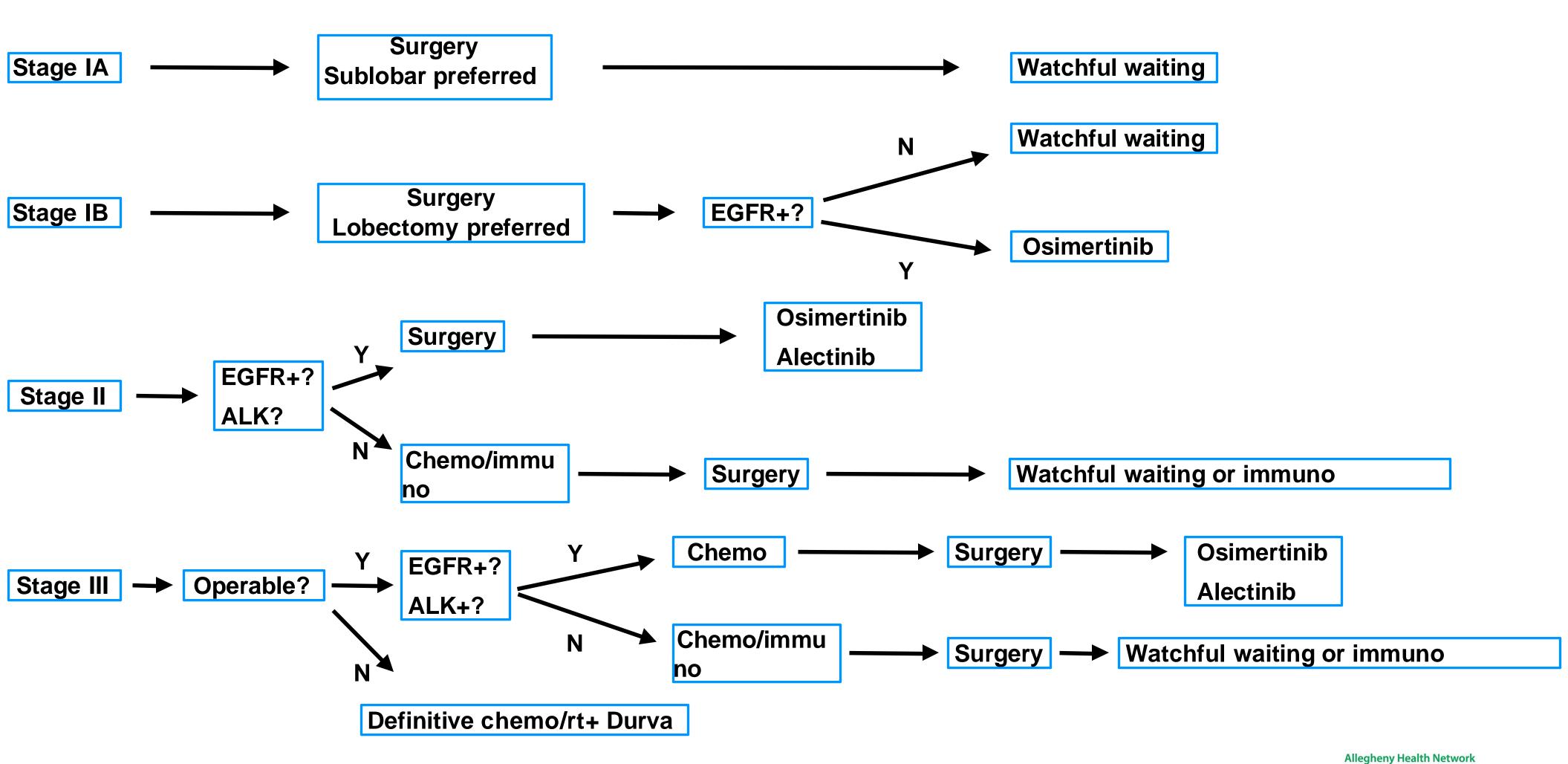




Old Paradigms







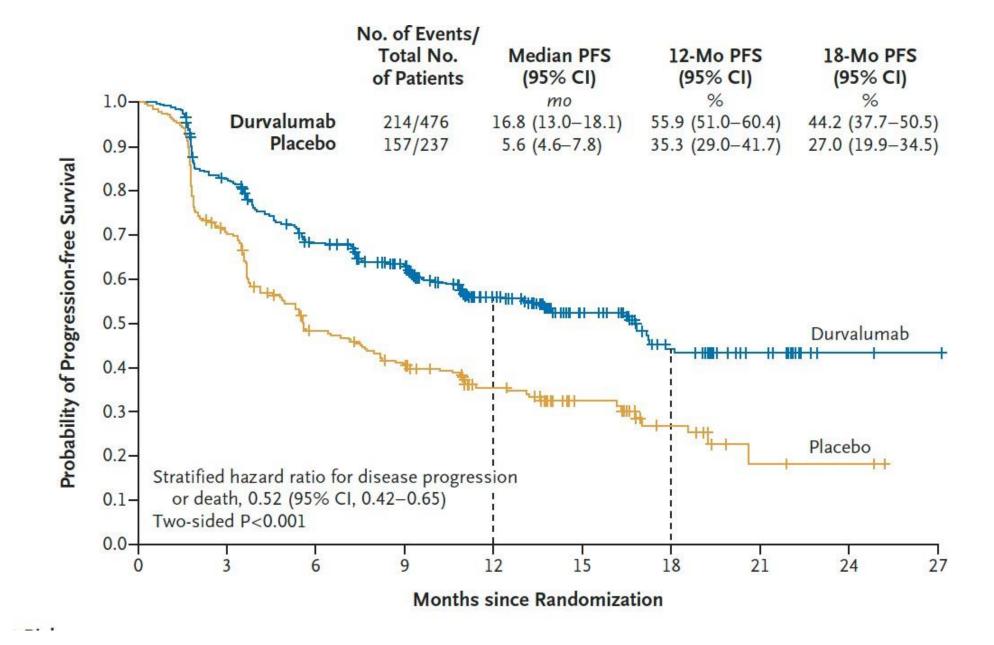


ORIGINAL ARTICLE

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

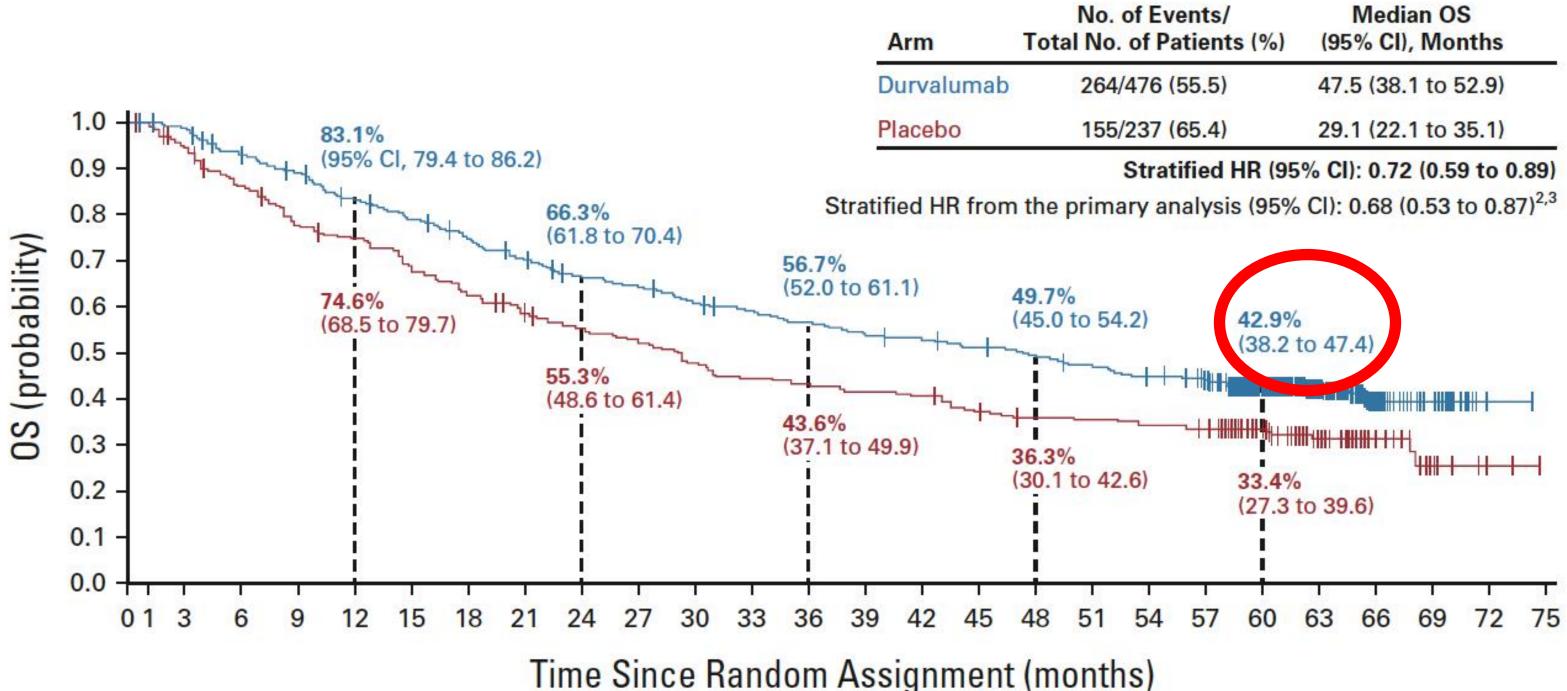




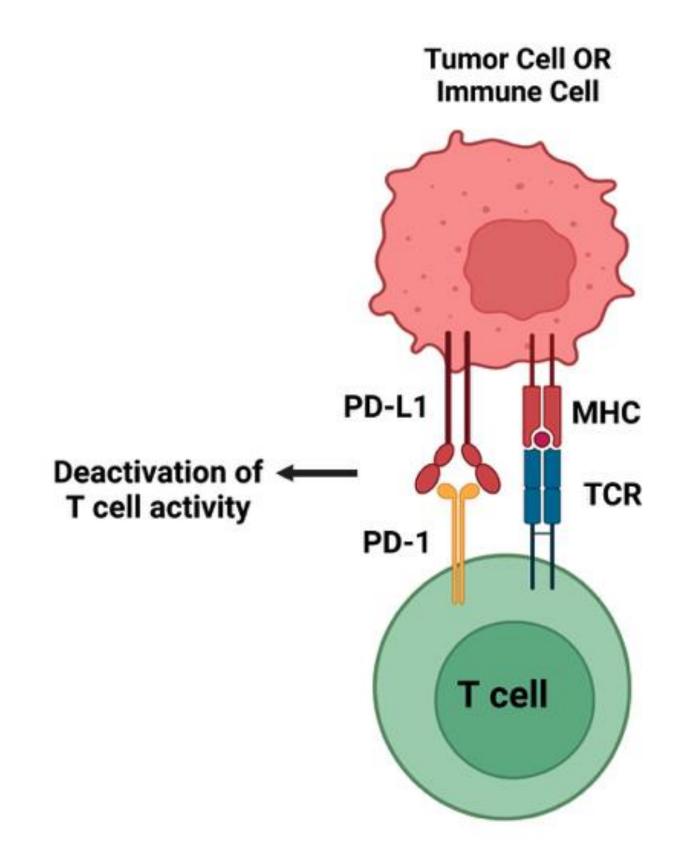
Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer

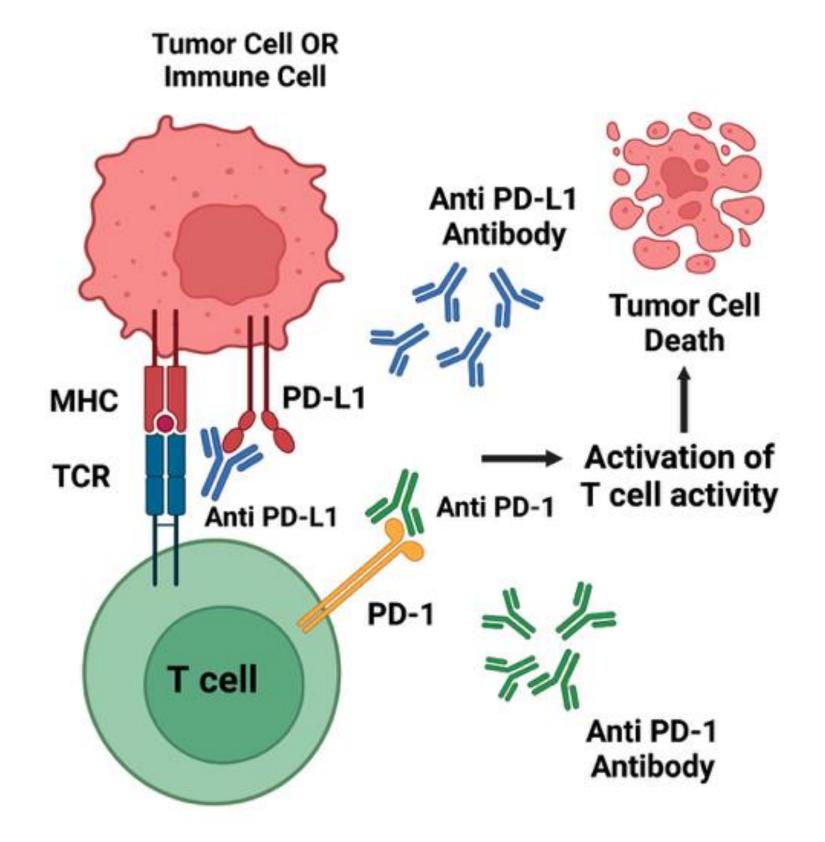
David R. Spigel, MD¹; Corinne Faivre-Finn, MD, PhD²; Jhanelle E. Gray, MD³; David Vicente, MD⁴; David Planchard, MD, PhD⁵; Luis Paz-Ares, MD, PhD⁶; Johan F. Vansteenkiste, MD, PhDˀ; Marina C. Garassino, MD³, Rina Hui, PhD¹⁰; Xavier Quantin, MD, PhD¹¹; Andreas Rimner, MD¹²; Yi-Long Wu, MD¹³; Mustafa Özgüroğlu, MD¹⁴; Ki H. Lee, MD¹⁵; Terufumi Kato, MD¹⁶; Maike de Wit, MD, PhD¹ˀ; Takayasu Kurata, MD¹³; Martin Reck, MD, PhD¹³; Byoung C. Cho, MD, PhD²⁰; Suresh Senan, PhD²¹; Jarushka Naidoo, MBBCH, MHS²²; Helen Mann, MSc²³; Michael Newton, PharmD²⁴; Piruntha Thiyagarajah, MD²³; and Scott J. Antonia, MD, PhD³; on behalf of the PACIFIC Investigators

J Clin Onc 2022





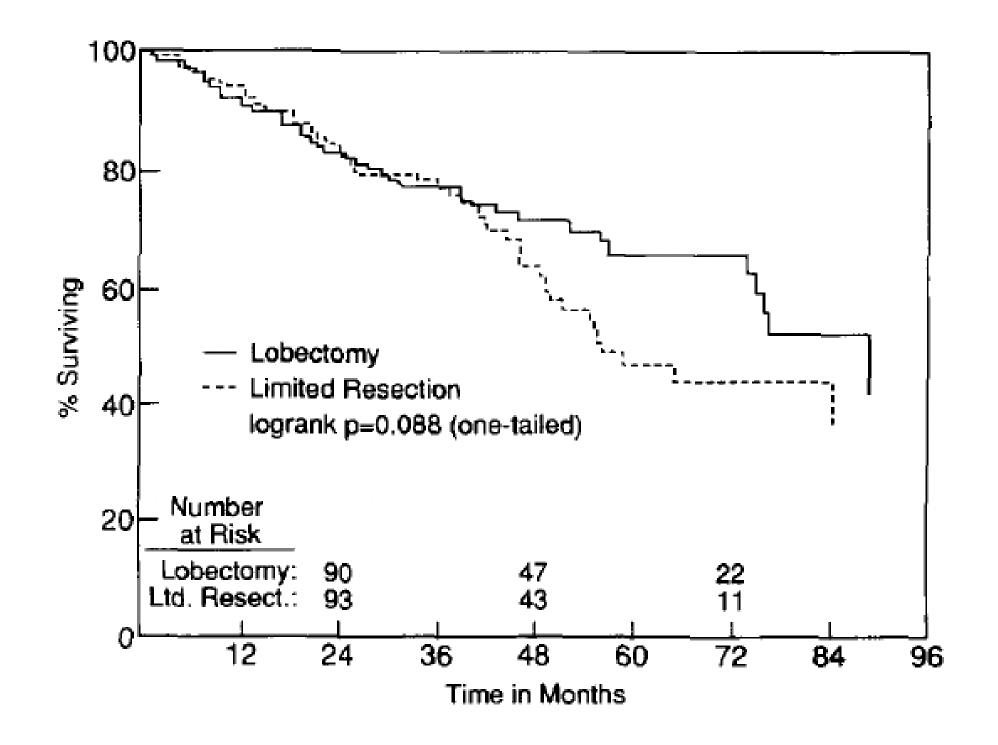


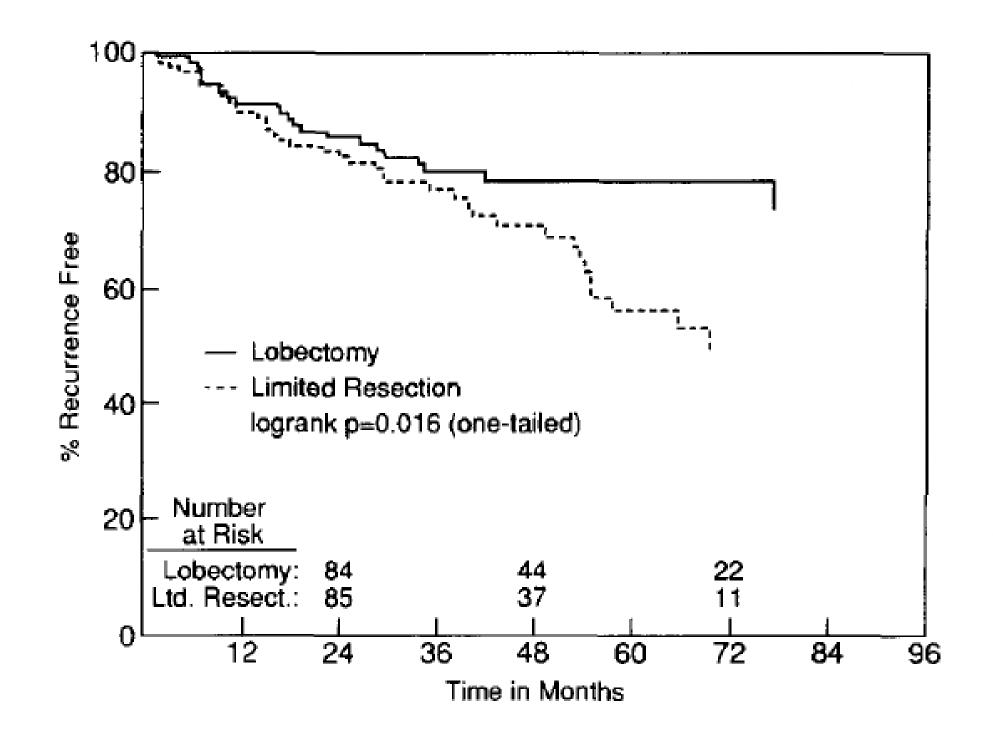




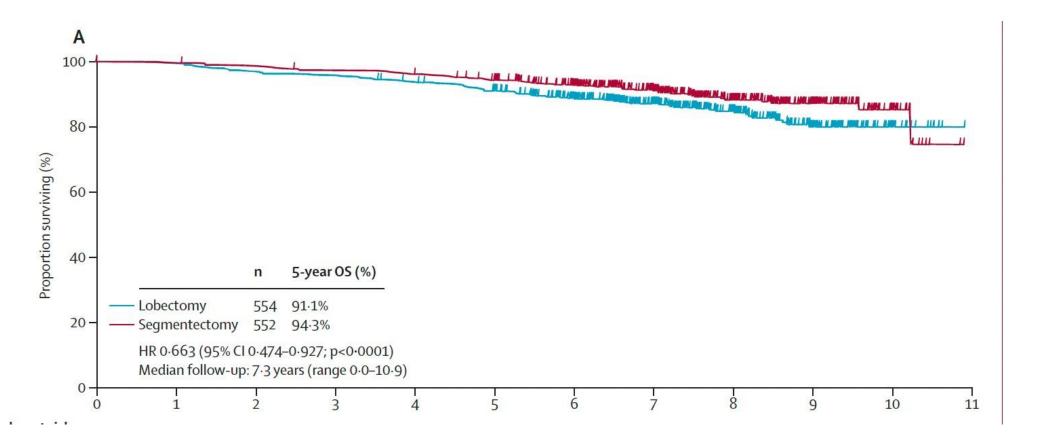
Randomized Trial of Lobectomy Versus Limited Resection for T1 N0 Non-Small Cell Lung Cancer

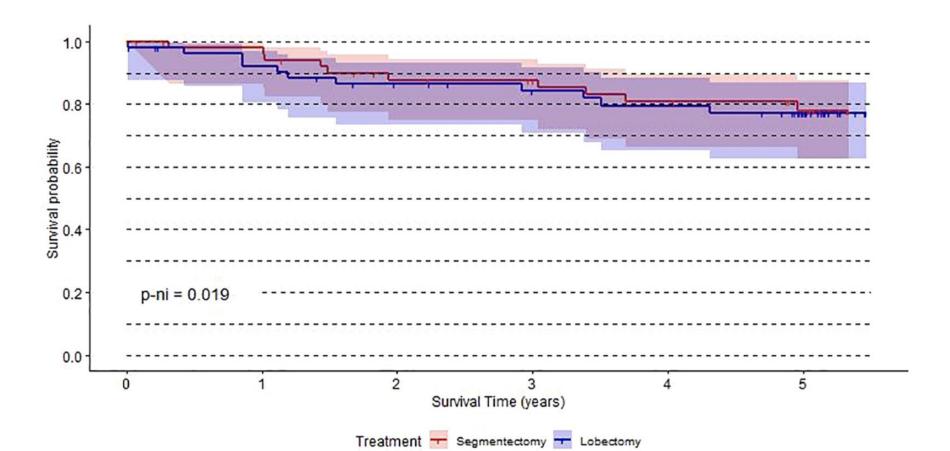
Lung Cancer Study Group (Prepared by Robert J. Ginsberg, MD, and Lawrence V. Rubinstein, PhD)



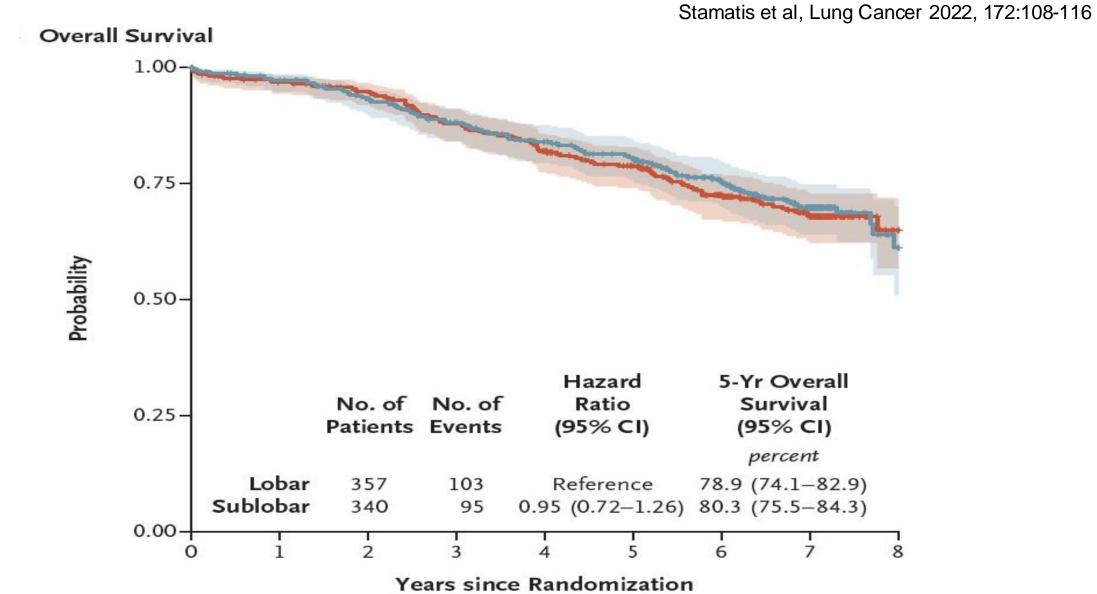






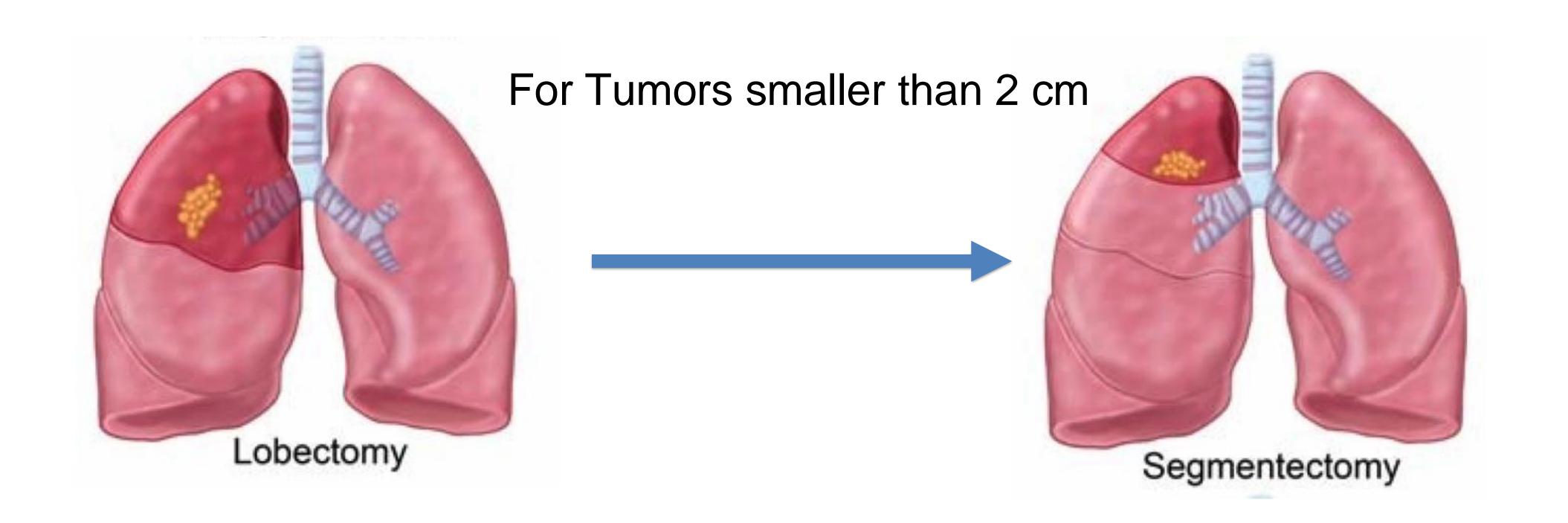


Saji et al, Lancet 2022, 399:1607-17





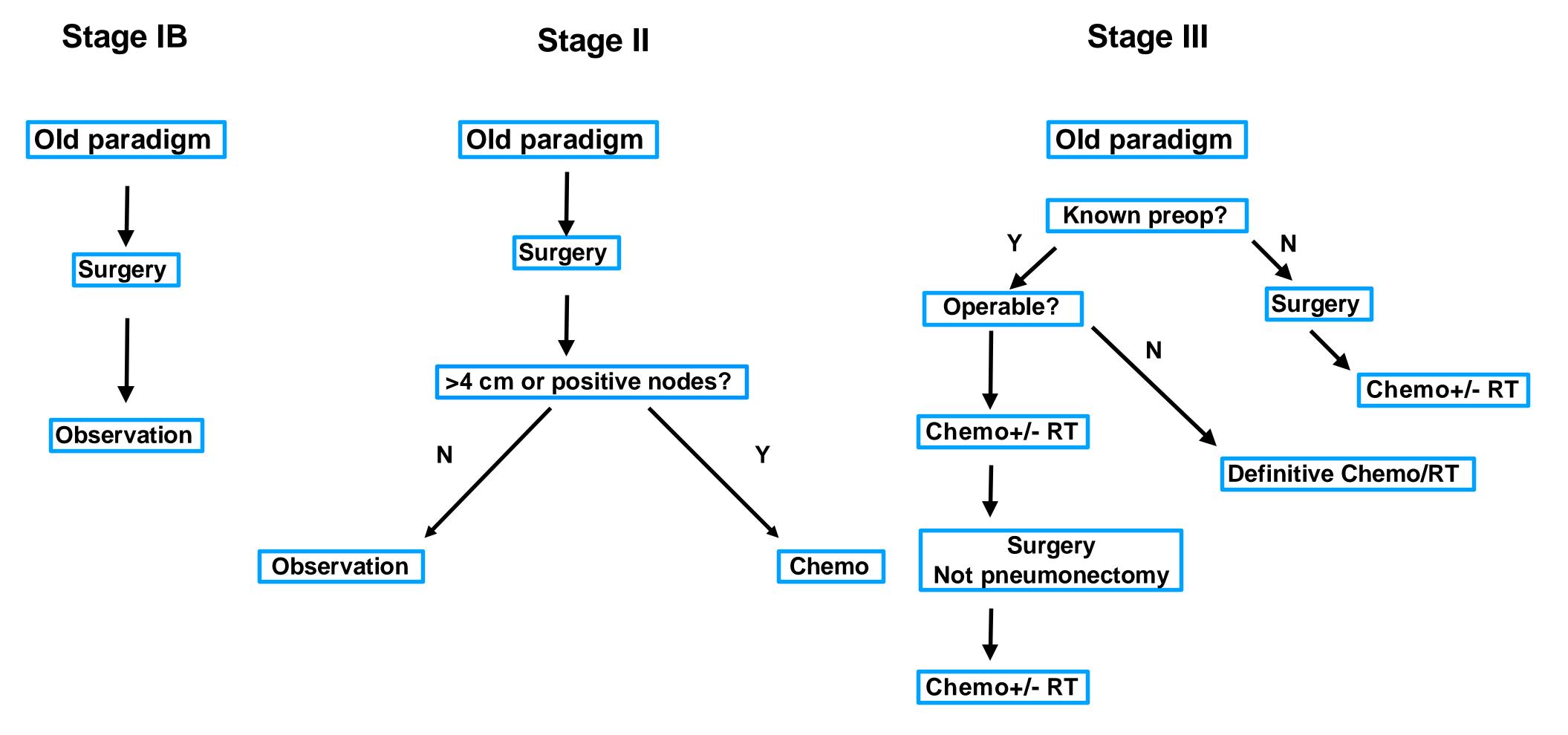
Altorki et al, NEJM 2023, 388:489-98





Stage IB-III





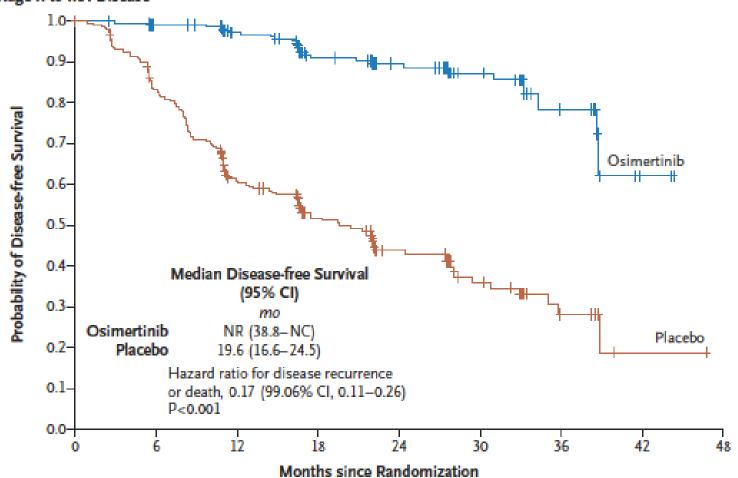


Osimertinib in Resected EGFR-Mutated Non-Small-Cell Lung Cancer

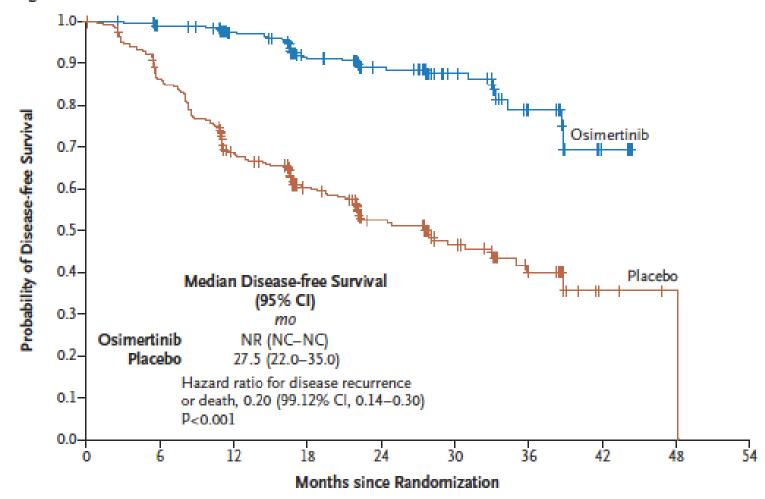
Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan 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



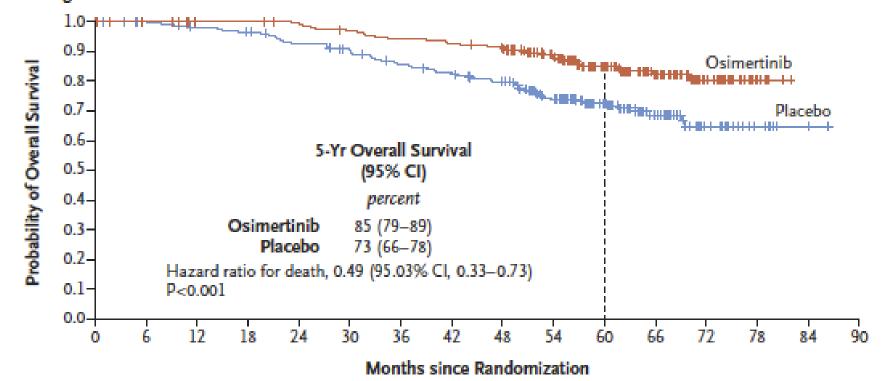


Overall Survival with Osimertinib in Resected EGFR-Mutated NSCLC

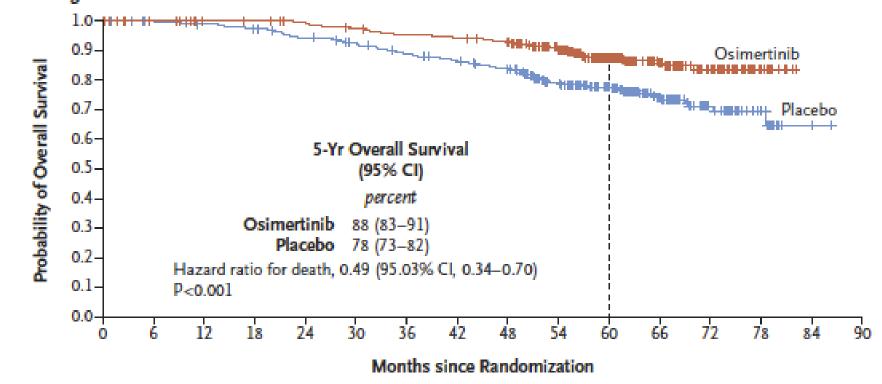
Masahiro Tsuboi, M.D., Roy S. Herbst, M.D., Ph.D.,
Thomas John, M.B., B.S., Ph.D., Terufumi Kato, M.D.,
Margarita Majem, M.D., Ph.D., Christian Grohé, M.D., Jie Wang, M.D., Ph.D.,
Jonathan W. Goldman, M.D., Shun Lu, M.D., Wu-Chou Su, M.D.,
Filippo de Marinis, M.D., Frances A. Shepherd, M.D., Ki Hyeong 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

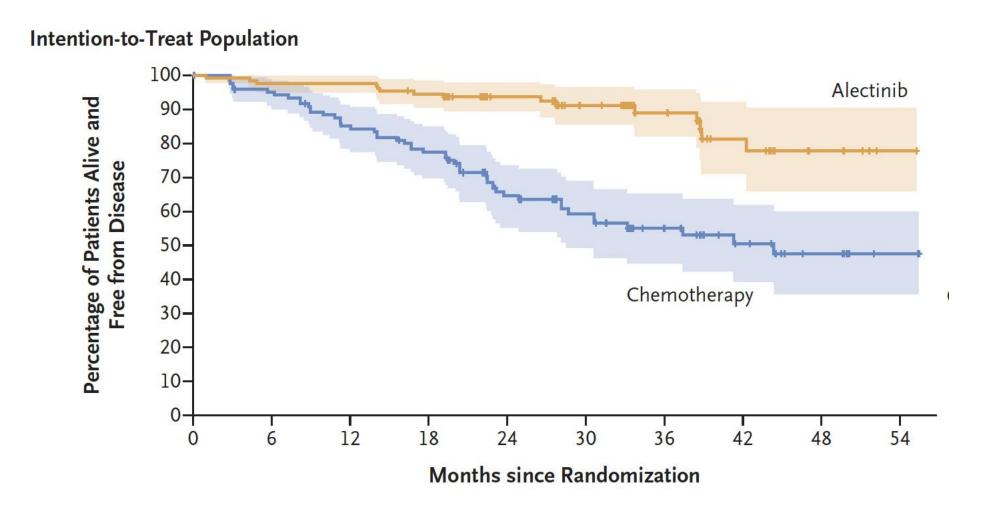


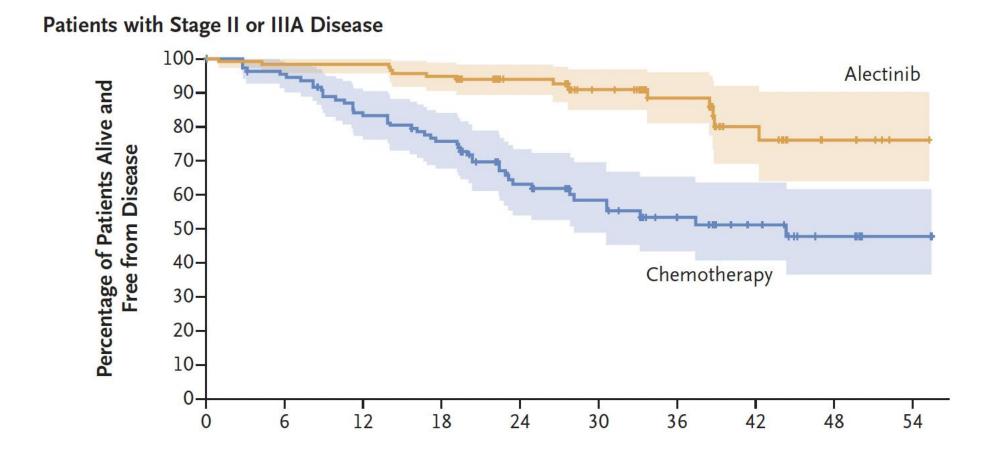


Alectinib in Resected ALK-Positive Non-Small-Cell Lung Cancer

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







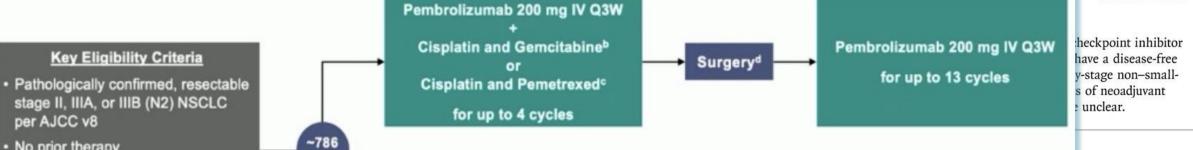


The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

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

Wakelee H et al. DOI: 10.1056/NEIMoa2302983



No prior therapy

Able to undergo surgery

Provision of tumor sample for PD-L1 evaluation^a

ECOG PS 0 or 1

Placebo IV Q3W Cisplatin and Gemcitabineb Placebo IV Q3W Surgery for up to 13 cycles Cisplatin and Pemetrexed^c

> 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

primary end rall survival.

domized, placebo-

padjuvant pembroliz-

surgical resection

improve outcomes,

otherapy and resec-

sly untreated, resect-

ge NSCLC.

prespecified first t-free survival was zumab group as rall survival did ups at the time of

> Grade ≥3 treatore often with

analysis of the and adjuvant

h limits conclu-

cisplatin-based

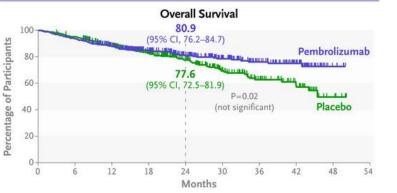
Links: Full Article | NEJM Quick Take | Editorial

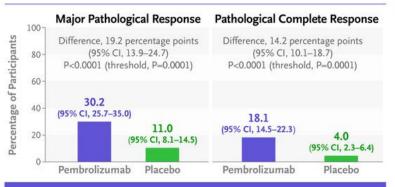
This Research Summary was updated on August 15, 2023, at NEJM.org. Copyright © 2023 Massachusetts Medical Society

Placebo (N=400)









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.

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

for up to 4 cycles

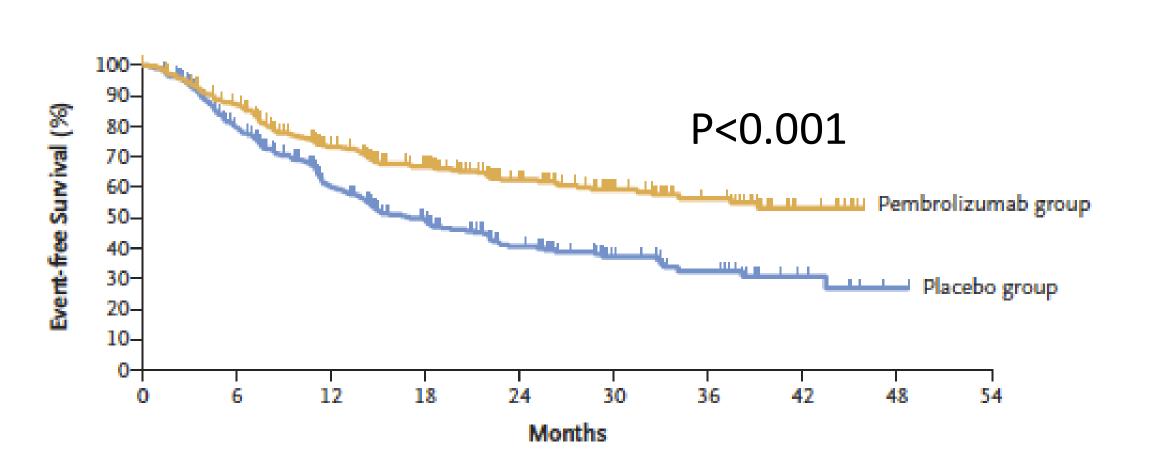
R 1:1

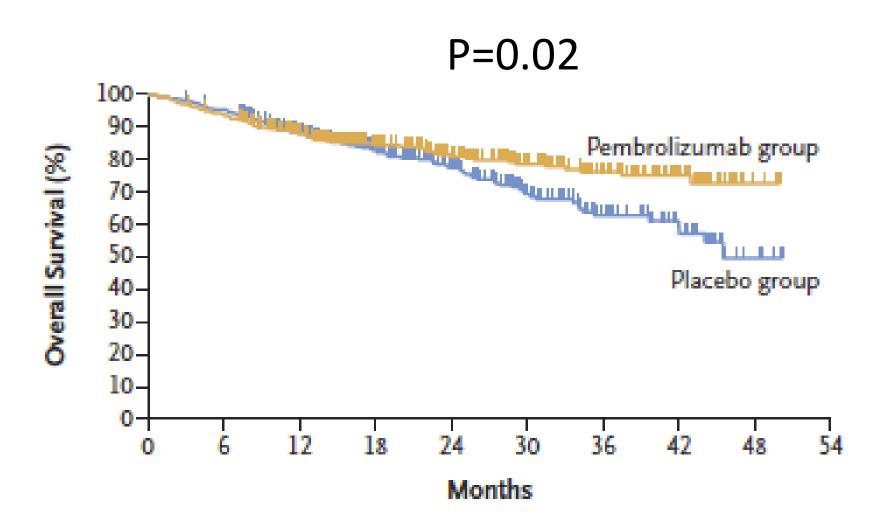
NCCN designated a class I recommendation

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





Pre specified threshold p=0.00462

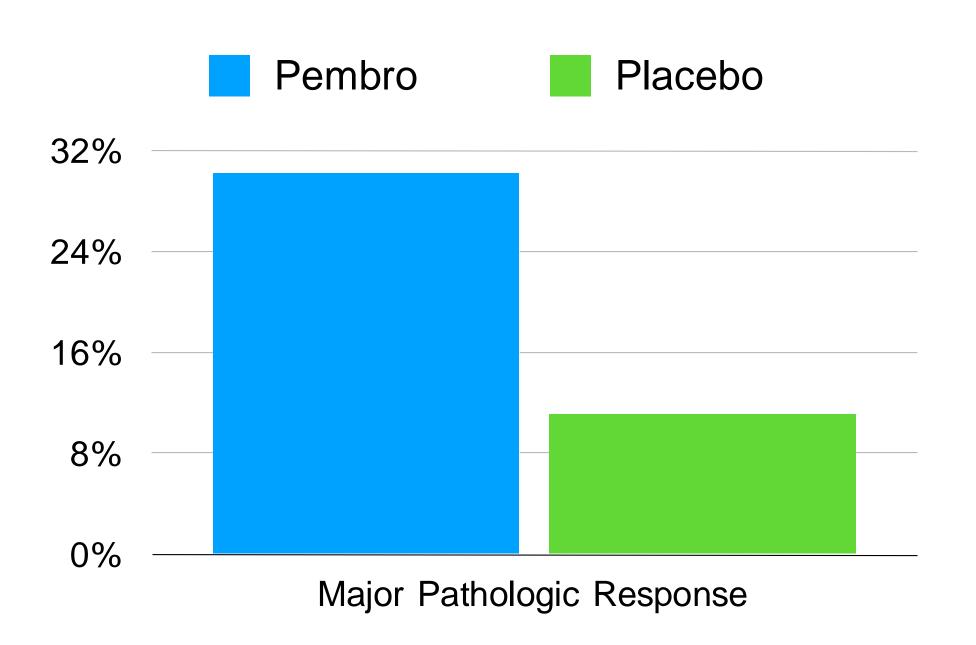
Pathological stage at baseline — no. (%)

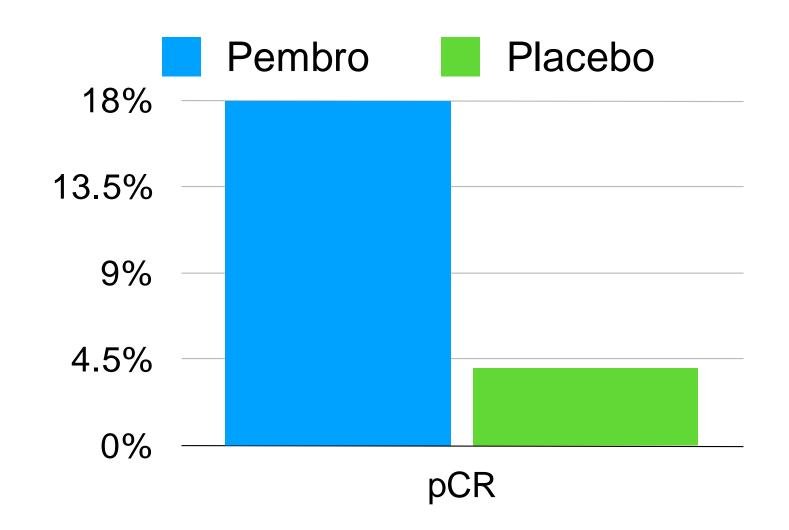
TH .	118 (29.7)	121 (30.2)
III	279 (70.3)	279 (69.8)
IIIA	217 (54.7)	225 (56.2)
IIIB	62 (15.6)	54 (13.5)



Pathologic Response

P<0.001







• Overall Survival • Median survival

- Pembro NR
- Placebo 52.4 months
- HR 0.72 (CI 0.56-0.93)
- p=0.005
- Median time from randomization 36 months
- 71% vs 64% overall 36 months survival

NSCLC, early stage

LBA56

Overall survival in the KEYNOTE-671 study of perioperative pembrolizumab for early-stage non-small-cell lung cancer (NSCLC)

J.D. Spicer¹, S. Gao², M. Liberman³, T. Kato⁴, M. Tsuboi⁵, S-H. Lee⁶, K-N. Chen⁷, C. Dooms⁸, M. Majem⁹, E. Eigendorff¹⁰, G. Martinengo¹¹, O. Bylicki¹², M.C. Garassino¹³, D. Rodriguez Abreu¹⁴, J. Chaft¹⁵, S. Novello¹⁶, J. Yang¹⁷, S.M. Keller¹⁸, A. Samkari¹⁸, H. Wakelee¹⁹

Presented at ESMO 2023

ARTICLES · Volume 404, Issue 10459, P1240-1252, September 28, 2024

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, MD <sup>a,*</sup> □ · Prof Marina C Garassino, MD <sup>b,*</sup> · Prof Heather Wakelee, MD <sup>c</sup> · Moishe Liberman, MD <sup>d</sup> · Terufumi Kato, MD <sup>e</sup> · Prof Masahiro Tsuboi, MD <sup>f</sup> · et al. Show more

Affiliations & Notes ∨ Article Info ∨ Linked Articles (1) ∨
```



Chemotherapy + Immunotherapy

Adjuvant

IMPower010

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



Keynote 091

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



Neoadjuvant

Checkmate-816

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



Sandwich

AEGEAN

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



Keynote 671

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



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

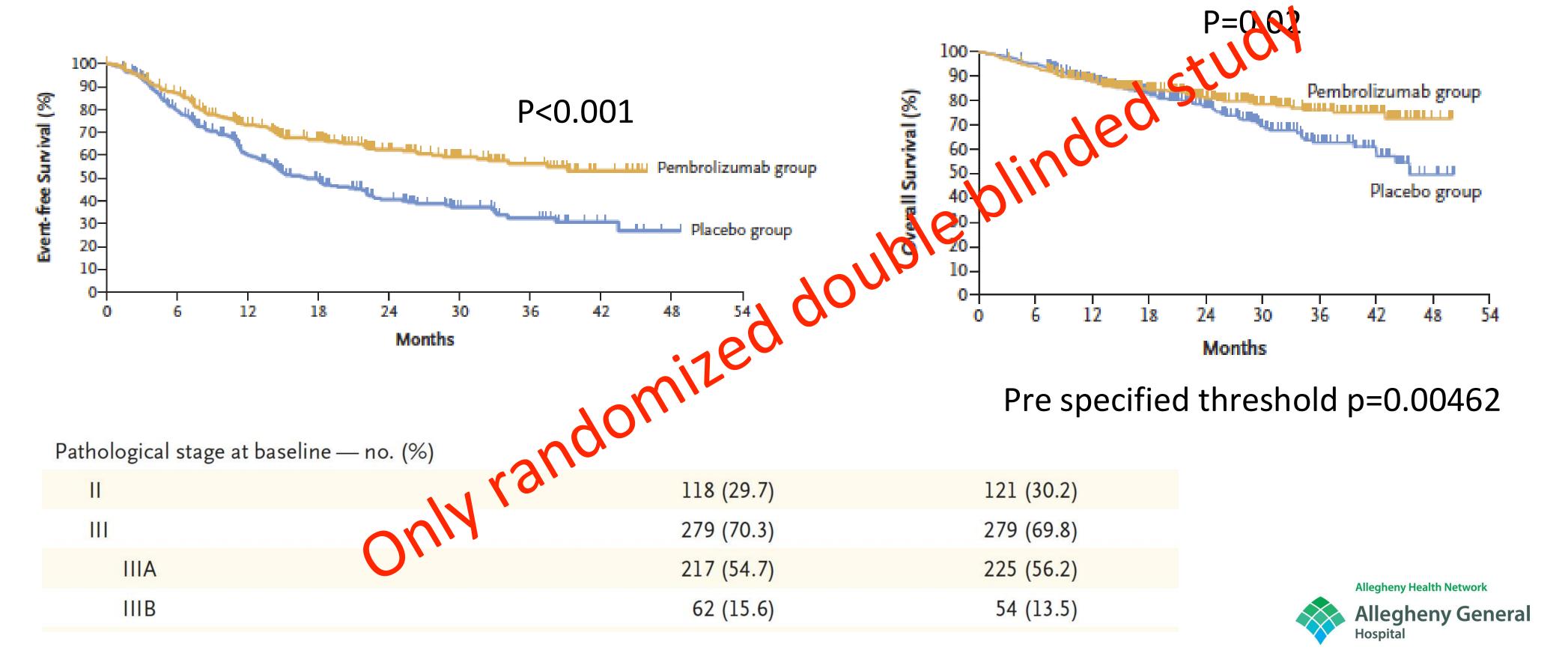
Tislelizumab 3-4c + 10M Resectable II-IIIA MPR OR:7.5



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

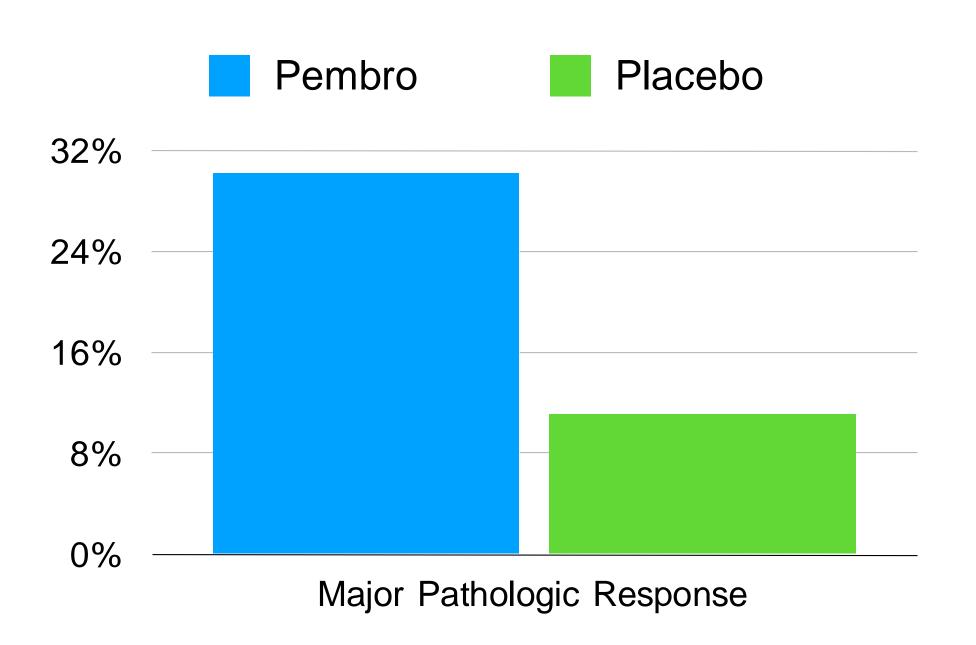
H. Wakelee, M. Liberman, T. Kato, M. Tsuboi, S.-H. Lee, S. Gao, K.-N. Chen, C. Dooms, M. Majem, E. Eigendorff, G.L. Martinengo, O. Bylicki, D. Rodríguez-Abreu, J.E. Chaft, S. Novello, J. Yang, S.M. Keller, A. Samkari, and J.D. Spicer, for the KEYNOTE-671 Investigators*

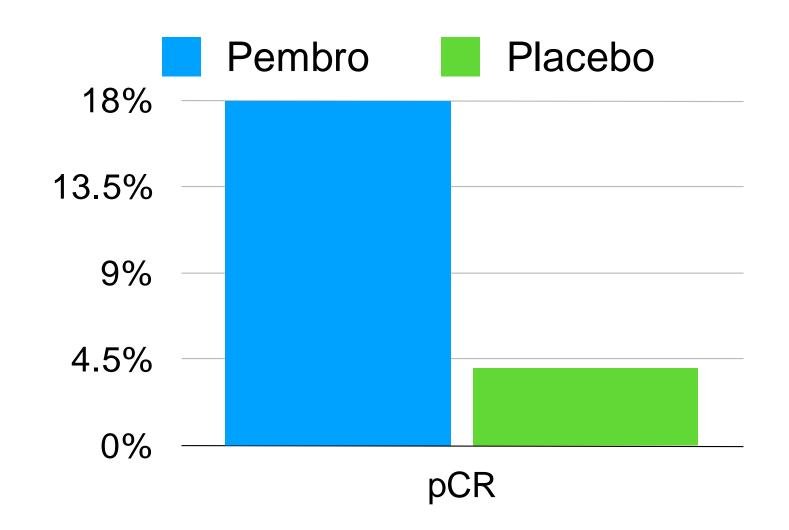
NEJM 2023



Pathologic Response

P<0.001







Emerging Therapies in Resectable NSCLC



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



Biomarker-directed therapies

Inhibit oncogenic drivers, which are present in

Does the tumor have a targetable mutation?

Atezolizumab (PD-1)

Durvalumab (PD-1)

Nivolumab (PD-L1)

Pembrolizumab (PD-L1)

Osimertinib (EGFR)
Alectinib (ALK)

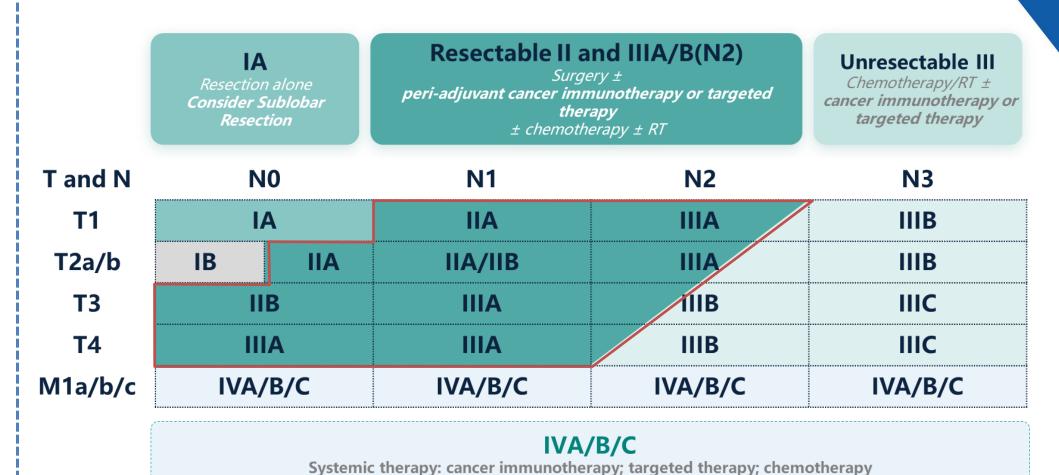


Decade of Change in NSCLC Treatment

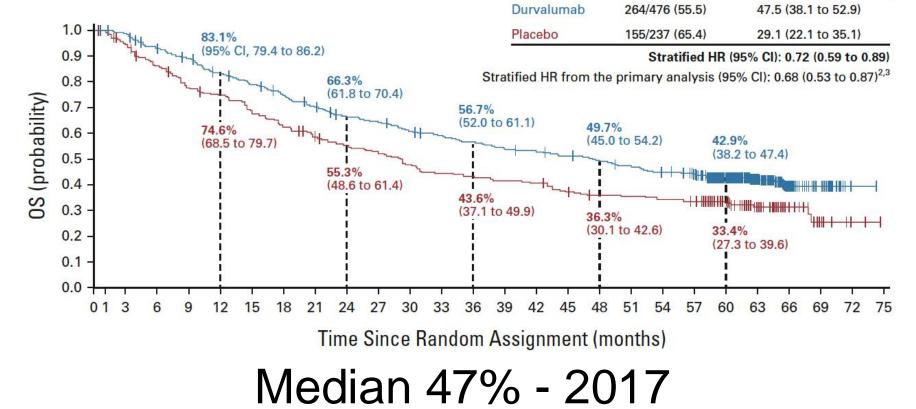
In 2015

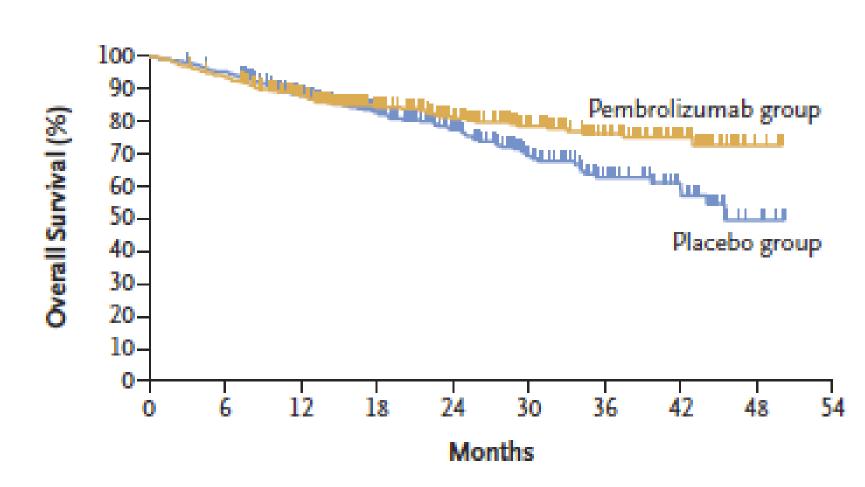
In 2024

	IA & small IB Resection alone		II and non-N2 IIIA Resection + adjuvant treatment	IIIA N2 Potential neoadjuvant treatment + resection, determined by bulk of nodal disease	IIIB/C Definitive chemotherapy/RT	
T and N	N0		N1	N2	N3	
T1	IA		IIA	IIIA	IIIB	
T2a/b	IB	IIA	IIA/IIB	IIIA	IIIB	
Т3	IIB		IIIA	IIIA	IIIC	
T4	IIIA		IIIA	IIIB	IIIC	
M1a/b/c	IVA/B/C		IVA/B/C	IVA/B/C	IVA/B/C	
	IVA/B/C Chemotherapy					









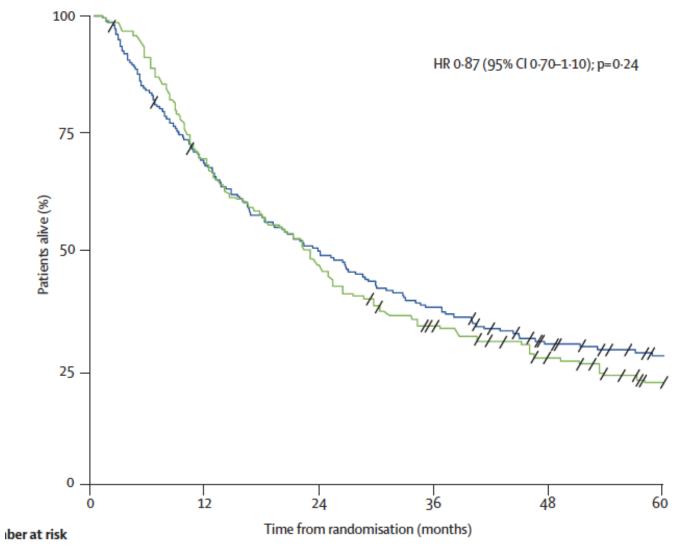
No. of Events/

Total No. of Patients (%)

Median OS

(95% CI), Months

Estimated 58 months 2024



Median 23 months - 2009





Screening

- A robust screening program is essential. Early diagnosis is key.
- 8000 screened patients a year at AHN.





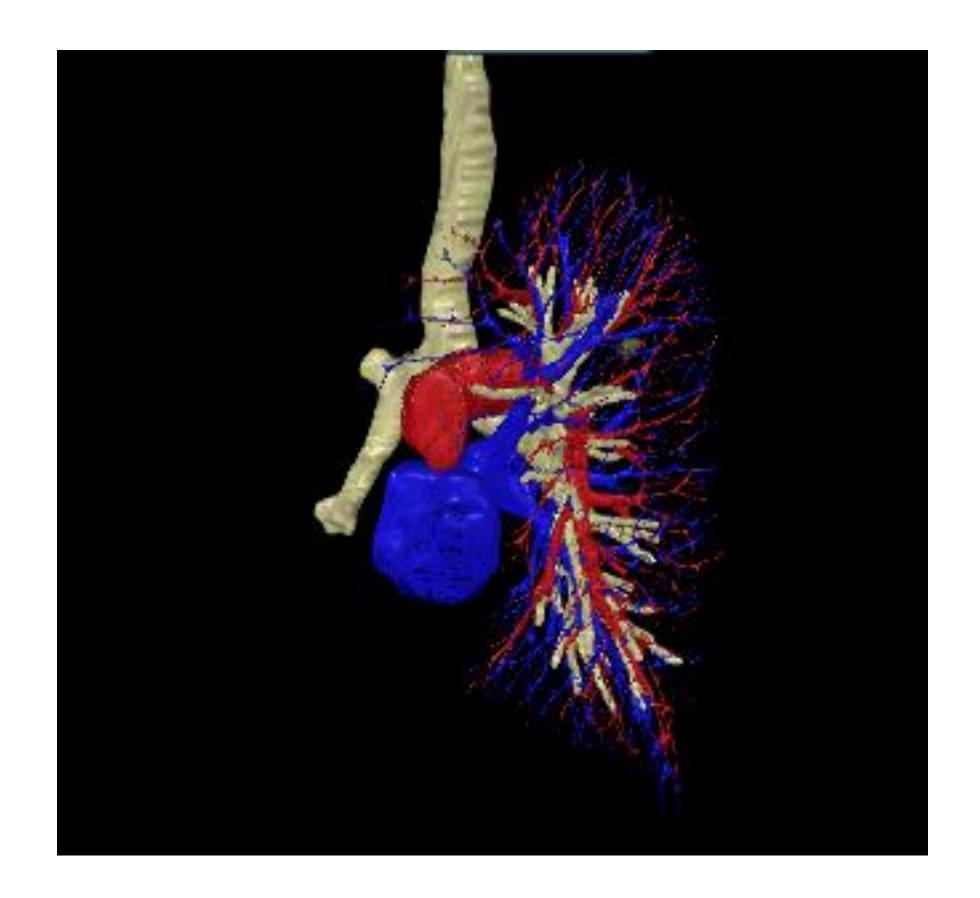


Speeding Up the Process

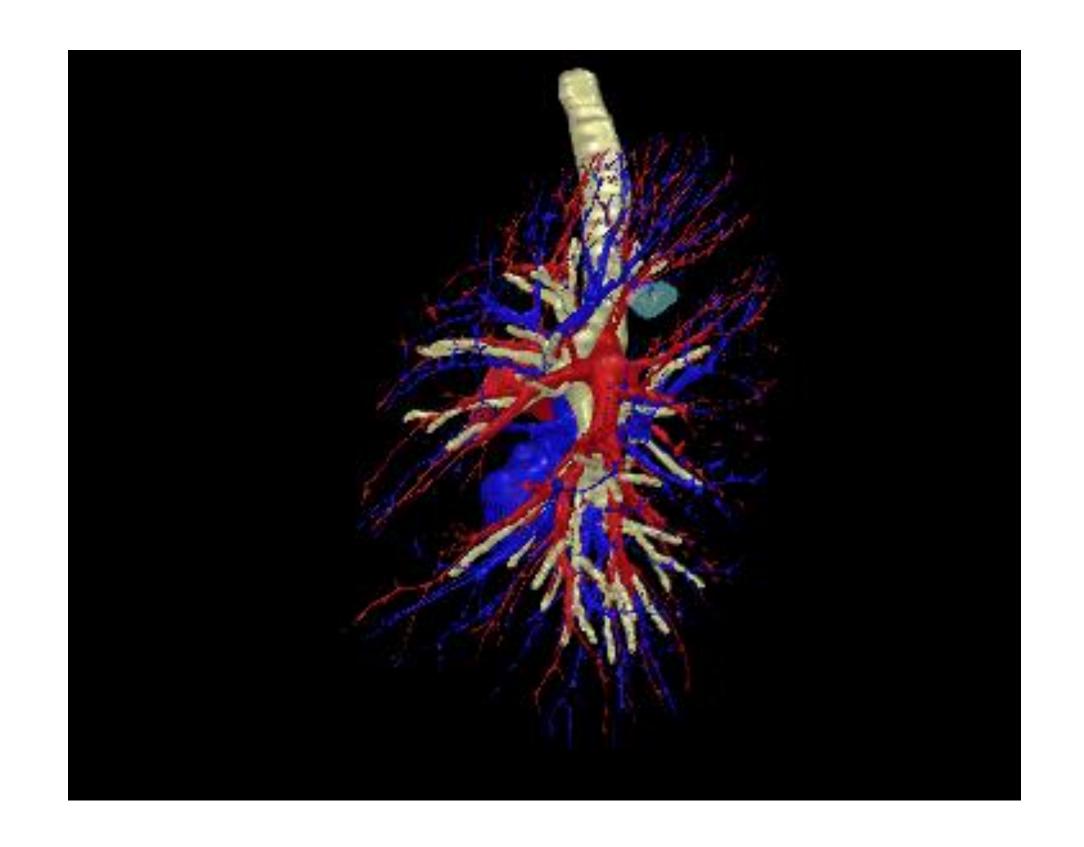
- Multidisciplinary clinics One stop shop.
 - See both IP and Surgery
 - Improve patients' satisfaction and decrease time from diagnosis to treatment
 - Reduces unnecessary surgical procedures
- Markers (PDL-1, EGFR, ALK) on all patients stage II and above
- Prospective TB and referrals for neoadjuvant/adjuvant therapy



















Summary

- Since 2017 lung cancer care has completely changed for every single stage
- Early detection, speedy treatment, minimally invasive surgery, and knowledge of targeted therapy are essential to good outcomes.



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

Nancy Gibbs









Thank You!

