HealthCare
MARKEY CANCER CENTER
Network

The Changing Care of Lung Cancer
- A Frustrating Past
- A Promising Future

Timothy Mullett, MD, MBA, FACS
Thoracic Surgeon - *Markey Cancer Center, University of Kentucky*
Commission on Cancer, Chair - *American College of Surgeons*
September 13, 2023

60-minute LIVE Webinar

All Guests on Mute

Submit Questions via Chat or Q&A

Stay Tuned for Future Webinars

Tuesday, November 7th
12:00PM

HealthCare
MARKEY CANCER CENTER
Network

WELCOME
Today's Moderator and Speaker

Michael Brooks, MD

Professor
Division of Radiology & Medicine
Radiology Vice Chair of Education
University of Kentucky, Markey Cancer

Timothy Mullett, MD, MBA, FACS

Professor
Division of Cardiothoracic Surgery and
Medical Director, University of
Kentucky, Markey Cancer Center
Network Development

HealthCare
MARKEY CANCER CENTER
Network

Learning Objectives

- Who is eligible for screening
- Management of positive findings
- Management of treatment options using a multidisciplinary care approach and the value of tumor boards
- Importance of clinical trial participation

30 Years of Walking with Patients Through the Cancer Journey

Commission on Cancer® | A QUALITY PROGRAM of the AMERICAN COLLEGE OF SURGEONS

- Role of Thoracic Surgeon in Lung Cancer
  - Detection
  - Evaluation
  - Treatment Decisions
  - Surgery
  - Follow-up

- Two Questions in patients with Lung Cancer:
  - Should I operate on you?
  - Can I operate on you?

Cancer PROGRAMS
AMERICAN COLLEGE OF SURGEONS


FT: 11 - 19
FT%: 57.9
KENTUCKY
5


Austin Nichols
WILD TURKEY
101
BUFFALO TRACE
Maker's Mark
WHISKY
FOUR ROSES
SINGLE BARREL
OLD HEAVEN HILL
10
JIM BEAM
BLACK
WOODFORD RESERVE

Lung Cancer Burden At a Glance

Nearly

1 in 4[1]

of all Cancer Deaths are From Lung Cancer

Only

16%[2]

of Lung Cancer Cases are Diagnosed in an Early Stage

*

[1] **American Cancer Society.** Cancer Facts and Figures. *Cancer.org.* [Online] 2019. https://www.cancer.org/latest-news/facts-and-figures-2019.html

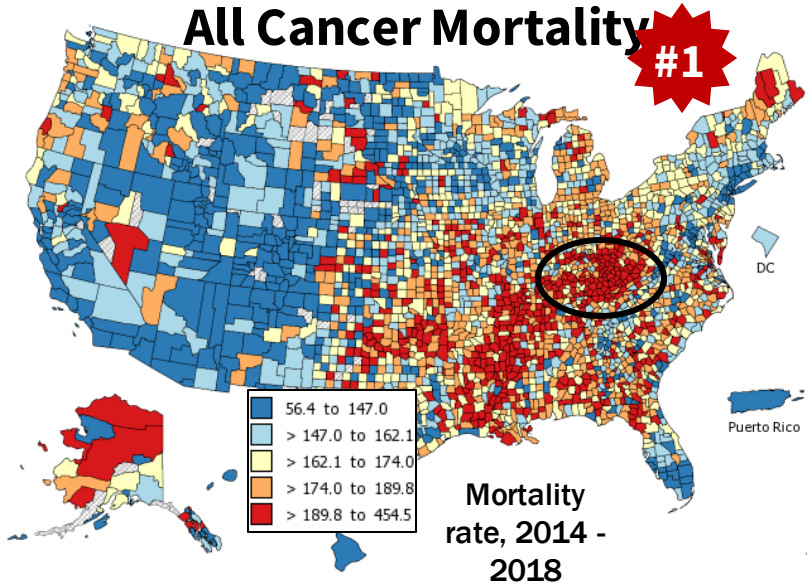
[2] **US National Institute of Health, National Cancer Institute.** *SEER Cancer Statistics Review, 1975-2015.*

HealthCare
MARKEY CANCER CENTER
Network

Kentucky's Cancer Burden

All Cancer Mortality

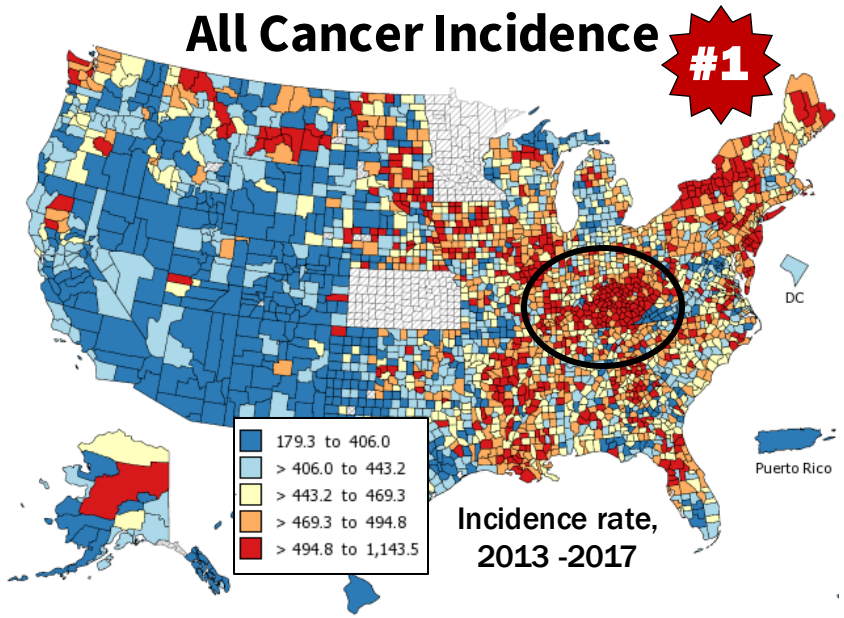
#1



Mortality rate, 2014 - 2018

All Cancer Incidence

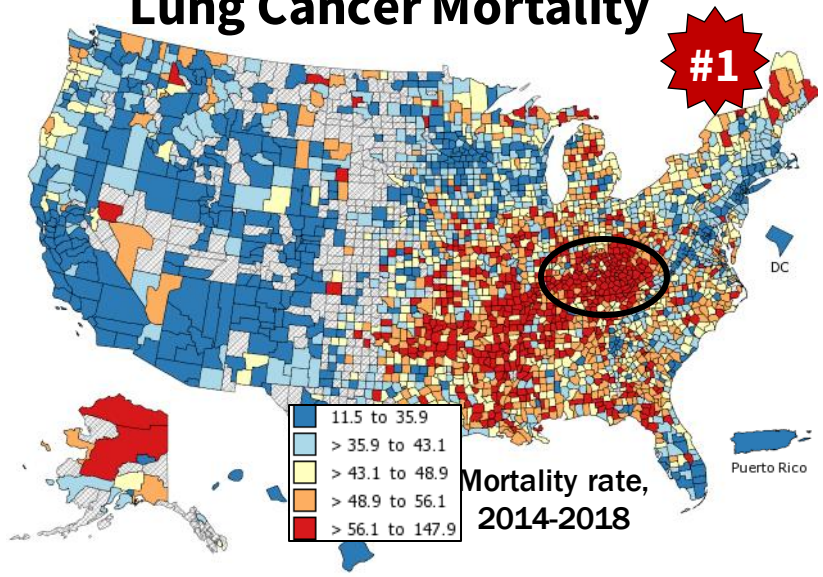
#1



Incidence rate, 2013 -2017

Lung Cancer Mortality

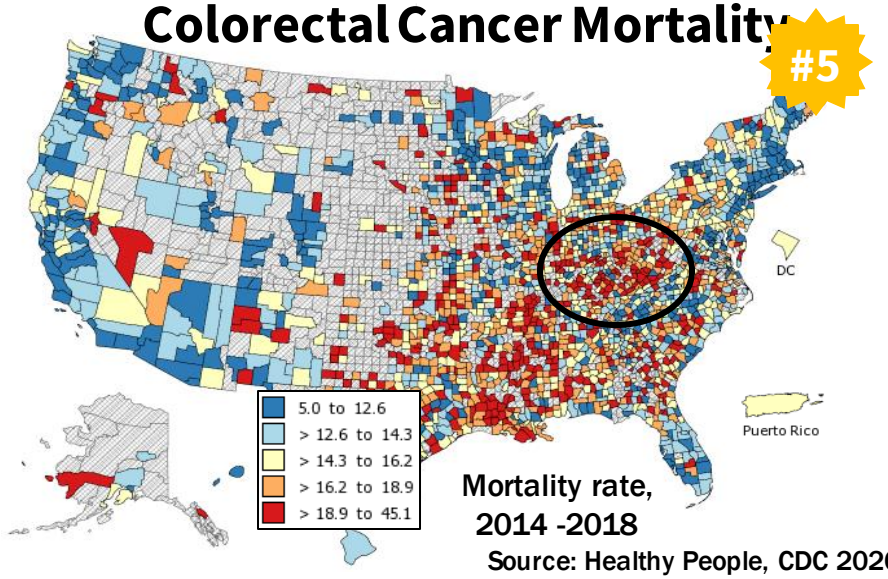
#1



Mortality rate, 2014-2018

Colorectal Cancer Mortality

#5

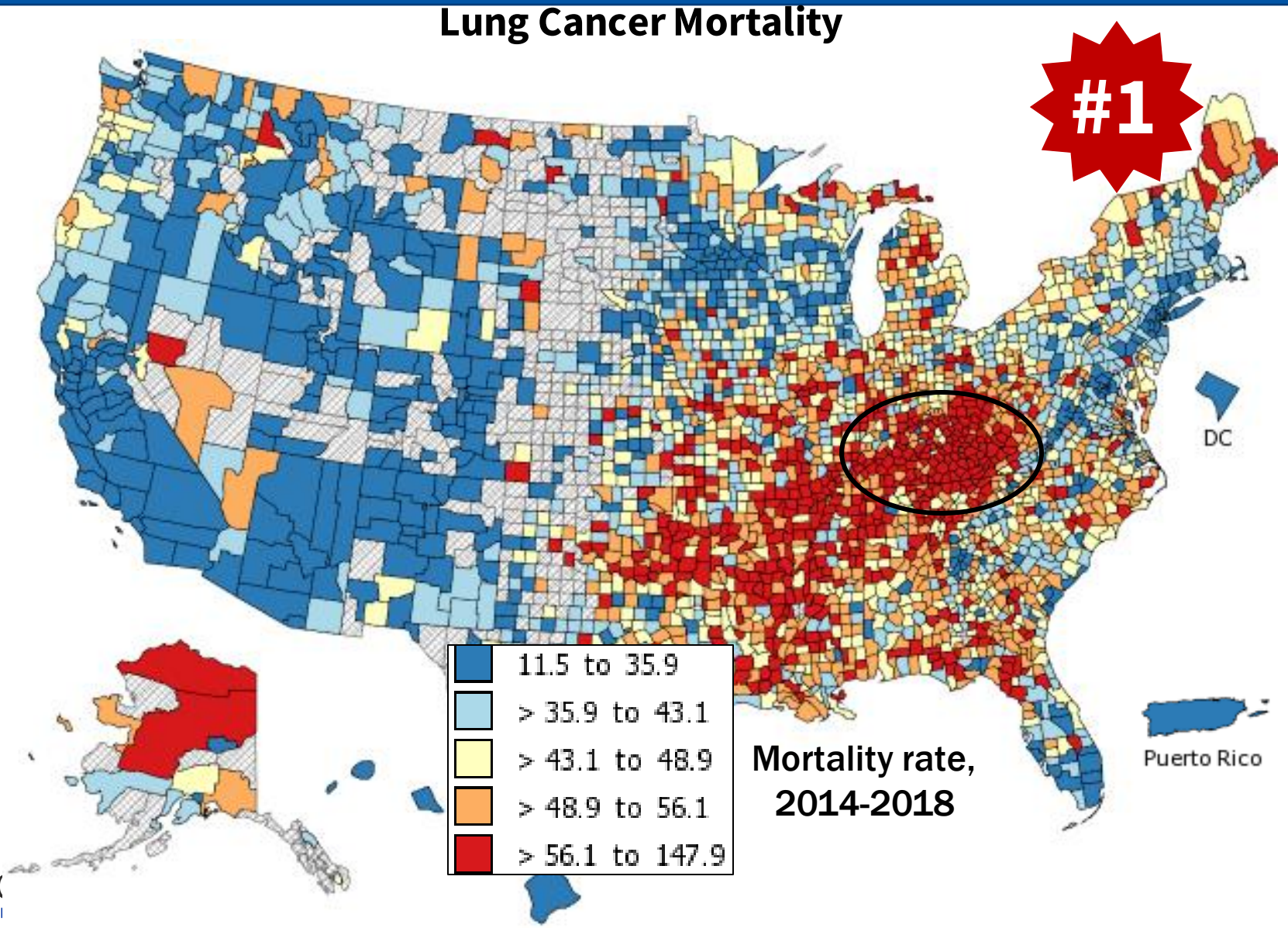


Mortality rate, 2014 -2018

Source: Healthy People, CDC 2020

HealthCare
MARKEY CANCER CENTER
Network

Kentucky's Cancer Burden

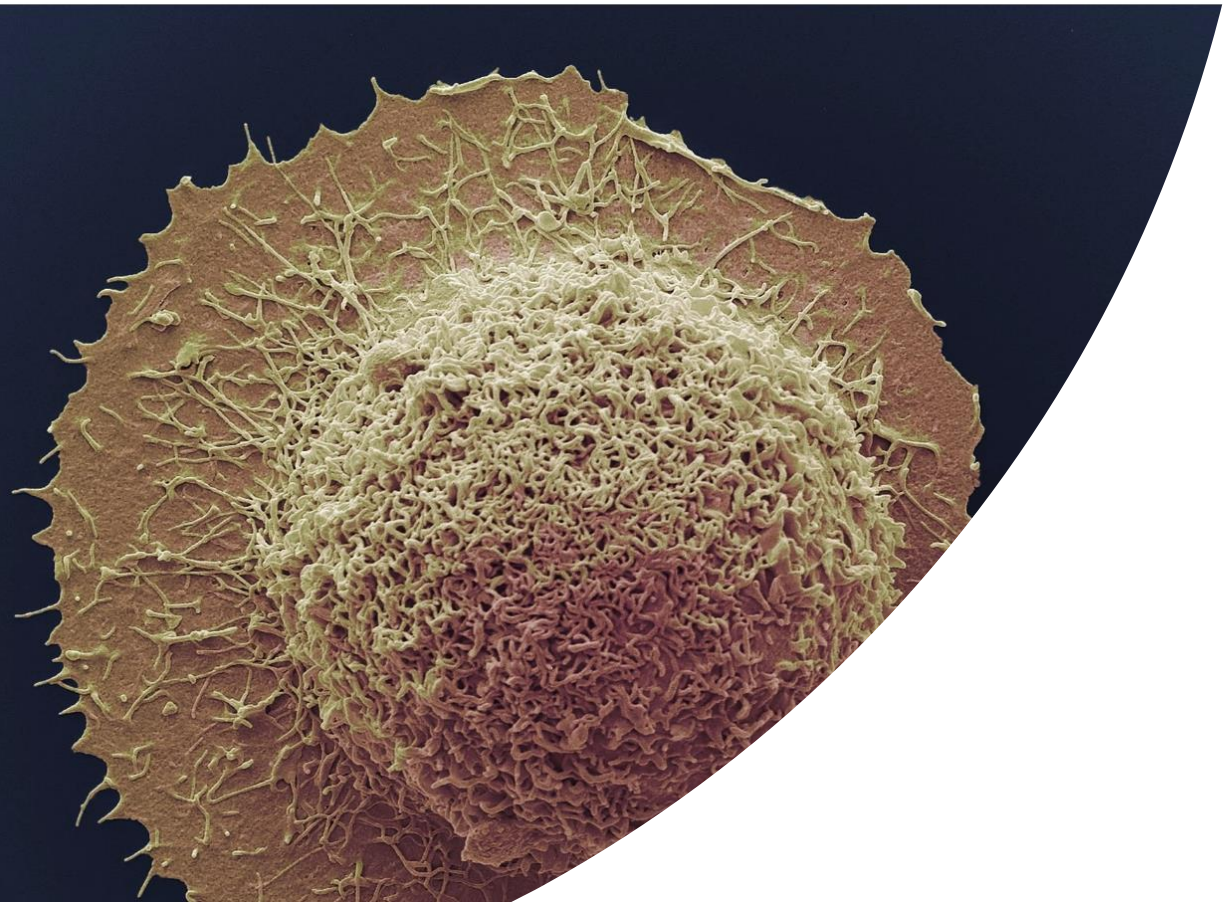


Health
MARKEY CANCER
Network

The New York Times

Cancer Death Rate in U.S. Sees Sharpest One-Year Drop

Breakthrough treatments for lung cancer and melanoma have driven down cancer mortality overall — and from 2016 to 2017 spurred the largest-ever decline.



Cancer Mortality is Decreasing

Lung Cancer as a Driving Force

Science News *from research organizations*

Cancer mortality continues steady decline, driven by progress against lung cancer

Drop of 2.2 percent from 2016 to 2017 is largest ever reported

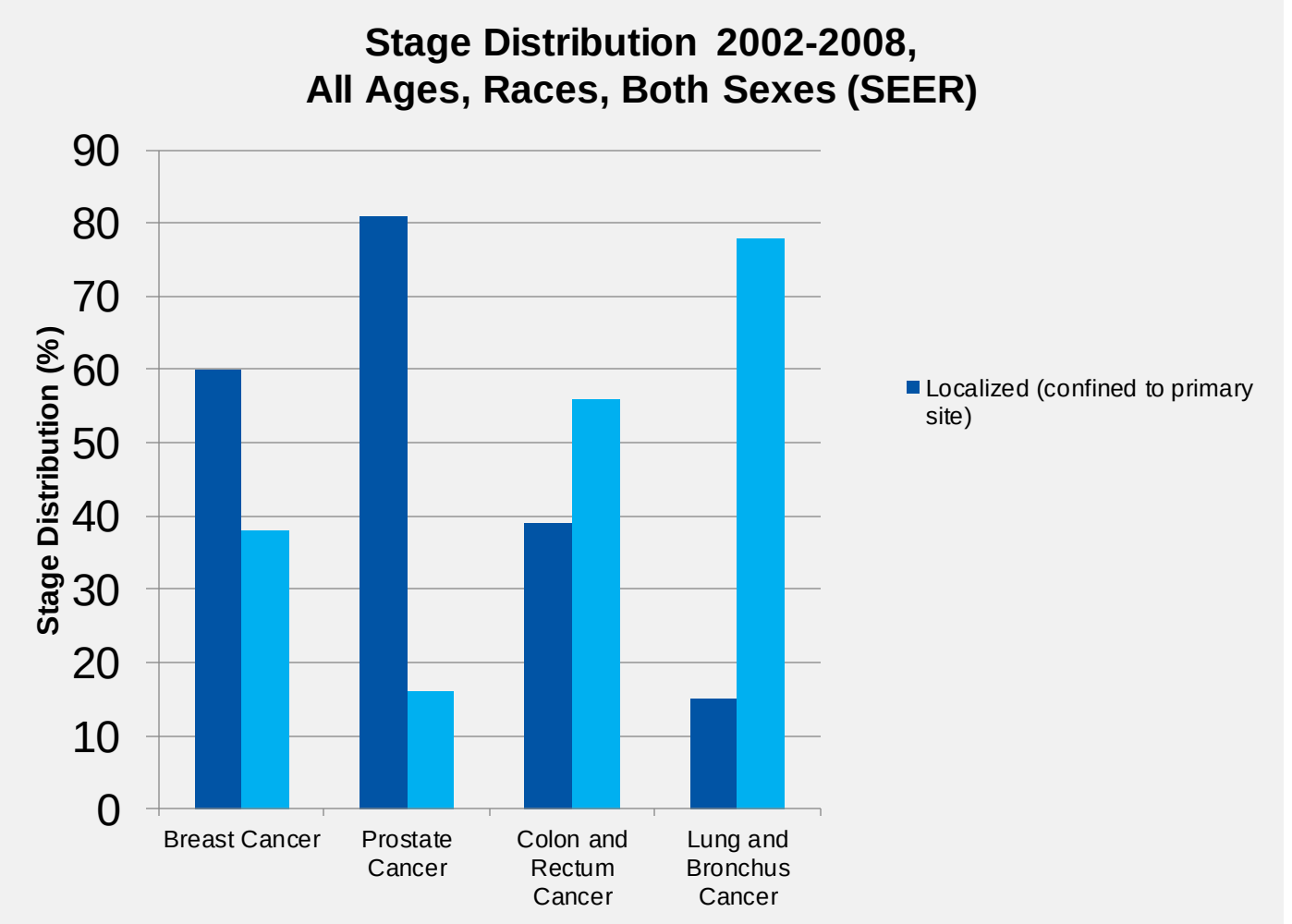
Date: January 8, 2020

Source: American Cancer Society

Summary: The cancer death rate declined by 29 percent from 1991 to 2017, including a 2.2 percent drop from 2016 to 2017, the largest single-year drop in cancer mortality ever reported, according to the American Cancer Society's annual report on cancer rates and trends.

- **Lung cancer death rates declined 48% among men and 23% among women.**
- **From 2011 to 2015, the rates of new lung cancer cases dropped by 3% per year in men and 1.5% per year in women.**

More than 75% of lung cancers are diagnosed in advanced stages.



HealthCare
MARKEY CANCER CENTER
Network

Lung Cancer Screening

- Currently screening eligibility is based on two blunt instruments:
  - Age
  - Smoking History
- Improvements may be seen when molecular targets are identified as risk factors
- Better able to predict which patients should be screened and when
- May predict who will respond better to treatment, etc.

Strongest Data that Lung Cancer Screening Works

- National Lung Screening Trial (US - 2011)
  - 54,000 participants
  - 20% reduction in mortality
- NELSON Trial (Netherlands-Belgium - 2019)
  - 15,500 subjects - 24% Reduction Men
  - 10-year follow-up - 33% Reductino Women
- MILD Trial (Italy - 2019)
  - 40% reduction in mortality
  - Nearly 60% mortality reduction at 10 years

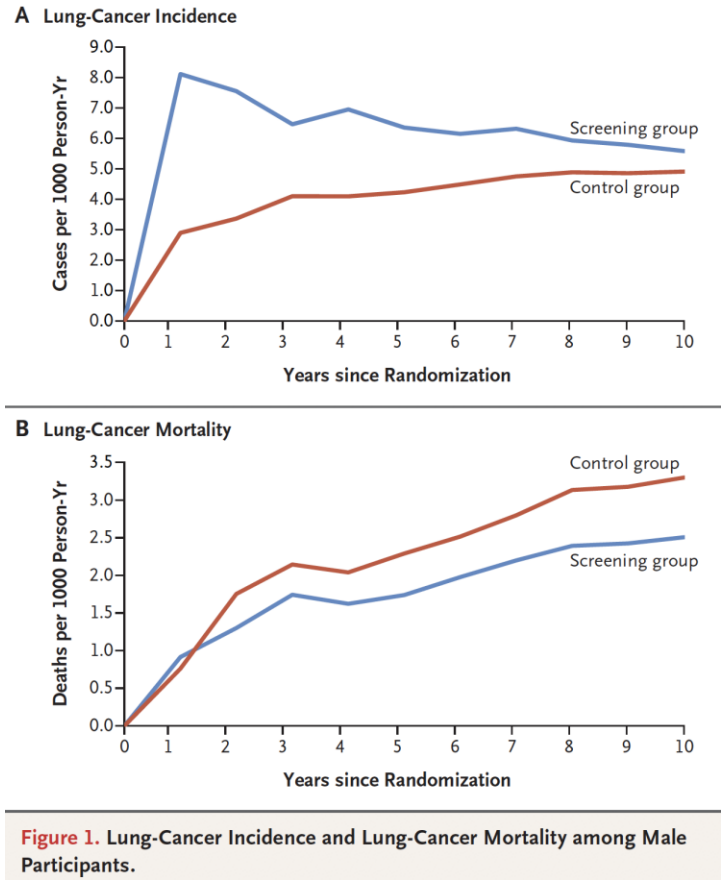


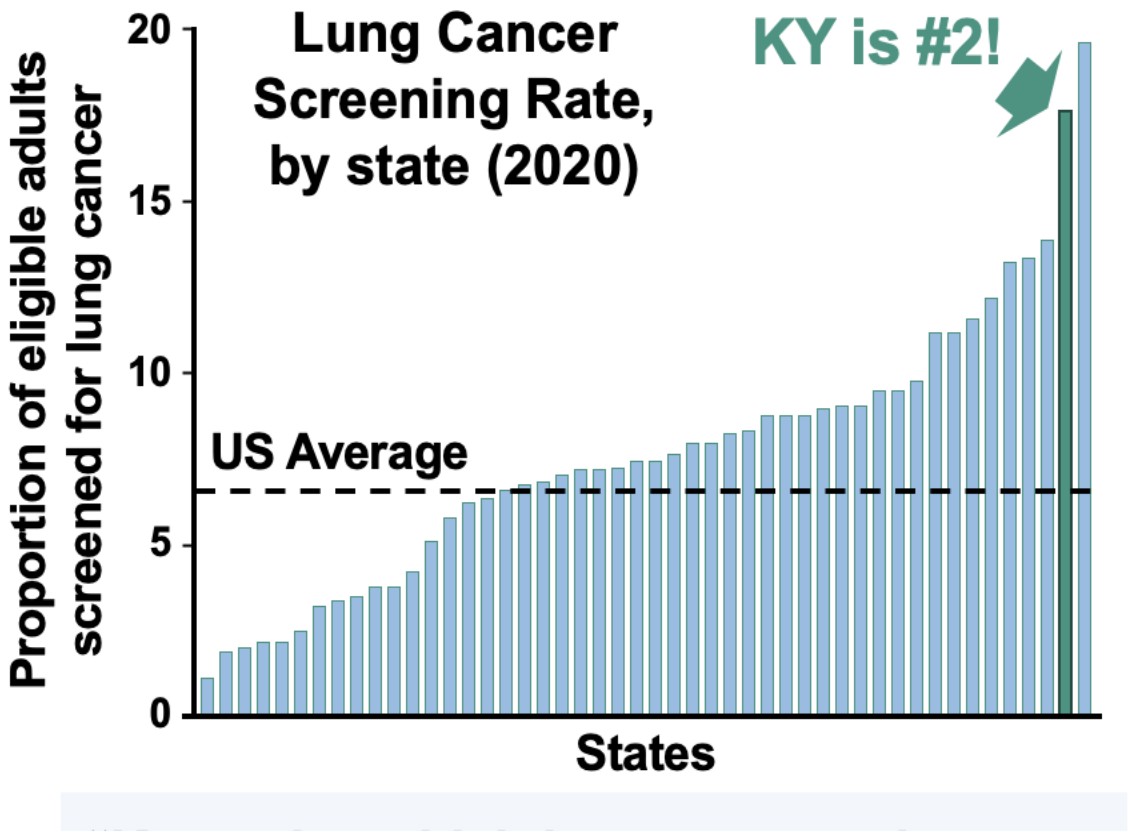
Figure 1. Lung-Cancer Incidence and Lung-Cancer Mortality among Male Participants.

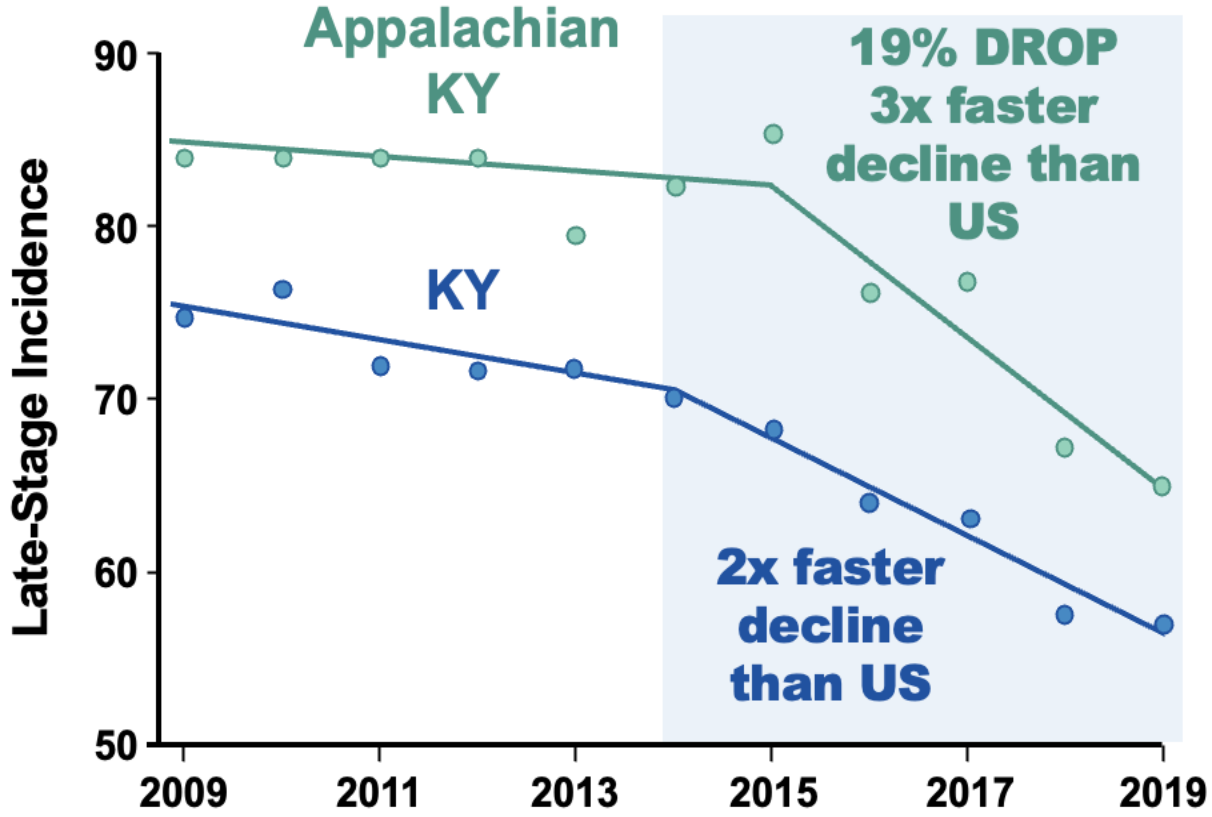
Nelson Data

HealthCare
MARKEY CANCER CENTER
Network

Lung Cancer Screening

- Complex Process
- Primary Care Providers identify patients
  - National average was approximately 5% of eligible patients….prior to COVID
  - Must identify patients 50-85 years old
  - 20 Pack-Year Tobacco Exposure (many interpretations of this number)
- Facilities that perform the technical aspects of scan
- Retention is a challenge
  - National average is less than 30%
- New standard of care
  - Fragile
  - Most impacted by impact of pandemic, slow to recover





HealthCare
MARKEY CANCER CENTER
Network

Deciding What is Suspicious

Table 2 Lung-RADS Classification System[14,15]

Category Descriptor	Lung-RADS Score	Findings	Management	Risk of Malignancy	Est. Population Prevalence
Incomplete	**0**	Prior chest CT examination(s) being located for comparison Part or all of lungs cannot be evaluated	Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed	n/a	1%
Negative No nodules and definitely benign nodules	**1**	No lung nodules Nodule(s) with specific calcifications: complete, central, popcorn, concentric rings and fat containing nodules	Continue annual screening with LDCT in 12 months	< 1%	90%
Benign Appearance or Behavior Nodules with a very low likelihood of becoming a clinically active cancer due to size or lack of growth	**2**	**Perifissural nodule(s)** *(See Footnote 11)* < 10 mm (524 mm^3) **Solid nodule(s):** < 6 mm (< 113 mm^3) new < 4 mm (< 34 mm^3) **Part solid nodule(s):** < 6 mm total diameter (< 113 mm^3) on baseline screening **Non solid nodule(s) (GGN):** <30 mm (<14137 mm^3) **OR** ≥ 30 mm (≥ 14137 mm^3) and unchanged or slowly growing **Category 3 or 4 nodules unchanged for ≥ 3 months**			
Probably Benign Probably benign finding(s) - short term follow up suggested; includes nodules with a low likelihood of becoming a clinically active cancer	**3**	**Solid nodule(s):** ≥ 6 to < 8 mm (≥ 113 to < 268 mm^3) at baseline **OR** new 4 mm to < 6 mm (34 to < 113 mm^3) **Part solid nodule(s)** ≥ 6 mm total diameter (≥ 113 mm^3) with solid component < 6 mm (< 113 mm^3) **OR** new < 6 mm total diameter (< 113 mm^3) **Non solid nodule(s)** (GGN) ≥ 30 mm (≥ 14137 mm^3) on baseline CT or new	6 month LDCT	1-2%	5%

HealthCare
MARKEY CANCER CENTER
Network

Deciding What is Suspicious

Suspicious Findings for which additional diagnostic testing is recommended	**4A**	**Solid nodule(s):** ≥ 8 to < 15 mm (≥ 268 to < 1767 mm^3) at baseline **OR** growing < 8 mm (< 268 mm^3) **OR** new 6 to < 8 mm (113 to < 268 mm^3)	3 month LDCT; PET/CT may be used when there is a ≥ 8 mm (≥ 268 mm^3) solid component	5-15%	2%
		Part solid nodule(s): ≥ 6 mm (≥ 113 mm^3) with solid component ≥ 6 mm to < 8 mm (≥ 113 to < 268 mm^3) **OR** with a new or growing < 4 mm (< 34 mm^3) solid component			
		Endobronchial nodule			
Very Suspicious Findings for which additional diagnostic testing and/or tissue sampling is recommended	**4B**	**Solid nodule(s)** ≥ 15 mm (≥ 1767 mm^3) **OR** new or growing, and ≥ 8 mm (≥ 268 mm^3)	Chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a ≥ 8 mm (≥ 268 mm^3) solid component. *For new large nodules that develop on an annual repeat screening CT, a 1 month LDCT may be recommended to address potentially infectious or inflammatory conditions*	> 15%	2%
		Part solid nodule(s) with: a solid component ≥ 8 mm (≥ 268 mm^3) **OR** a new or growing ≥ 4 mm (≥ 34 mm^3) solid component			
	4X	Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy			
Other Clinically Significant or Potentially Clinically Significant Findings (non lung cancer)	**S**	**Modifier - may add on to category 0-4 coding**	As appropriate to the specific finding	n/a	10%

Adapted from American College of Radiology. Lung CT Screening Reporting & Data System.[14†]
CT, computed tomography; LDCT, low-dose computed tomography; Lung-RADS, Lung Imaging Reporting and Data System; PET, positron emission tomography.
Negative screen does not mean that an individual does not have lung cancer. Once a patient is diagnosed with lung cancer, further management (including additional imaging such as PET/CT) may be performed for purposes of lung cancer staging; this is no longer screening. A negative screen is defined as categories 1 and 2; a positive screen is defined as categories 3 and 4. Category 3 and 4A nodules that are unchanged on interval CT should be coded as category 2, and individuals returned to screening in 12 months.
*Additional resources available at www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-RADS.
†Link to Lung-RADS calculator: https://brocku.ca/lung-cancer-screening-and-risk-prediction/risk-calculator.

HealthCare
MARKEY CANCER CENTER
Network

Work up of a Suspicious nodule

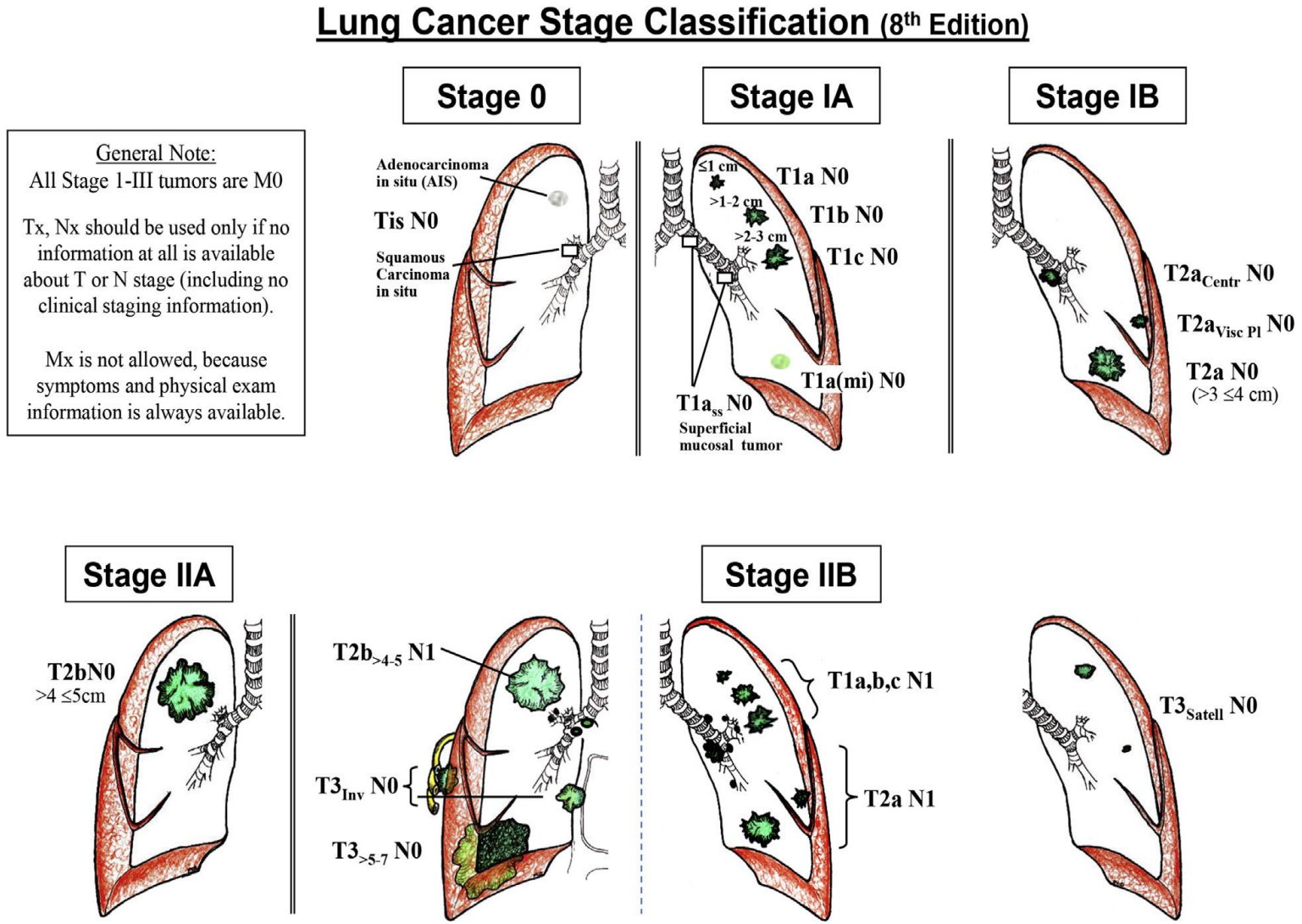
- Imaging
  - CT Thorax
  - PET CT
    - Not routinely used for the workup of nodules
    - False negatives
      - <8-10mm
      - Less metabolically active tumors (insitu, mucinous adenocarcinomas, carcinoids)
    - False positives
      - Infectious or inflammatory conditions

Should I Operate on You?

- Treatment is guided by 3 things:
  - Stage
  - Stage
  - Stage
- Stage is determined by
  - Size and Location of Tumor (T)
  - Whether tumor has spread to local/regional nodes (N)
  - Whether tumor has spread to other sites (M)

Treatment depends on Stage

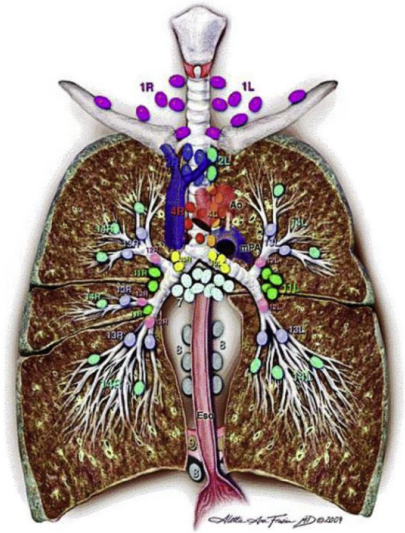
Lung Cancer Stage Classification



HealthCare
MARKEY CANCER CENTER
Network

Detterbeck. TNM 8. Chest Surg 2017

Lymph Nodes of the Chest



Supraclavicular zone
- 1 Low cervical, supraclavicular, and sternal notch nodes

SUPERIOR MEDIASTINAL NODES

Upper zone
- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3a Prevascular
- 3p Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)

AORTIC NODES

AP zone
- 5 Subaortic
- 6 Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone
- 7 Subcarinal

Lower zone
- 8 Paraesophageal (below carina)
- 9 Pulmonary ligament

N1 NODES

Hilar/Interlobar zone
- 10 Hilar
- 11 Interlobar

Peripheral zone
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

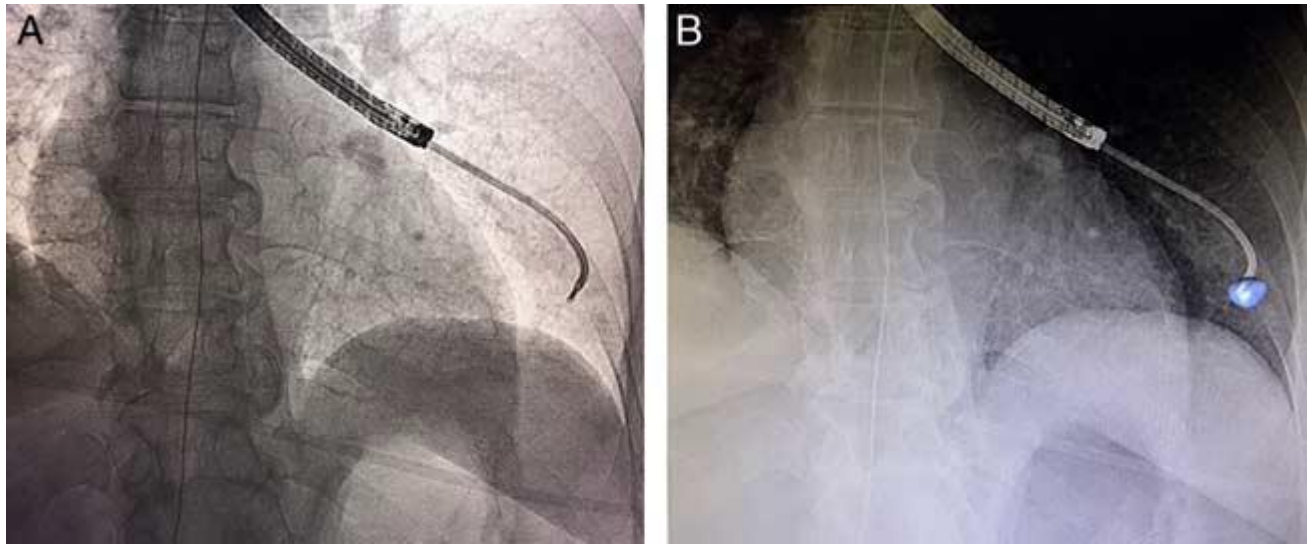
HealthCare
MARKEY CANCER CENTER
Network

Detterbeck. TNM 8. Chest Surg 2017

Biopsy

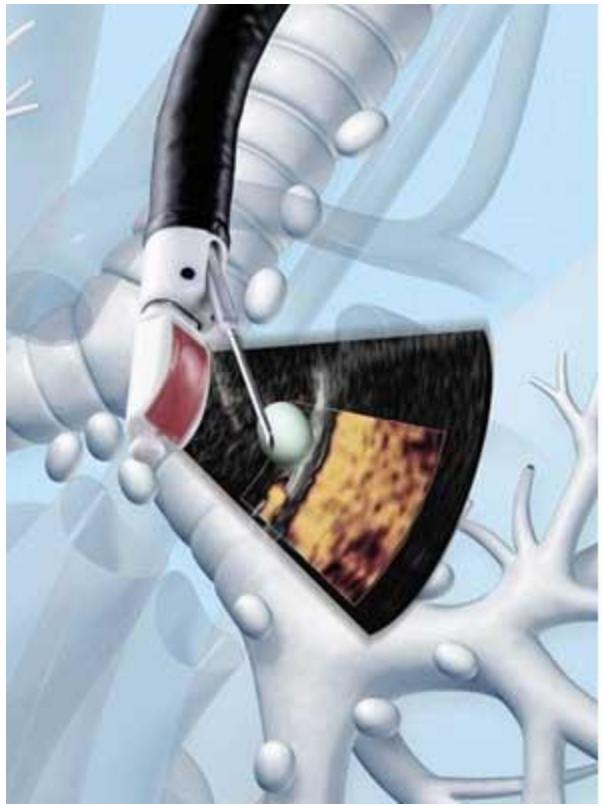
- CT guided biopsy
- Bronchoscopy
  - EBUS
  - Navigational bronchoscopy

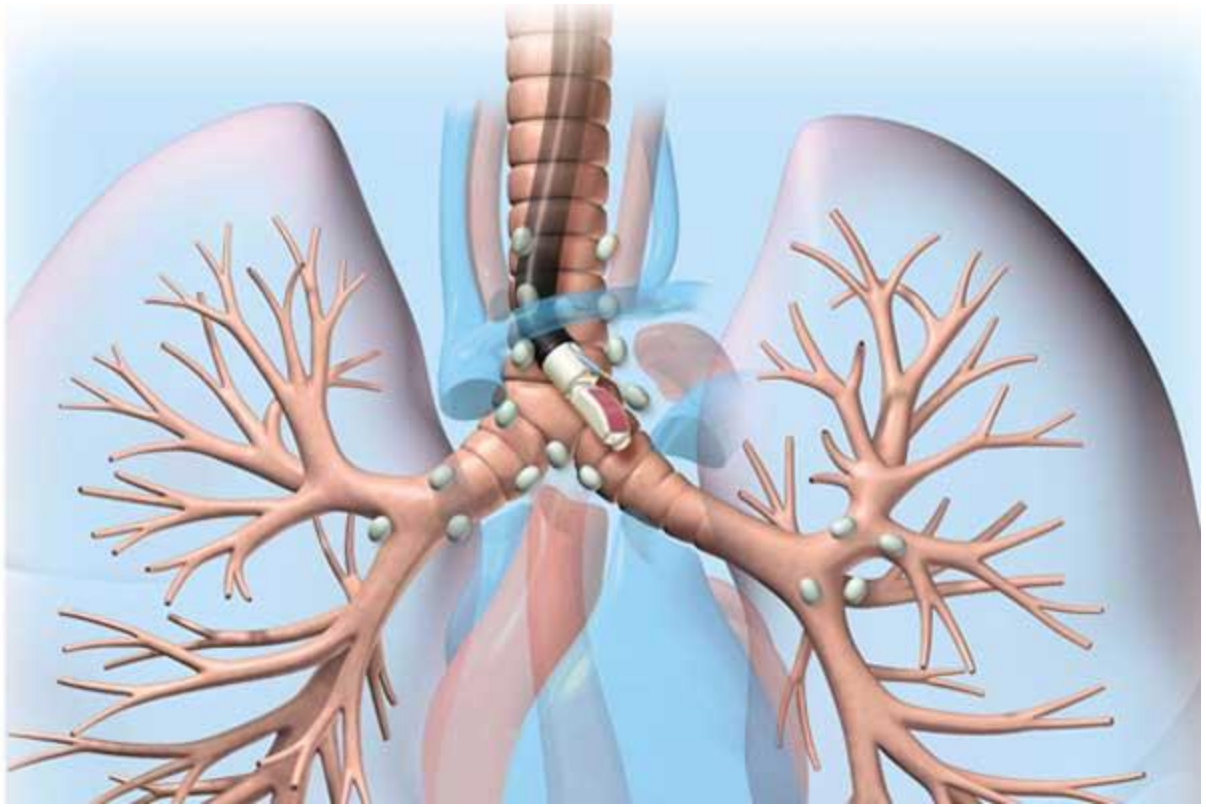
Navigational Bronchoscopy



Future Oncol. 2018 Sep;14(22):2247-2252
J Bronchol Intervent Pulmonol Volume 25, Number 4, October 2018

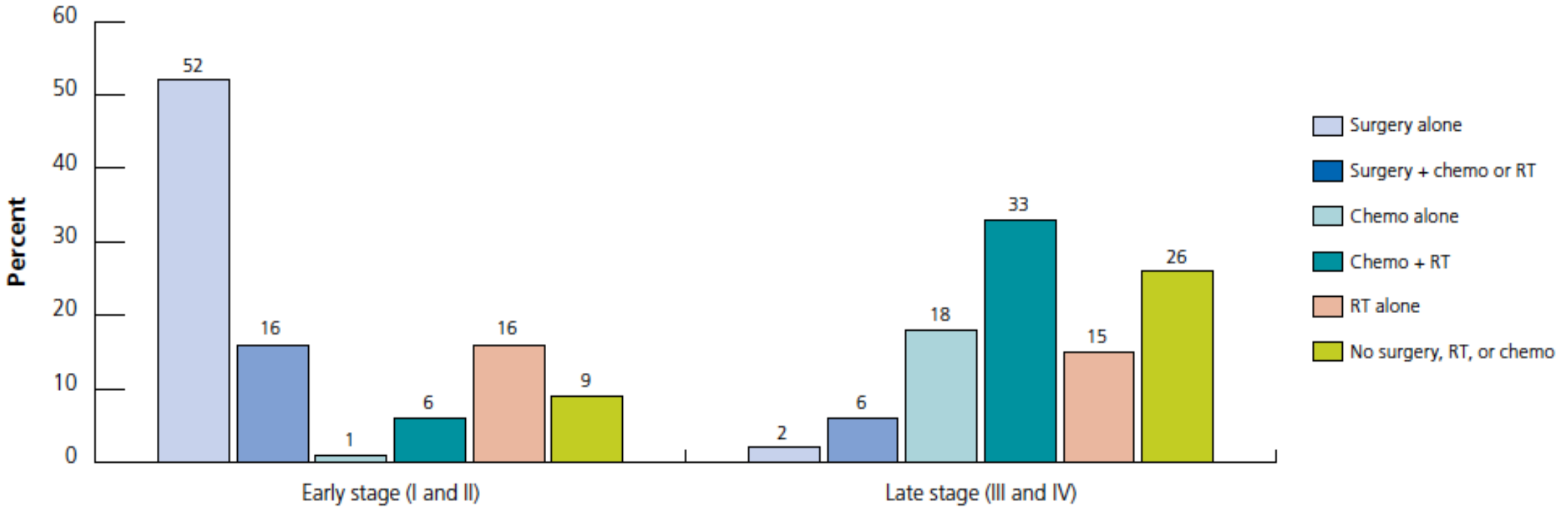
Endobronchial Ultrasound





HealthCare
MARKEY CANCER CENTER
Network

Non-Small Cell Lung Cancer Treatment Patterns



Chemo = chemotherapy and includes targeted therapy and immunotherapy drugs; RT = radiation therapy.

Source: National Cancer Data Base, 2011.[38]

American Cancer Society, Surveillance and Health Services Research, 2014

HealthCare
MARKEY CANCER CENTER
Network

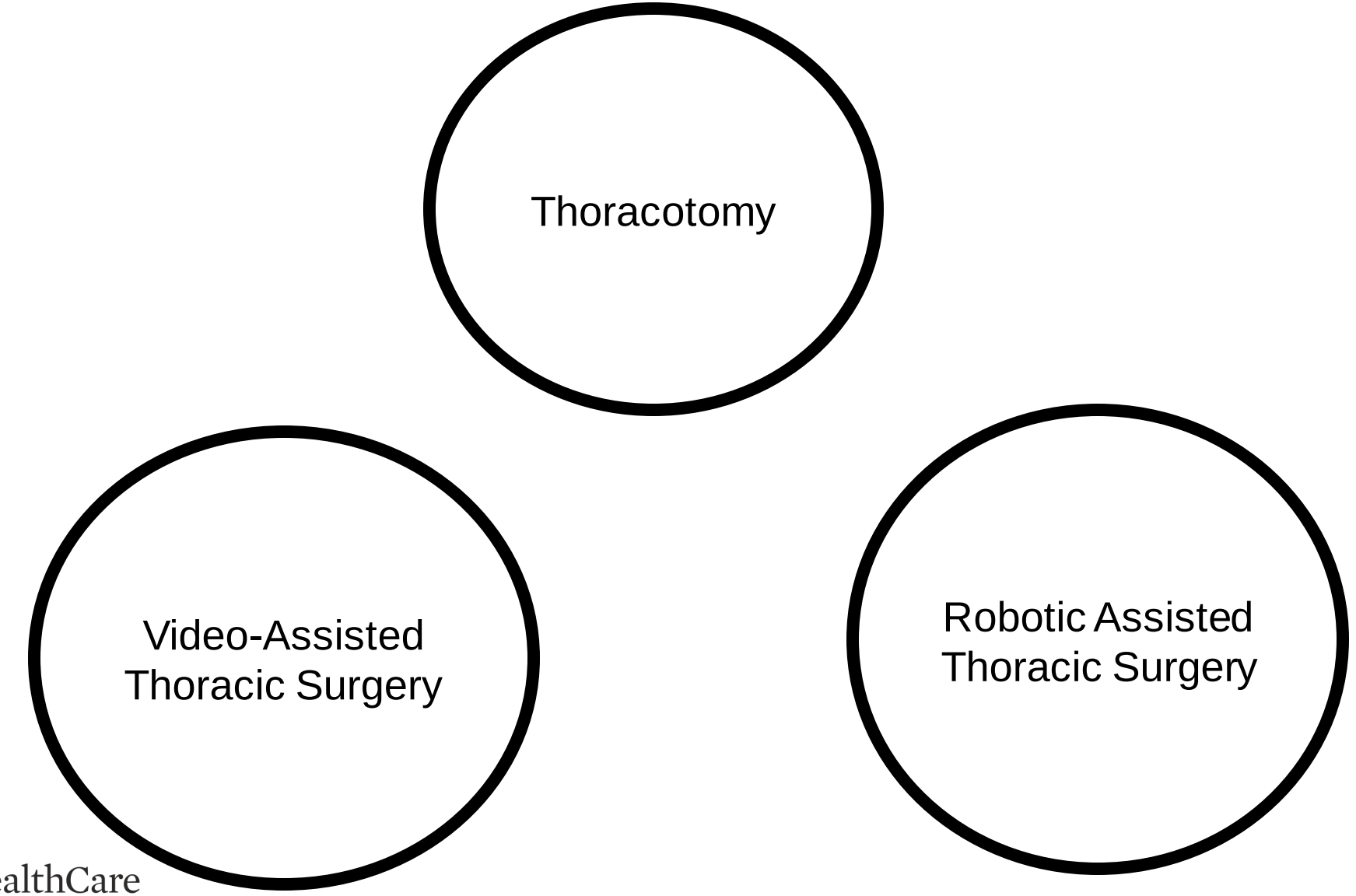
Can I Operate on You?

- Is it SAFE to operate on a patient?
  - Already determined stage and, most often, diagnosis
- Determined by several factors:
  - Patient Interest in Curative Intent
  - Can patient tolerate impact of surgery
    - Heart function
    - Lung function
    - Performance Status
      - Liver, kidney, other diseases that may limit success of surgery
      - Activity Level

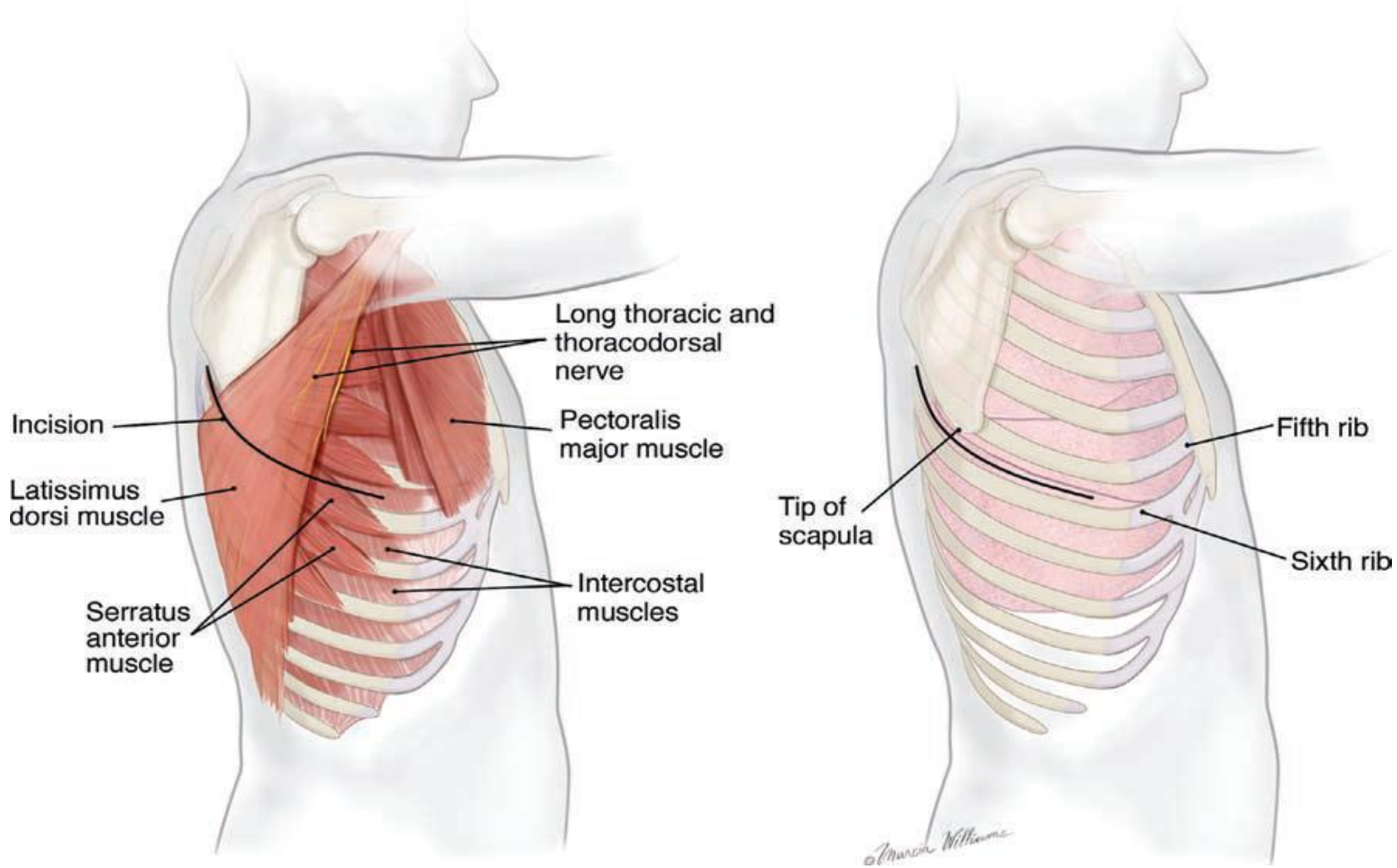
Treatment Options

- Can the patient tolerate surgery?
  - Surgery
    - Gold standard
    - Increasing Surgery for the “marginal patient”
      - Minimally Invasive techniques expand who we can operate on
  - Nonsurgical options
    - SBRT – Stereotactic Body Radiation Therapy
      - Targeted Radiation Therapy
      - 3-year survival ranges from 43 – 95%
      - Important to understand limitations
    - RFA – Radiofrequency Ablation
      - Can be delivered by bronchoscopy or by an external needle
      - Experimental – gaining experience

Surgical Approaches



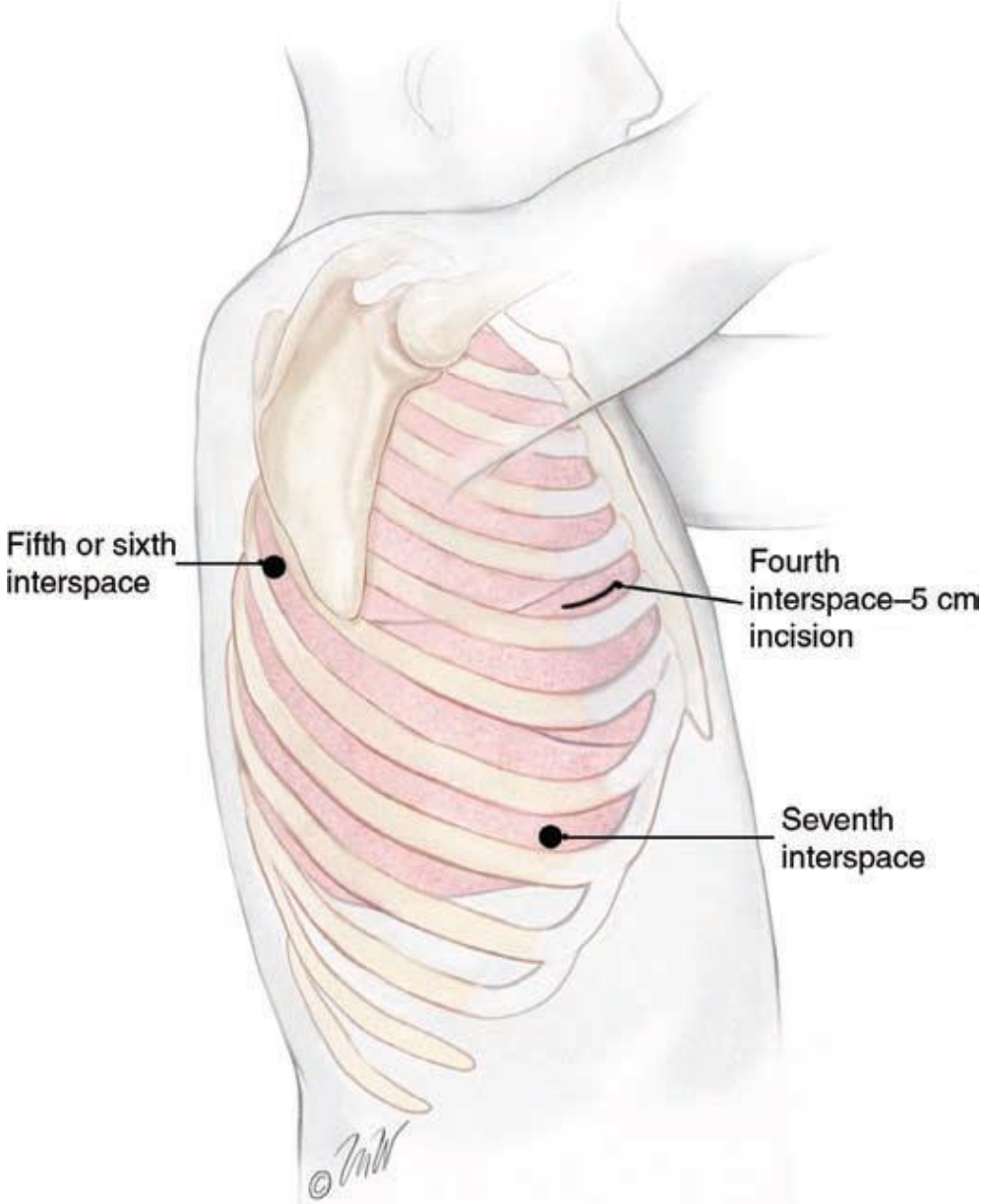
Thoracotomy



HealthCare
MARKEY CANCER CENTER
Network

Sugarbaker et al. Adult Chest Surgery

Video-Assisted or Robotic Approach



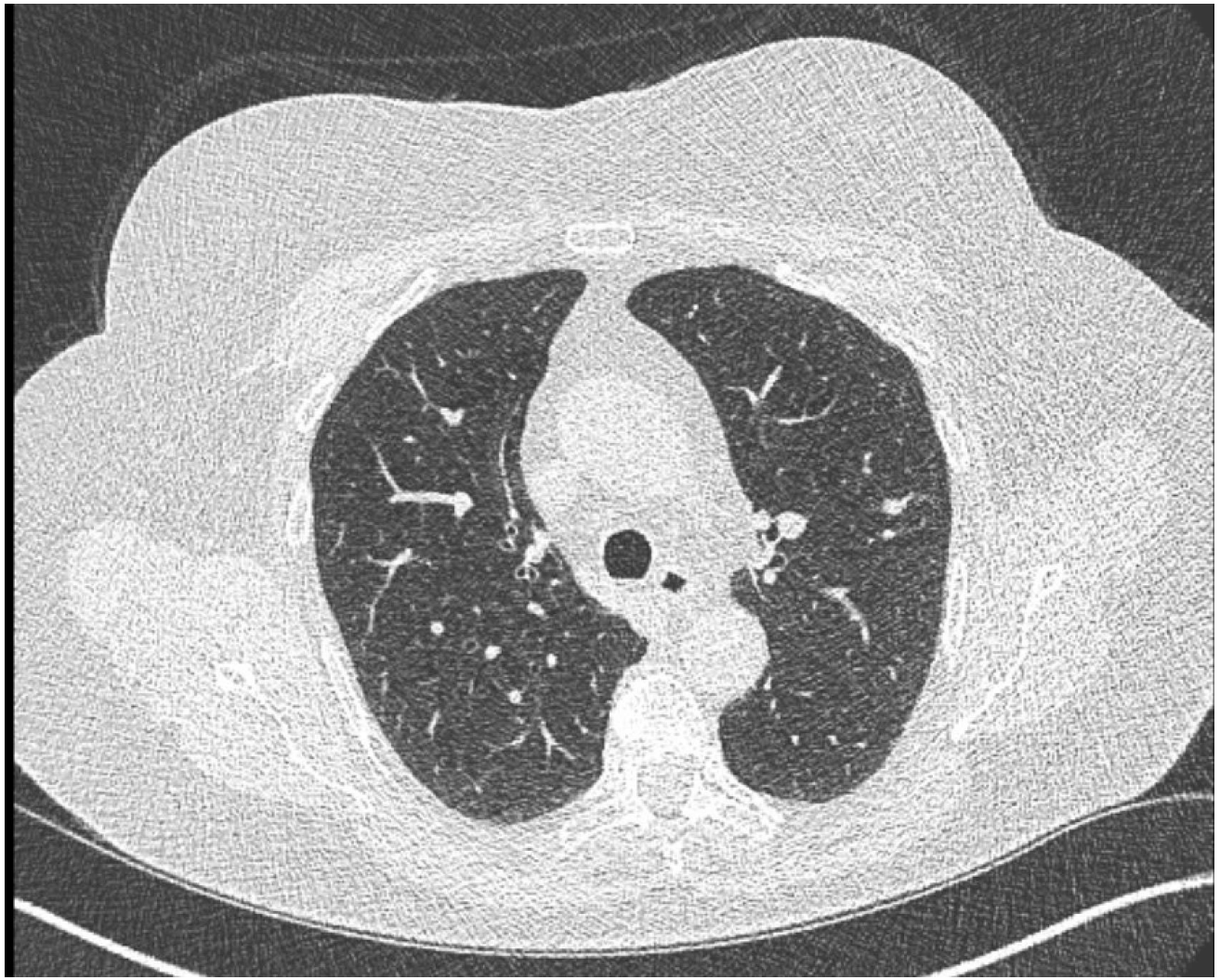
HealthCare
MARKEY CANCER CENTER
Network

Sugarbaker et al. Adult Chest Surgery

Patient Experience

Approach	Hospital Stay	ICU Stay	Pain	Chronic Pain	Efficacy
Thoracotomy	4-6 days	0-2 days	++++	>10%	++++
VATS	1-2 days	none	+	<1%	++++
RATS	1-2 days	none	+	<1%	++++

68yo Female, Former Smoker



Followed for 2 years

Low-Dose Chest CT

Small stable lung nodule
Left Lung

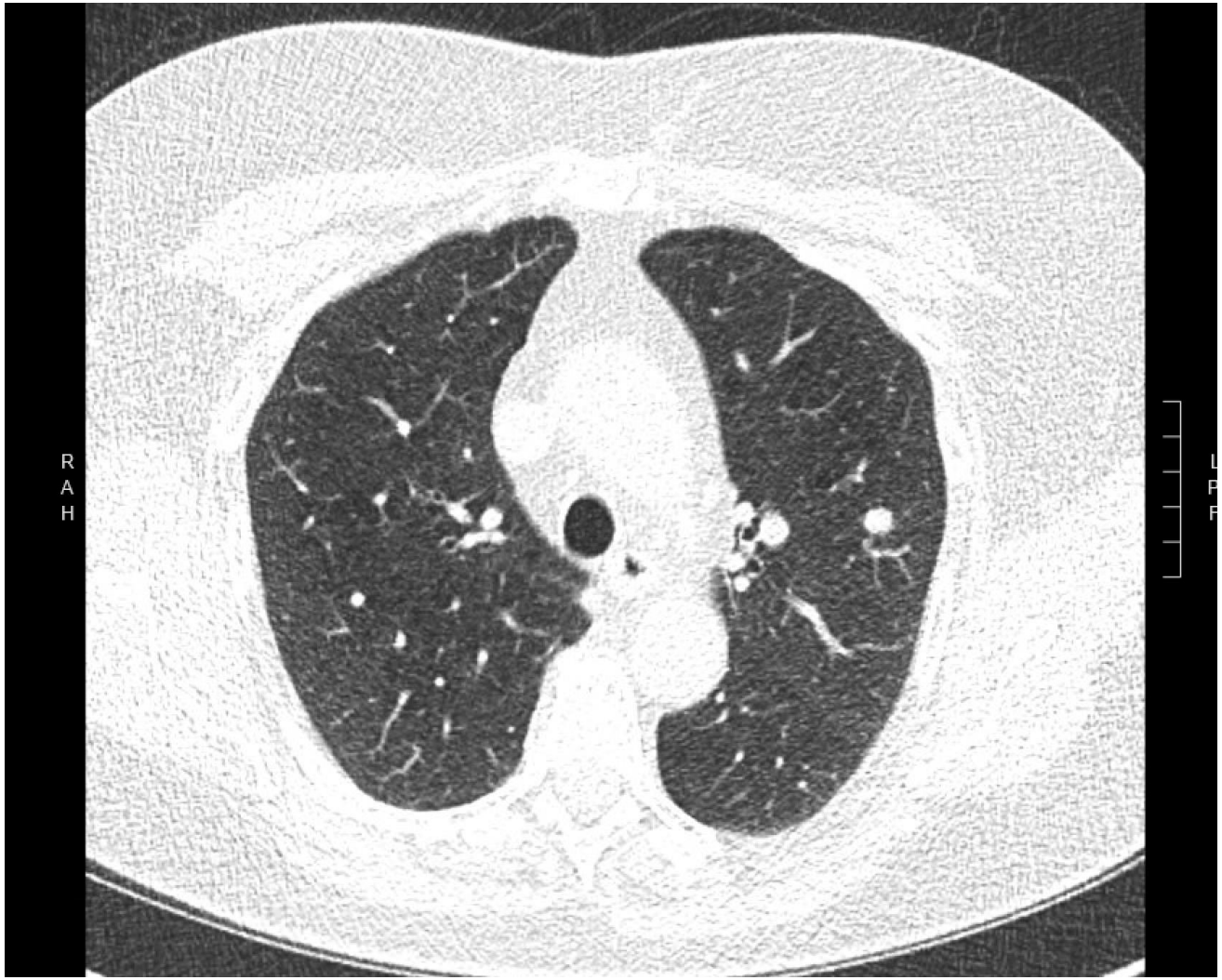
HealthCare
MARKEY CANCER CENTER
Network

One Year Later…

Left lung abnormality persists

Low-Dose Chest CT

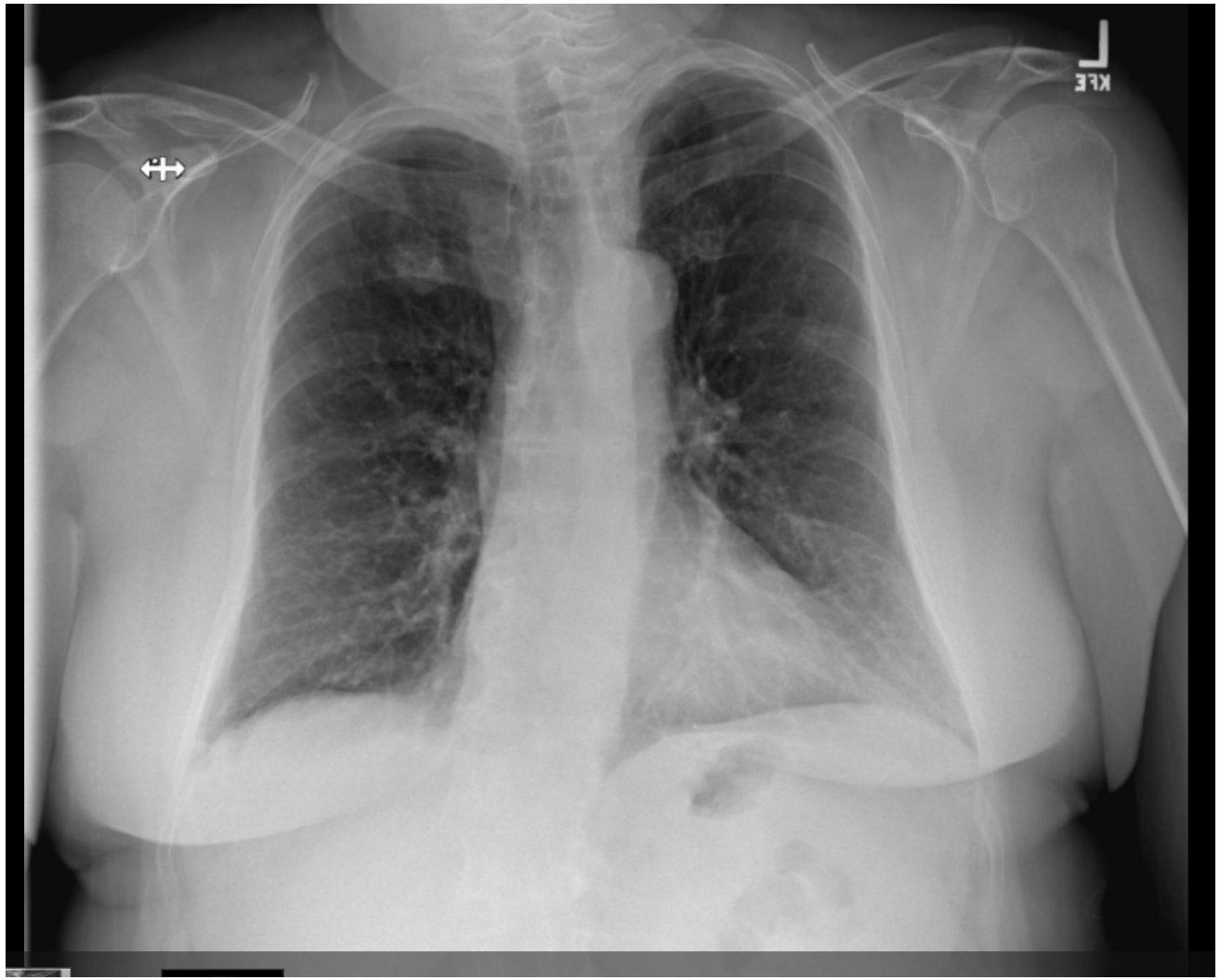
More dense…suspicious



HealthCare
MARKEY CANCER CENTER
Network

Chest X-Ray

CXR not sensitive enough



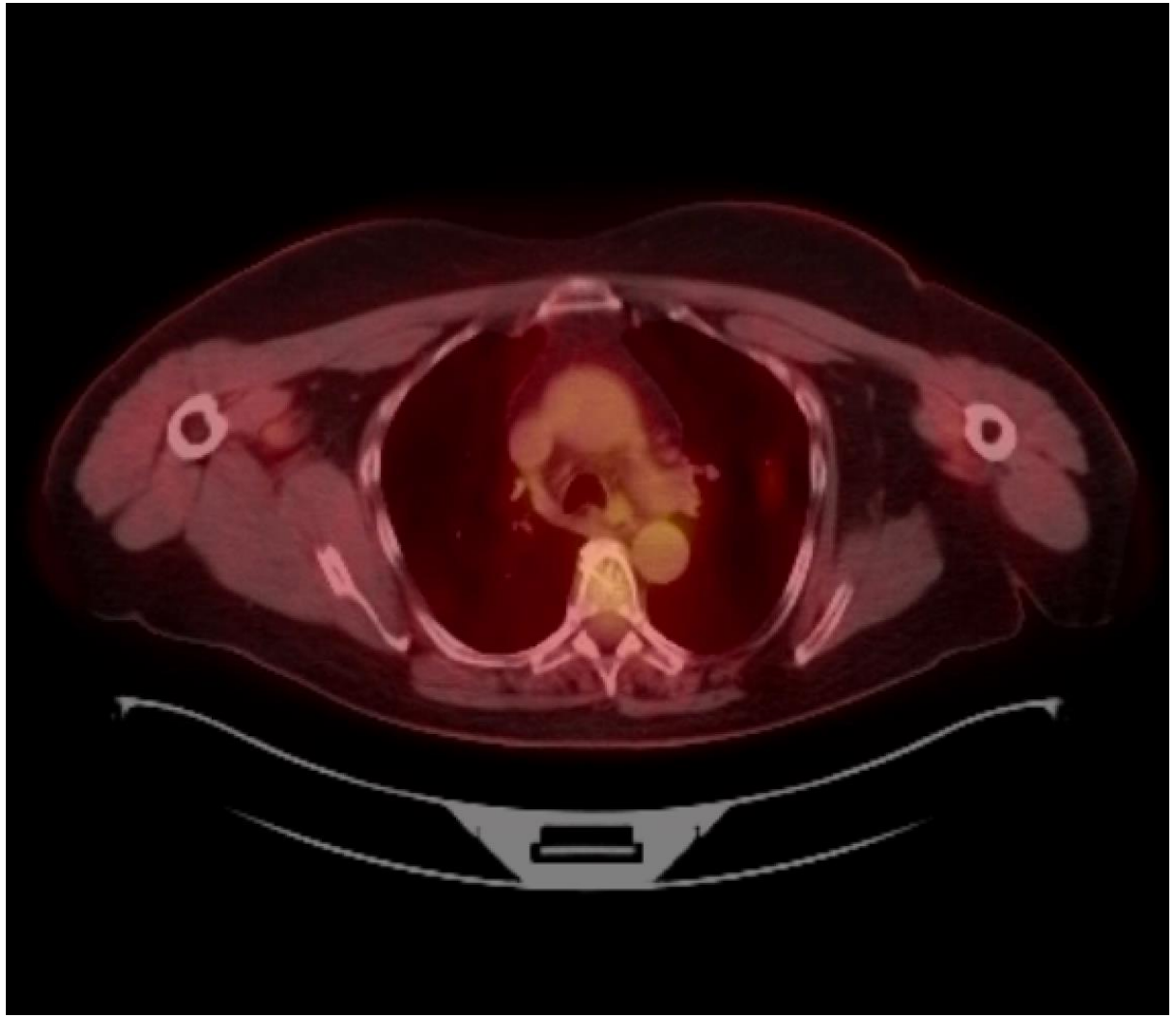
HealthCare
MARKEY CANCER CENTER
Network

PET Scan

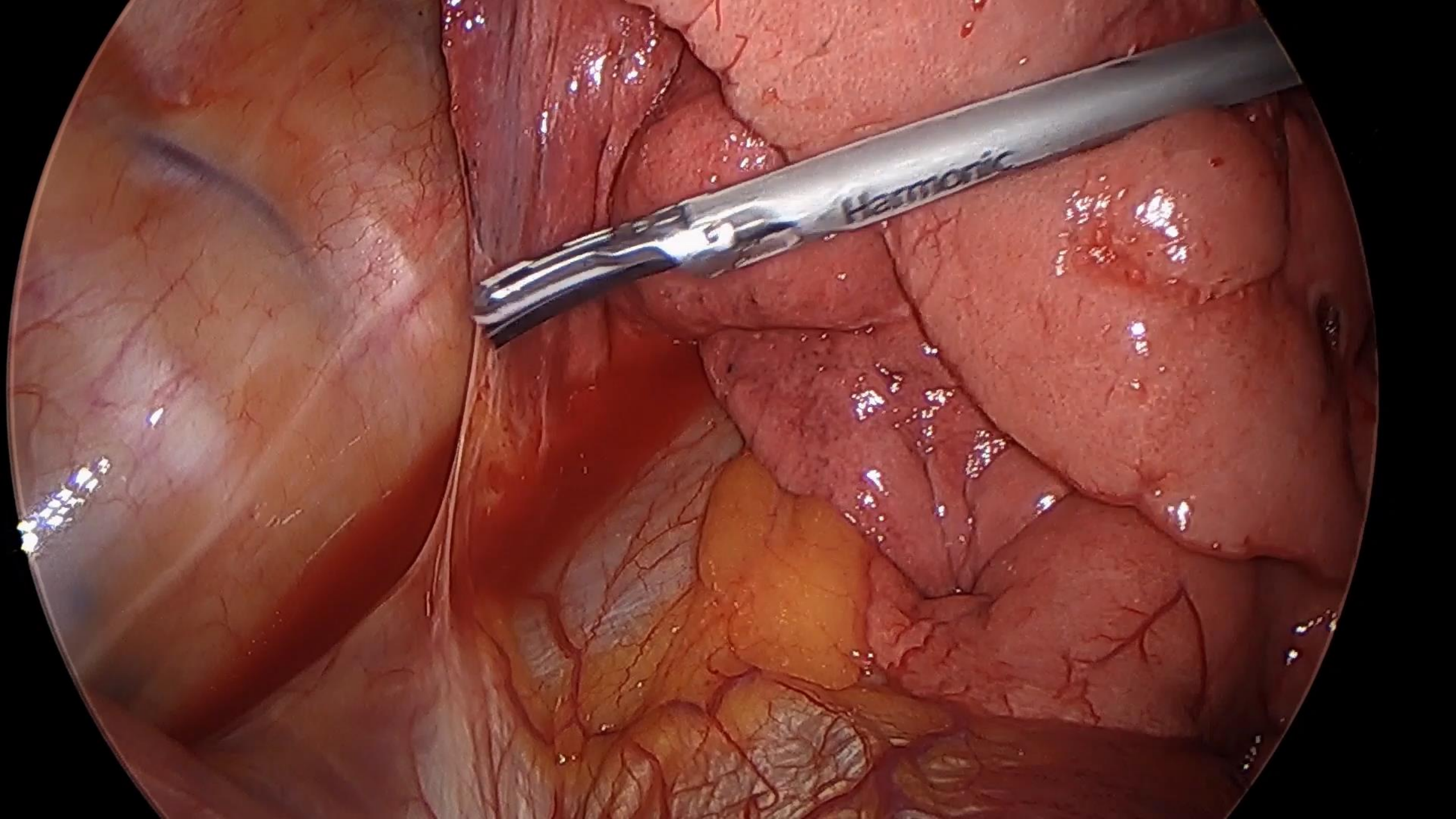
PET Scan mildly positive

Lesion continued to grow on Short term follow-up

Proceed to OR for diagnosis and removal

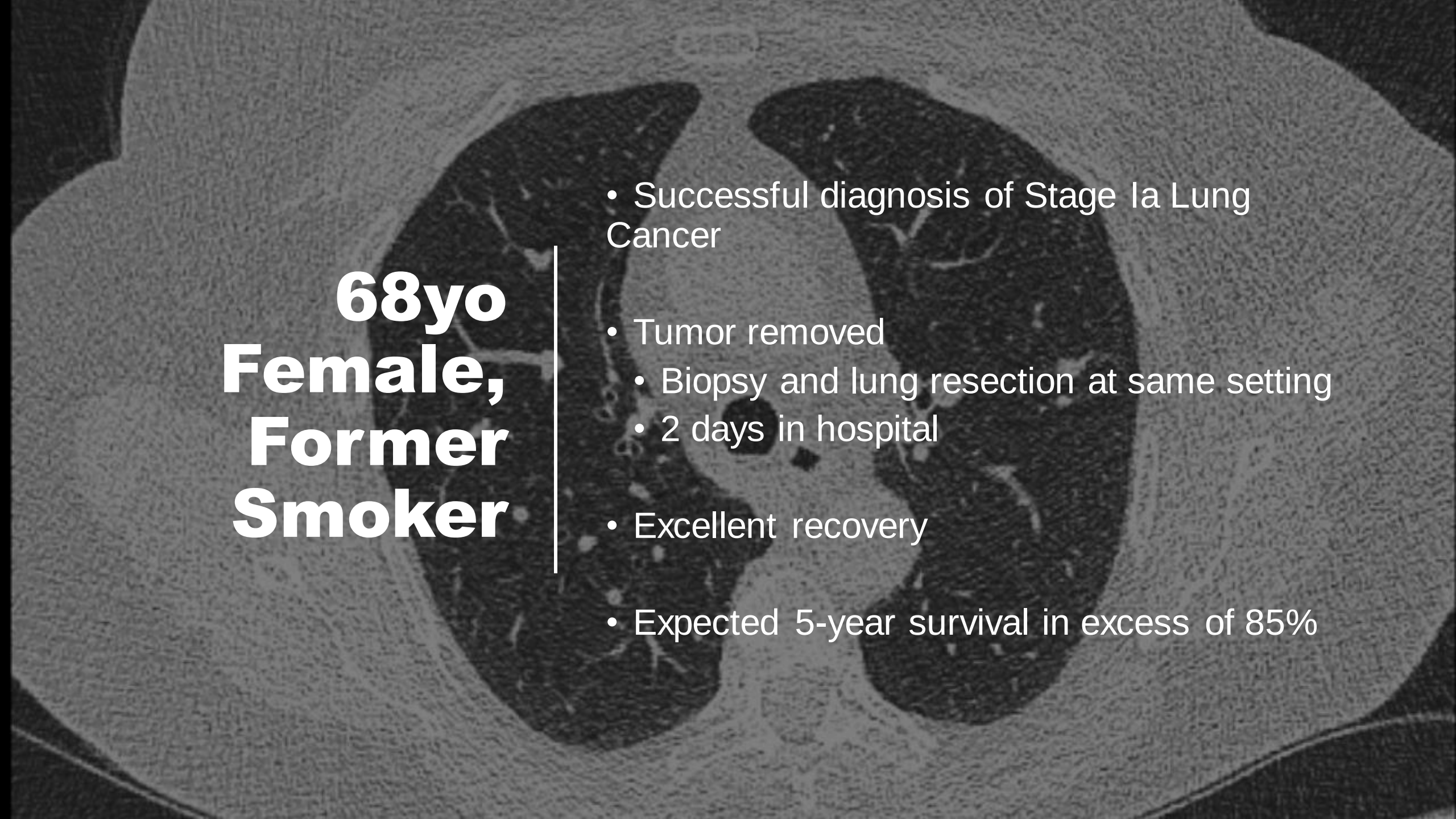


HealthCare
MARKEY CANCER CENTER
Network


Harmonic

Follow up (NCCN guidelines)

- Stage I and II (surgery / chemotherapy)
  - CT thorax every 6 months for 2-3 years then yearly
- Stage I and II (RT)
  - CT Thorax every 3-6 months for 3 years, every 6 months for 2 years then yearly
- Routine use of PET/CT and Brain MRI is not recommended



68yo Female, Former Smoker

- Successful diagnosis of Stage Ia Lung Cancer
- Tumor removed
  - Biopsy and lung resection at same setting
  - 2 days in hospital
- Excellent recovery
- Expected 5-year survival in excess of 85%

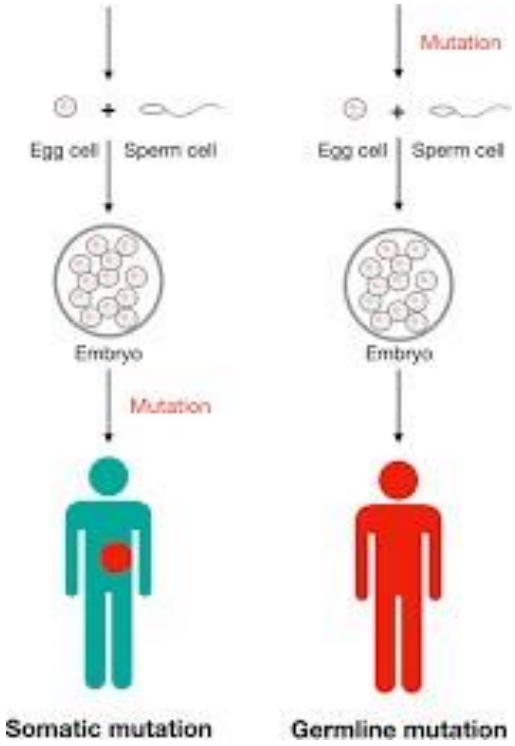
Advances

- Early diagnosis and treatment
- Less invasive options
- Better postoperative care

- Best outcomes are achieved from programs that have dedicated team that perform a high volume of these cases, most often led by Thoracic Surgeons where lung cancer is a large part of their practice

Somatic versus Inherited Genetic Variability

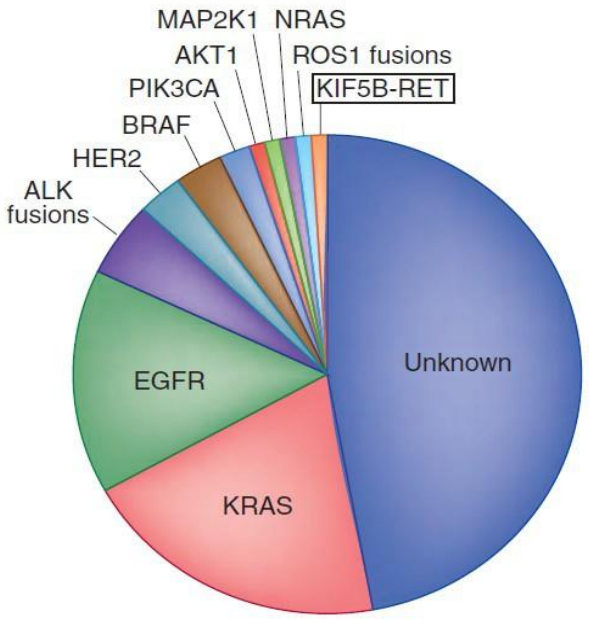
(Mutation)



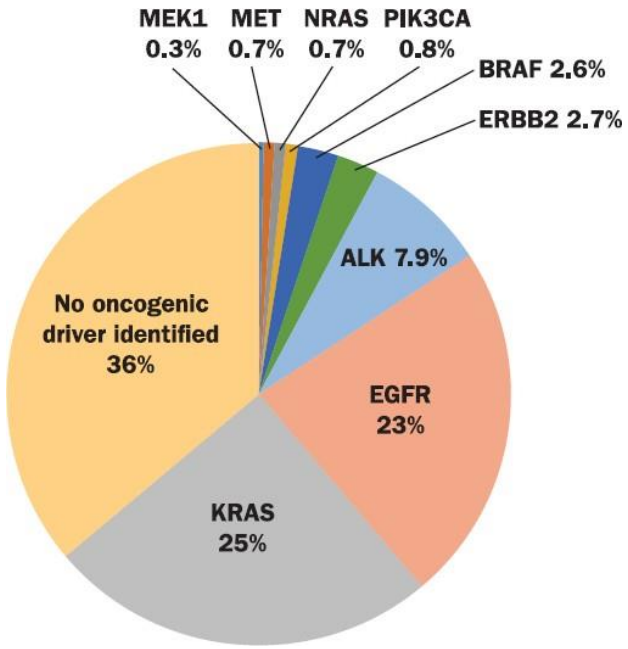
	Somatic	Germline
Location	Only some cells	All cells
Heritability	Not passed to children	Passed to children
Diseases	Cancer (90%)	Cancer (10%) Inborn errors of metabolism Cardiac defects Malignant hyperthermia Drug metabolism
How to test	Tumor tissue (biopsy needed) Liquid biopsy (detects circulating cancer cells shed from tumor)	Blood sample Buccal swab
Use	Diagnosis of cancer Selection of treatment	Selection of treatment Prevention of disease Prevention of adverse effects
Cost	~$2500	Varies of number of genes sequence

HealthCare
MARKEY CANCER CENTER
Network

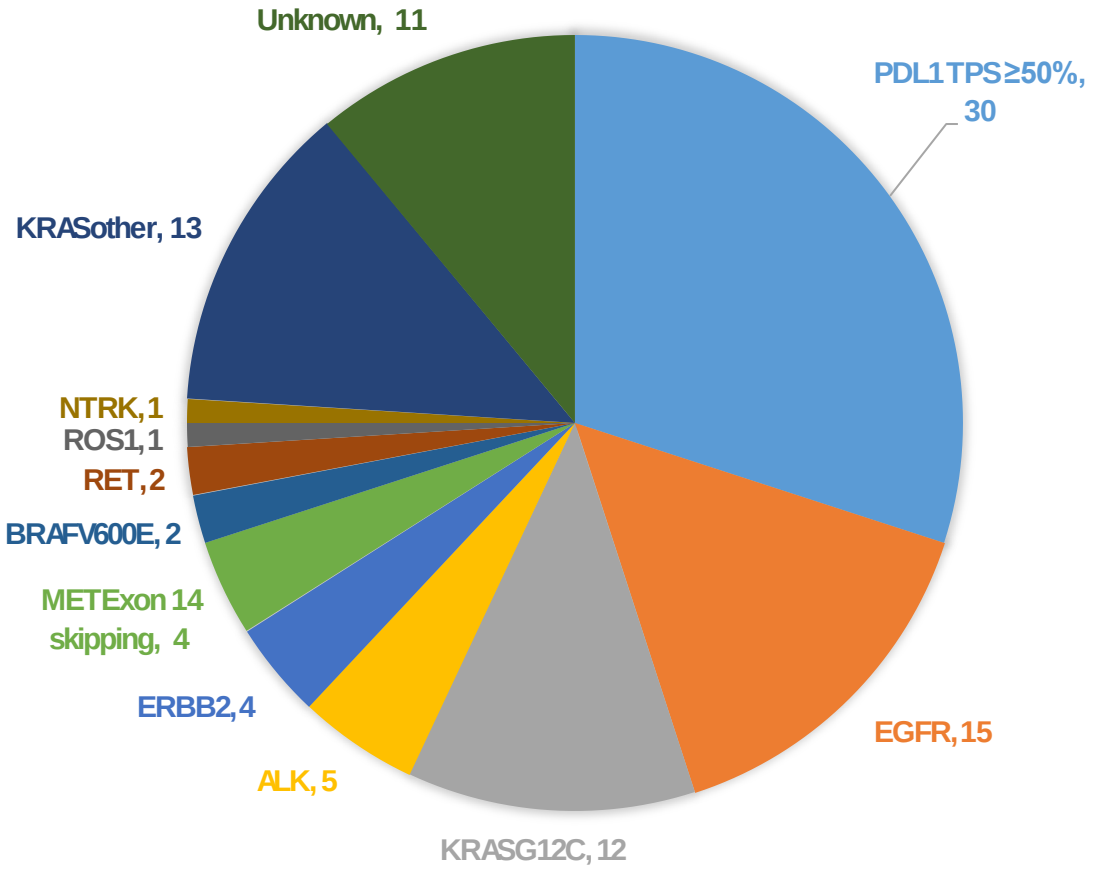
The Accelerated Progression: 2012 to 2020



Pao and Hutchinson 'Chipping away at the lung cancer genome'
Nature Medicine. **March 2012**



Scholl et al. Lung Cancer Mutation Consortium
J Thorac Oncol. **May 2015**



2020: biomarkers with drug targets

HealthCare
MARKEY CANCER CENTER
Network

Current NSCLC Lung Cancer Biomarker Guidelines

NCCN

The National Comprehensive Cancer Network® NCCN has released updated evidence-based guidelines on comprehensive biomarkers in lung cancer

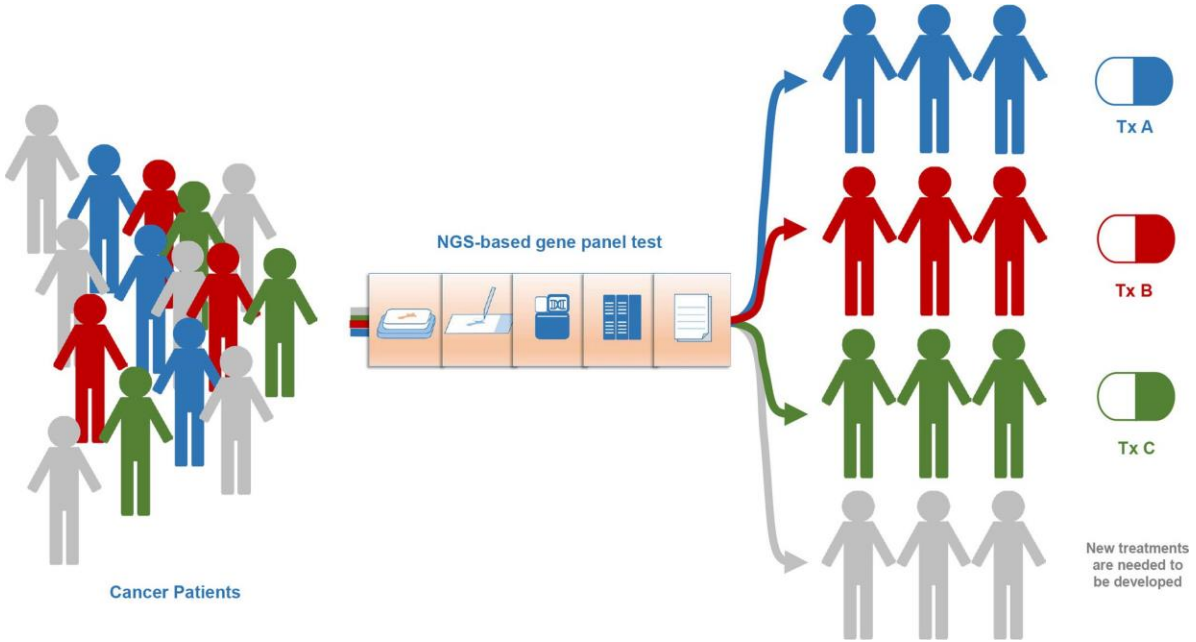
CAP, IASLC, & AMP

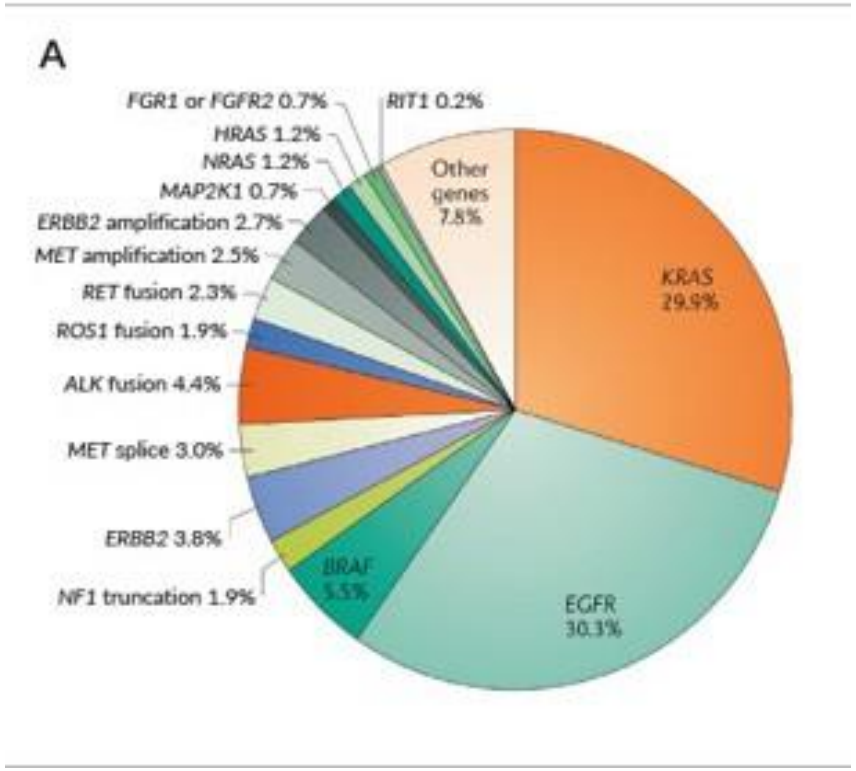
Evidence-based consensus guidelines on biomarker testing in NSCLC from **the College of American Pathologists (CAP)**, **International Association of Lung Cancer (IASLC)**, and the **Association for Molecular Pathologists (AMP)** recommend that all late-stage NSCLC patients with advanced stage lung adenocarcinoma should receive biomarker testing for three mutations (EGFR, ALK, and ROS1)[1] in 2018

ASCO

The American Society of Clinical Oncology (ASCO) released an update in February 2021 to their 2017 guideline on systemic therapy for patients with stage IV NSCLC with driver alterations

Next Generation Sequencing (Somatic, Tumor Only) for Lung Cancer



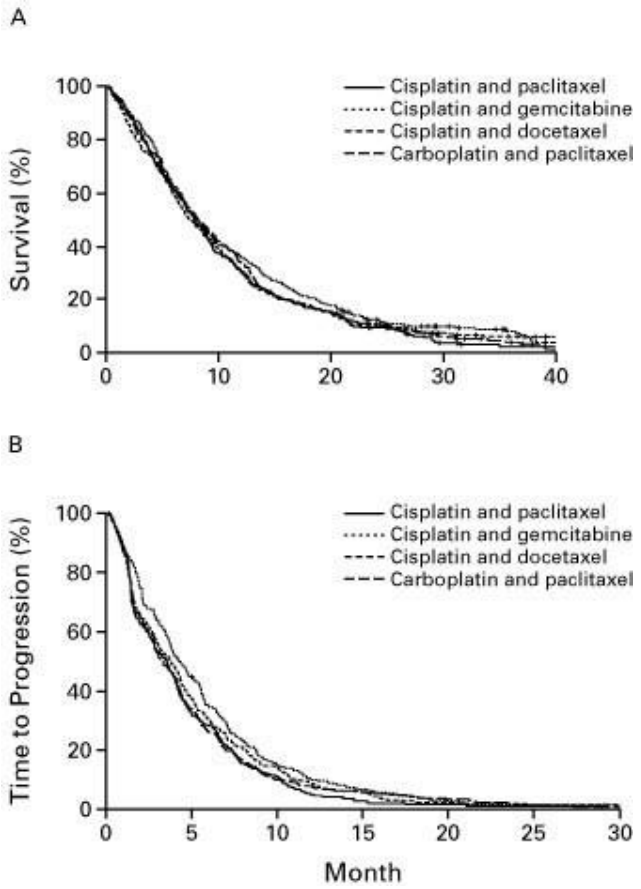


~40% of NSCLC will have a targetable mutation, of these ~30% are EGFR and ~30% are KRAS

HealthCare
MARKEY CANCER CENTER
Network

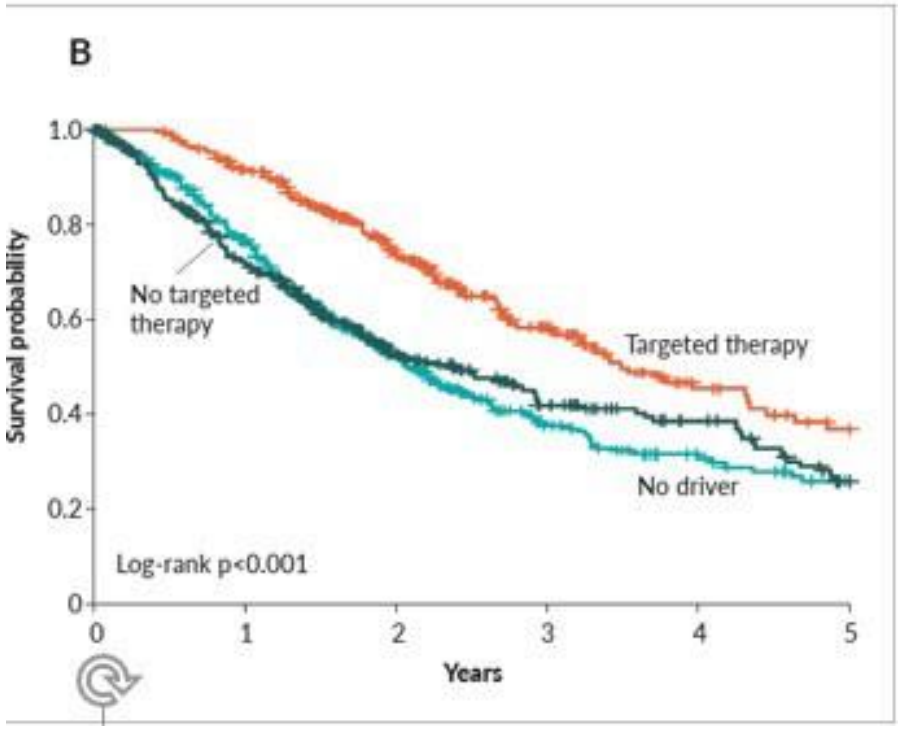
NSCLC Treatment After Genomics

2002: Survival 8 Months



Schiller JH. NEJM 2002; 346:92-98

2022: Survival 4 Years



Meisel 2020, Healthbook

HealthCare
MARKEY CANCER CENTER
Network

Current Treatment of First Line IIIb/IV NSCLC

Genetics	%	PS	Treatment
EGFR	~15%	0-4	Erlotinib, gefitinib, afatinib, osimertinib, dacomitinib Mobocertinib, amivantinamab-lpyl (exon 20 only)
ALK	~4%	0-4	Crizotinib, ceritinib, alectinib, brigatinib, lorlatinib
ROS1	~1%	0-4	Crizotinib, entrectinib, lorlatinib
BRAF V600E	~3%	0-4	Dabrafenib + trametinib
KRAS G12C	~13%	0-4	Sotorasib
NTRK gene fusion	<1%	0-4	Larotrectinib, entrectinib
HER2 (mutations and amplifications)	~1-3%	0-4	Fam-trastuzumab deruxtecan
RET	~1-3%	0-4	Selpercatinib, pralsetinib
MET (exon 14 skipping or > 5 fold CN)	~3%	0-4	Crizotinib, capmatinib, tepotinib
TMB > 10	~35	0-4	Pembrolizumab
PD-L1 positive (>1%)	~60%	0-4	Pembrolizumab +/- chemotherapy
MSI-High	<1%	0-4	Pembrolizumab
No target		0-1	Doublet chemotherapy** +/- immunotherapy +/- bevacizumab

Cancer Mutation Testing in Kentucky

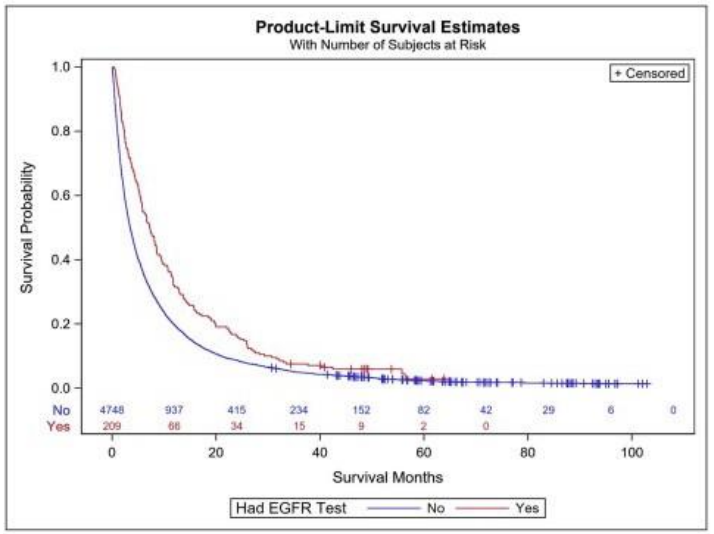
Population: Stage IIIb-IV NSCLC in SEER with associated claims data (Medicare or private)

- EGFR Testing Rate 2010: 5.9%
- EGFR Testing Rate 2011: 10.6%
- EGFR Testing Rate 2021: 22%

Table 3. Factors associated with having EGFR somatic mutation testing in Stage IIIb–Stage IV NSCLC patients.

Modeling Had EGFR Testing		
Variable	**OR (95% CI)**	**P-Value**
Age (ref = 75+)		0.0001
20–49	4.15 (2.17–7.91)	
50–64	1.76 (1.16–2.67)	
65–74	1.39 (0.98–1.98)	
Sex (ref = Male)		0.0142
Female	1.44 (1.08–1.93)	
Appalachian Status (ref = Non-Appalachia/Metro)		0.0011
Appalachian/Metro	0.67 (0.28–1.59)	
Appalachian/Non-Metro	0.51 (0.36–0.73)	
Non-Appalachian/Non-Metro	0.60 (0.40–0.89)	
Year of Diagnosis (ref = 2007)		<0.0001
2008	3.81 (0.43–34.68)	
2009	22.30 (3.00–165.41)	
2010	58.56 (8.12–422.26)	
2011	113.47 (15.81–814.21)	
Insurance (ref = Private)		<0.0001
Medicaid	0.19 (0.09–0.40)	
Medicare	0.61 (0.44–0.84)	

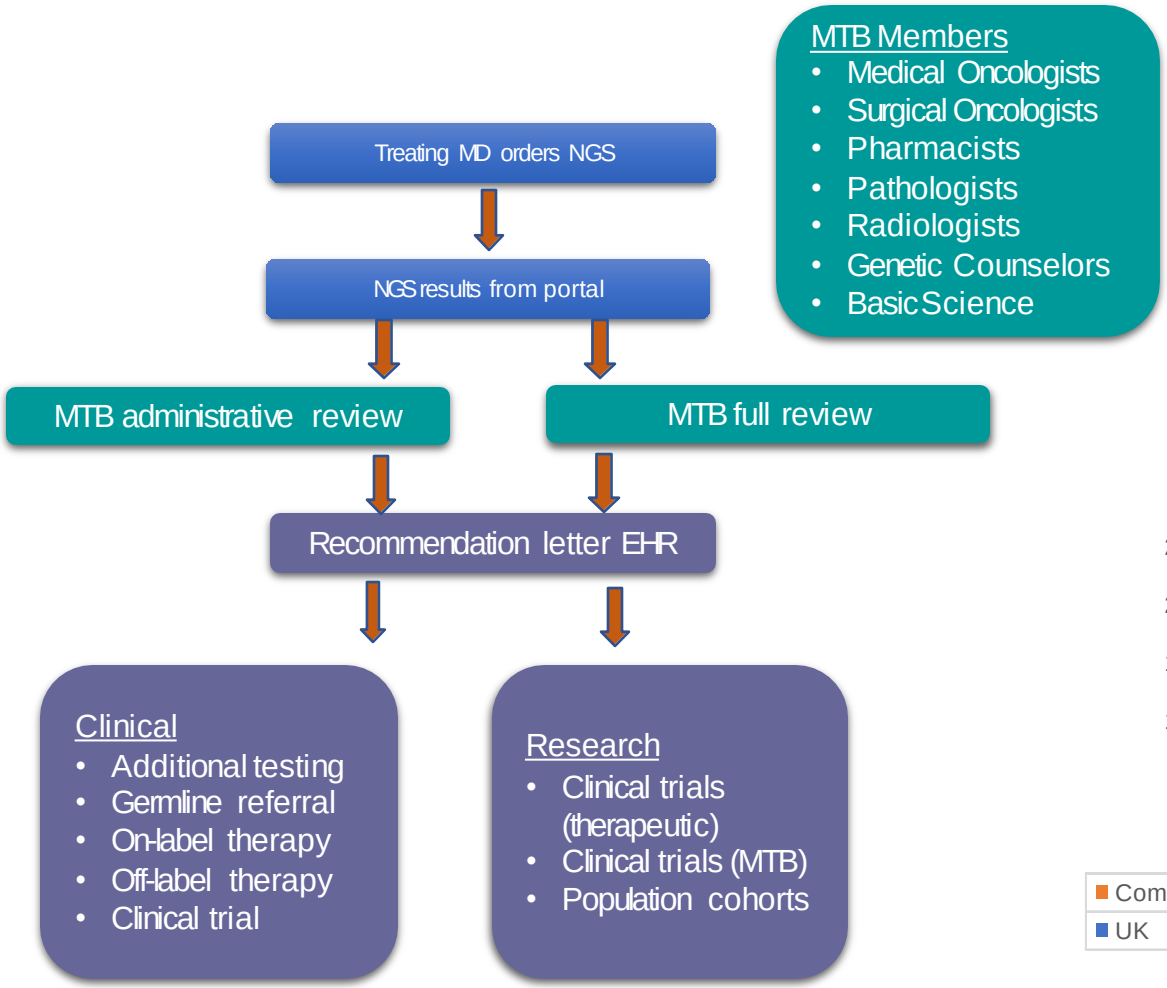
HR:0.77; 95% CI 0.67-0.79 p=0.0003



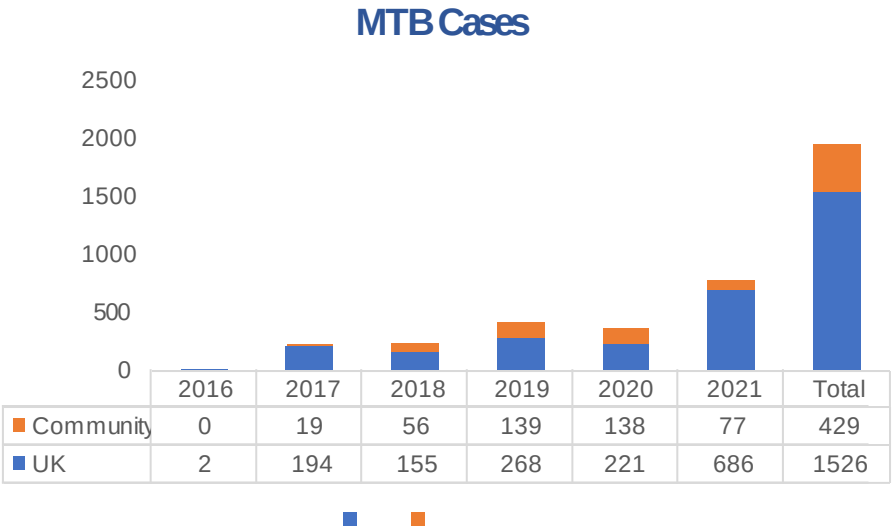
Kolesar, etal 2020, PLOS One

HealthCare
MARKEY CANCER CENTER
Network

Molecular Tumor Boards: An Implementation Strategy for Precision Oncology



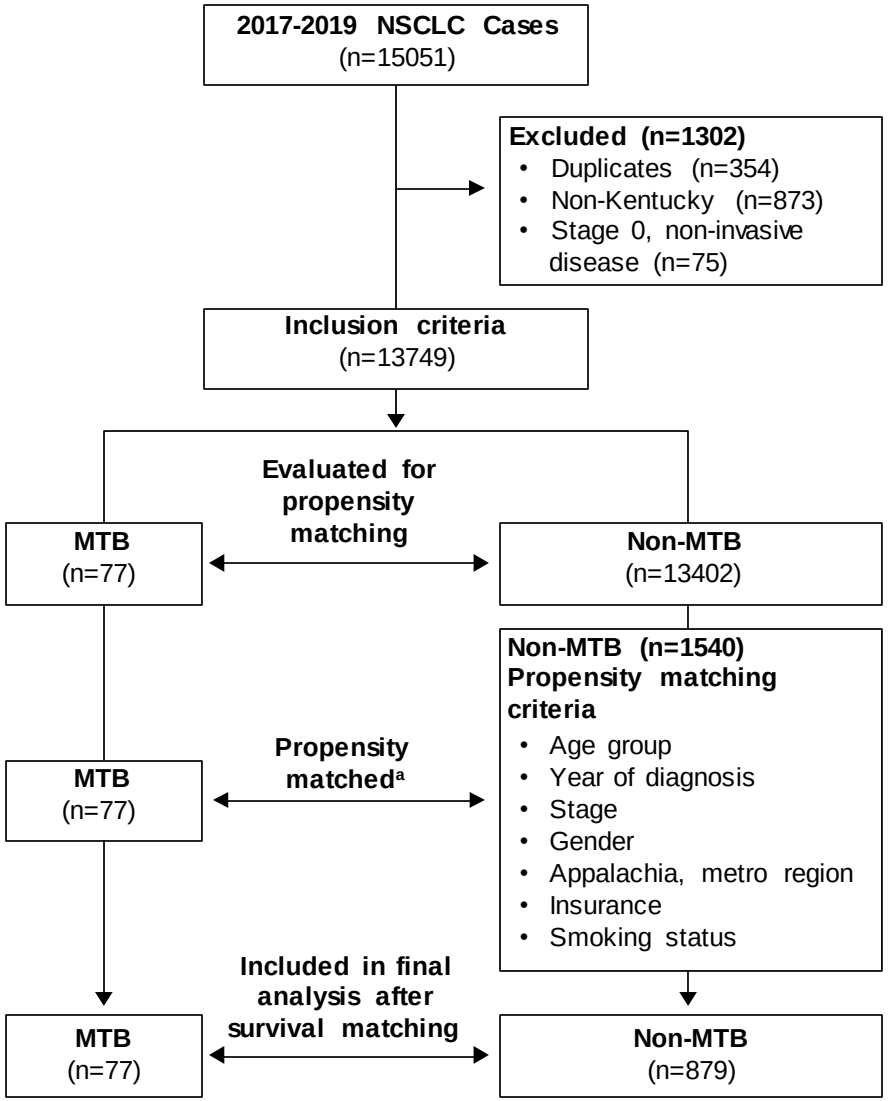
MTB Members
- Medical Oncologists
- Surgical Oncologists
- Pharmacists
- Pathologists
- Radiologists
- Genetic Counselors
- Basic Science



HealthCare MARKEY CANCER CENTER Network

JCO Precision Oncology (2017); J Rural Health (2020); PLOS One (2020); JCO Precision Oncology 2021; Current Problems in Cancer 2021; JCO Precision Oncology 2021; JCO Precision Oncology 2022 (in revision).

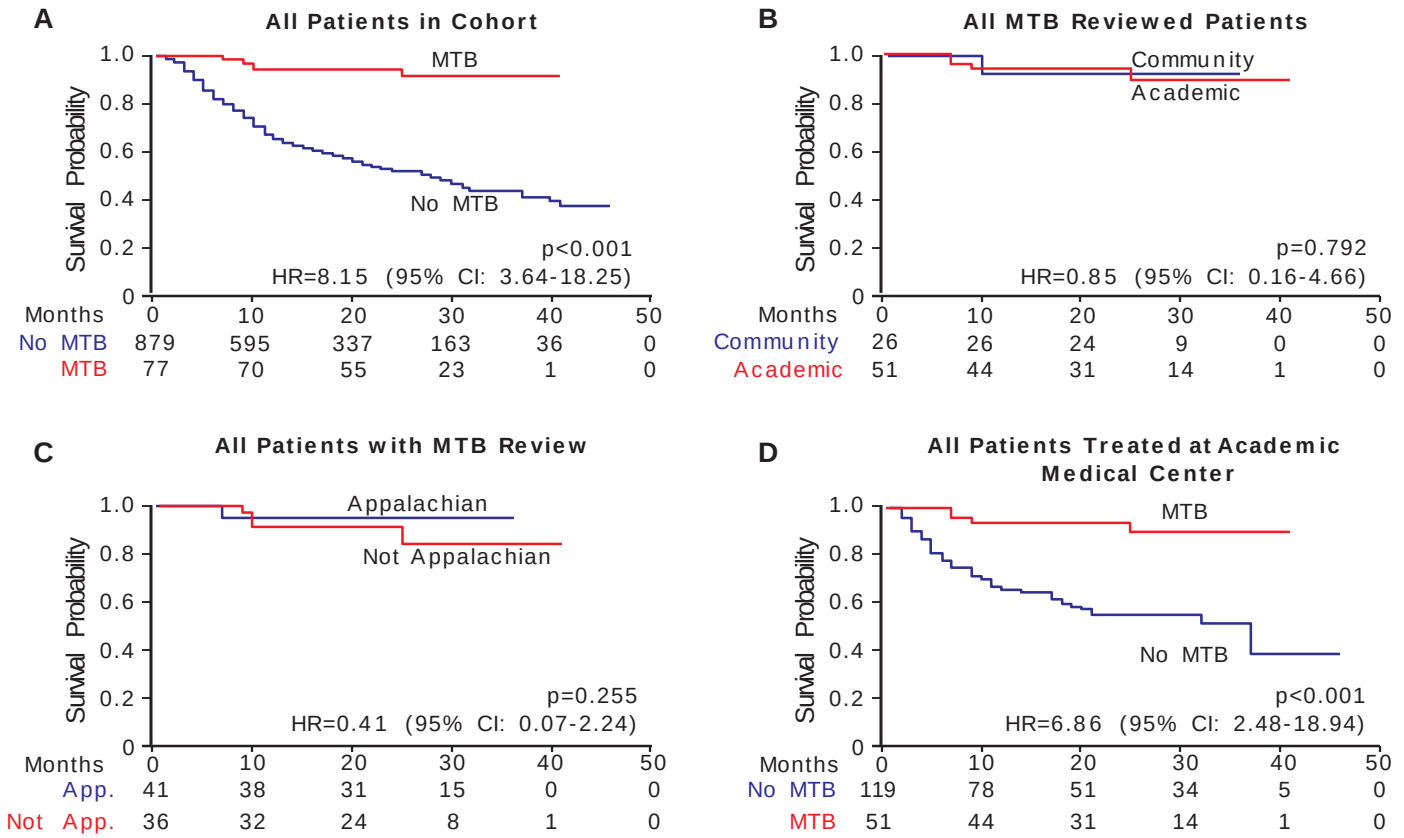
Background: Design Case Control Study in NSCLC



HealthCare
MARKEY CANCER CENTER
Network

Kolesar, etal 2021, JCO Precision Oncology

Background – Outcomes of Case Control Study



HealthCare
MARKEY CANCER CENTER
Network

Kolesar, etal 2021, JCO Precision Oncology

2023 ASCO ANNUAL MEETING

Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC)

Roy S. Herbst[1], Masahiro Tsuboi[2], Thomas John[3], Terufumi Kato[4], Margarita Majem[5], Christian Grohé[6], Jie Wang[7], Jonathan Goldman[8], Shun Lu[9], Wu-Chou Su[10], Filippo de Marinis[11], Frances A. Shepherd[12], Ki Hyeong Lee[13], Nhieu Thi Le[14], Arunee Dechaphunkul[15], Dariusz Kowalski[16], Lynne Poole[17], Marta Stachowiak[18], Yuri Rukazenkov[19], Yi-Long Wu[20]

[1]Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA; [2]Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [3]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia; [4]Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; [5]Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6]Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; [7]Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China; [8]David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA; [9]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [10]Department of Oncology, National Cheng Kung University, Tainan, Taiwan; [11]Thoracic Oncology Division, European Institute of Oncology (IEO), IRCCS, Milan, Italy; [12]Department of Medical Oncology and Hematology, University Health Network, Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [13]Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, Republic of Korea; [14]Ho Chi Minh City Oncology Hospital, Binh Thanh District, Ho Chi Minh City, Vietnam; [15]Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; [16]Department of Lung Cancer and Thoracic Tumours, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [17]Oncology Biometrics, AstraZeneca, Cambridge, UK; [18]Late Oncology Research & Development, AstraZeneca, Warsaw, Poland; [19]Oncology Research & Development, AstraZeneca, Cambridge, UK; [20]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China

2023 ASCO ANNUAL MEETING #ASCO23

PRESENTED BY: Roy S. Herbst

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

HealthCare MARKEY CANCER CENTER Network

ADAURA overall survival: summary and impact

The ADAURA study has demonstrated a statistically significant and clinically meaningful OS benefit with adjuvant osimertinib vs placebo in patients with resected EGFRm stage IB–IIIA NSCLC

>2 million
new cases of lung cancer worldwide annually[1]

NSCLC represents **~80%** of all diagnoses[1]

Approximately **30%** of patients have resectable disease[2–4]

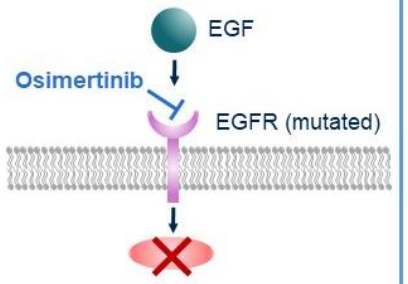
EGFR mutation prevalence ranges from **10–50%** in patients with NSCLC[5–9]

ADAURA

Surgery → Adjuvant Therapy

Osimertinib vs placebo

Adjuvant osimertinib



Osimertinib is the first EGFR-TKI to show significant OS benefit in a Phase III adjuvant study

Reinforces osimertinib as standard of care

EGFR mutation testing

Best treatments early

New era for targeted treatment in early-stage disease

1. Cancer.net 2023. Available at: https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics; 2. Datta et al. Chest 2003;123:2096–2103; 3. Le Chevalier Ann Oncol 2010;21(Suppl 7):vii196–8; 4. Cagle et al. Arch Pathol Lab Med 2013;137:1191–1198; 5. Pi et al. Thorac Cancer 2018;9:814–819; 6. Hondelink et al. Eur J Cancer 2023;181:53–61; 7. Zhang et al. Oncotarget 2016;7:78985–78993; 8. Stone et al. Intern Med J 2014;44:1188–1192; 9. Kim et al. Pathology 2020;52:410–420.

HealthCare
MARKEY CANCER CENTER
Network

Herbst et al, ASCO2023#LBA3

ADAURA Phase III study design

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
≥18 years (Japan / Taiwan: ≥20)
WHO performance status 0 / 1
Confirmed primary non-squamous NSCLC Ex19del / L858R‡
Brain imaging, if not completed pre-operatively
Complete resection with negative margins§
Maximum interval between surgery and randomization:
- 10 weeks without adjuvant chemotherapy
- 26 weeks with adjuvant chemotherapy

Stratification by:
Stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
Race (Asian vs non-Asian)

Randomization 1:1 (N=682)

- **Osimertinib 80 mg, once daily**
- **Placebo, once daily**

Planned treatment duration:
3 years

Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

Endpoints
- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

*At the time of recruitment, staging was determined by the AJCC / UICC Staging Manual 7th edition. Patients with stage IB disease were not eligible in Japan. †Pre-operative, post-operative, or planned radiotherapy was not allowed. ‡Centrally confirmed in tissue. §Patients received a CT scan after resection and within 28 days prior to treatment.

Adjuvant osimertinib has significantly improved CNS DFS

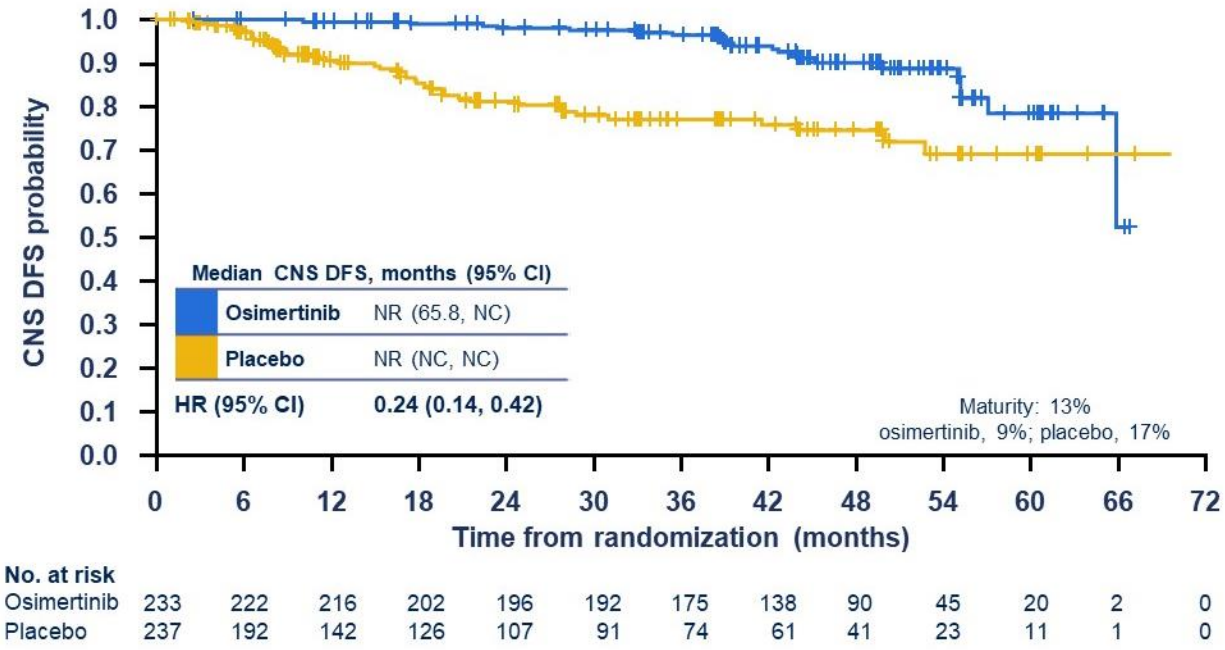
- CNS metastases are a poor prognostic factor among patients with NSCLC, and are associated with deterioration in quality of life[1]

Improved CNS efficacy with osimertinib treatment

- Osimertinib has shown greater penetration of the blood-brain barrier and higher exposure in the brain compared with other EGFR-TKIs[2–4]
- Adjuvant osimertinib demonstrated CNS DFS* benefit vs placebo in both the stage II–IIIA and IB–IIIA populations[5,6]

ADAURA updated CNS DFS analysis[5,6] (stage II–IIIA)

JCO January 2023



No. at risk													
Osimertinib	233	222	216	202	196	192	175	138	90	45	20	2	0
Placebo	237	192	142	126	107	91	74	61	41	23	11	1	0

Data cut-off: April 11, 2022.

*CNS DFS events were defined as CNS disease recurrence or death by any cause.

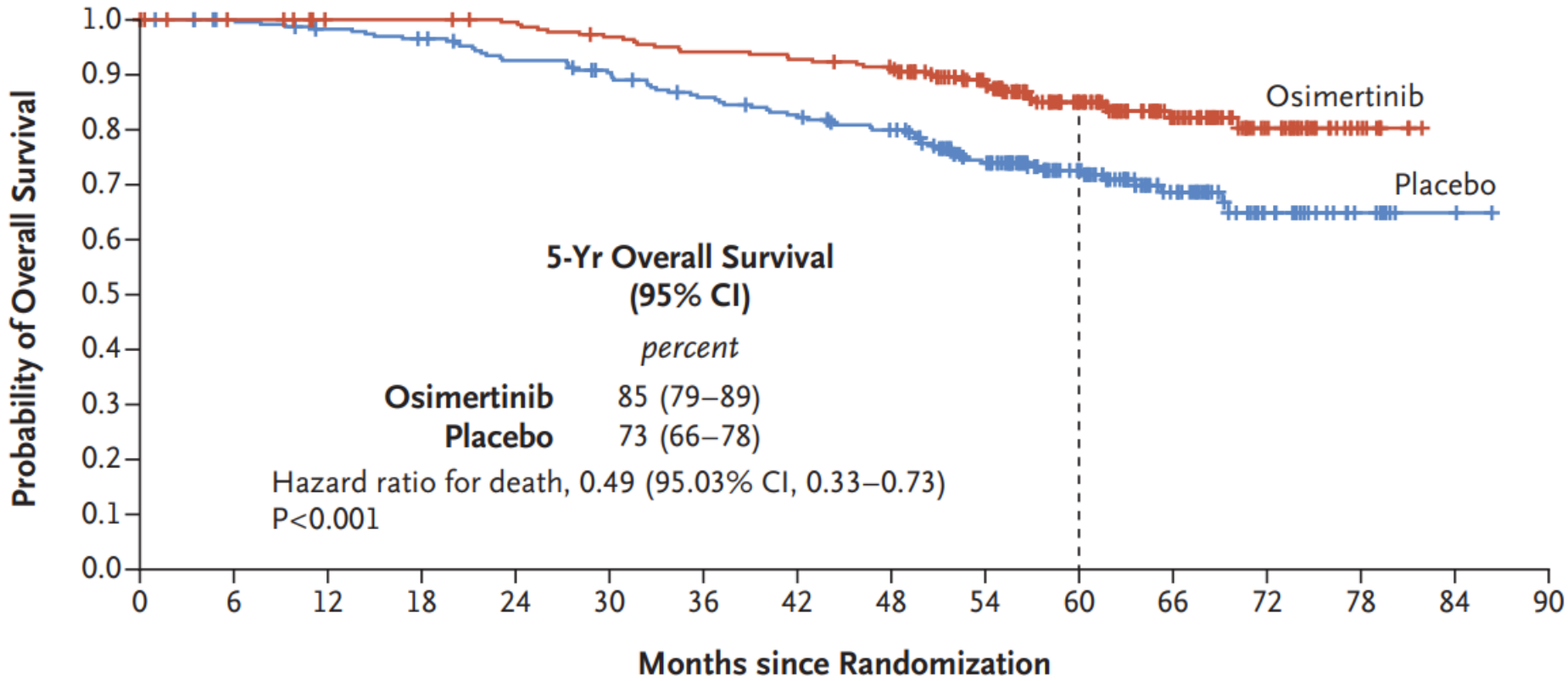
1. Peters et al. Cancer Treat Rev 2016;45:139–162; 2. Colclough et al. Eur J Cancer 2016;69:S28; 3. Ballard et al. Clin Cancer Res 2016;22:5130–5140; 4. Vishwanathan et al. Cancer Res 2018; 78:CT013; 5. Herbst et al. J Clin Oncol 2023;41:1830–1840; 6. Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract / oral LBA47.

HealthCare
MARKEY CANCER CENTER
Network

Herbst et al, ASCO2023#LBA3

Overall Survival among Patients with Stage II to IIIA Disease and in the Overall Population

Adjuvant osimertinib demonstrated improvement in OS vs placebo in the primary population of stage II-IIIA disease

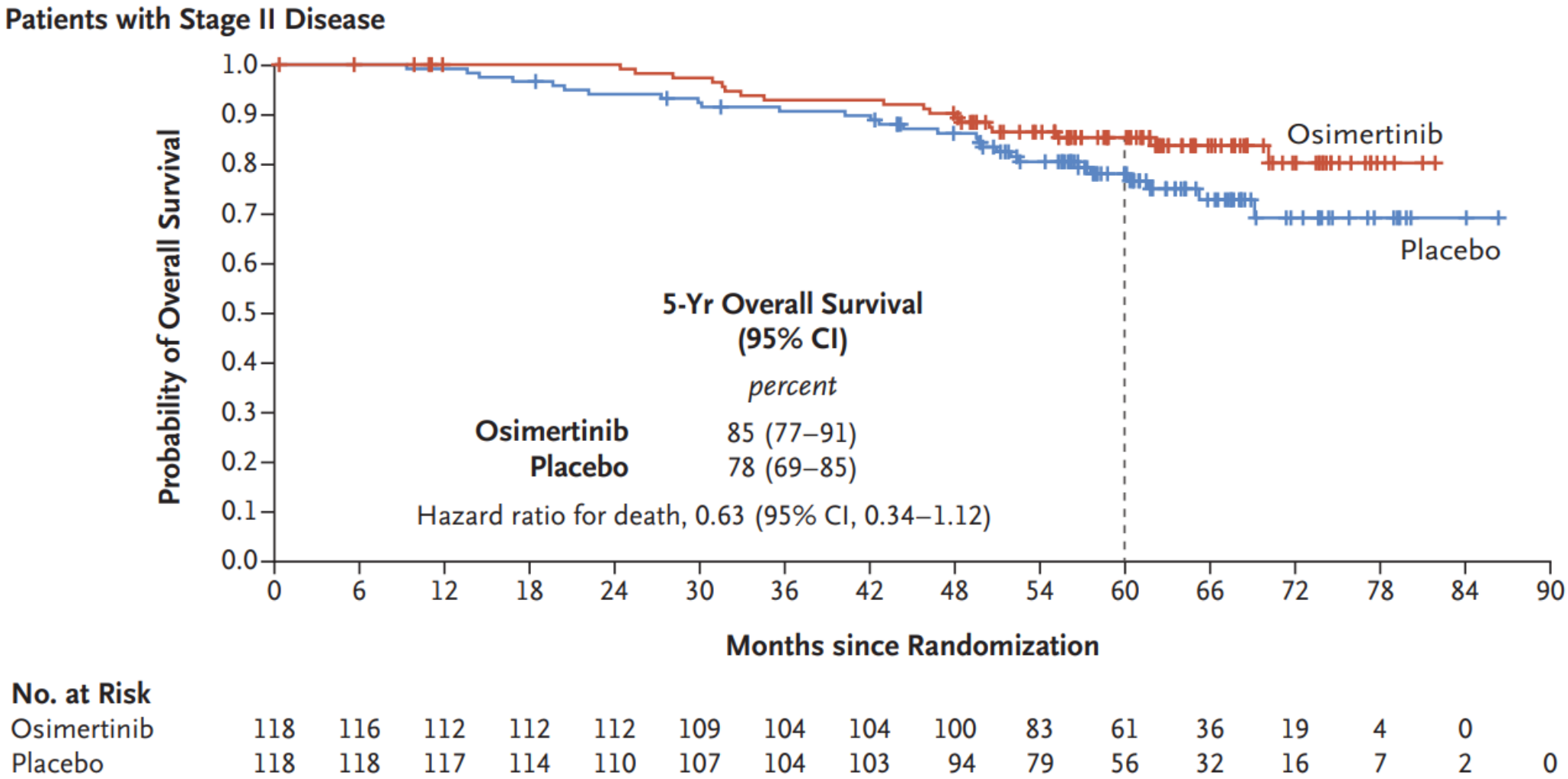


No. at Risk															
Osimertinib	233	229	224	224	221	214	208	205	200	170	115	69	33	9	0
Placebo	237	232	226	221	210	202	190	182	171	138	94	53	25	8	2	0

HealthCare
MARKEY CANCER CENTER
Network

Wu YL et al, NEJM 2023

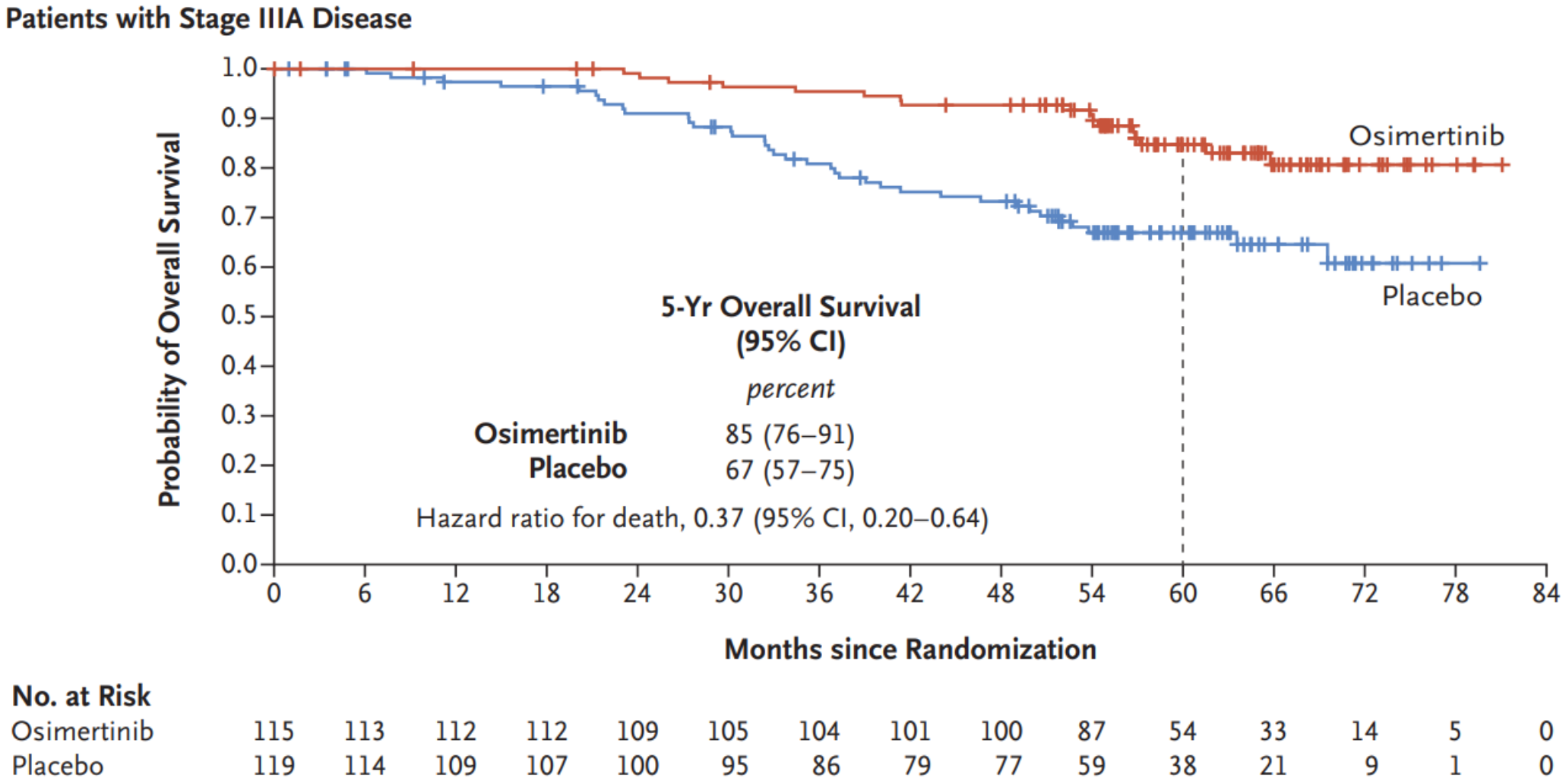
Overall survival by disease stage



HealthCare
MARKEY CANCER CENTER
Network

Wu YL et al, NEJM 2023

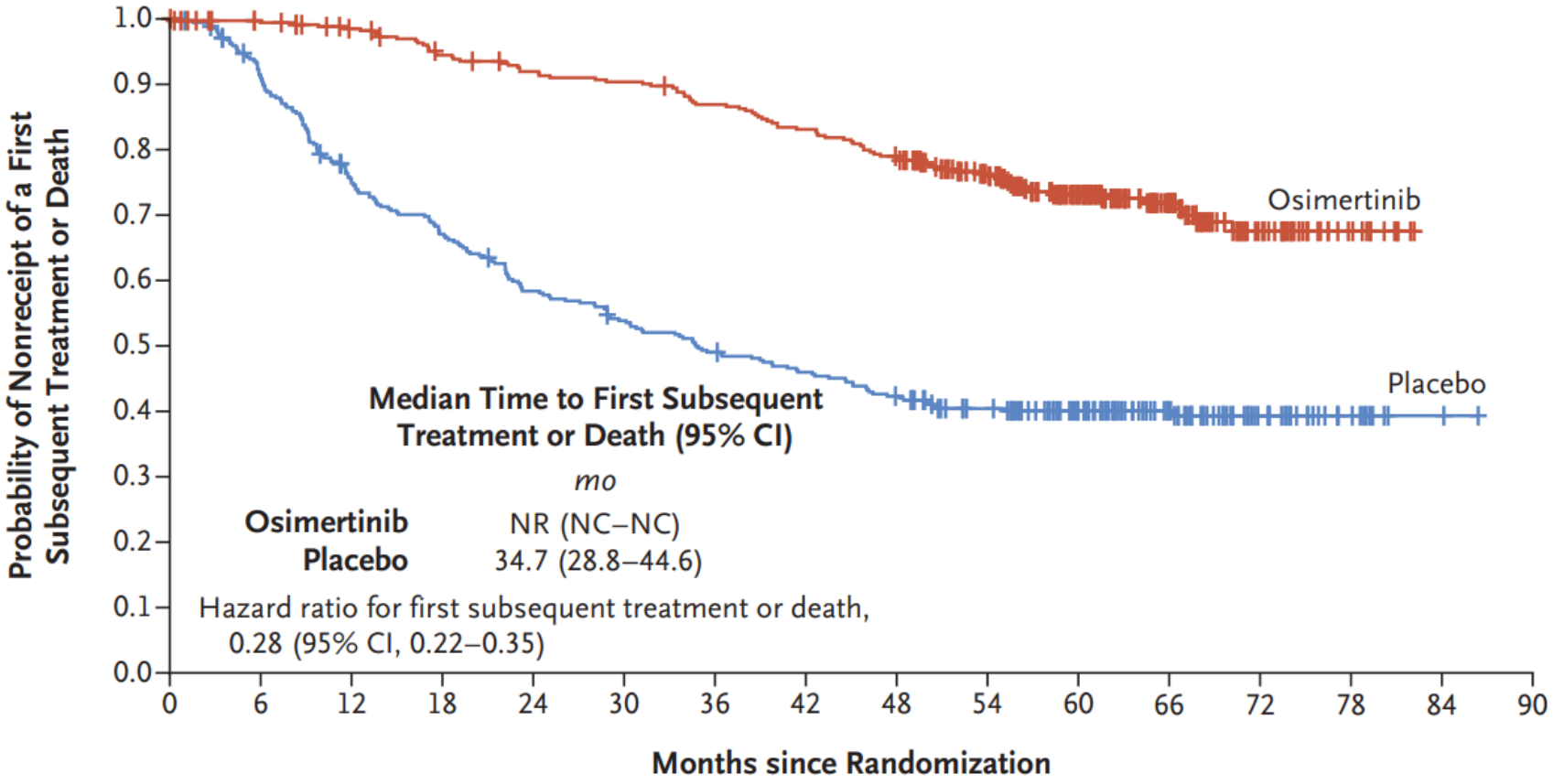
Overall survival by disease stage



HealthCare
MARKEY CANCER CENTER
Network

Wu YL et al, NEJM 2023

Time to First Subsequent Treatment or Death in the Overall Population



No. at Risk															
Osimertinib	339	328	318	302	292	287	275	263	249	208	147	87	37	12	0
Placebo	343	308	250	224	194	178	162	151	138	118	89	54	27	10	2	0

HealthCare MARKEY CANCER CENTER Network

Wu YL et al, NEJM 2023

ADAURA Conclusions

- In the ADAURA primary analysis, adjuvant osimertinib demonstrated a statistically significant[1] and clinically meaningful DFS benefit vs placebo in resected EGFRm stage IB–IIIA NSCLC, along with improved CNS DFS and a tolerable safety profile[1,2]
- **DFS benefit in ADAURA has translated into a statistically significant OS benefit with adjuvant osimertinib vs placebo**
  - **Primary (stage II–IIIA) population, OS HR 0.49; 95.03% CI 0.33, 0.73; p=0.0004**
  - **Overall (stage IB–IIIA) population, OS HR 0.49; 95.03% CI 0.34, 0.70; p<0.0001**
- OS benefit with adjuvant osimertinib vs placebo was generally consistent across subgroups, including by disease stage (IB / II / IIIA) and prior adjuvant chemotherapy use (yes / no)

ADAURA is the first global Phase III study to demonstrate statistically significant and clinically meaningful OS benefit with targeted treatment in this patient population, reinforcing adjuvant osimertinib as the standard of care for patients with resected EGFRm stage IB–IIIA NSCLC

Data cut-off: January 27, 2023.

1. Wu et al. N Engl J Med 2020;383:1711–1723; 2. Herbst et al. J Clin Oncol 2023;41:1830–1840.

Herbst et al, ASCO2023#LBA3


IASLC
2022 World Conference on Lung Cancer
AUGUST 6-9, 2022 | VIENNA, AUSTRIA
IMpower010: Overall survival interim analysis of a phase III study of atezolizumab vs best supportive care in resected NSCLC
Enriqueta Felip,[1] Nasser Altorki,[2] Eric Vallieres,[3] Ihor O. Vynnychenko,[4] Andrey Akopov,[5] Alex Martinez-Marti,[1] Antonio Chella,[6] Igor Bondarenko,[7] Shunichi Sugawara,[8] Yun Fan,[9] Hirotsugu Kenmotsu,[10] Yuh-Min Chen,[11] Yu Deng,[12] Meilin Huang,[12] Virginia McNally,[13] Elizabeth Bennett,[12] Barbara J. Gitlitz,[12] Caicun Zhou,[14] Heather A. Wakelee[15]
[1]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [2]NewYork-Presbyterian Hospital, Weill Cornell Medicine, New York, NY, USA; [3]Swedish Cancer Institute, Seattle, WA, USA; [4]Regional Municipal Institution Sumy Regional Clinical Oncology Dispensary, Sumy State University, Sumy, Ukraine; [5]Pavlov State Medical University, Saint Petersburg, Russia; [6]Pneumology Unit, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy; [7]Dnipro State Medical University, Dnipro, Ukraine; [8]Sendai Kousei Hospital, Miyagi, Japan; [9]Zhejiang Cancer Hospital, Hanzhou, China; [10]Shizuoka Cancer Center, Shizuoka, Japan; [11]Taipei Veterans General Hospital and National Yang Ming Chiao Tung University, Taipei, Taiwan; [12]Genentech Inc, South San Francisco, CA, USA; [13]Roche Products Ltd, Welwyn Garden City, United Kingdom; [14]Tongji University Affiliated Shanghai Pulmonary Hospital, Shanghai, China; [15]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA.
IMpower010 OS IA. https://bit.ly/3InK8SP
Presented by Dr Enriqueta Felip

IMpower010: Phase III randomised trial of atezolizumab vs BSC in early-stage NSCLC

Completely resected stage IB-IIIA[a] NSCLC

- Stage IB tumors ≥4 cm
- ECOG 0-1
- Lobectomy
- Tumor tissue for PD-L1 analysis

Cisplatin + pemetrexed, gemcitabine, docetaxel or vinorelbine

1-4 cycles

N=1280

R 1:1

No crossover

Atezolizumab 1200 mg q21d x 16 cycles or 1 year

N = 1005

BSC

Survival follow-up

Stratification factors

- Sex | Stage | Histology | PD-L1 status

Primary endpoint

- Investigator-assessed DFS tested hierarchically

Key secondary endpoints

- OS in ITT | DFS in PD-L1 TC ≥50% | 3-yr and 5-year DFS

Key exploratory endpoints

- OS biomarker analyses

Clinical cutoff: 18 April 2022. Both arms included observation and regular scans for disease recurrence on the same schedule. ECOG, Eastern Cooperative Oncology Group, q21d, every 21 days.
[a] Per UICC/AJCC staging system, 7th edition. [b] Two-sided α=0.05.

Hierarchical statistical testing of endpoints

DFS in PD-L1 TC ≥1% stage II–IIIA population[b]

If positive:

DFS in all-randomized stage II–IIIA population[b]

If positive:

DFS in ITT population (stage IB-IIIA)[b]

If positive:

OS in ITT population[b]

Endpoint was met at DFS IA

Endpoint was not met at DFS IA and follow up is ongoing

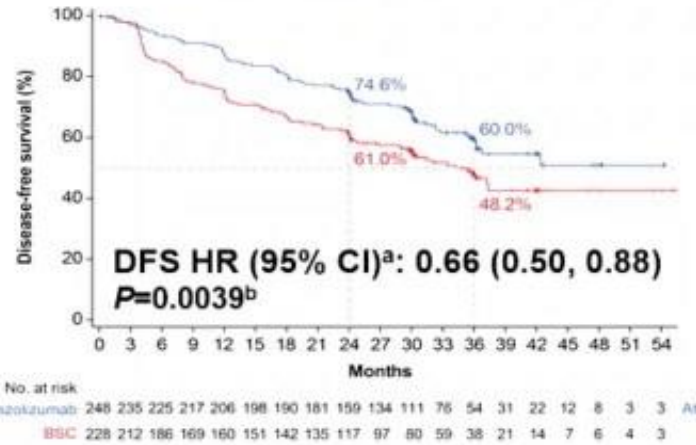
Endpoint was not formally tested

IMpower010 OS IA. https://bit.ly/3InK8SP
Presented by Dr Enriqueta Felip

Recap of DFS and OS data from the DFS IA[1,2]

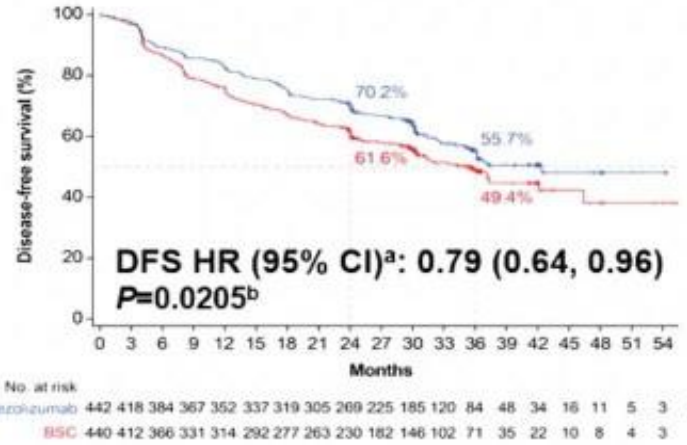
(data cutoff: 21 Jan '21, median follow-up: 32 months)

DFS: PD-L1 TC ≥1% stage II-IIIA population



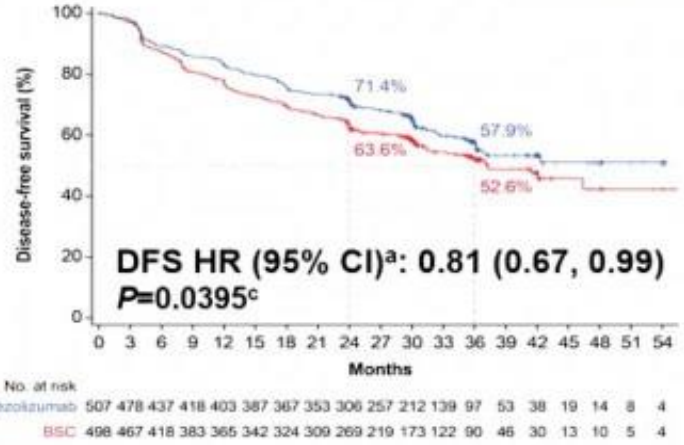
DFS HR (95% CI)[a]: 0.66 (0.50, 0.88)
***P*=0.0039[b]**

DFS: All-randomised stage II-IIIA population



DFS HR (95% CI)[a]: 0.79 (0.64, 0.96)
***P*=0.0205[b]**

DFS: ITT (randomised stage IB-IIIA) population



DFS HR (95% CI)[a]: 0.81 (0.67, 0.99)
***P*=0.0395[c]**

- **OS data** were not mature (event to patient ratio in ITT was 19% in atezolizumab arm, 18% in BSC arm)
  - PD-L1 TC ≥1% stage II-IIIA population: OS HR, 0.77 (95% CI: 0.51, 1.17)[a]
  - All-randomised stage II-IIIA population: OS HR, 0.99 (95% CI: 0.73, 1.33)[a]
  - ITT (randomised stage IB-IIIA) population: OS HR, 1.07 (95% CI: 0.80, 1.42)[a]

Clinical cutoff: 21 Jan 2021. [a] Stratified. [b] Statistical significance boundary for DFS crossed. [c] Statistical significance boundary for DFS not crossed.

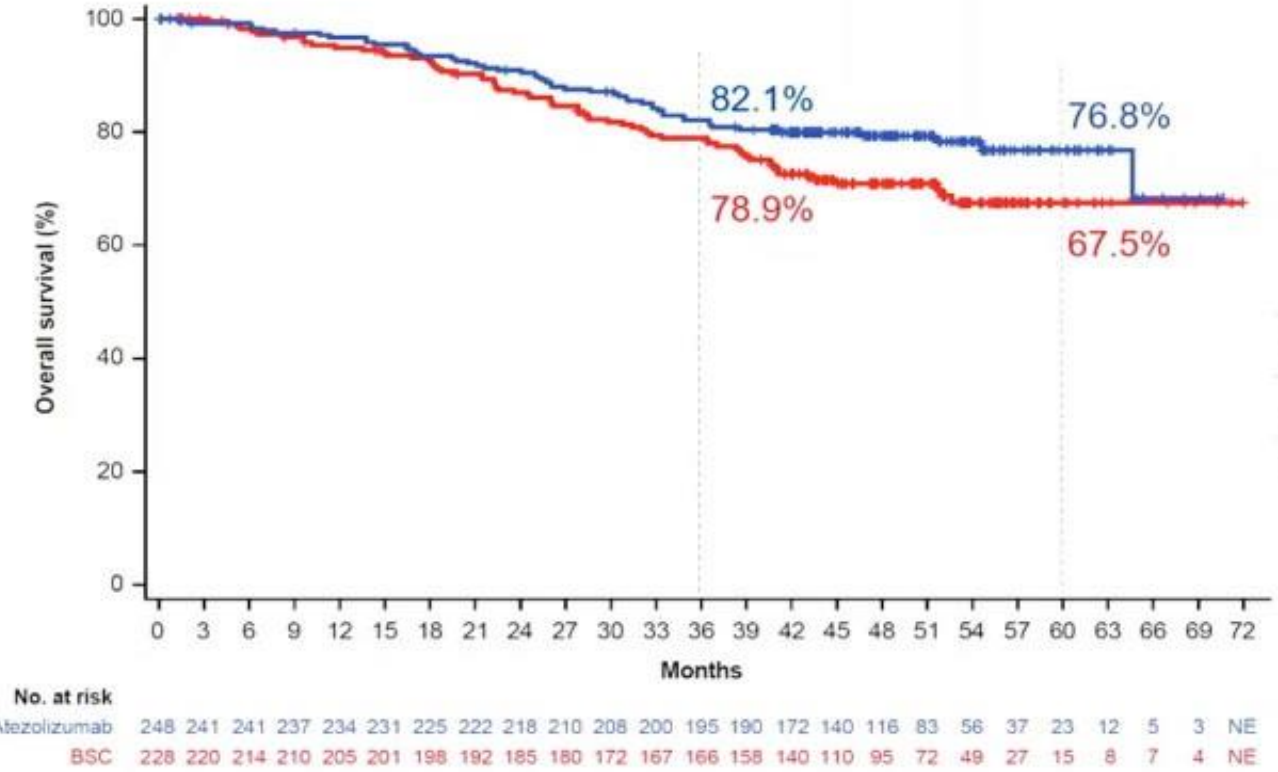
1. Felip, E et al Lancet 2021; 938; 1344-1357; 2. Wakelee. HA et al ASCO 2021; abs #8500.

IMpower010 OS IA. https://bit.ly/3InK8SP
Presented by Dr Enriqueta Felip

HealthCare
MARKEY CANCER CENTER
Network

Results of OS IA: PD-L1 TC ≥1%[a] (stage II-IIIA)

(data cutoff: 18 Apr '22, median follow-up: 46 months)



	Atezo (n=248)	BSC (n=228)
Events, n (%)	52 (21.0%)	64 (28.1%)
mOS (95% CI), mo	NR	NR
HR (95% CI)[b]	0.71 (0.49, 1.03)	

mOS, median overall survival; NR, not reached. [a]By SP263 assay. [b]Stratified.

IMpower010 OS IA. https://bit.ly/3InK8SP
Presented by Dr Enriqueta Felip

HealthCare
MARKEY CANCER CENTER
Network

Conclusion

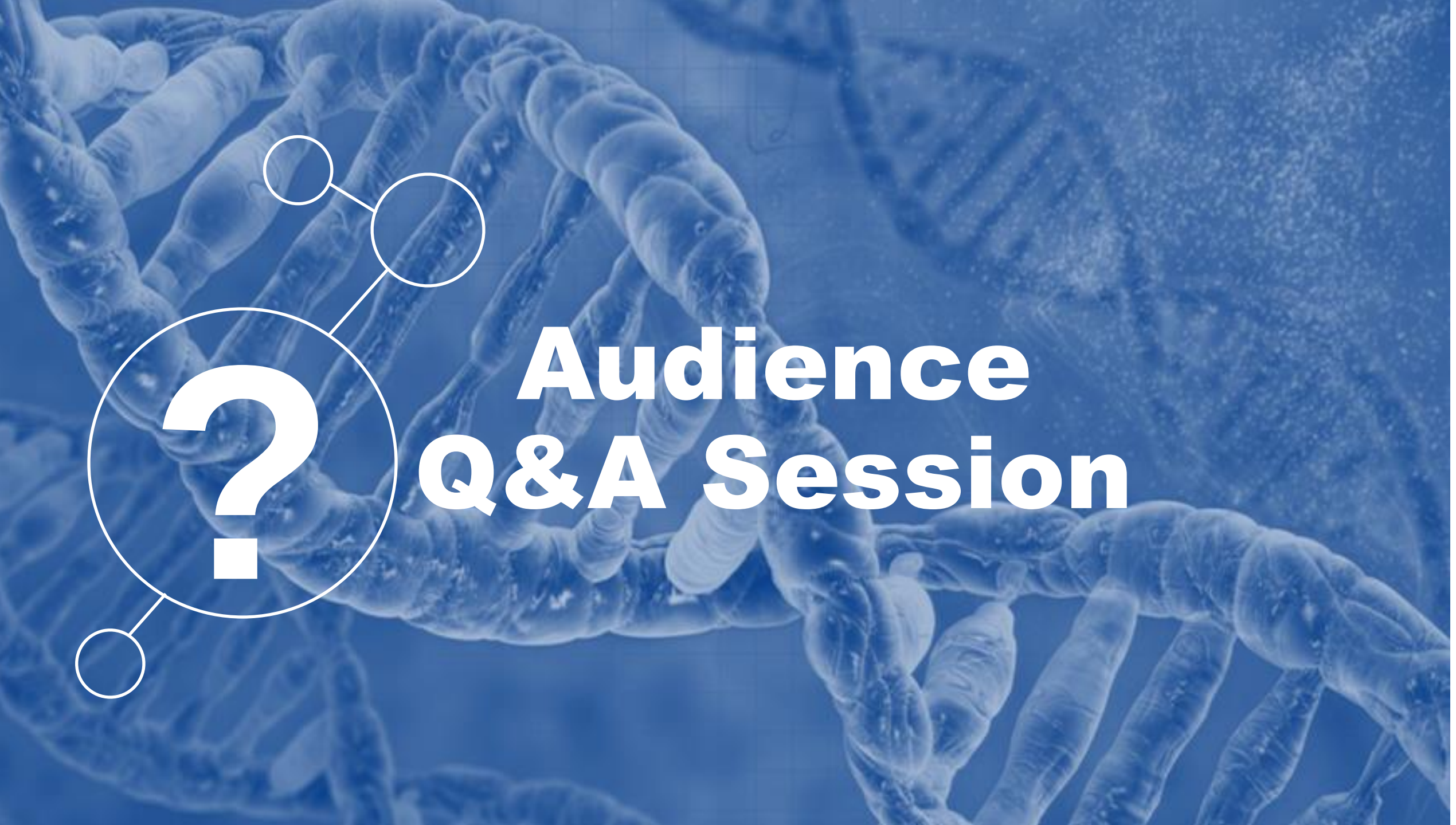
- Lung cancer screening leads to early detection and treatment.
- There is a drop off in cancer survival after Stage I
- Minimally invasive approaches to lung resection are considered the standard of care in Stage I NSCLC

- Advances in genomic testing are *Expanding the Scope* of patients amenable to surgical management
- Multidisciplinary Management (tumor boards and molecular tumor boards) are critical to improving communication

HealthCare
MARKEY CANCER CENTER
Network

A Time of Change
New technology
Promising Outcomes

A Time for Hope


Audience
Q&A Session

Thank you for Attending!

Join us for the next session: Tuesday, November 7th from 12 – 1 PM EDT

"Optimizing the Management of Newly Diagnosed Ovarian Cancer Including Maintenance"

Tricia Fredericks, MD

Learn More:


OncoLens.com


info@OncoLens.com

UK HealthCare MARKEY CANCER CENTER Network

Powered by: ONCOLENS

Sponsored by: AstraZeneca