



**Practical Updates
in Primary Care**

Empowering Primary Care Providers in Non-Small Cell Lung Cancer Care: Strategies to Enhance Screening, Treatment, Adverse Event Management, and Multidisciplinary Care

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Disclosures

- **Michael Gieske, MD:** Consultant – ACCC, AstraZeneca, Eisai, Exact Sciences, Gilead, GlaxoSmithKline, Inivata, LUNgevity, Merck, Novartis, Pfizer, Roche; Advisory Board – AstraZeneca, Eisai, Exact Sciences, Gilead, GlaxoSmithKline, Inivata, Merck, Novartis, Pfizer, Roche
- **Sandip Patel, MD, FASCO** has nothing to disclose in relation to this activity



Learning Objectives

- Apply guideline-recommended strategies for the screening and early detection of NSCLC
- Interpret the clinical data of available/emerging treatment options for EGFR-mutant NSCLC
- Employ strategies to mitigate, manage, and anticipate treatment-related adverse events associated with EGFR-targeted therapies
- Optimize the identification, treatment, and survivorship of patients with NSCLC through personalized and multidisciplinary care





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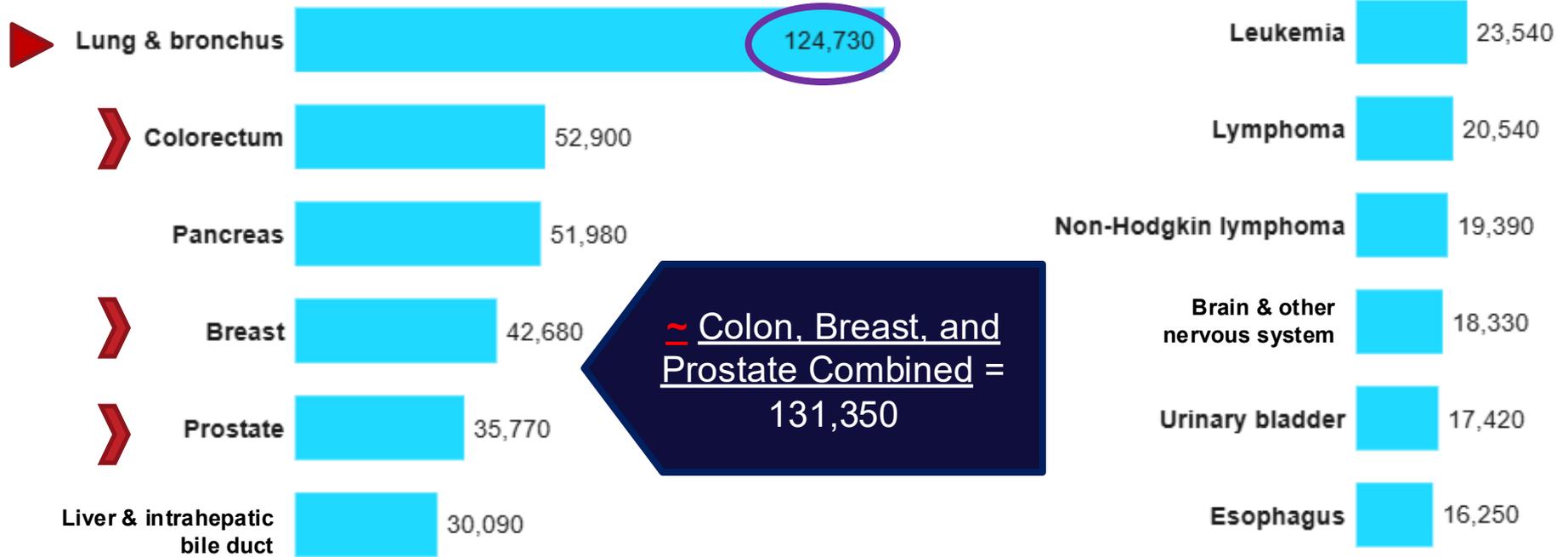
The State of Lung Cancer

Michael Gieske, MD
Director, Lung Cancer Screening
St. Elizabeth Healthcare

Cancer Death Estimates: American Cancer Society

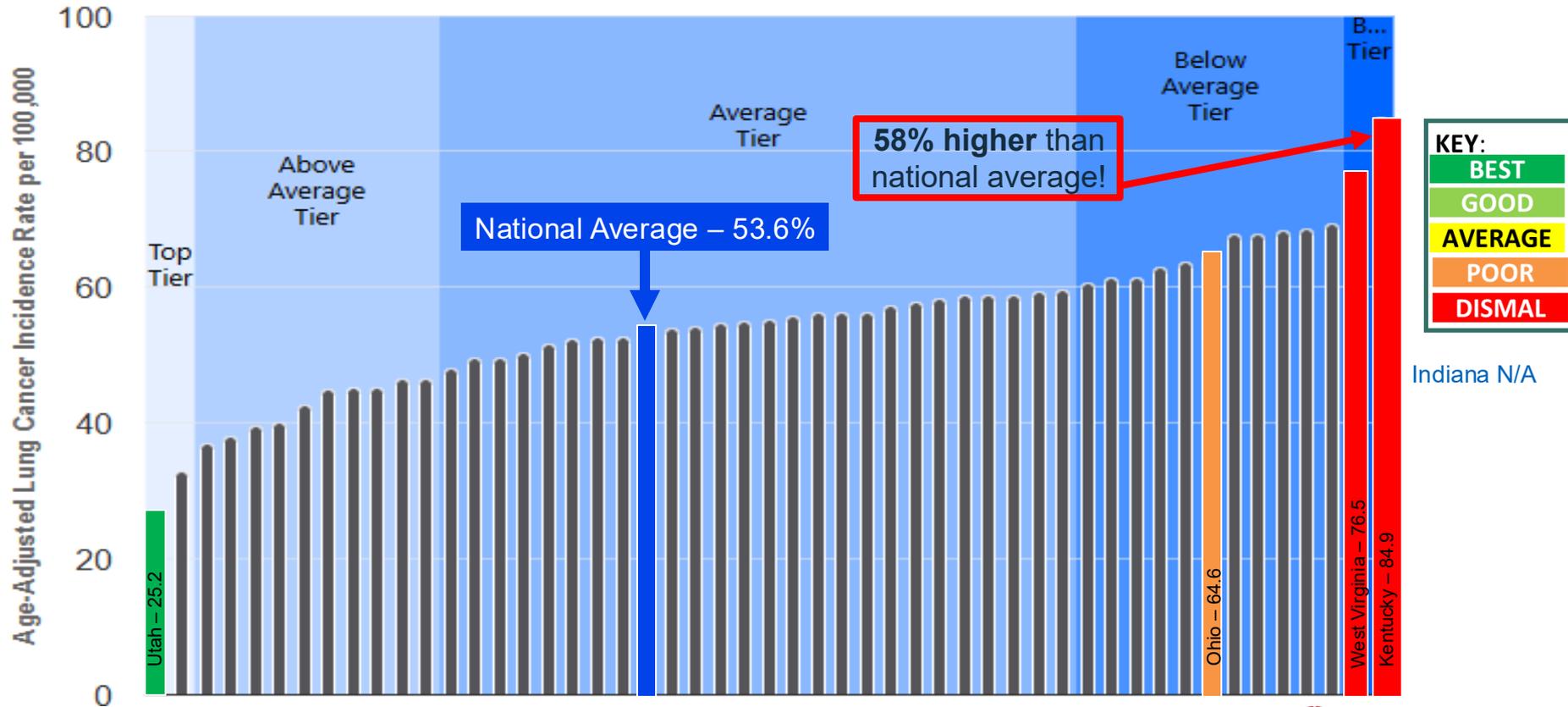
2025 Estimated Cancer Deaths

#1 Cancer Killer in the USA
and the World



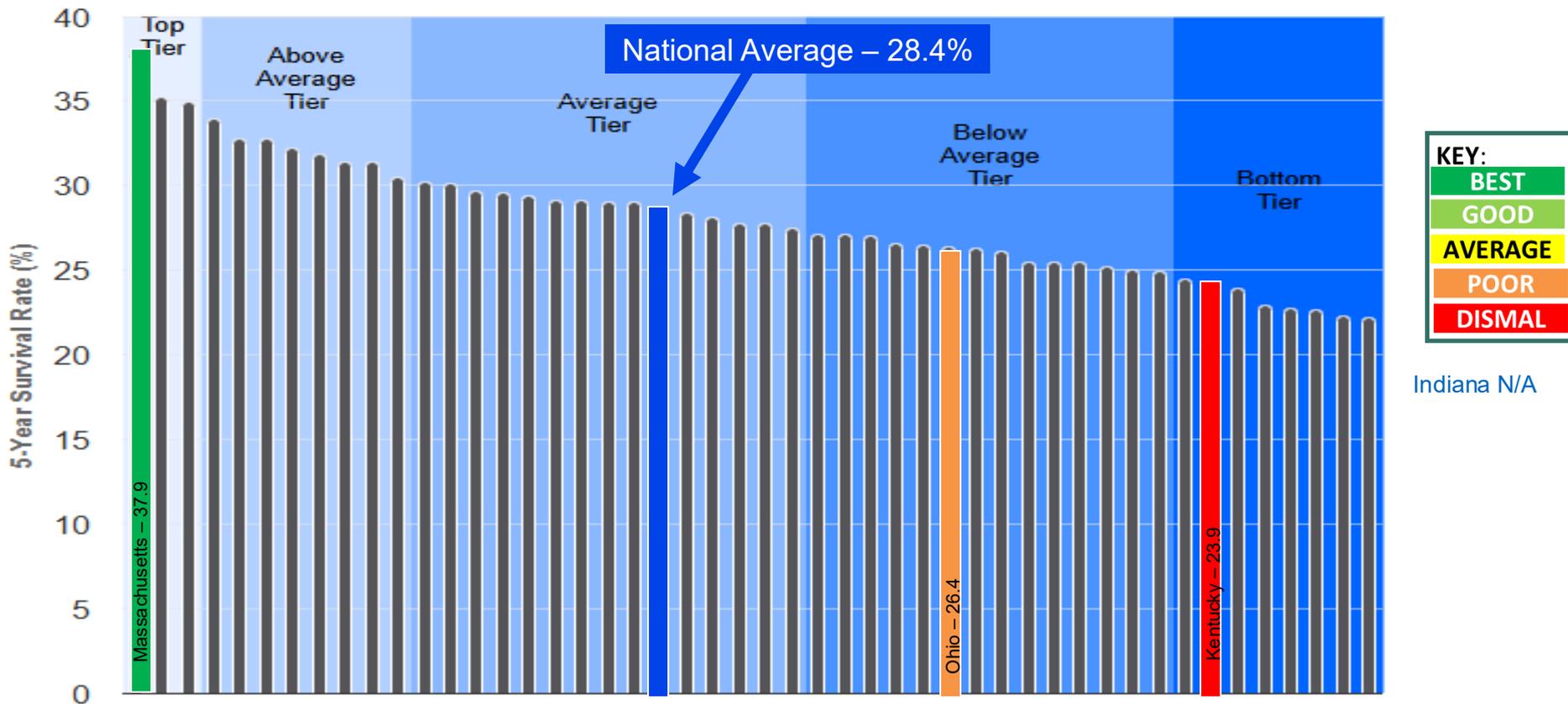
National Lung Cancer Incidence

State Rankings by Rate of New Cases



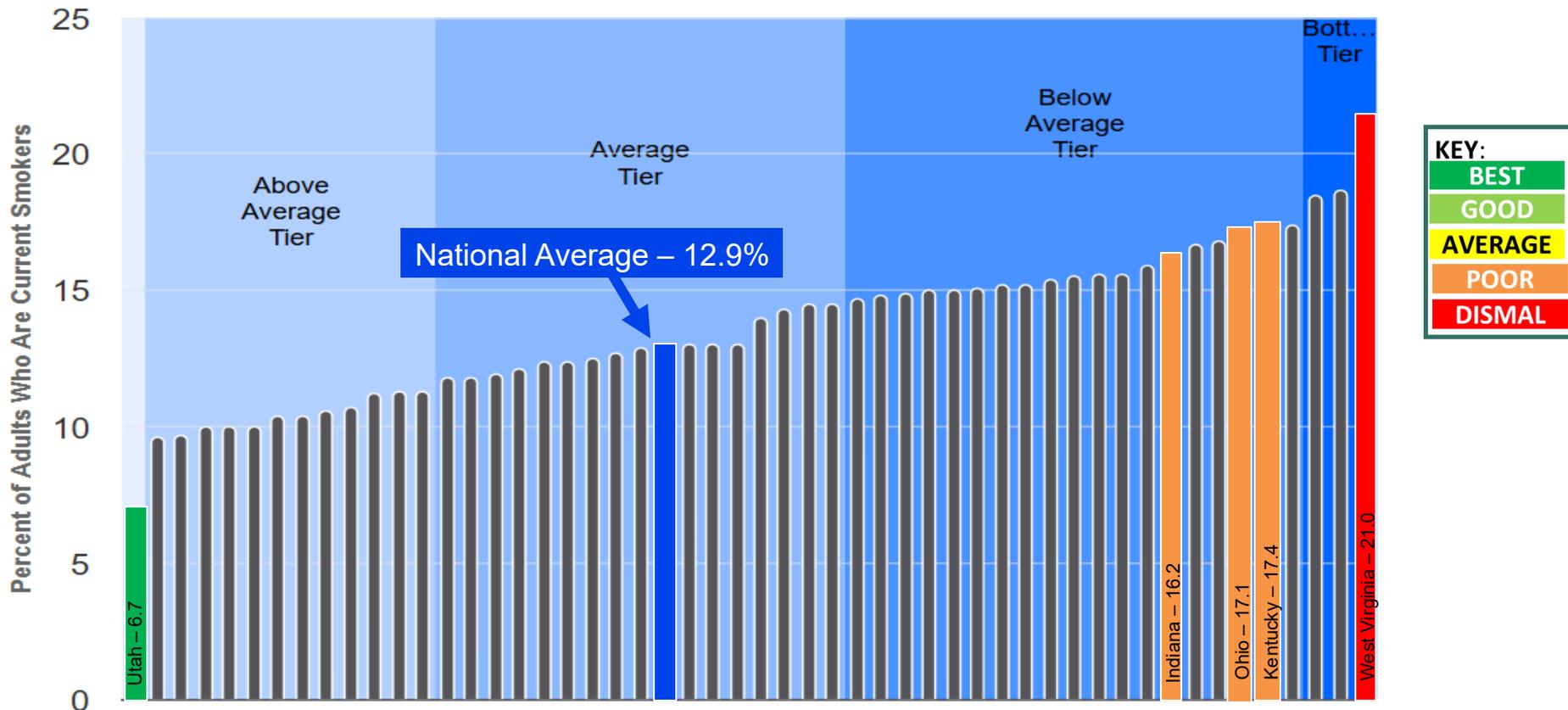
National Lung Cancer 5-Year Survival

State Ranking by Survival Rate



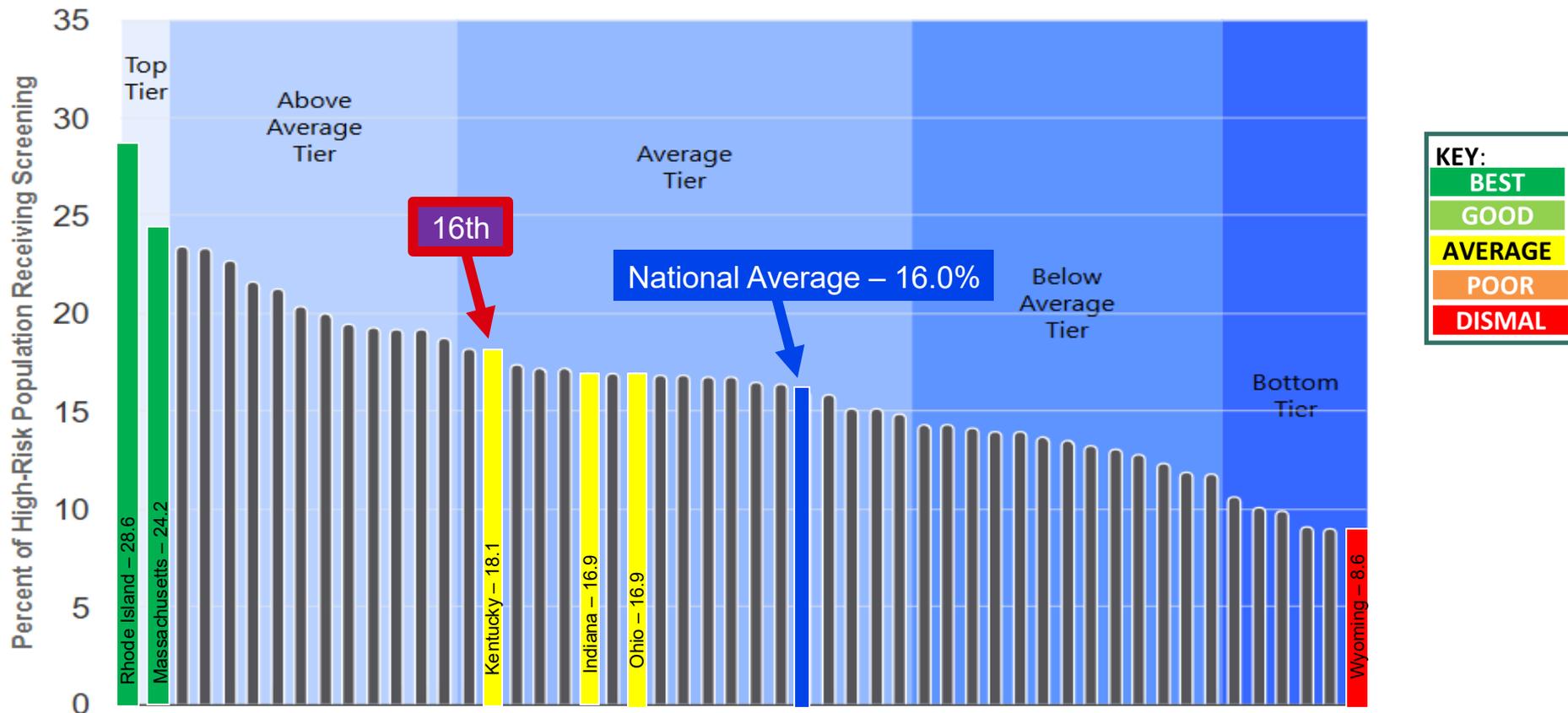
National Smoking Prevalence

State Ranking by Smoking Rate



National Lung Cancer Screening Rates

State Ranking by High-Risk Screening Rate



When it Comes to Survival, STAGE MATTERS

5-Year Survival Rates from 2018 American Cancer Society

5-Year Survival Rate Non-Small Cell Lung Cancer (NSCLC)		
Stage	IA1	92%
	IA2	83%
	IA3	77%
	IB	68%
	IIA	60%
	IIB	53%
	IIIA	36%
	IIIB	26%
	IIIC	13%
	IVA	10%
	IVB	<1%

These numbers come from thousands of people from all over the world who were diagnosed with NSCLC between 1999 and 2010. Although the numbers are based on people diagnosed several years ago, they are the most recent rates published for the current AJCC staging system.

5-Year Survival Rate Small Cell Lung Cancer (SCLC)		
Stage	I	31%
	II	19%
	III	8%
	IV	2%

These numbers are relative survival rates calculated from the National Cancer Institute's SEER database, based on people who were diagnosed with SCLC between 1988 and 2001.

These survival rates are based on the TNM staging system in use at the time, which has since been modified slightly for the latest version. Because of this, the survival numbers may be slightly different for the latest staging system.

Stage Matters!

American Joint Committee on Cancer (AJCC). *Cancer Staging Manual*. 8th ed. Springer; 2017.
National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) Program. Updated
2023. Accessed May 1, 2025. Available at: <https://seer.cancer.gov/statfacts/html/lungb.html>.



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Making a Difference!

**Michael Gieske, MD
Director, Lung Cancer Screening
St. Elizabeth Healthcare**

LDCT – The Patient Experience



- Overall, the entire process takes about 15 minutes or so; the scan itself takes less than 3 minutes
- LDCT uses X-rays to scan the entire chest in about 5 to 10 seconds during a single breath-hold; less than background dose of radiation for 1 yr, 1.3 mSv
- The process is performed without needles or contrast/dye

LDCT = low-dose computed tomography.
Lowenstein LM, et al. *Transl Lung Cancer Res.* 2018;7(3):254-271.



Practical Updates
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USPSTF Recommendation – March 9, 2021



St. Elizabeth implemented March 1, 2022

Recommendation Summary

Population	Recommendation	Grade
Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	The USPSTF recommends <u>annual screening</u> for lung cancer with low-dose computed tomography (LDCT) in adults aged <u>50 to 80 years</u> who have a <u>20 pack-year</u> smoking history and currently smoke or have quit within the <u>past 15 years</u> . Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

Commercial insurance payers have 1 year after the USPSTF guidelines are finalized to cover A and B recommendations under the PPACA; year begins after date of insurance contract renewal.

USPSTF = US Preventive Services Task Force; PPACA = Patient Protection and Affordable Care Act.
USPSTF. March 9, 2021. Accessed May 1, 2025.

<https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening>.



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CMS Coverage Determination – February 10, 2022

2022 CMS Criteria

- 50 to **77 yo**
- **≥20 pack-year**
- **Smoked in last 15 years**
- **Asymptomatic**
- **SDM mandated for baseline screen**

Reasoning

We find that the human clinical evidence is not sufficient to conclude that lung cancer screening with low-dose CT is reasonable and necessary for Medicare beneficiaries with the specific eligibility criterion for stopping low-dose CT screening at age 80 years. The Medicare beneficiary eligibility criterion for stopping age will not be changed and will remain at 77 years old.



American Cancer Society's Lung Cancer Screening Guidelines – Updated November 1, 2023



Cigarette smoking significantly increases the risk of lung cancer and mortality

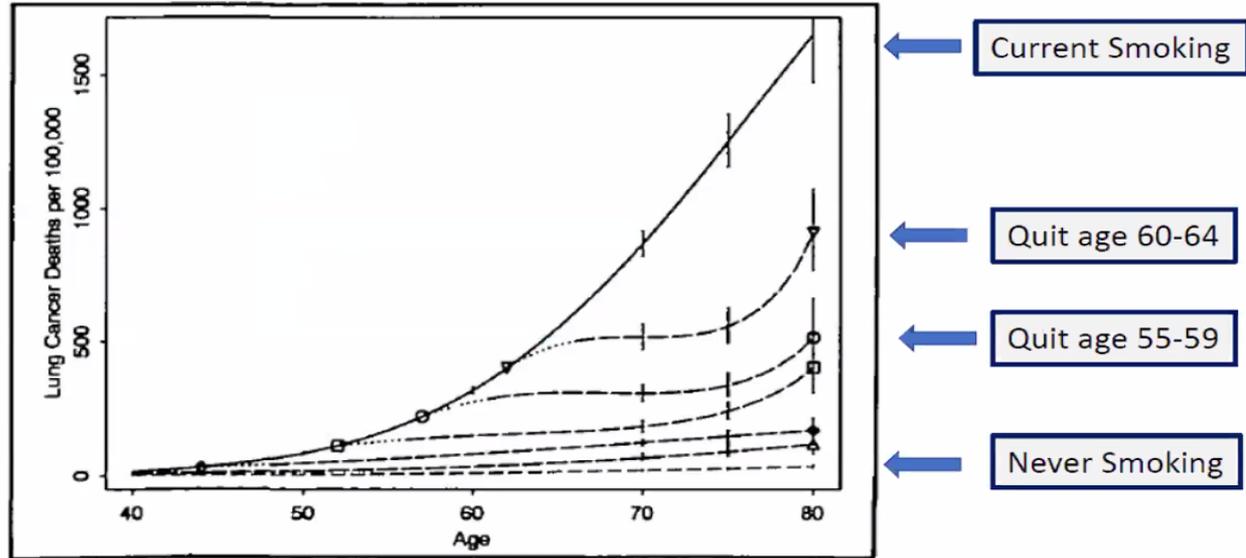
In 2013, the American Cancer Society (ACS) recommended that persons, aged 55–74 years with a 30 or greater pack-year smoking history, including those who had quit smoking within 15 years, undergo annual screening with low-dose computed tomography (LDCT)

However, evidence suggests that the risk of lung cancer remains high beyond 15 years after quitting and increases with age

 **The updated guideline recommends annual LCS with LDCT for asymptomatic persons who smoke or used to smoke (aged 50 to 80 years) and have a 20 or more pack-year smoking history.**

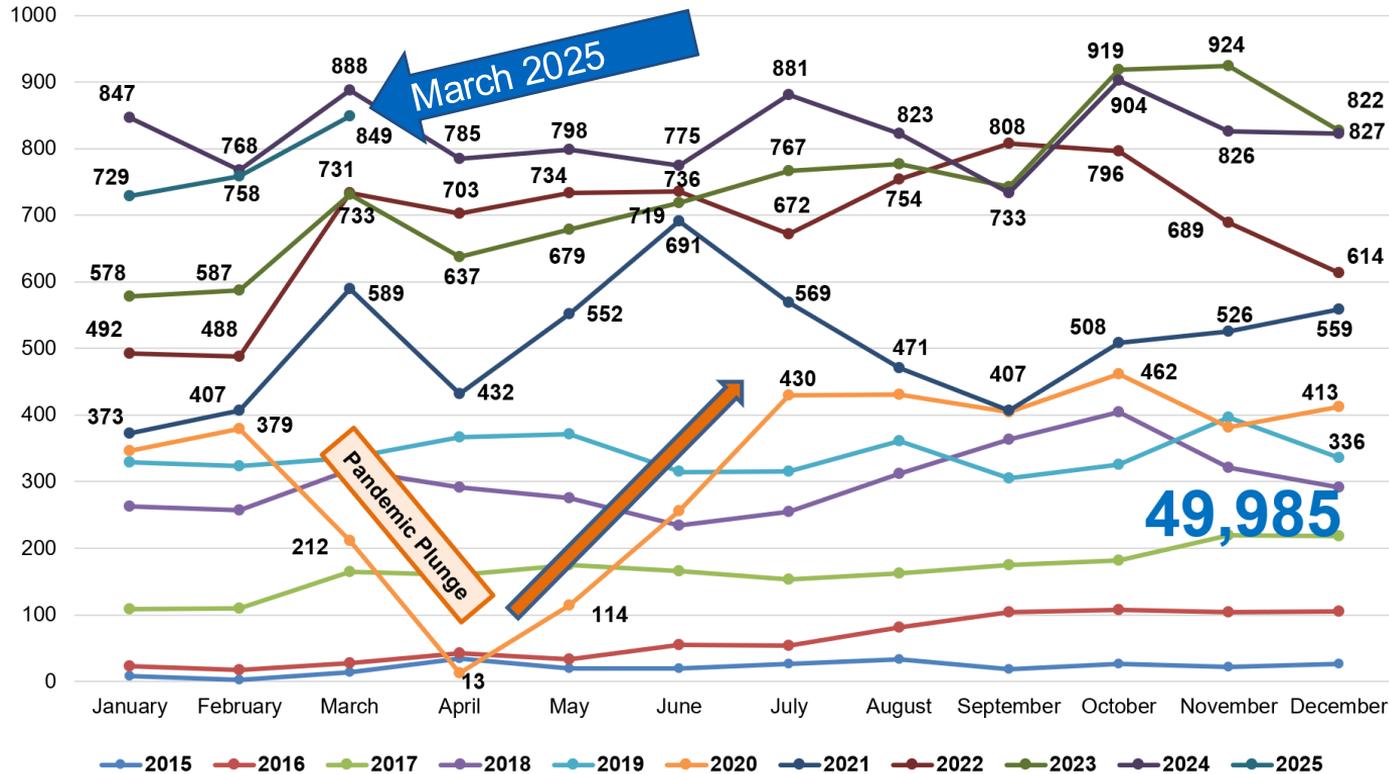
Lung Cancer Mortality and Age

Quitting after age 50 reduces the risk of lung cancer death compared with people who continue to smoke, but following a plateau after cessation, risk of lung cancer death rises significantly.



Tracking Our Progress

St. Elizabeth LDCT Screening Volumes (2015 – 2025 YTD)



Year	Total LDCT Screening
2013	7
2014	121
2015	252
2016	753
2017	1,965
2018	3,585
2019	4,082
2020*	3,843
2021	6,084
2022**	8,219
2023	8,888
2024	9,850
2025	2,336

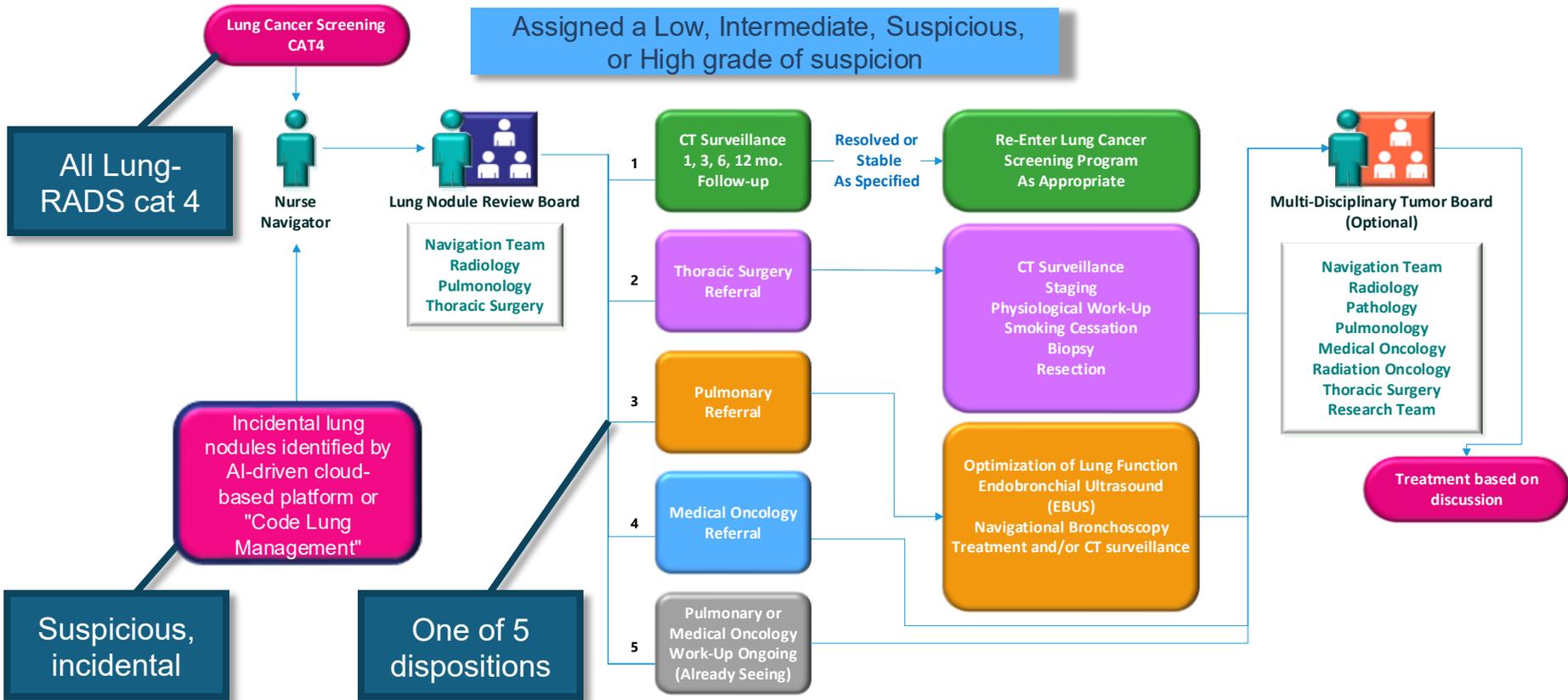
*5.81% pandemic reduction 2020 vs 2019; **Methodology to include incident and interval screens starting 2022.
LCS = lung cancer screenings.

50,000 LCS completed as of 3/17/25!



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Our Nodule Review Board



EMR – Health Maintenance Prompt

← Snapshot Chart Review Plan Wrap-Up Rooming Results Immunizations Medications **HM** History Care Everywhere Teams Growth Problems Flow

Health Maintenance

Address Topic Remove Override Edit Modifiers Report Refresh Guidelines

New data from outside sources

Problems and Immunizations need attention. [Go Reconcile](#)

Topic	Due Date	Frequency	Date Completed
Diabetic Eye Exam	Overdue since 6/19/2021	2 year(s)	6/19/2019 - HM DIABETES EYE EX...
Influenza Vaccine (1)	Due soon on 9/1/2021	Imm Details	12/8/2017 (Declined)
Upcoming			
Hemoglobin A1c	Next due on 2/10/2022	6 month(s)	8/10/2021 - HEMOGLOBIN A1C
Wellness Exam Medicare	Next due on 7/16/2022	1 year(s)	7/16/2021 - AMB Last Preventative...
Fall Risk Assessment	Next due on 7/16/2022	1 year(s)	7/16/2021 - Fall Risk Filing Date
Lipids	Next due on 8/10/2022	1 year(s)	8/10/2021 - LIPID SCREEN
Low Dose Lung Cancer Screening	Ordered on 8/27/2021	1 year(s)	8/26/2021 - CT LUNG CANCER SC...
DTaP/TDaP/Td (2 - Td or Tdap)	Next due on 2/20/2023	Imm Details	2/20/2013 - Tdap

Satisfied

Overdue!

Low Dose Lung Cancer Screening

Low Dose Lung Cancer Screening

Satisfied

COVID-19 Vaccine (1)	Overdue - never done	Imm Details	
DTaP/TDaP/Td (1 - Tdap)	Overdue since 9/2/1996	Imm Details	9/1/1996 - Td, Unspecified Formulati...
Colon Cancer Screening: Colonoscopy	Overdue - never done	10 year(s)	
Zoster (2 of 3)	Overdue since 2/14/2015	Imm Details	12/20/2014 - Zoster 2013 - Zoster
Low Dose Lung Cancer Screening	Overdue since 4/14/2019	1 year(s)	4/14/2018 - CT LUNG CANCER SC... 14/2014 - CT CHEST W CONTRA...
Annual Wellness Exam	Overdue since 1/20/2021	1 year(s)	1/20/2020 - AMB Last Preventative... 3/1/2017 (Postponed)
Fall Risk Assessment	Overdue - never done	1 year(s)	
AAA Screening	Overdue - never done	Once	
Influenza Vaccine (1)	Due soon on 9/1/2021	Imm Details	10/23/2018 - Influenza Virus Vaccin... 3/24/2018 (Declined)
Upcoming			
Pneumococcal Vaccine 65+ (2 of 2 - PPSV23)	Next due on 10/23/2023	Imm Details	10/23/2018 - Pneumococcal Polysac...



LDCT LCS BPA – Best Practice Advisory/Alert

HospF/U,TCM COPD CHF PCMH DMHTL PCMH HT PCMH HLipidemia PCMH COPD PCMH CHF
PCMH Office Note PCMH Welcome MC PCMH MC Wellness, Subsequent APSO PREOP APSO Office LONG
APSO Hospital F/U PCMH PRE-OP 2.15.18 PCMH Dynamic SOAP Note 2.15.18 COVID19PROGRESSNOTEMG
VIRTUAL VISIT VV or TV - OFFICE NOTE Virtual Health Center Note

BestPractice Advisory

Important (1)

ⓘ Your patient has not had CT low dose lung cancer screening this year. Please address whether a screening order should be done at today's office visit.

Open SmartSet Do Not Open Low Dose Lung Cancer Screening [Preview](#)

Acknowledge Reason _____

Patient Refused Contraindicated Previously Ordered-Pending Completion Other-See Comments

✓ **Accept** **Dismiss**

H & P Notes

+ Create Note in NoteWriter + Create Note See All Notes Refresh

BPA = best practice advisory.

Our LCS EMR SmartSet

Low Dose Lung Cancer Screening [Manage User Versions](#)

**** Advise patients to check with their insurance carrier to determine coverage benefits prior to completing this screening ****

▼ **Diagnosis**

▶ Diagnosis [Click for more](#)

▼ **Testing**

▼ **Testing**

CT LUNG CANCER SCREENING LOW DOSE - Baseline (\$)

Expires: 9/19/2023, Routine, Ancillary Performed

▼ **Uninsured/Underinsured Assistance Referral for Lung Screening**

Uninsured/Underinsured Referral - Lung Screening

▼ **Documentation**

▼ **Documentation**

AMB LUNG CANCER SCREENING SHARED DECISION MAKING NOTE

▼ **Education**

▼ **Education**

Lung Cancer Screening Education

▼ **Charges**

▼ **Additional Code**

PR VISIT TO DETERMINE LDCT ELIG
[Clinic Performed, Qty-1](#)

G0296

**0.52
wRVU**

▼ **Diagnosis**

- Encounter for screening for lung cancer [Z12.2]
- Cigarette smoker [F17.210]
- Cigarette nicotine dependence in remission [F17.211]
- Cigarette nicotine dependence with withdrawal [F17.213]
- Nicotine dependence, cigarettes, with other nicotine-induced disorders [F17.218]
- Cigarette nicotine dependence with nicotine-induced disorder [F17.219]
- Personal history of tobacco use, presenting hazards to health [Z87.891]
- Nicotine dependence [F17.200]

Best collectively covered codes for MC/MC, commercial; F17.210 and Z87.891



Our LCS EMR SmartSet, Baseline or Annual

CT LUNG CANCER SCREENING LOW DOSE - Annual (\$)

Confirmed

Is the patient Asymptomatic? Yes No

Is this the first (baseline) LDCT lung cancer screen or an annual exam? Baseline Annual Baseline

I have discussed with the patient the benefits and harms of lung cancer screening, including potential follow-up testing. Yes No Annual - no SDM discussion

I have counseled the patient on the importance of adhering to the annual screening and their ability or willingness to undergo diagnosis and treatment. Yes No Annual - no SDM discussion

I have counseled the patient on the importance of smoking cessation and provided smoking cessation information, or discussed the importance of continued smoking abstinence. Yes No Annual - no SDM discussion

⚠ Has the patient been exposed to a high level of radon (4 pCi/L or higher)? Yes No Unknown

⚠ Has the patient been occupationally exposed to agents that are carcinogens targeting the lungs? Yes No

⚠ Does the patient have a history of other smoking-related cancer(s), for example, lymphoma, leukemia, head and neck, esophageal, stomach, colon, liver, pancreas, bladder, kidney, or cervical cancer? Yes No

Accept Cancel Remove

CT LUNG CANCER SCREENING LOW DOSE - Annual (\$)

Confirmed

Is the patient Asymptomatic? Yes No

Is this the first (baseline) LDCT lung cancer screen or an annual exam? Annual Annual Baseline Comments

I have discussed with the patient the benefits and harms of lung cancer screening, including potential follow-up testing. Yes No Annual - no SDM discussion

I have counseled the patient on the importance of adhering to the annual screening and their ability or willingness to undergo diagnosis and treatment. Yes No Annual - no SDM discussion

I have counseled the patient on the importance of smoking cessation and provided smoking cessation information, or discussed the importance of continued smoking abstinence. Yes No Annual - no SDM discussion

⚠ Has the patient been exposed to a high level of radon (4 pCi/L or higher)? Yes No Unknown

⚠ Has the patient been occupationally exposed to agents that are carcinogens targeting the lungs? Yes No

⚠ Does the patient have a history of other smoking-related cancer(s), for example, lymphoma, leukemia, head and neck, esophageal, stomach, colon, liver, pancreas, bladder, kidney, or cervical cancer? Yes No

Accept Cancel Remove



EMR System Progress Note – Problem-Focused Charting, LDCT SDM Component

Diagnoses and all orders for this visit:

Needs flu shot

- QUADRIVALENT FLUZONE HIGH

Chronic anxiety (Chronic)

Overview:

Stable, continue meds, and

Orders:

- clonazepam, 1 mg Oral Tablet; Take 1 Tablet by mouth 3 times daily as needed for Anxiety. Dispense: 90 Tablet; Refill: 2

Benzodiazepine dependence, continued

Overview:

Stable, continue meds, and

Orders:

- clonazepam, 1 mg Oral Tablet; Take 1 Tablet by mouth 3 times daily as needed for Anxiety. Dispense: 90 Tablet; Refill: 2

Need for pneumococcal vaccination

- PNEUMOCOCCAL CONJUGATE VACCINE 20 VALENT IM

Screening for osteoporosis

- DX BONE DENSITY AXIAL SKELETON: Future

Postmenopausal

- DX BONE DENSITY AXIAL SKELETON: Future

Nicotine dependence, cigarettes, with other nicotine-induced disorders

- CT LUNG CANCER SCREENING LOW DOSE: Future

- PR VISIT TO DETERMINE LDCT ELIG



Gieske, Michael R, MD
Physician
Specialty: Family Medicine

Progress Notes
Signed

Creation Time: 9/19/2022 9:49 AM

Customized entry into progress note,
meeting CMS LDCT criterion

During this visit [REDACTED] was found to be a candidate for lung cancer screening.

The patient is a 66 y.o. female and reports that she has been smoking cigarettes. She started smoking about 47 years ago. She has a 22.50 pack-year smoking history. She has never used smokeless tobacco. The patient is asymptomatic. They were counseled on the importance of annual adherence and are willing to continue annual screening if appropriate.

The patient was counseled on the benefits and risks of screening, including the potential need for further diagnostic testing, and they are willing to proceed. The patient was also counseled on the importance of smoking cessation or continued abstinence, as appropriate, along with interventions available to assist in cessation if presently smoking.

Qualifying diagnosis is added to the
Assessment and Plan



Current smoker = currently smokes any amount, even occasionally

Former smoker = if they have quit smoking (does not include those in the process of quitting)

Smoking History

Smoking Status:

Start date: Should be patient's **very first** start date, not a re-start date

Start Date:

Most current quit date if patient has quit; this will reset the 15-year rule for screenings

Quit Date:

Types:

Packs/day: This will be the **average** of how many packs per day when the patient smoked full time ("I smoked between 1 and 2 packs a day when I smoked all the time" = 1.5) [Could also just use the **maximum** amount for simplicity]

Type: Needs to be marked cigarettes to qualify for lung cancer screening

Packs/Day:

Years:

Update the years smoked every year if a current smoker (eg, 2018 = 40 years, 2019 = 41 years)



If a patient starts smoking again

- Remove quit date from box
- Do not update start date

Ready to Quit:

Counseling Given:

Comments:

Years: Use the calculator to calculate if patient gives you a start date (eg, 2018-1966 = 52)

To be used for: Patients who are weaning down (eg, "pt down to 8 cigarettes a day), using electronic cigarettes, etc; **do not** include dates for starting and stopping



New! July 11, 2023 – Longitudinal Smoking History

The new way to document smoking history for our patients in the EMR

Substance Use

Tobacco

Smoking

Never Former **Every Day** Some Days Unknown

Passive exposure: Never Past Cu

Types: Cigarettes Pipe Cigars

Total pack years: **58.4**

Cigarettes

First smoked: 1980 Last attempt to quit: 1990 - 2000 Current use: 1 pack/day since 2015

Update current usage: Quit 0.5 1 2

Packs / Day	From	To	Years
1	2015	(56 y.o.) Current	(64 y.o.) ≈ 8.4
2	2000	(41 y.o.) 2015	(56 y.o.) 15
<input checked="" type="checkbox"/> Quit	1990	(31 y.o.) 2000	(41 y.o.) 10
2	1980	(21 y.o.) 1990	(31 y.o.) 10

- Each time the patient's smoking history changes, a new line item is entered, and the total pack-years amount automatically adjusts
- This continues to update automatically until the patient's smoking status or current use changes



Registry Summary – 2015-2025 YTD

Analysis of Positive Scans - St. Elizabeth Healthcare --- 1/1/2015 - 2025 YTD															
Year	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	TOTAL	% Scans	False Positive	False Discovery
Total LDCT LC Scr. SCANS	252	753	1965	3585	4082	3854	6084	7729	8339	9050	1357	47050	*	**	***
Tot. # Unique Patients Scanned	237	716	1649	2751	2267	1332	1964	2770	2651	2157	259	18753			
Annual					1815	2511	4120	4959	5688	6898	1102	27093			
Baseline					2267	1332	1964	2770	2651	2157	259	13400			
Annual LCS - % of total					44.5%	65.3%	67.7%	64.2%	68.2%	76.2%	81.0%	49.5%			
Follow-Up/Interval Screens	9	32	100	168	293	286	430	490	549	800	130	2357			
Annual, Baseline, Interval	261	785	2065	3753	4375	4140	6514	8219	8888	9850	1487	49407			
Cat 1	127	457	1164	2194	2312	2289	3630	4399	4752	4974	760	27058	57.51%		
Cat 2	76	201	506	887	1250	1121	1760	2357	2342	2718	398	13616	28.94%		
Cat 3 (Indeterminate)	22	47	143	240	250	258	401	533	643	848	112	3497	7.43%		
Cat 4 (Suspicious) - Total	27	48	152	264	270	190	303	423	586	500	86	2849	6.06%	4.43%	73.15%
Cat 4A	16	33	108	186	188	138	238	343	502	454	76	2282	4.85%		
Cat 4B	11	15	44	78	82	45	60	74	76	41	8	534	1.13%		
Cat 4X					8	5	6	6	8	5	2	34	0.07%		
Cat 3 + Cat 4 - Combined	49	95	295	504	520	448	704	956	1229	1348	198	6346	13.49%	11.86%	87.95%
Lung Cancer	5	16	37	82	81	51	66	120	144	151	12	765	1.63%	#Lung Cancer Screens to find 1 LC	61.5
													4.08%	#Unique Patients Screened to find 1 LC	24.5



SEP Attributed Patients – Ranked by Site – 2024 Year-End

USPSTF
2021
uptake
ranked
by PC
site (41)

Presented
quarterly to
PCPs,
oncology
team,
management

**Distribution of Lung Cancer Screening per USPSTF 2021 Criteria - Eligible & Attributed Patients - By Practice
2024 Q4 - Listed by Percentage of Eligible Patients Captured YTD**

Rank	Department	Metric	Measure Date	Benchmark	Numerator	Denominator	%	Gap/Site
	SEP Site Overall	USPSTF 2021	12/31/2024	> 45.00%	10,690	20,680	51.7%	33.8
1	SEP CONCIERGE MEDICINE	Screening: Lung Cancer	12/31/2024	> 45.00%	6	7		
2	SEP CVH IM/PEDS	Screening: Lung Cancer	12/31/2024	> 45.00%	316	503	62.82%	
3	SEP EDGEWOOD IM/PEDS	Screening: Lung Cancer	12/31/2024	> 45.00%	27	43	62.79%	
4	SEP LBG WILSON CRK PC	Screening: Lung Cancer	12/31/2024	> 45.00%	131	214	61.21%	
5	SEP BURLINGTON PC	Screening: Lung Cancer	12/31/2024	> 45.00%	249	411	60.58%	64
6	SEP NEWPORT OVATION PC	Screening: Lung Cancer	12/31/2024	> 45.00%	124	207	59.90%	31
7	SEP AURORA PC	Screening: Lung Cancer	12/31/2024	> 45.00%	134	228	58.77%	31
8	SEP CRESTVIEW HILLS IM	Screening: Lung Cancer	12/31/2024	> 45.00%	386	662	58.31%	88
9	SEP GREENDALE PC	Screening: Lung Cancer	12/31/2024	> 45.00%	211	362	58.29%	48
10	SEP FORT MITCHELL PC	Screening: Lung Cancer	12/31/2024	> 45.00%	517	897	57.64%	113
11	SEP HIGHLAND HTS PC	Screening: Lung Cancer	12/31/2024	> 45.00%	567	989	57.33%	122
12	SEP AURORA 107 PC	Screening: Lung Cancer	12/31/2024	> 45.00%	100	176	56.82%	21
13	SEP UNION BRISTOW PC	Screening: Lung Cancer	12/31/2024	> 45.00%	298	550	54.18%	51
14	SEP COVINGTON PC	Screening: Lung Cancer	12/31/2024	> 45.00%	499	923	54.06%	84
15	SEP CRITTENDEN PC	Screening: Lung Cancer	12/31/2024	> 45.00%	675	1,258	53.66%	109
16	SEP UNION US 42 PC	Screening: Lung Cancer	12/31/2024	> 45.00%	492	922	53.36%	77
17	SEP FLO TURFWAY PC	Screening: Lung Cancer	12/31/2024	> 45.00%	560	1,055	53.08%	85
18	SEP FLORENCE EWING PC	Screening: Lung Cancer	12/31/2024	> 45.00%	358	676	52.96%	54
19	SEP SOUTHGATE IM	Screening: Lung Cancer	12/31/2024	> 45.00%	197	377	52.25%	27
20	SEP NPTFTT PC	Screening: Lung Cancer	12/31/2024	> 45.00%	268	515	52.04%	36
21	SEP HEBRON CONNER PC	Screening: Lung Cancer	12/31/2024	> 45.00%	319	621	51.37%	40
22	SEP BELLEVUE PC	Screening: Lung Cancer	12/31/2024	> 45.00%	293	572	51.22%	36
23	SEP HEBRON LITTON PC	Screening: Lung Cancer	12/31/2024	> 45.00%	304	594	51.18%	37
24	SEP INDEPENDENCE PC	Screening: Lung Cancer	12/31/2024	> 45.00%	393	785	50.06%	40
25	SEP LBG STABELINE PC	Screening: Lung Cancer	12/31/2024	> 45.00%	155	316	49.05%	13
26	SEP LBG ELM STREET PC	Screening: Lung Cancer	12/31/2024	> 45.00%	343	707	48.51%	25
27	SEP WALTON PC	Screening: Lung Cancer	12/31/2024	> 45.00%	239	494	48.38%	17
28	SEP BRIGHT PC	Screening: Lung Cancer	12/31/2024	> 45.00%	145	301	48.17%	10
29	SEP COVINGTON IM	Screening: Lung Cancer	12/31/2024	> 45.00%	123	258	47.67%	7
30	SEP BUTLER PC	Screening: Lung Cancer	12/31/2024	> 45.00%	370	791	46.78%	14
31	SEP EDGEWOOD PC	Screening: Lung Cancer	12/31/2024	> 45.00%	106	232	45.69%	2
32	SEP WILLIAMSTOWN PC	Screening: Lung Cancer	12/31/2024	> 45.00%	245	537	45.62%	3
33	SEP TAYLOR MILL PC	Screening: Lung Cancer	12/31/2024	> 45.00%	333	731	45.55%	4
34	SEP RISING SUN PC	Screening: Lung Cancer	12/31/2024	> 45.00%	156	343	45.48%	2
35	SEP ALEXANDRIA PC	Screening: Lung Cancer	12/31/2024	> 45.00%	398	888	44.82%	-2
36	SEP DRY RIDGE PC	Screening: Lung Cancer	12/31/2024	> 45.00%	427	966	44.20%	-8
37	SEP MILAN PC	Screening: Lung Cancer	12/31/2024	> 45.00%	57	133	42.86%	-3
38	SEP AT MUBEA	Screening: Lung Cancer	12/31/2024	> 45.00%	15	36	41.67%	-1
39	SEP VEVAY PC	Screening: Lung Cancer	12/31/2024	> 45.00%	87	211	41.23%	-8
40	SEP DILLSBORO NS IM	Screening: Lung Cancer	12/31/2024	> 45.00%	62	174	35.63%	-16
41	SEP AT AURORA CASKET	Screening: Lung Cancer	12/31/2024	> 45.00%	5	15	33.33%	-2
42								
43								
44								
					10,690	20,680	51.7%	33.8

The
“Hawthorne Effect”

Finished 2023 at 46.8% uptake

Finished 2022 at 44.1% uptake

National average 16.0%
of 14.2 million
eligible population

SEP = St. Elizabeth physicians.
American Lung Association.
State of Lung Cancer.
November 13, 2024.
Available at:
<https://www.lung.org/research/state-of-lung-cancer/states>.



Practical Updates
in Primary Care

Performance of SEHC LCSP, Histology, PY, Sex, 2024

Overall Lung Cancer Discovery		
Stage - all yrs	N	%
Stage I	493	64.03%
Stage II	78	10.13%
Stage III	126	16.36%
Stage IV	73	9.48%
Unknown	0	0.00%
Total	770	100.00%
Stage I & II	74.16%	

Lung Cancer Type		
Type	N	%
adenocarc.	349	45.3%
squamous	230	29.9%
small cell	80	10.4%
limited	50	
extensive	30	
large cell	12	1.6%
carcinoid	16	2.1%
other	16	2.1%
unknown	67	8.7%
	770	100%

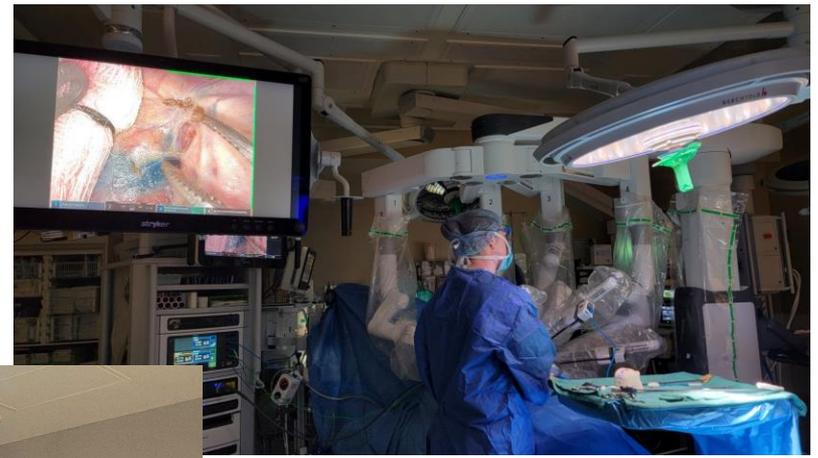
74.2% found in early stages

Male	368	47.8%
Female	402	52.2%
	770	100%

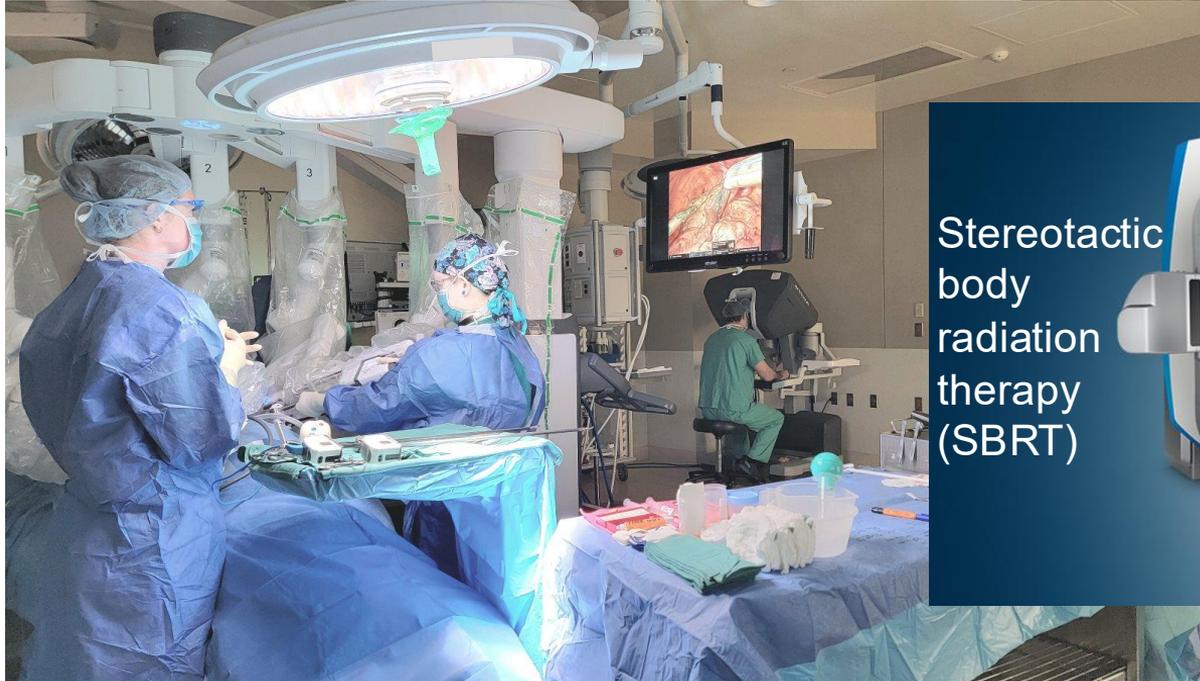
Average (Mean) PY =	61.0
Median PY =	52.0

2024: 151 lung cancers discovered;
109 in stage I = 72.2% stage I, 76.8% in early stage I & II

Early-Stage Treatment



RATS – robotic-assisted thoracic surgery



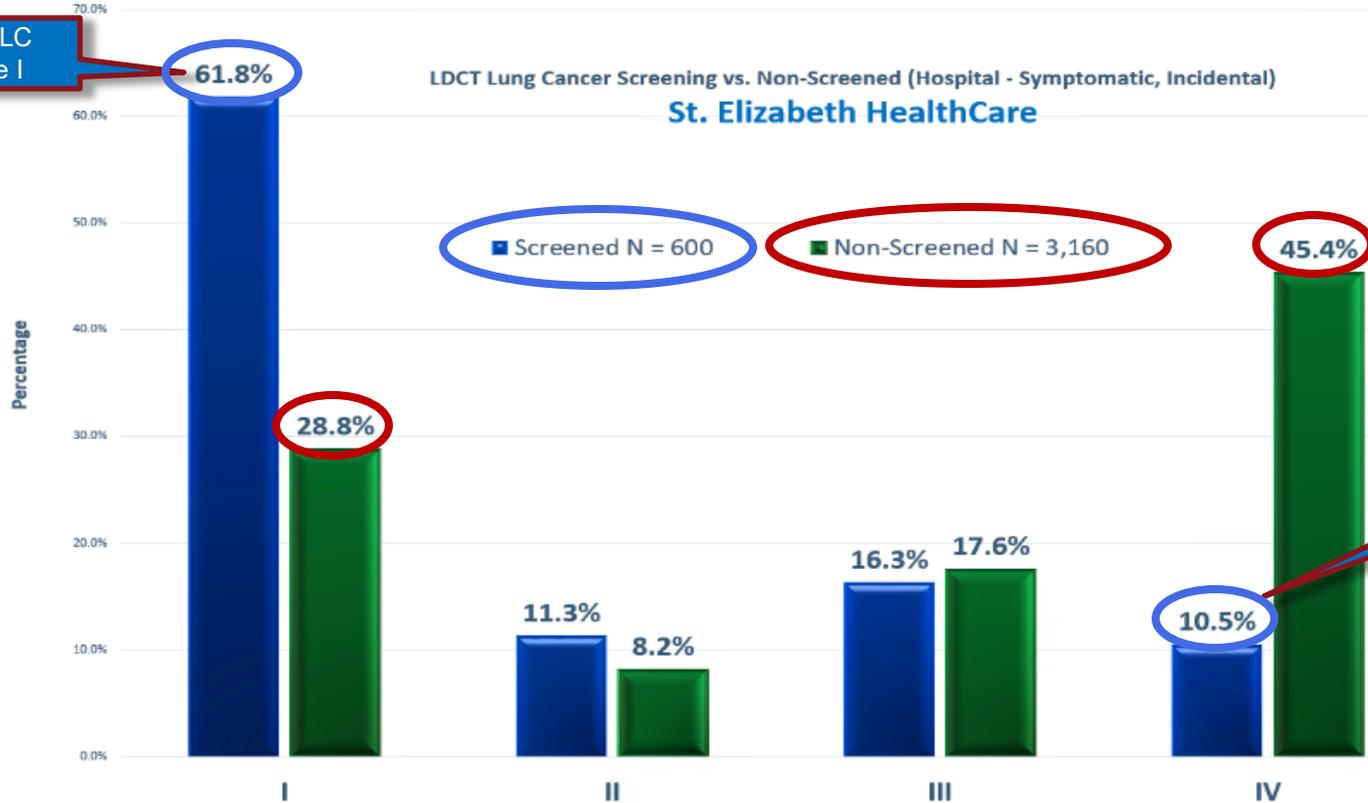
Stereotactic
body
radiation
therapy
(SBRT)



Practical Updates
in Primary Care

Stage Migration 2015-2023

Lung Cancers Discovered – 3760 over 9 Years



114.6% more LC found in stage I

76.9% less found in stage IV

73.1% Found in Early Stages (I and II) Screened

63.0% Found in Late Stages (III & IV) Non-Screened

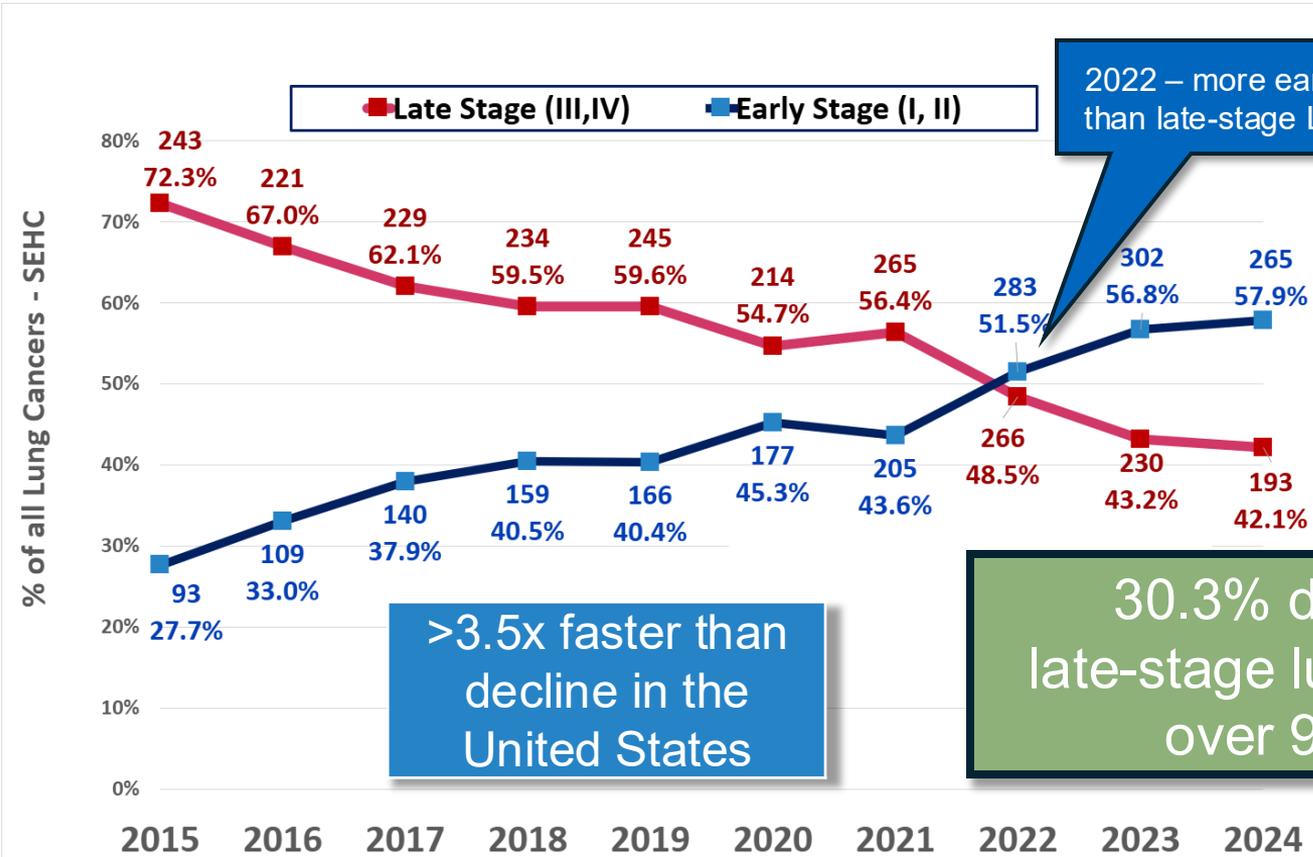
Lung Cancer Stage



Practical Updates in Primary Care

Decline in Late-Stage Lung Cancer – 4239 Lung Cancers (SEHC)

Lung Cancer – Early vs Late Stage – 2015-2024 3Q – A Decade of Evolution



2022 – more early- than late-stage LC!

1899
2340

>3.5x faster than decline in the United States

30.3% decline in late-stage lung cancers over 9 years

LCS Criteria Still Missing Many Patients

Review of our first 30,000+ LCS

Overcoming barriers to lung cancer screening using a systemwide approach with additional focus on the non-screened, ASPIRED

[Michael R Gieske](#)  , [Jessica Kerns](#), [..], and [Royce F Calhoun](#) 

Distribution of non-screened cohort respective of patients who could have qualified for screening, either with existing EMR data or upon audit of substance use history

Non-screened lung cancers	CMS 2015		USPSTF 2021	
	N	%	N	%
Met criteria—existing EMR	720	31.96%	1020	45.27%
Met criteria—on audit	294	13.05%	272	12.07%
Subtotal	1014	45.01%	1292	57.35%
Eligibility could not be determined	87	3.86%	120	5.3%
Did not meet screening criteria	1152	51.13%	841	37.3%
Total	2253	100.00%	2253	100.00%

42.6% of patients with lung cancer, even after an audit, did not qualify for any insurance-recognized LCS criteria



We Need a Better Risk Prediction Model/Algorithm

- 20% of lung cancers in the United States occur in individuals without a history of smoking
- SEHC: 42.7% of lung cancers not within USPSTF 2021 criteria after audit
- Radon is considered a major risk factor for non-smoking-related lung cancers
- In Asia and Africa, cooking oils and open wood burning without ventilation are major risk factors
- Family history is a substantial risk factor and increases with the number of relatives affected; biomarkers will become an increasingly important part of the equation
- Air pollution is a major risk factor in many areas of the world
- In Taiwan, 53% of lung cancer cases occur in individuals with no smoking history; 60% are found in stage IV; globally, more than 60% of lung cancer cases occur in females who have never smoked (in the US, 15%)



Risk Prediction Models

PLCOM2012

We have implemented and utilized the PLCOM2012 risk prediction model to calculate risk; use $\geq 1.3\%$ chance of lung cancer in 6 years. Incorporates **11 predictors**: (1) age; (2) smoking status (former or current); (3) average number of cigarettes smoked per day; (4) duration smoked; (5) years of quitting smoking; (6) highest level of education obtained; (7) body mass index (BMI); (8) chronic obstructive pulmonary disease (COPD); (9) personal history of cancer; (10) family history of lung cancer; (11) race and ethnicity.

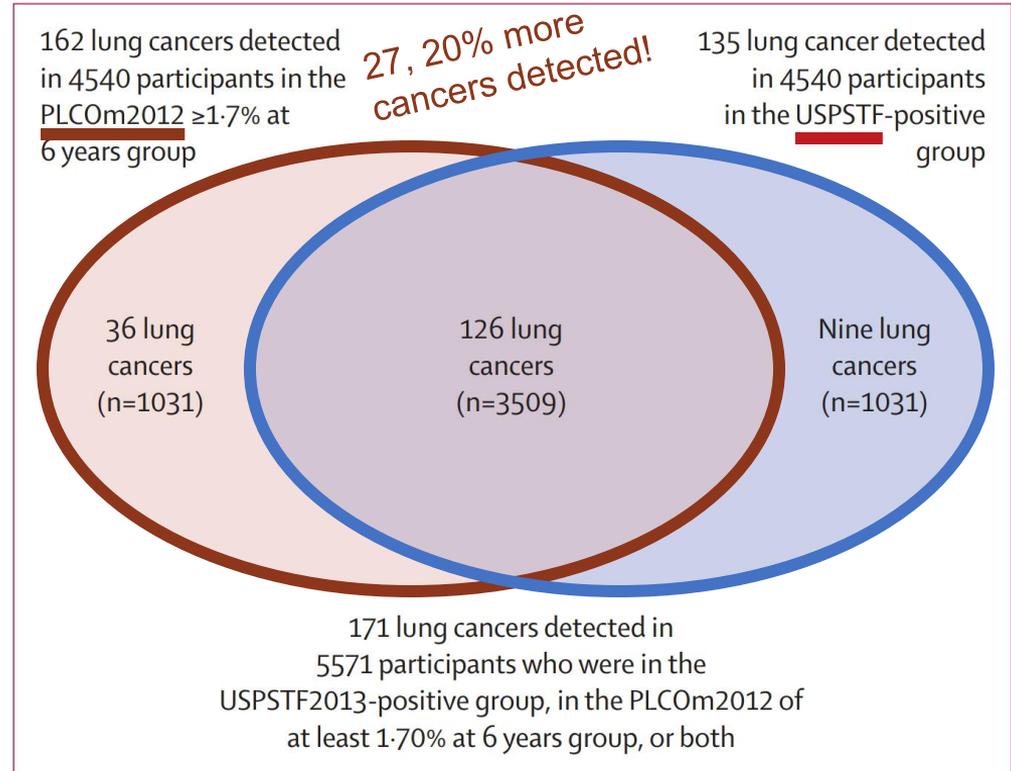


Figure: Venn diagram describing the distribution of individuals and lung cancer cases by criteria (USPSTF2013 positivity and PLCOM2012 $\geq 1.7\%$ at 6 years status)





**Practical Updates
in Primary Care**

The Future Is Now: Applying Innovation and Evolving Technology

Michael Gieske, MD
Director, Lung Cancer Screening
St. Elizabeth Healthcare

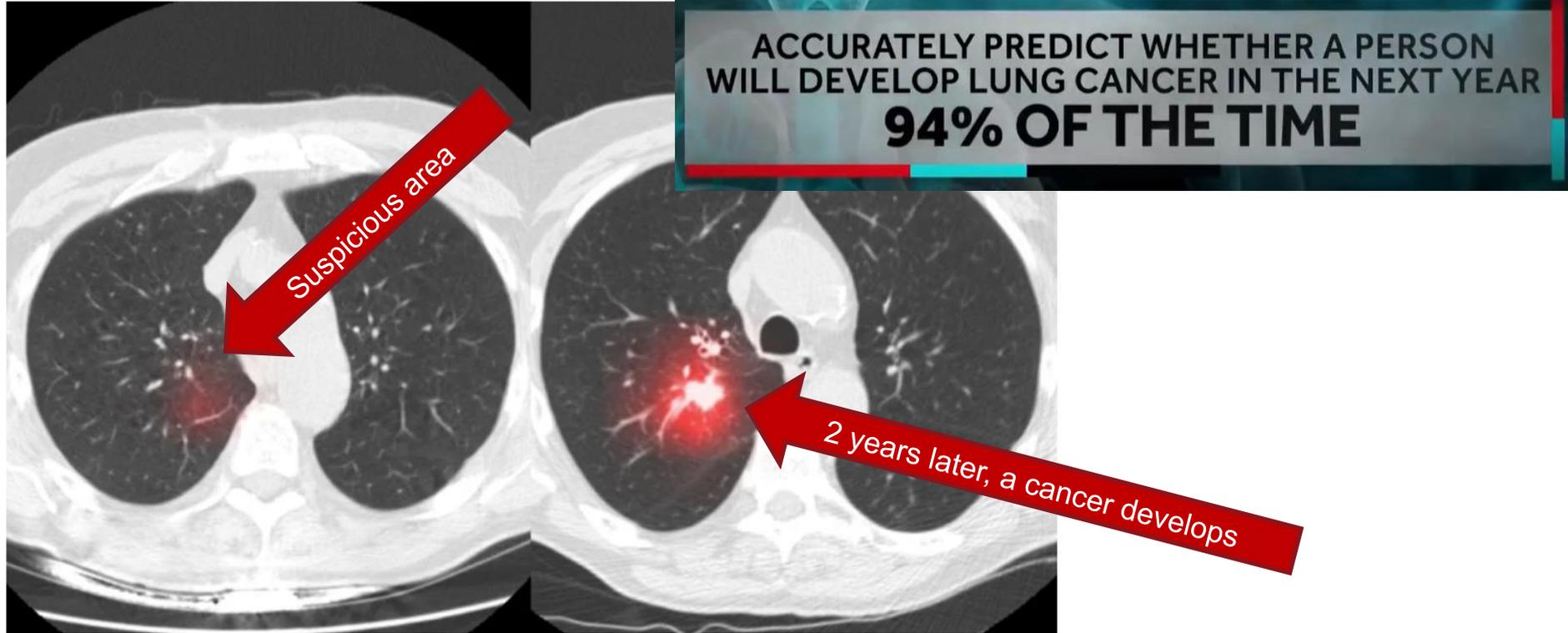
AI Tool for Prediction of Lung Cancer

Promising new AI can detect early signs of lung cancer that doctors can't see

The tool looks for signs of where cancer is likely to turn up so doctors can spot it as early as possible.



AI Tool for Prediction of Lung Cancer



This AI tool is able to detect early signs of lung cancer. These CT scans, from the same patient, were taken 2 years apart. In the scan on the left, the area highlighted in red is what the AI tool detected. The scan on the right shows what the radiologists saw 2 years later.

MIT and Mass General

Lovelace Jr. B, et al. *NBC News*. April 11, 2023. Accessed May 1, 2025. <https://www.nbcnews.com/health/health-news/promising-new-ai-can-detect-early-signs-lung-cancer-doctors-cant-see-rcna75982>.



Practical Updates
in Primary Care

Biomarkers

Cancer **predilection** – prediction, risk modeling

- Genetic markers
- Proteins/genes – genetic predeterminants

Cancer **detection** – determine presence of disease

- cfDNA and RNA
- Proteins shed into blood
- MCED – multi-cancer early detection, SCED – single-cancer early detection

Cancer **direction** – treatment

- Liquid biopsies
 - MRD – minimal residual disease
 - Precision medicine – targeted treatments
- Tissue biopsies
 - Determining treatments – driver mutations – precision medicine – targeted therapies
 - Tracking therapy – cancers change and evolve – keeping ahead – determining aggressiveness
 - Monitoring success of treatment – predicting how the patient will respond

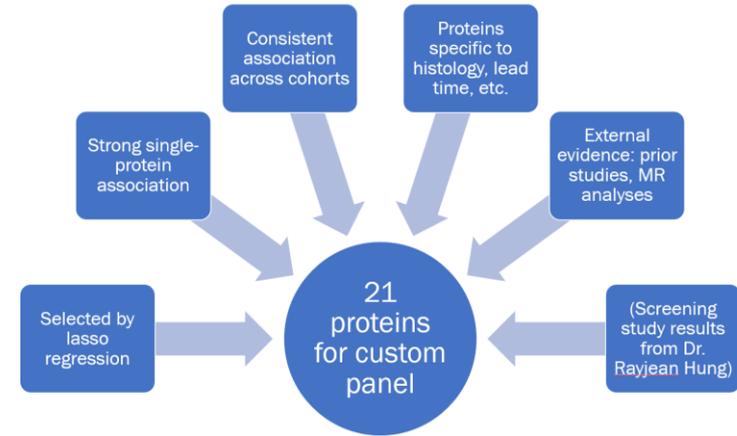


Prediction – Protein Markers – Proteomics

Hilary A. Robbins, PhD, MHS, MSPH
International Agency for Research on Cancer | RobbinsH@iarc.fr

World Health Organization (WHO)

Initial studies indicated that protein markers can improve lung cancer risk models.

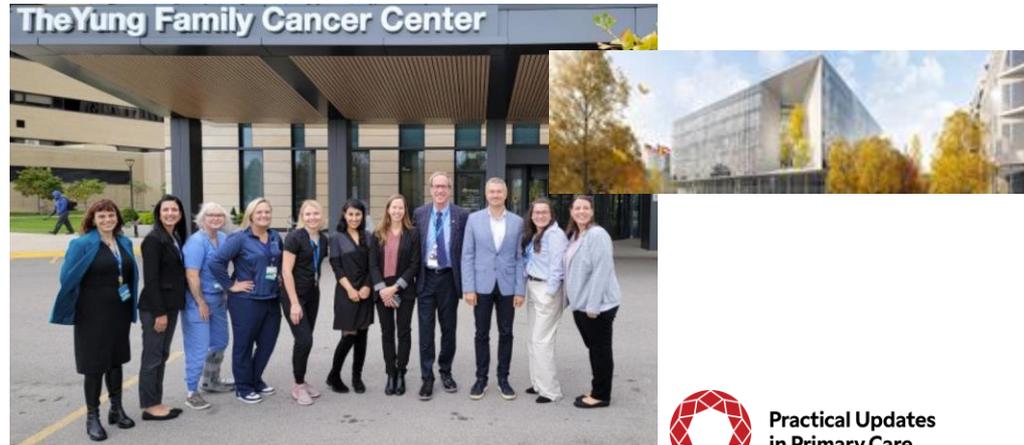


Robust answers to a few questions:

Can circulating proteins **improve** the discrimination of **standard** lung cancer **risk prediction models**? By how much?

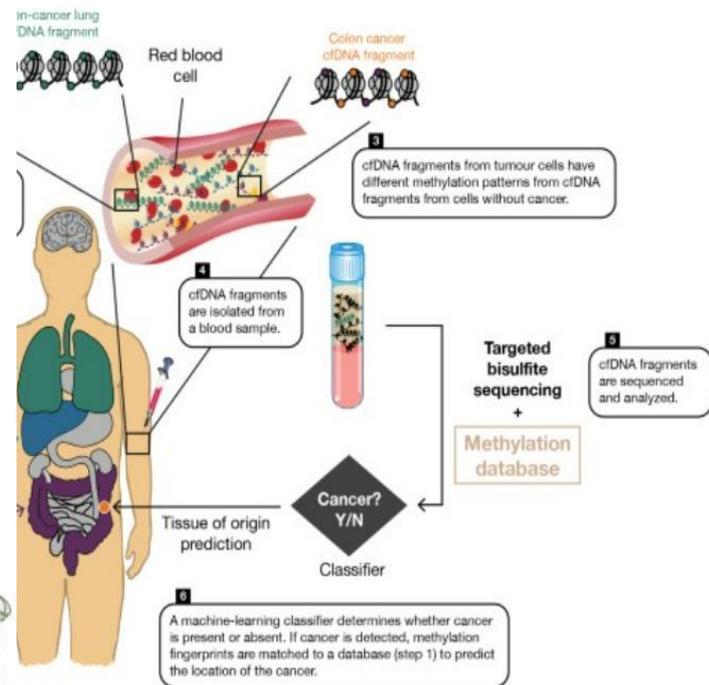
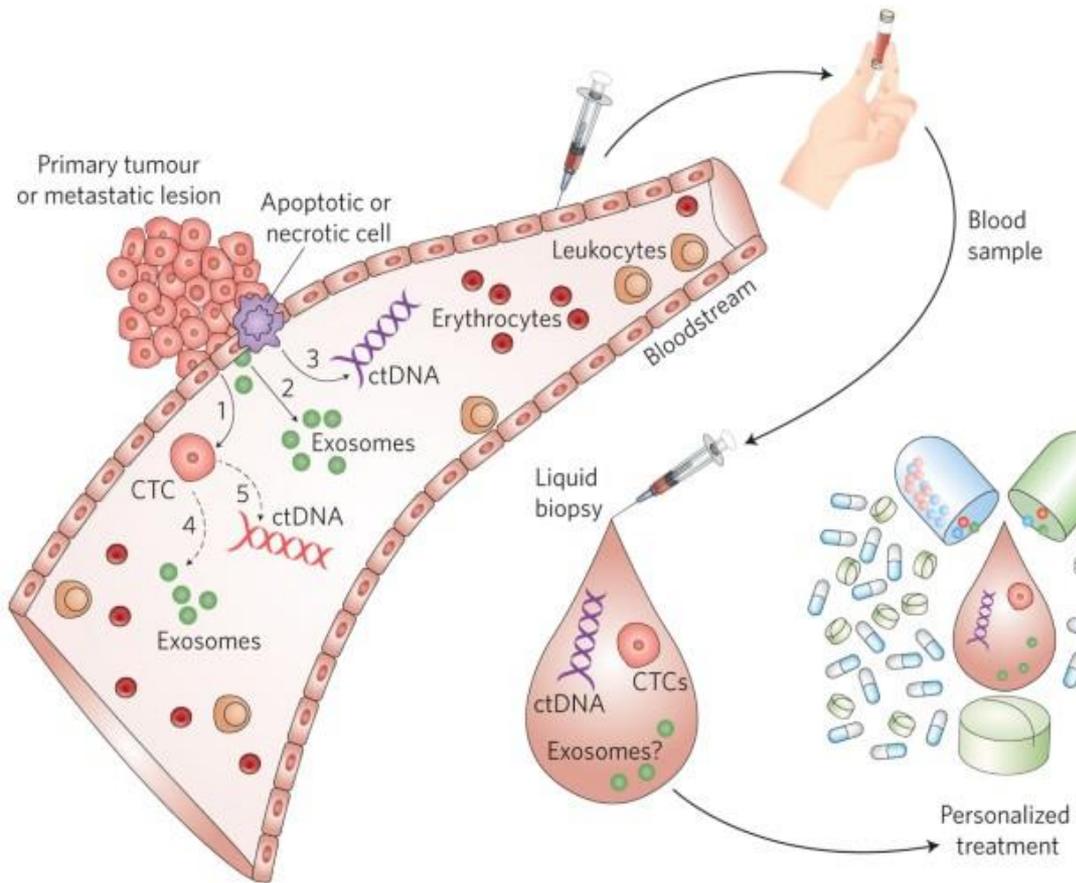
How does this affect who is classified as screening-eligible?

How does the performance of lung cancer risk models vary across **geography and ethnicity**?



Practical Updates
in Primary Care

Detection – MCEd



DNA methylation patterns in blood. A targeted methylation-recognize differences in DNA methylation patterns in cell-free. These patterns are characteristic of different cell types and to detect cancer and map its location in the body.

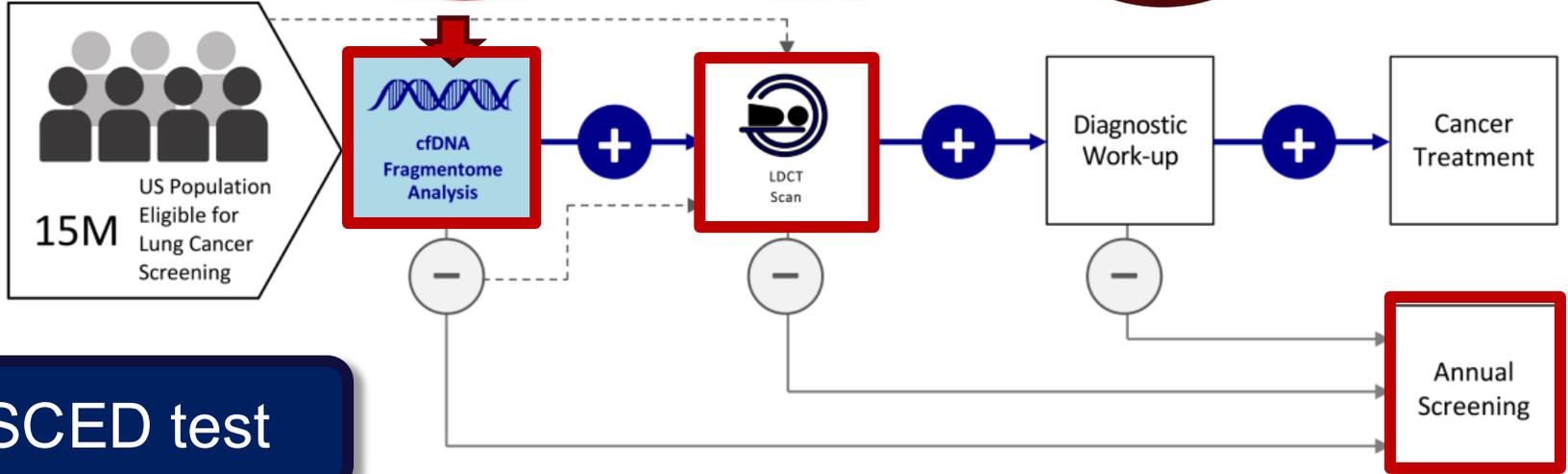
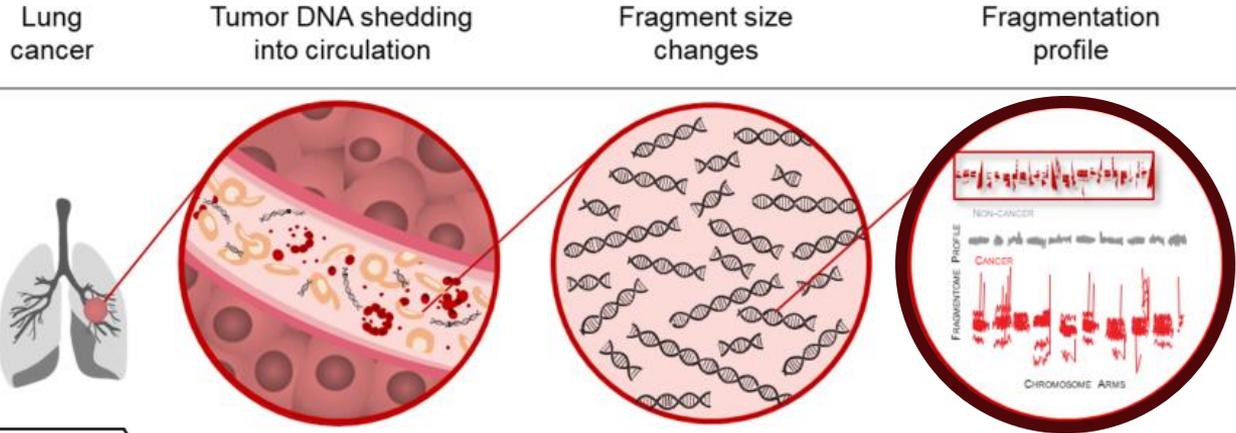


Detection – MCED

- We've proven that early detection reduces mortality for 6 cancers: Cervix, lung, breast, colon, rectal, prostate (25% of all cancer deaths)
- Only 14% of diagnosed cancers are detected by current screening tests (NORC, University of Chicago, December 14, 2022)
- Some MCEDs can detect over 50 cancers
 - Expensive
 - Not included in present screening guidelines, not covered by insurance
 - Looming questions of mortality reduction
 - Low sensitivity for early-stage cancers (<40%), though very high specificity or low false positive (~98%); <25% sensitivity for stage I lung cancer



Clinical Validation of a Cell-Free DNA Fragmentome Assay for Augmentation of Lung Cancer Early Detection



SCED test

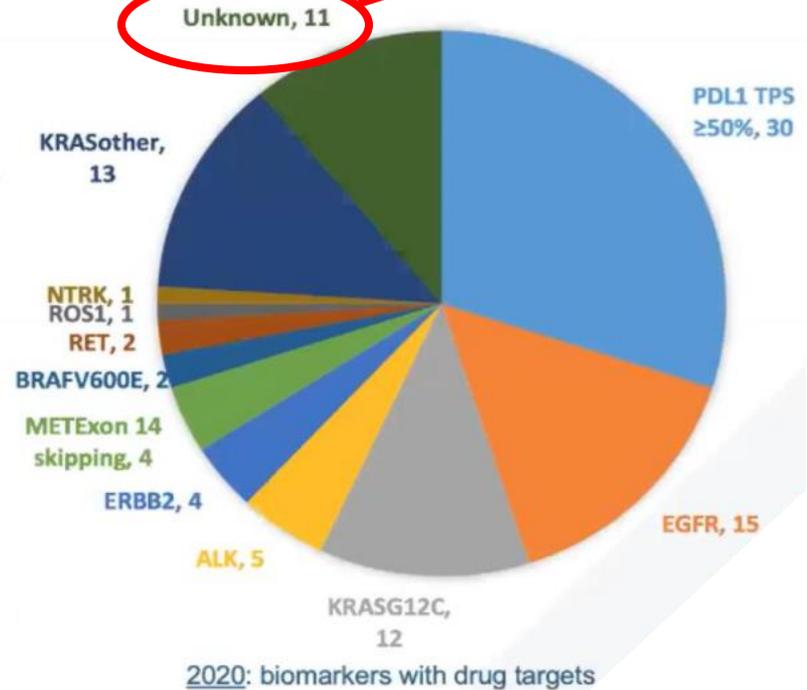
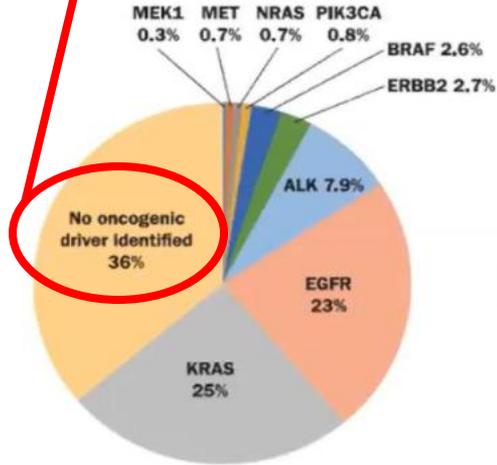
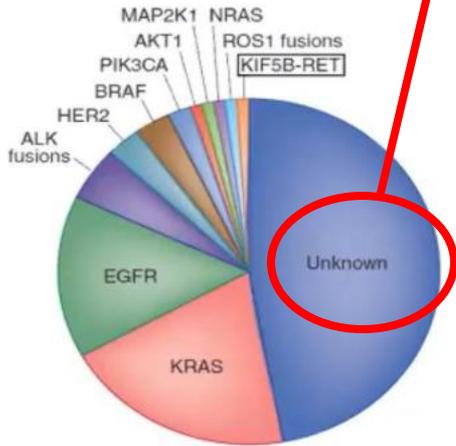
Direction: Confronting Nihilism – The New Frontier

Non-Squamous Non-Small Cell Lung Cancer Biomarkers

~50%

36%

11%



2020: biomarkers with drug targets

There is a targeted therapy revolution, being led by lung cancer



Practical Updates
in Primary Care

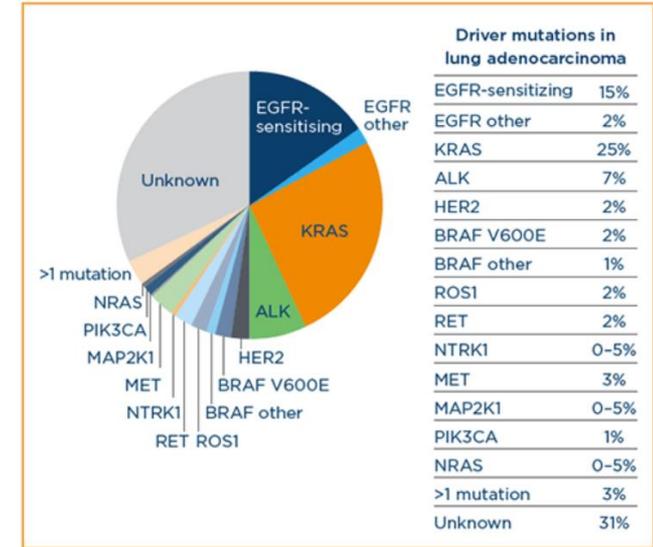
Biomarkers – Cancer Treatment

Targeted therapies: For mutations, genetic abnormalities (variants) in cancer cells

>9 genes with driver mutations, for which there are FDA-approved targeted therapies (TKIs) for the treatment of lung cancer.

- ALK – crizotinib, alectinib, brigatinib, ceritinib, lorlatinib
- BRAF V600E – combined dabrafenib and trametinib
- EGFR – erlotinib, afatinib, gefitinib, osimertinib (2015), amivantamab, necitumumab, ~~mabocertinib~~ (9/15/21)
- KRAS G12C – sotorasib
- MET exon 14 skipping – crizotinib, cabozantinib
- NTRK – larotrectinib, entrectinib
- RET – pralsetinib, cabozantinib
- ROS1 – crizotinib, entrectinib, lorlatinib
- HER2/not amplifications – trastuzumab, TDM-1 ado-trastuzumab emtansine

DRIVER MUTATIONS IN LUNG ADENOCARCINOMA



All current FDA-approved targeted therapies treat NSCLC.
There are as yet no approved targeted therapies for small cell lung cancer.

TKIs = tyrosine kinase inhibitors.

Drugs@FDA: FDA-Approved Drugs. Accessed May 1, 2025. <https://www.accessdata.fda.gov/scripts/cder/daf/>.

LUNGeVity. Accessed May 1, 2025. www.lungevity.org/lung-cancer-basics/types-of-lung-cancer.



Practical Updates
in Primary Care

Immunotherapy – Another Expanding Frontier

Immunotherapy drugs are treatments that work by essentially boosting the ability of the immune system to fight cancer.

One category of immunotherapy drugs is checkpoint inhibitors, of which 7 drugs are currently available for treating non-small cell lung cancer (with different indications)

- Nivolumab
- Pembrolizumab
- Atezolizumab
- Durvalumab
- Ipilimumab
- Cemiplimab
- Tremelimumab

Not everyone responds to immunotherapy, but in some cases, the results can be very dramatic, with long-term control of the disease.



Ongoing Research, Therapeutic Trials

- Unfortunately, even when cancers respond favorably and succumb to treatment, they eventually outsmart the treatments and **develop resistance** to the targeted therapies
- **Previously**, we did not know this to be the case, as patients with lung cancer **did not outlive their first lines of treatment**
- Now, we are discovering that we need to be nimble and correct course as cancers outsmart the targeted therapies; we need new **replacement therapies or combined therapies** that are less likely to succumb to resistance



ADCs – Antibody Drug Conjugates

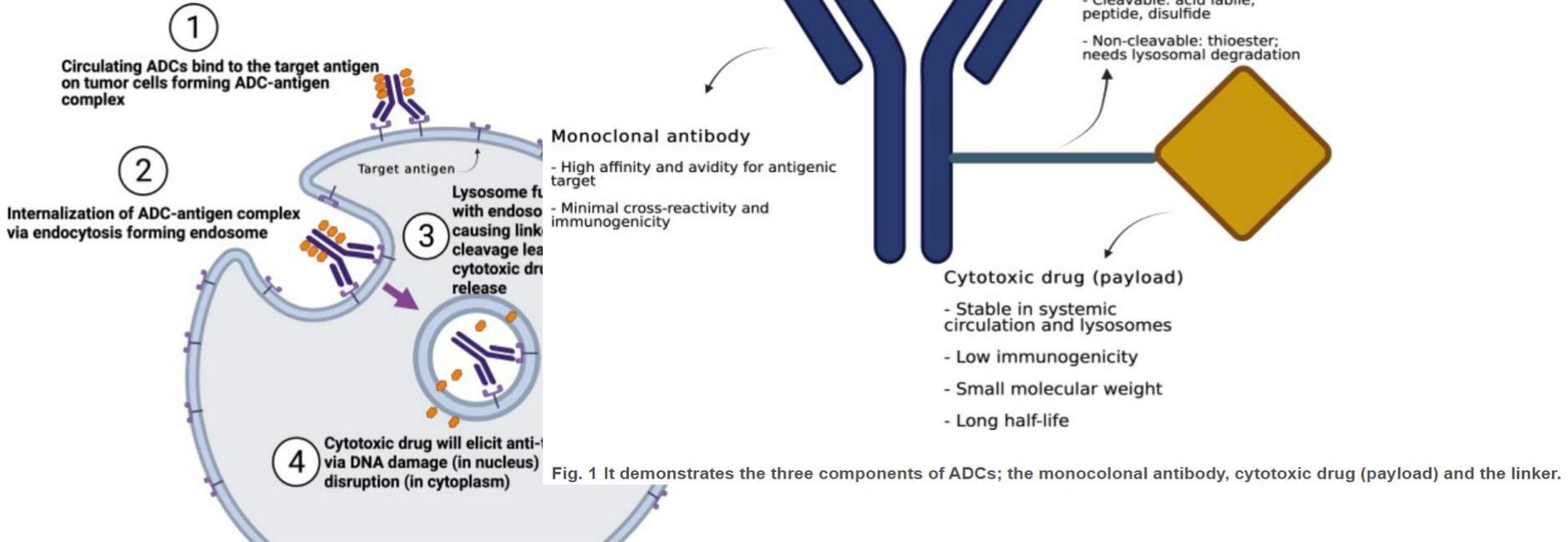
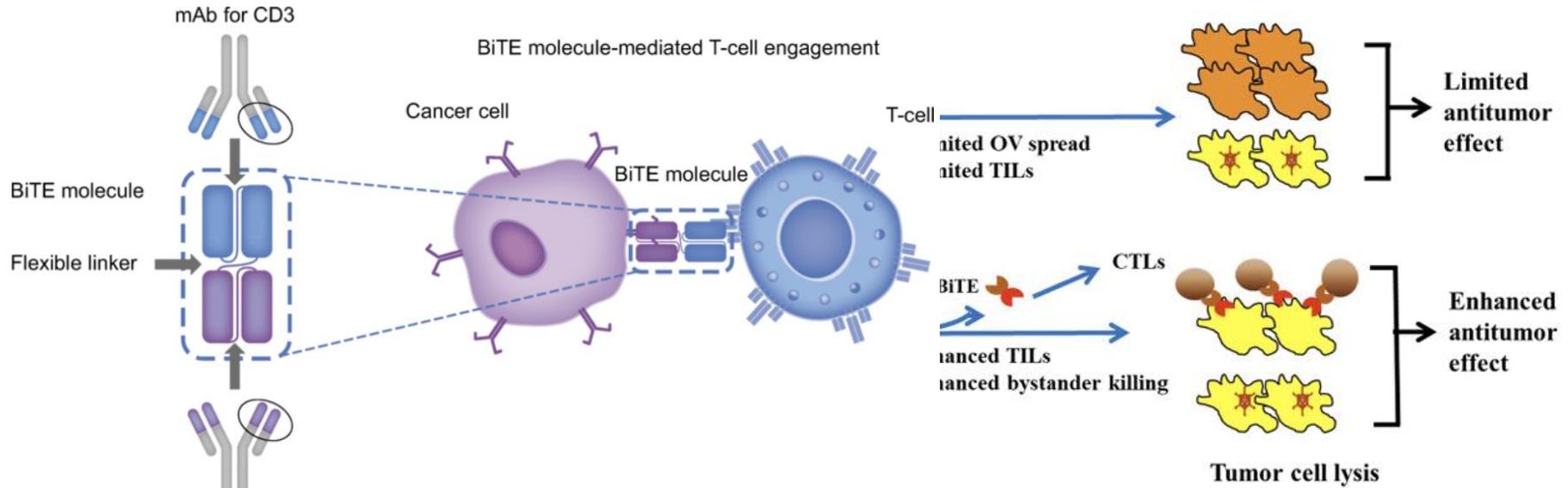


Fig. 2 It shows the step by step mechanism of action of ADCs. Circulating ADCs bind to the target antigen forming an ADC-antigen complex (1). Then, the complex is internalized via endocytosis (2). Linker cleavage leads to cytotoxic drug release (3) and elicit anti-tumor effects (4).

BITEs – Bispecific T-Cell Engagers – Oncolytic Virotherapy



Mechanism of action of BiTE technology. BiTE bispecific T cell engager, CD3 cluster of differentiation 3, mAb monoclonal antibody

and secrete these BiTEs that diffuse within the tumor tissue, activating and directing endogenous T cells to recognize and kill the tumor cells or/and stromal cells effectively (even if not directly infected by the OV), resulting in improved antitumor efficacy. This is a modified version of a figure originally published by Song XT, Discovery Med, 2013 [71].

BiTE-armed oncolytic virus (OV). The efficacy of a “pure” OV is limited by the OV throughout the tumor tissue and induction of tumor immune response. BiTE-armed OV may overcome these limitations as the armed OV produces



The White Ribbon Project





...From the Mountaintops

HOPE...
Thank You!



**Practical Updates
in Primary Care**

Management of EGFR-Mutant NSCLC

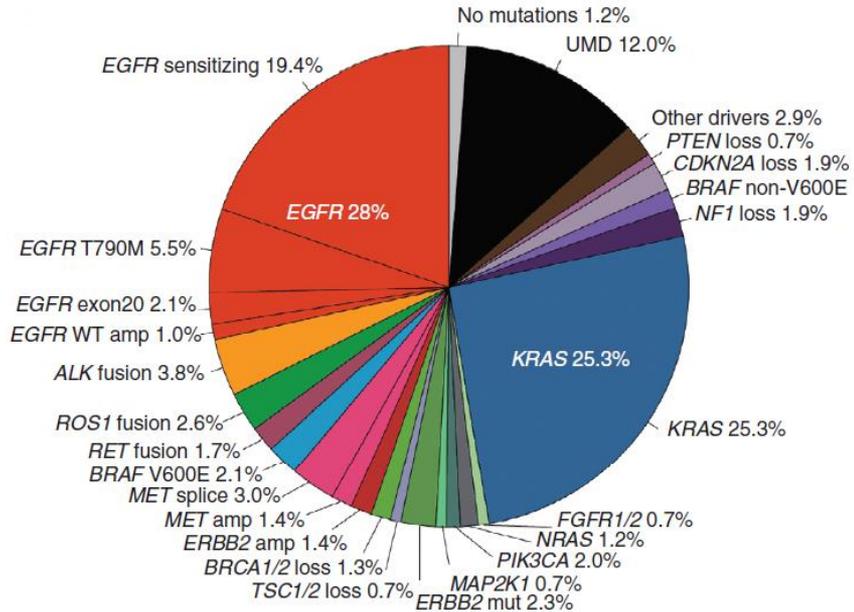
**Sandip Patel, MD, FASCO
Professor, Medical Oncology
UCSD**

Before Treatment

- **Radiographic diagnosis**: CNS imaging and CT CAP (or PET)
- **Pathologic diagnosis AND stage** by biopsy of highest-stage non-bone lesion
 - Ensure at least 4 passes of a larger-bore needle for molecular analyses
- **Molecular diagnosis**
 - cfDNA or tissue-based multiplex for EGFR/ALK/ROS1/BRAF/HER2/MET/others
 - PD-L1 IHC helpful
 - Even in PD-L1 >50%, make sure to wait for NGS prior to starting treatment



Molecular Revolution: Targeted Therapy



Mutation	Treatment
EGFR exon 19/21 EGFR exon 20	Osimertinib [±] Amivantamab* Mobocertinib*
ALK rearrangement	Alectinib, Brigatinib, Lorlatinib
ROS1 rearrangement	Entrectinib, Crizotinib
BRAF V600E	Dabrafenib & Trametinib
NTRK rearrangement	Larotrectinib, Entrectinib
RET rearrangement	Selpercatinib, Pralsetinib
MET exon 14	Capmatinib, Tepotinib
HER2 exon 20	Trastuzumab deruxtecan*
KRAS G12C	Sotorasib*, Adagrasib*

*2nd-line approval; [±]Adjuvant approval.

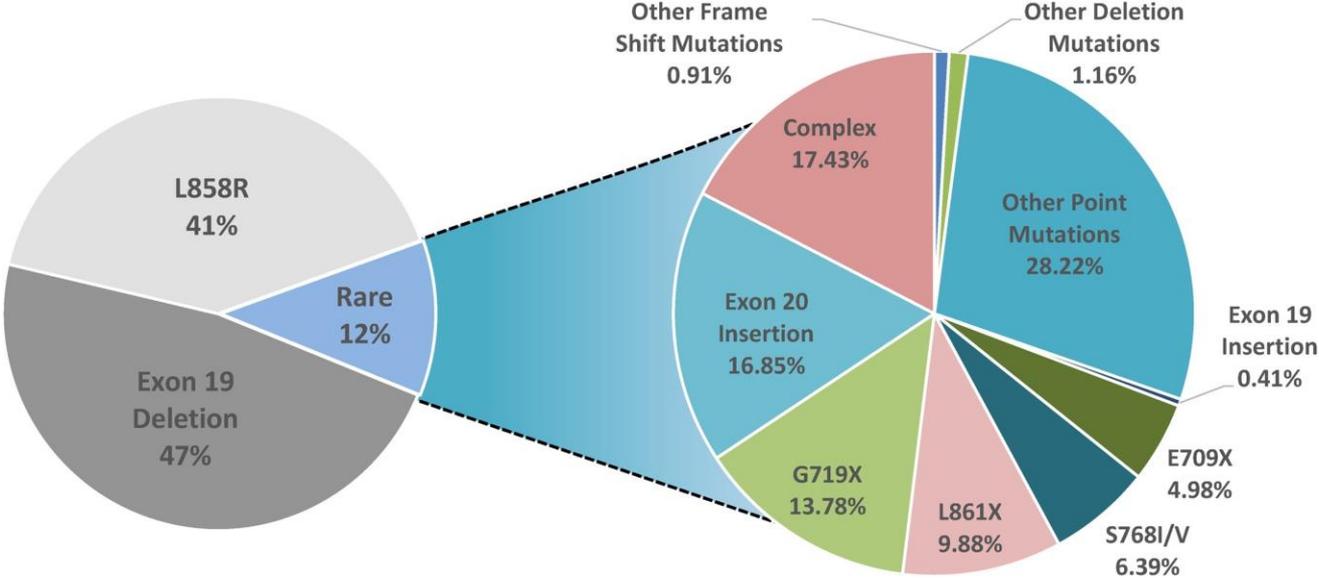
Jordan EJ, et al. *Cancer Discov.* 2017;7(6):596-609. Ettinger DS, et al. *J Natl Compr Canc Netw.* 2022;20(5):497-530.



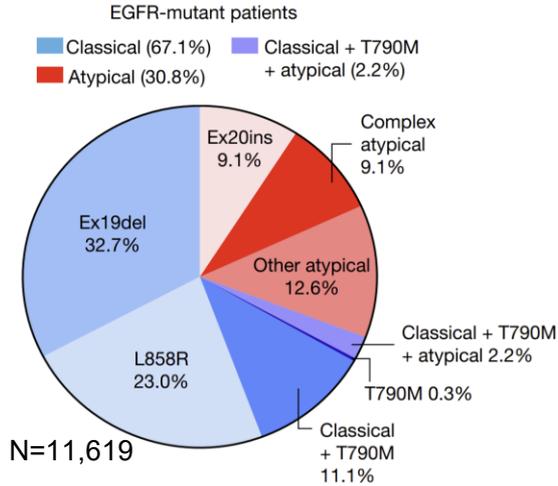
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EGFR Mutations are Identified in 15% of Lung Adenocarcinomas; More Common in Females, Asian Population, and Non-Smokers

Frequency of EGFR mutations



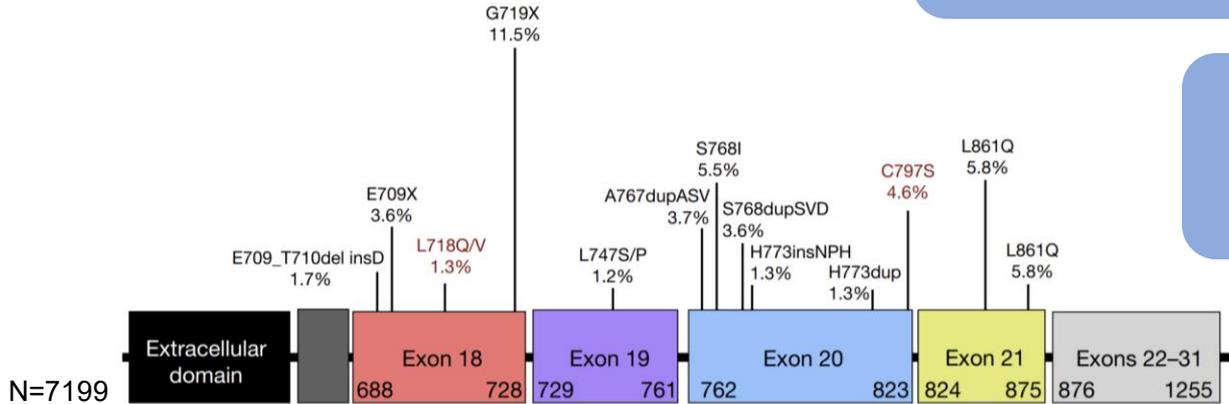
The Spectrum of EGFR-Activating Mutations in NSCLC



~80-90% classic EGFR-activating mutations
EGFR del19 and L858R

~10% atypical EGFR-activating/TKI sensitizing mutations at exon 18, 20
EGFR G719X, V769L, S768I

~10% EGFR exon 20 insertion mutations



Targeted Therapy for Actionable Drivers, ChemolO for Everyone Else

Table 2: PFS according to primary oncogenic driver from initiation of ICI

	EVT/N	Median PFS [95%CI] (months)	6-months PFS [95%CI]	12-months PFS [95%CI]
KRAS	208/271	3.2 [2.7; 4.5]	37.9 [32.1; 49.8]	25.6 [20.2; 31.3]
EGFR	117/125	2.1 [1.8; 2.7]	18.4 [12.1; 25.6]	6.4 [2.7; 12.1]
BRAF	34/43	3.1 [1.8; 4.6]	32.1 [18.3; 46.6]	18.0 [7.2; 32.7]
HER2	23/29	2.5 [1.8; 3.5]	22.7 [8.9; 40.2]	13.6 [3.6; 30.1]
MET	26/36	3.4 [1.7; 6.2]	36.5 [20.7; 52.4]	23.4 [10.6; 39.0]
ALK	21/23	2.5 [1.5; 3.7]	11.8 [2.2; 30.2]	5.9 [0.4; 23.0]
ROS1	-	-	-	-
RET	15/16	2.1 [1.3; 4.7]	14.1 [2.3; 35.9]	7.0 [0.4; 27.1]

EVT Event; N Number

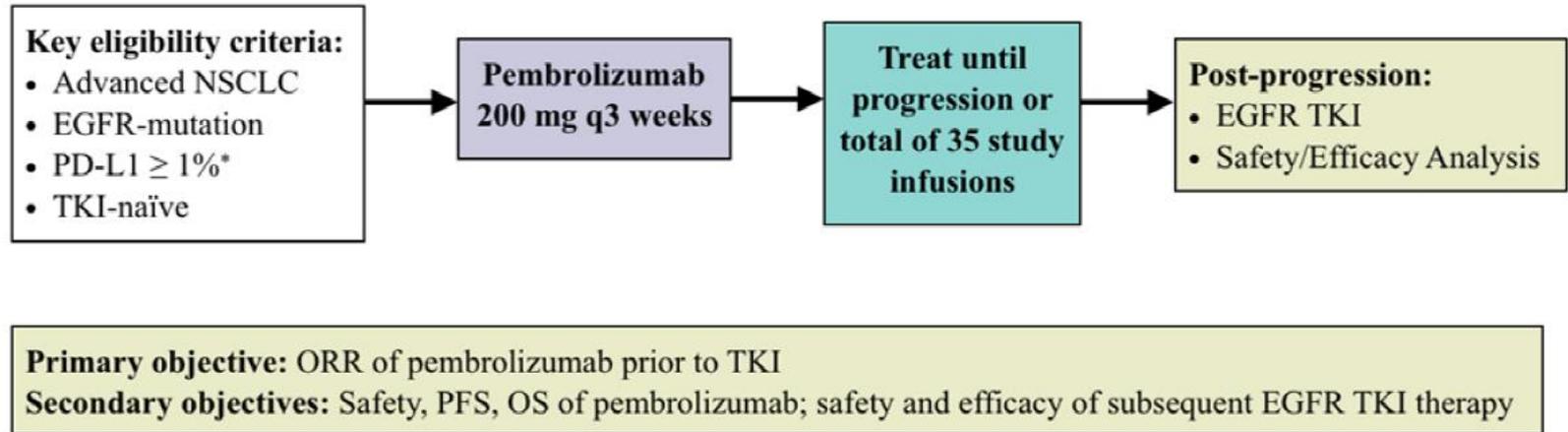
	EGFR N=125	KRAS N=271	ALK N=23	BRAF N=43	ROS1 N=7	HER2 N=29	RET N=16	MET N=36
PDL1 Status available	N = 49	N = 95	N = 11	N = 10	N = 5	N = 15	N = 8	N = 20
PDL1 Status								
Negative	18 36.7%	32 33.7%	4 36.4%	3 30%	0 0%	7 46.7%	2 25%	5 25%
Positive (>1%)	31 63.3%	63 66.3%	7 63.6%	7 70%	5 100%	8 53.3%	6 75%	15 75%
% of tumor cells								
PDL1 staining <10%	21 55.3%	39 48.8%	5 50%	3 33.3%	0 0%	11 84.6%	3 50%	6 40%
≥10%	17 44.7%	41 51.3%	5 50%	6 66.7%	5 100%	2 15.4%	3 50%	9 60%
missing	11	15	1	1	0	2	2	5
% of tumor cells								
PDL1 staining <50%	27 71.1%	54 67.5%	6 60%	4 44.4%	2 40%	13 100%	3 50%	8 53.3%
≥50%	11 28.9%	26 32.5%	4 40%	5 55.6%	3 60%	0 0%	3 50%	7 46.7%
missing	11	15	1	1	0	2	2	5
% of tumor cells								
PDL1 positive								
Median	3.5	12.5	7.5	50	90	0	26	30
Range	0-90	0-100	0-90	0-90	20-100	0-25	0-80	0:100
missing	11	15	1	1	0	2	2	5

IO = immuno-oncology; PFS = progression-free survival; ICI = immune checkpoint inhibitor.
Mazieres J, et al. *Ann Oncol.* 2019;30(8):1321-1328.



Practical Updates
in Primary Care

Pembrolizumab in PD-L1 >1%, EGFR-Mutated mNSCLC



*Performed with an IHC assay in a CLIA-approved laboratory.

ORR = overall response rate; OS = overall survival; CLIA = clinical laboratory improvement amendments.

Lisberg AE, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; June 1-5, 2018; Chicago, IL.



Potentially Fatal Pneumonitis with Anti-PD-1 with Subsequent EGFR TKI – Safety Data

Pembrolizumab: Treatment related adverse events (trAEs)

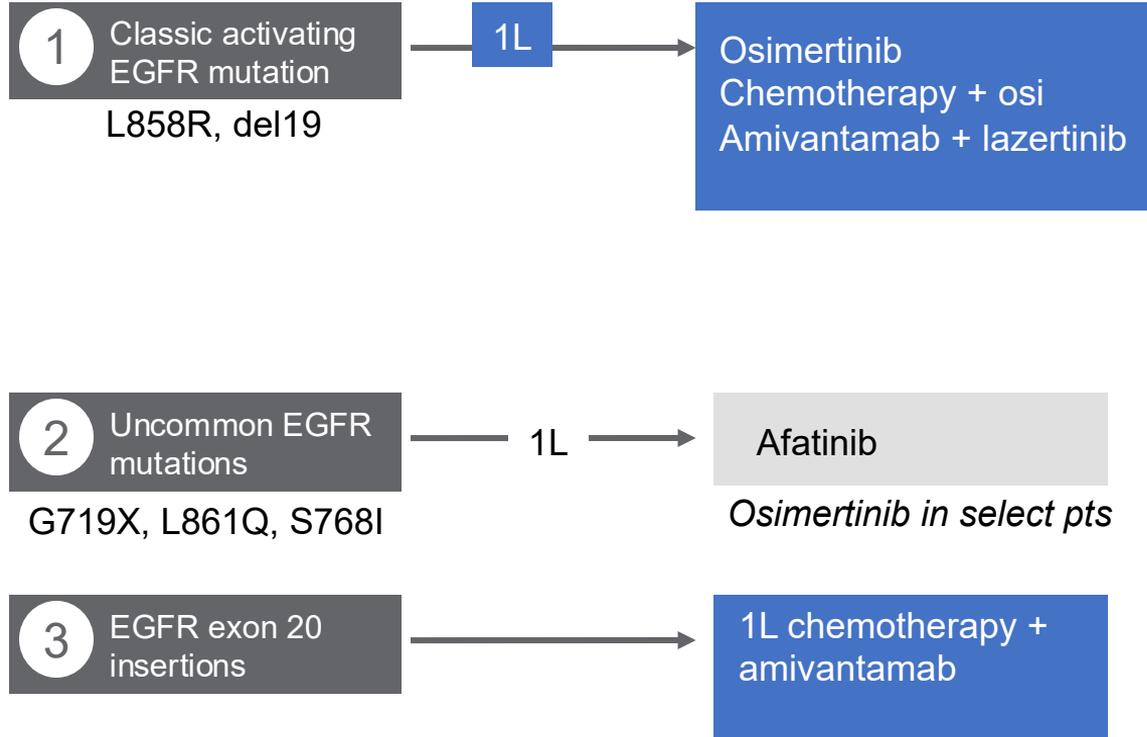
AE Term	Any trAE N = 11 (%)	trAE Grade 3-5 N = 11 (%)
Integument		
Rash	3 (27.3%)	0
Endocrine		
Adrenal insufficiency	1 (9.1%)	0
Gastrointestinal		
Diarrhea	2 (18.2%)	0
Other		
Flu-like symptoms	2 (18.2%)	0
Chills	1 (9.1%)	0
Laboratory Abnormalities		
Alanine & Aspartate Aminotransferase increased	1 (9.1%)	1 (9.1%)
Alkaline phosphatase increased	1 (9.1%)	0
Thyroid-stimulating hormone decreased	1 (9.1%)	0

Subsequent TKI: Treatment related adverse events (trAEs)

AE Term	Any trAE N = 7 (%)	trAE Grade 3-5 N = 7 (%)
Integument		
Rash	4 (57.1%)	0
Respiratory		
Pneumonitis	1 (14.3%)	1 (14.3%)
Gastrointestinal		
Diarrhea	2 (28.6%)	1 (14.3%)
Laboratory Abnormalities		
Transaminitis	1 (14.3%)	1 (14.3%)



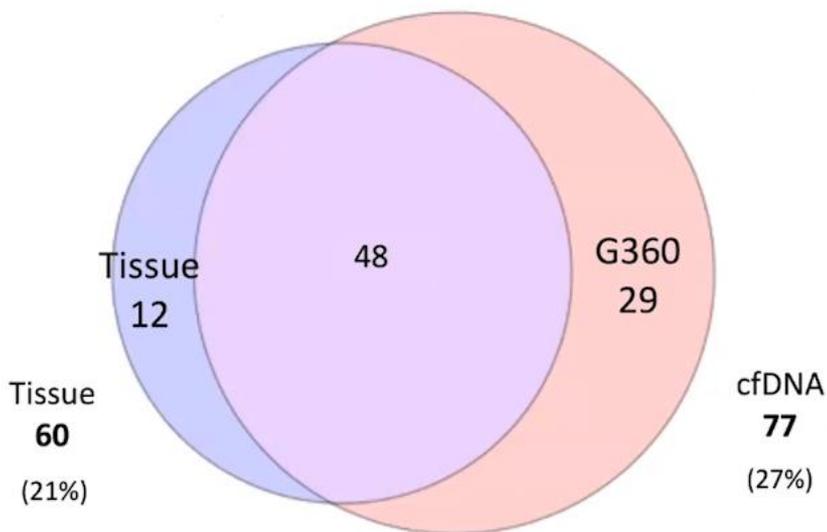
Updates in Management of EGFR-Mutated NSCLC



Non-Invasive vs Invasive Lung Evaluation (NILE)

EGFR point mutation, indel; ALK fusion; ROS1 fusion; BRAF V600E; RET fusion; ERBB2 point mutation; MET exon 14 skip, amplification

cfDNA identified 27%, tissue testing 21%
p<0.0001 for non-inferiority



89/282 (32%) positive by either method

Concordance >98%;
PPV 100%

Tissue

	Pos	Neg	Total
cfDNA			
Pos	48	29	77
Neg	12	193	205
Total	60	222	282

PPV = positive predictive value.

Leigh NB, et al. *Clin Cancer Res.* 2019;25(15):4691-4700.



Practical Updates
in Primary Care



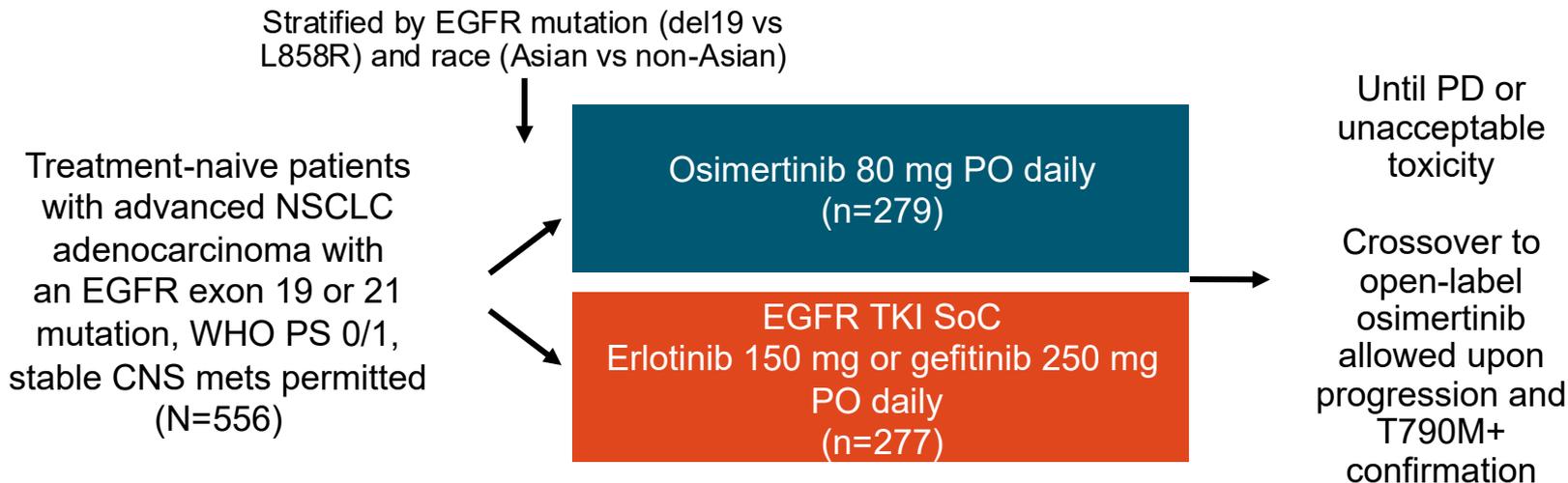
**Practical Updates
in Primary Care**

EGFR TKI Therapy for Metastatic NSCLC

**Sandip Patel, MD, FASCO
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UCSD**

FLAURA: 1st-Line Osimertinib vs Erlotinib or Gefitinib for EGFR-Mutated Advanced NSCLC

- Double-blind phase III study



- Primary endpoint: Investigator-assessed PFS (RECIST v1.1)
- Secondary endpoints, including ORR, DoR, DCR, depth of response, OS, PROs, safety

DoR = duration of response; DCR = disease control rate; PROs = patient-reported outcomes; SoC = standard of care; PD = progressive disease.

Soria JC, et al. *N Engl J Med.* 2018;378(2):113-125. Ramalingam SS, et al. *N Engl J Med.* 2020;382(1):41-50.

FLAURA: Survival

PFS

Median PFS,
Mo (95% CI)

Osimertinib 18.9 (15.2-21.4)

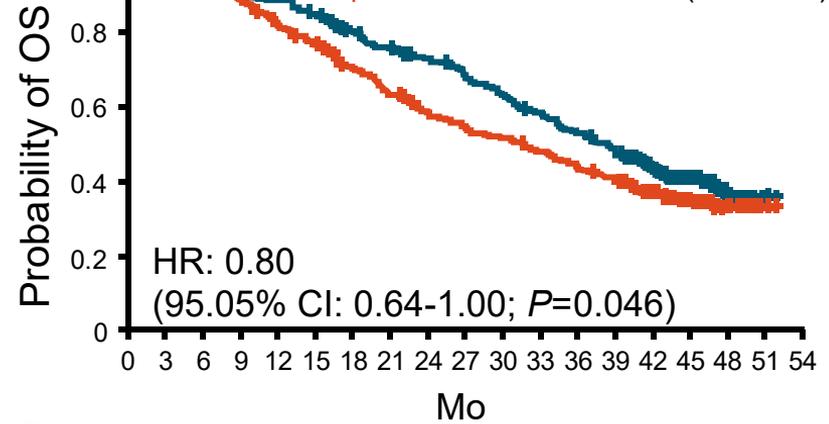
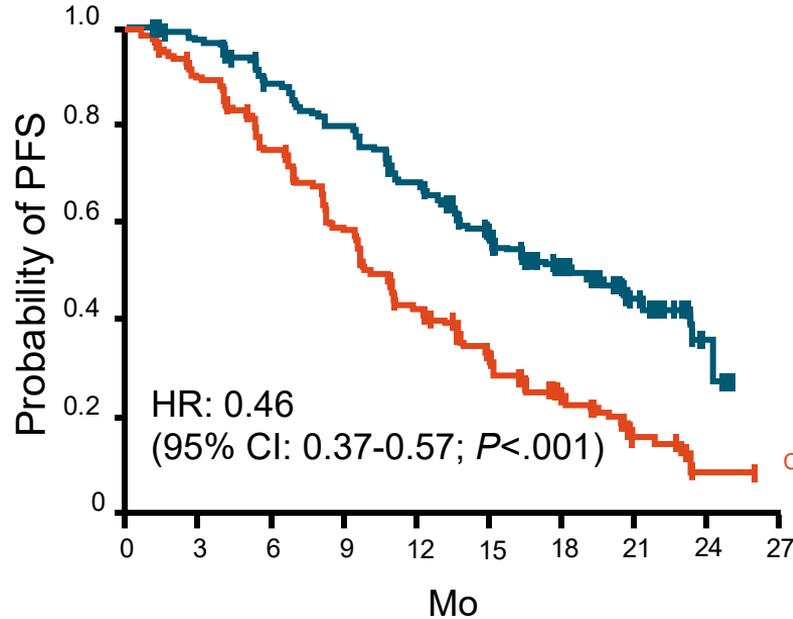
Comparator EGFR TKI 10.2 (9.6-11.1)

Updated OS

Median OS,
Mo (95% CI)

Osimertinib 38.6 (34.5-41.8)

Comparator EGFR TKI 31.8 (26.6-36.0)



Patients at Risk, n

Mo	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54
Osimertinib	279	276	270	254	245	236	217	204	193	180	166	153	138	123	86	50	17	2	0
Comparator EGFR-TKI	277	263	252	239	219	205	182	165	148	138	131	121	110	101	72	40	17	2	0

Patients at Risk, n

Mo	0	3	6	9	12	15	18	21	24	27
Osimertinib	279	262	233	210	178	139	71	26	4	0
Comparator EGFR TKI	277	239	197	152	107	78	37	10	2	0

CI = confidence interval; HR = hazard ratio.

Soria JC, et al. *N Engl J Med.* 2018;378(2):113-125. Ramalingam SS, et al. *N Engl J Med.* 2020;382(1):41-50.

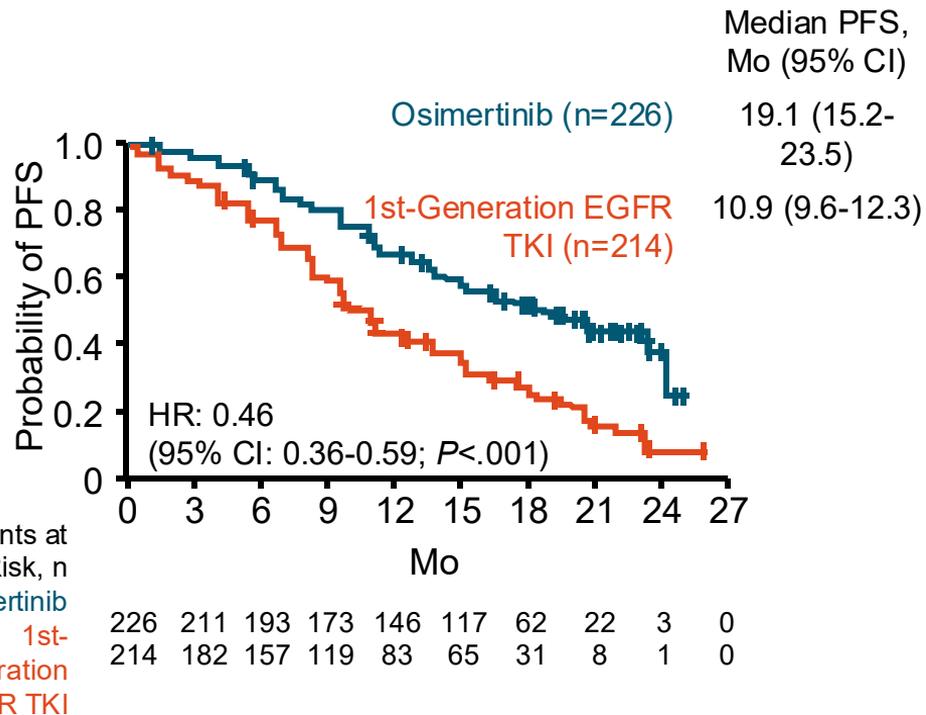
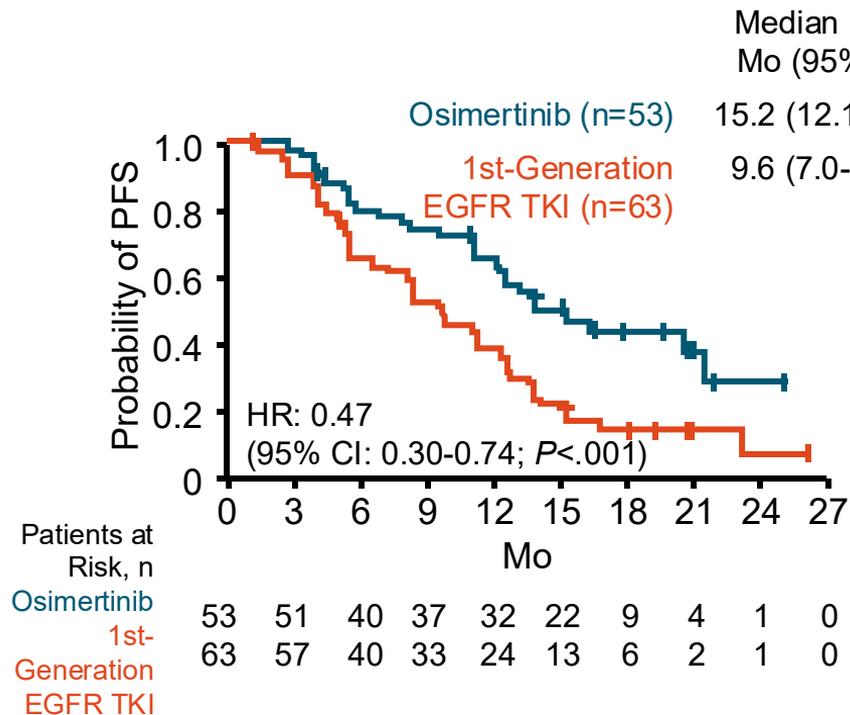


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FLAURA: PFS by CNS Metastases at Baseline

With CNS Metastases at BL (n=116)

Without CNS Metastases at BL (n=440)



CNS progression occurred in 17 patients (6%) with osimertinib vs 42 (15%) with 1st-generation EGFR TKI

FLAURA: Updated Safety

AE, n (%)	Osimertinib (n=279)			Comparator EGFR TKI (n=277)		
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
Diarrhea	119 (43)	41 (15)	7 (3)	118 (43)	35 (13)	7 (3)
Rash or acne	132 (47)	29 (10)	3 (1)	111 (40)	88 (32)	20 (7)
Nail effects	61 (22)	45 (16)	2 (1)	58 (21)	35 (13)	2 (1)
Dry skin	89 (32)	16 (6)	1 (<1)	78 (28)	21 (8)	3 (1)
Stomatitis	66 (24)	14 (5)	1 (<1)	51 (18)	8 (3)	1 (<1)
Decreased appetite	32 (11)	27 (10)	7 (3)	29 (10)	24 (9)	5 (2)
Cough	42 (15)	18 (6)	0	33 (12)	17 (6)	0
Nausea	37 (13)	18 (6)	0	31 (11)	23 (8)	0
Constipation	42 (15)	9 (3)	0	29 (10)	10 (4)	0
Pruritus	41 (15)	8 (3)	1 (<1)	33 (12)	14 (5)	0
Increased ALT	11 (4)	6 (2)	2 (1)	30 (11)	19 (7)	21 (8)

- No new cases of ILD or pneumonitis observed since primary analysis of osimertinib vs comparator EGFR TKI: ILD, 2% vs 1%; pneumonitis, 2% vs 1%
- Pooled analysis of osimertinib-treated patients from FLAURA and AURA3 reported LVEF decreases to <50% in 3.9% and cardiac failure-related AEs in 2.6%; no dose-response relationship observed

ILD = interstitial lung disease; LVEF = left ventricular ejection fraction; ALT = alanine aminotransferase.
 Ramalingam SS, et al. *N Engl J Med*. 2020;382(1):41-50. Soria JC, et al. *N Engl J Med*. 2018;378(2):113-125.
 Ewer MS, et al. *J Clin Oncol*. 2021;39(4):328-337.



FLAURA2: Osimertinib + Chemotherapy Phase III Trial Design

Safety run-in period (N=30)
Published in *ESMO Open*, 2021



Patients with untreated locally advanced/metastatic EGFRm NSCLC

Key inclusion criteria

- Aged ≥ 18 years (Japan: ≥ 20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del/L858R (local/central test)
- WHO PS 0/1
- No prior systemic therapy for advanced NSCLC
- Stable CNS metastases were allowed
- Brain scans at baseline (MRI/CT)



Stratification by

- **Race** (Chinese Asian/non-Chinese Asian/non-Asian)
- **EGFRm** (local/central test)
- **WHO PS** (0/1)

Osimertinib 80 mg (QD)
+ pemetrexed 500 mg/m²
+ carboplatin AUC5
or cisplatin 75 mg/m²
(Q3W for 4 cycles for platinum-based treatments)

Maintenance osimertinib 80 mg (QD)
+ pemetrexed (Q3W)

Randomization
1:1 (N=557)



Osimertinib 80 mg (QD)



Follow-up

- RECIST 1.1 assessment at 6 and 12 weeks, then every 12 weeks until RECIST 1.1-defined radiological disease progression or other withdrawal criteria were met

- **Primary endpoint:** PFS by investigator assessment per RECIST 1.1
 - **Sensitivity analysis:** PFS by BICR assessment per RECIST 1.1
- **Secondary endpoints:** OS, ORR, DoR, DCR, HRQoL, safety (AEs by CTCAE v5) and PFS2

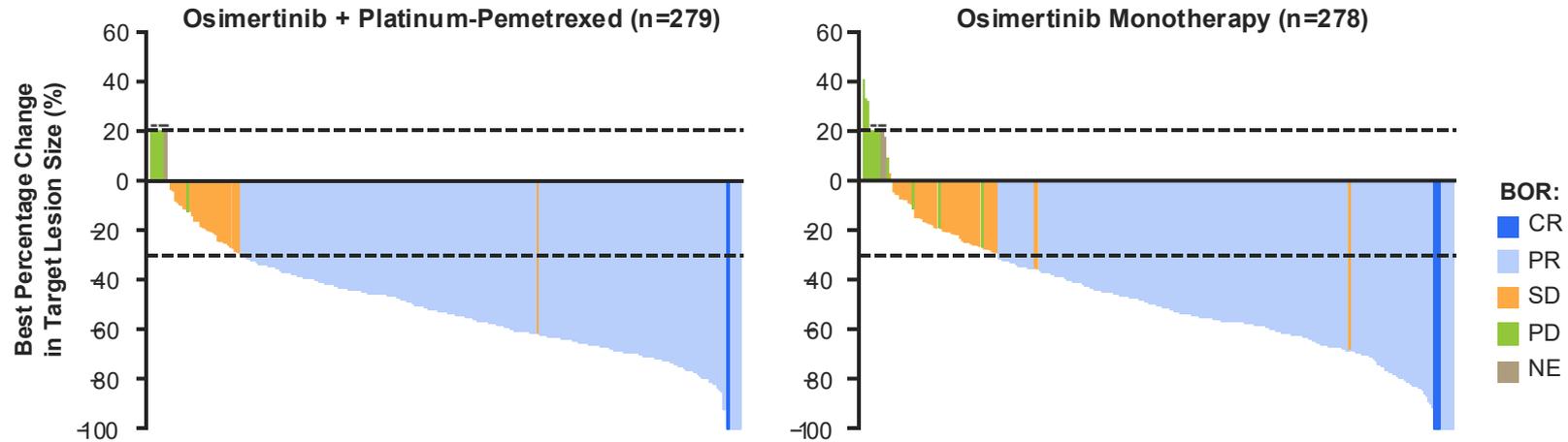
PS = performance status; MRI = magnetic resonance imaging; HRQoL = health-related quality of life; CTCAE = Common Terminology Criteria for Adverse Events.

Jänne PA, et al. Presented at: World Conference on Lung Cancer (WCLC); September 9-12, 2023; Singapore.



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FLAURA2: Tumor Response per Investigator



	Osimertinib + Platinum-Pemetrexed (n=279)	Osimertinib Monotherapy (n=278)
Median best percentage change in target lesion size, % (range)	-52.6 (-100.0, 20.0)	-50.0 (-100.0, 40.4)
Objective response rate, % (95% CI)	83 (78, 87)	76 (70, 80)
Adjusted odds ratio (95% CI)	1.61 (1.06, 2.44)	
Complete response, n (%)	1 (<1)	2 (1)
Partial response, n (%)	231 (83)	208 (75)
Stable disease ≥35 days, n (%)	34 (12)	51 (18)
Progression, n (%)	7 (3)	12 (4)
Median duration of response, months (95% CI)	24.0 (20.9, 27.8)	15.3 (12.7, 19.4)

BOR = best overall response; CR = complete response; PR = partial response; SD = stable disease.

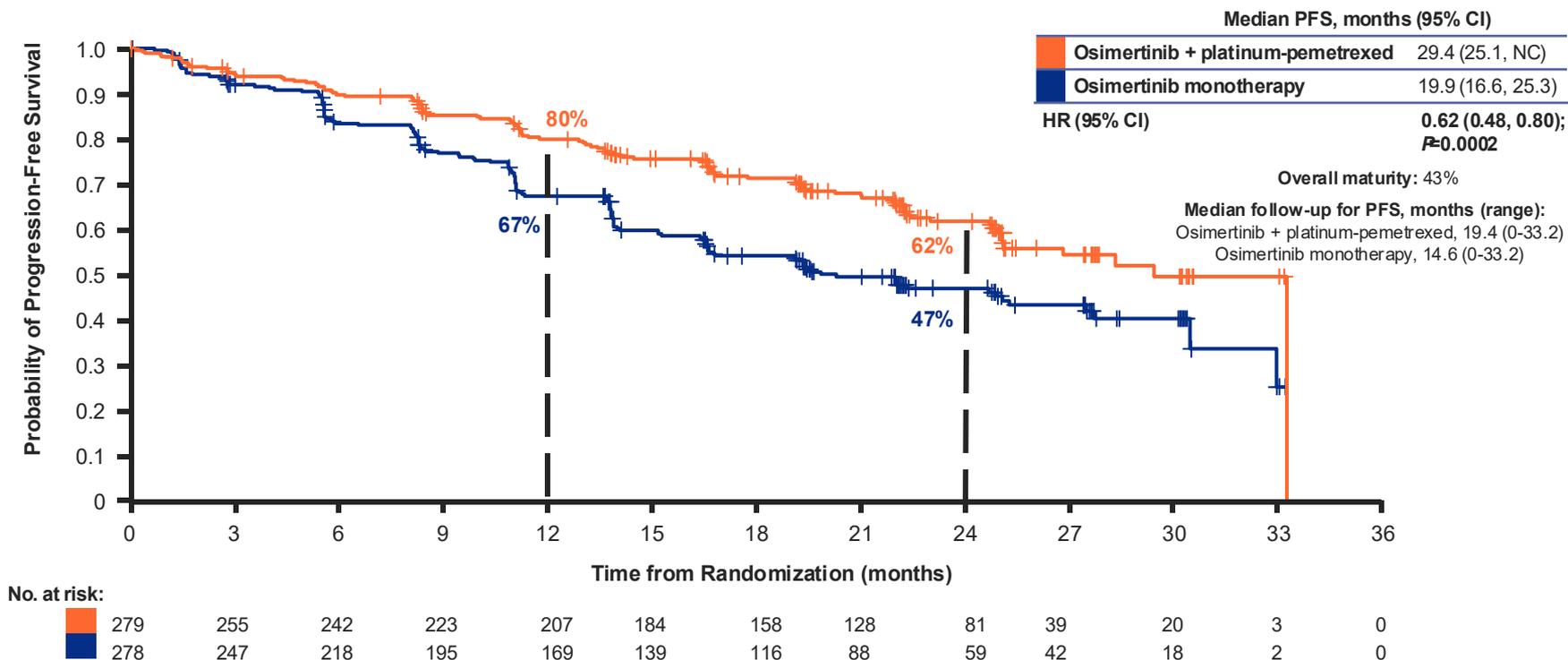
Jänne PA, et al. Presented at: WCLC; September 9-12, 2023; Singapore.



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FLAURA2: PFS per BICR

Median PFS was improved by ~9.5 months with osimertinib plus platinum-pemetrexed vs osimertinib monotherapy



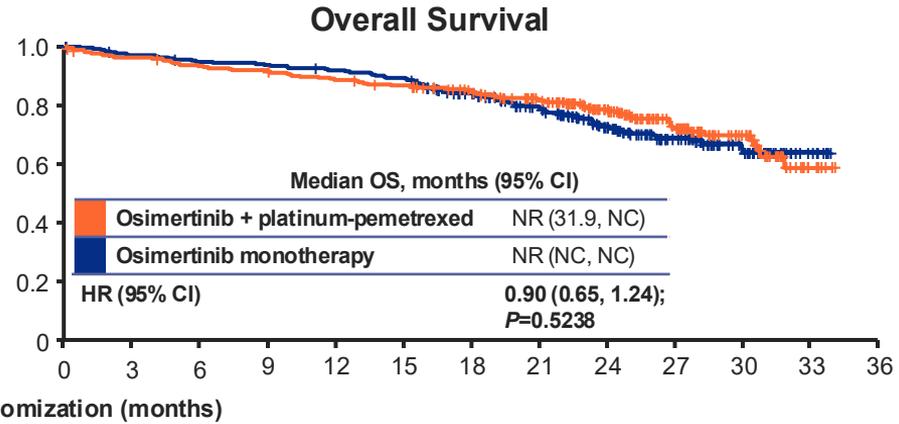
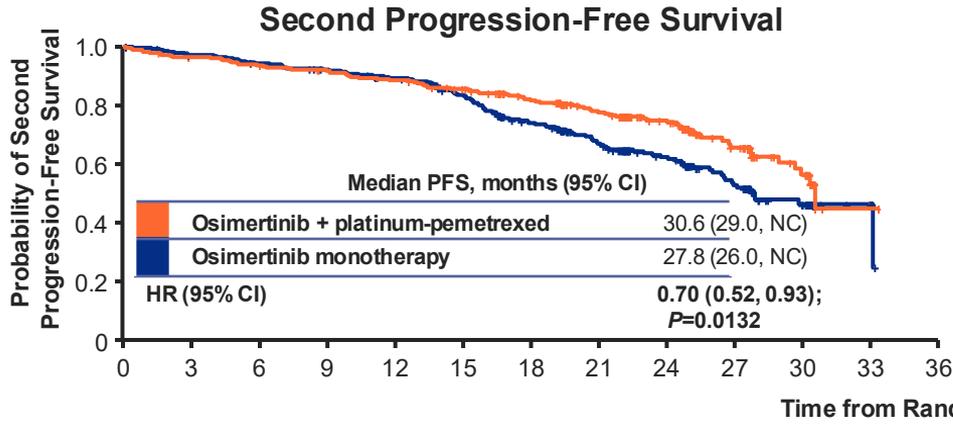
BICR = blinded independent central review.

Jänne PA, et al. Presented at: WCLC; September 9-12, 2023; Singapore.



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FLAURA2: PFS2 and Interim OS Analysis



No. at risk:

279	263	254	247	236	220	194	158	107	54	26	3	0	279	267	258	253	244	237	219	191	139	84	46	7	0
278	265	255	246	232	206	166	130	90	58	26	3	0	278	267	260	257	251	244	214	185	133	85	46	10	0

- PFS2 and OS were immature at this interim analysis (34% and 27% data maturity, respectively)
- At DCO, 57/123 patients (46%) in the osimertinib plus platinum-pemetrexed arm and 91/151 patients (60%) in the osimertinib monotherapy arm received any subsequent anti-cancer treatment
 - In both arms, cytotoxic chemotherapy was the most common subsequent anti-cancer treatment (33% and 54% in the combination and monotherapy arms, respectively)

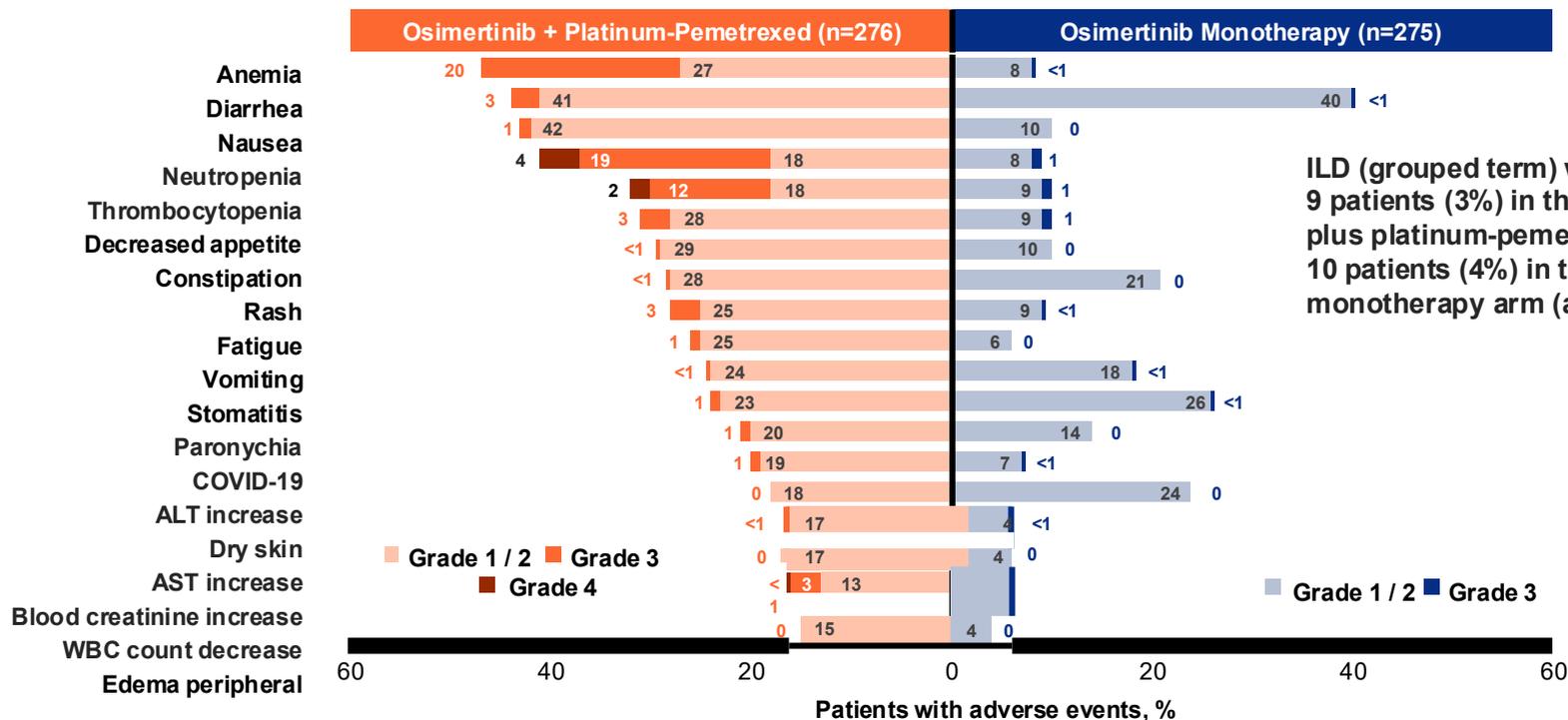
DCO = data cutoff.

Jänne PA, et al. Presented at: WCLC; September 9-12, 2023; Singapore.



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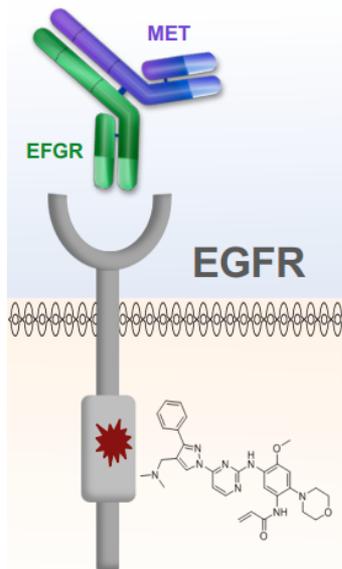
FLAURA2: Common AEs (>15% of Patients)



ILD (grouped term) was reported in 9 patients (3%) in the osimertinib plus platinum-pemetrexed arm, and 10 patients (4%) in the osimertinib monotherapy arm (all grades)

Of the most common AEs (occurring in $\geq 15\%$ of patients in either arm), all Grade 4 AEs in the osimertinib plus platinum-pemetrexed arm were hematological toxicities, known to be associated with chemotherapy; there were no common Grade 4 AEs in the monotherapy arm

Amivantamab and Lazertinib

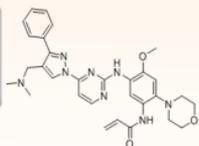


Amivantamab (JNJ372)

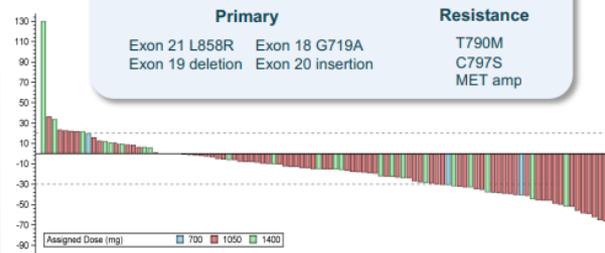
- Fully human bispecific antibody that targets EGFR and MET
- Has immune cell-directing activity¹
- Demonstrated clinical activity across diverse EGFRm NSCLC²
- Granted FDA Breakthrough Therapy Designation for EGFRm Exon20ins NSCLC post-chemotherapy

Lazertinib

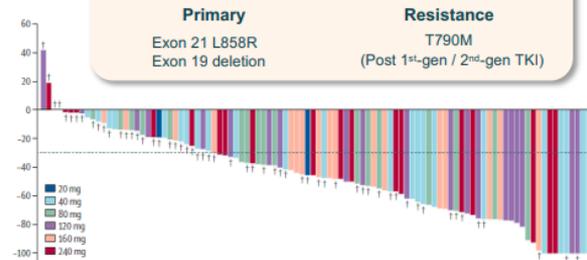
- Potent 3rd-gen TKI with efficacy seen in activating mutations, T790M, and CNS disease³
- Low rates of EGFR-related toxicity such as rash and diarrhea³
- Safety profile that supports combination with other anti-EGFR molecules



Efficacy in Primary and Resistance Mutations



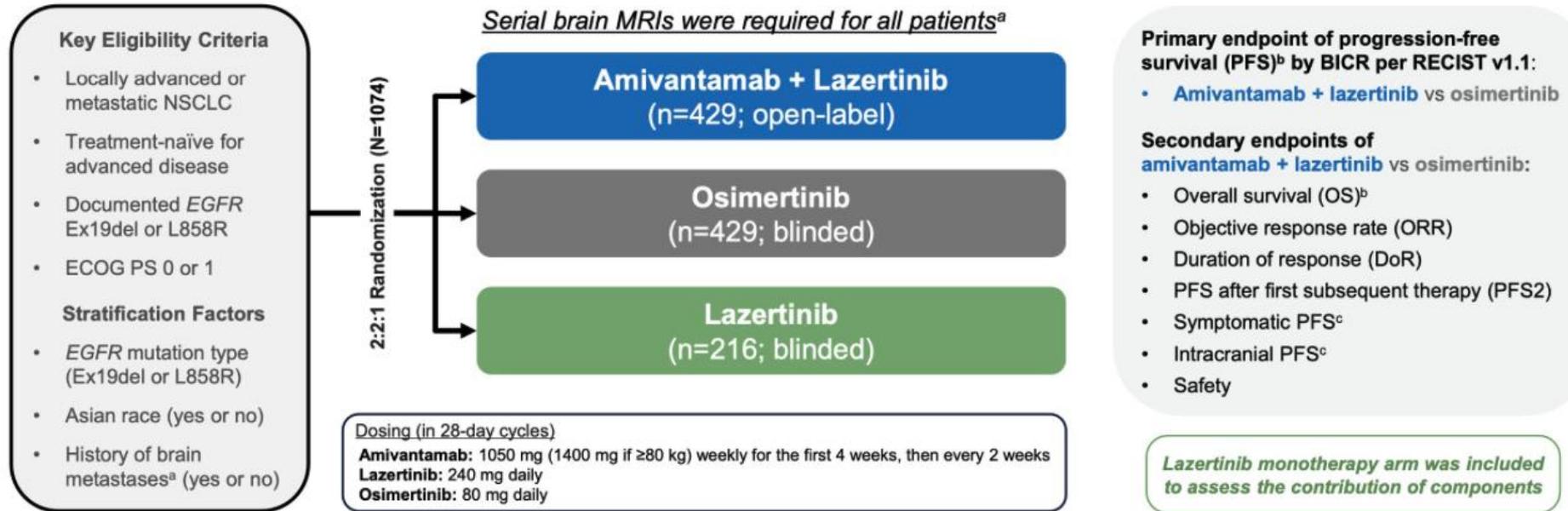
Efficacy in Primary and Resistance Mutations



¹Vijayaraghavan *Mol Cancer Ther* Aug 3, 2020 ²Haura ASCO 2019 Oral Abstract #9009; ³Ahn *Lancet Oncol* 20(12):P1681 (Reprinted from *The Lancet* 2020, with permission from Elsevier). amp, amplification; BT, Breakthrough Therapy Designation; EGFR, epidermal growth factor receptor; EGFRm, EGFR mutant; gen, generation; MET, mesenchymal epithelial transition; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor



MARIPOSA: Phase 3 Study Design



MARIPOSA (ClinicalTrials.gov Identifier: NCT04487080) enrollment period: November 2020 to May 2022; data cut-off: 11-Aug-2023.

^aBaseline brain MRI was required for all patients and performed ≤28 days prior to randomization; patients who could not have MRIs were allowed to have CT scans. Brain scan frequency was every 8 weeks for the first 30 months and then every 12 weeks thereafter for patients with a history of brain metastasis and every 24 weeks for patients with no history of brain metastasis. Extracranial tumor assessments were conducted every 8 weeks for the first 30 months and then every 12 weeks until disease progression is confirmed by BICR.

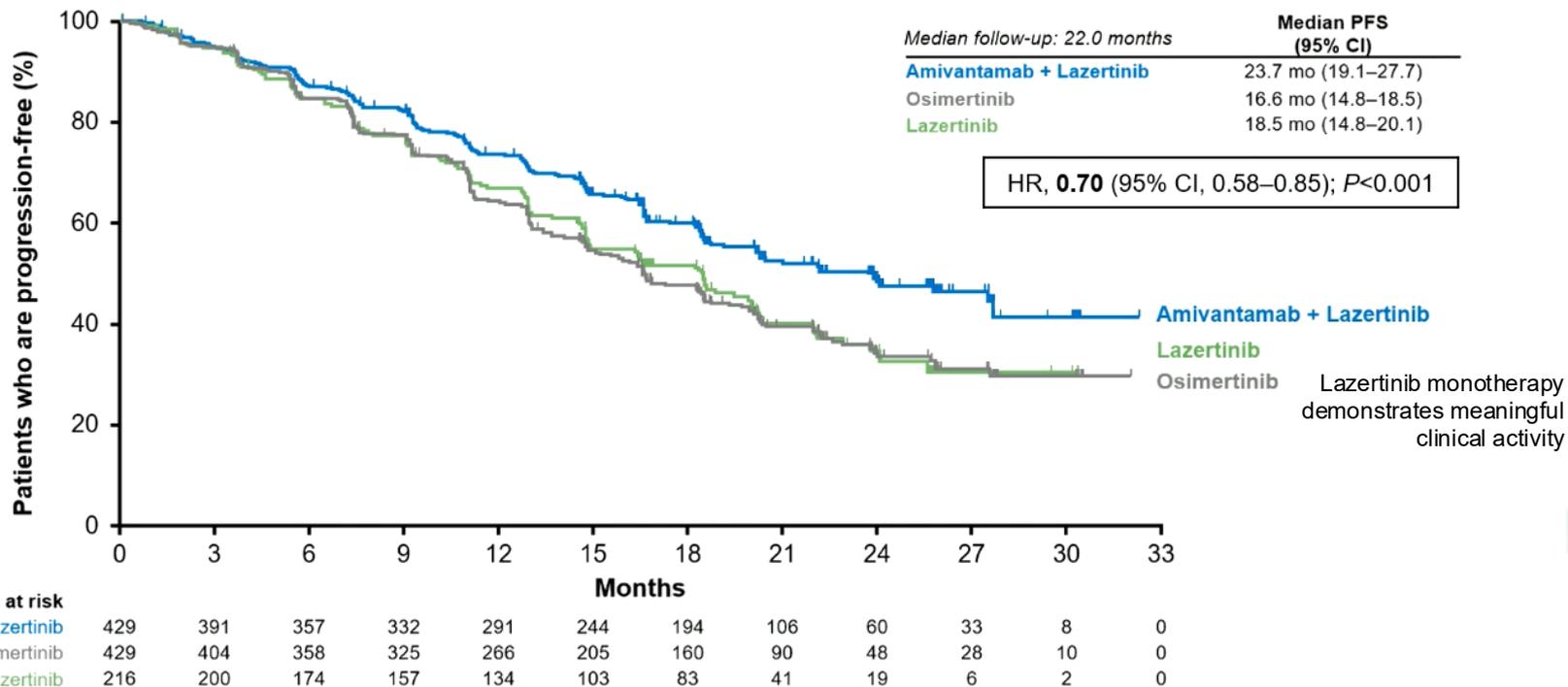
^bKey statistical assumptions: 800 patients with 450 PFS events would provide approximately 90% power for amivantamab + lazertinib vs osimertinib to detect a HR of 0.73 using a log-rank test, with an overall two-sided alpha of 0.05 (assuming an incremental median PFS of 7 months). Statistical hypothesis testing included PFS and then OS.

^cThese secondary endpoints (symptomatic and intracranial PFS) will be presented at a future congress.



Progression-Free Survival by BICR

Amivantamab + lazertinib reduced the risk of progression or death by 30% and improved PFS by 7.1 months



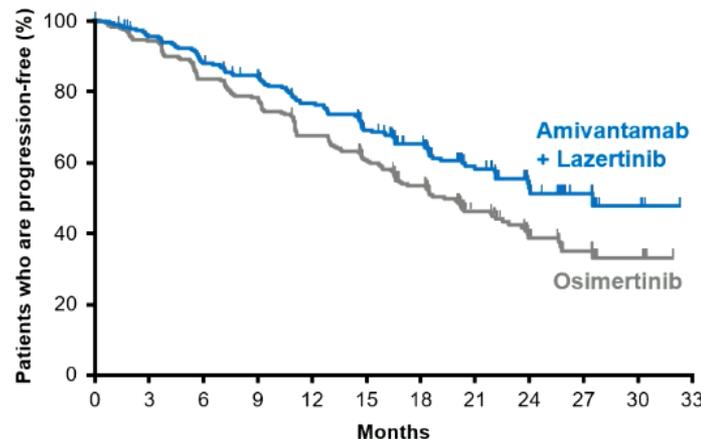
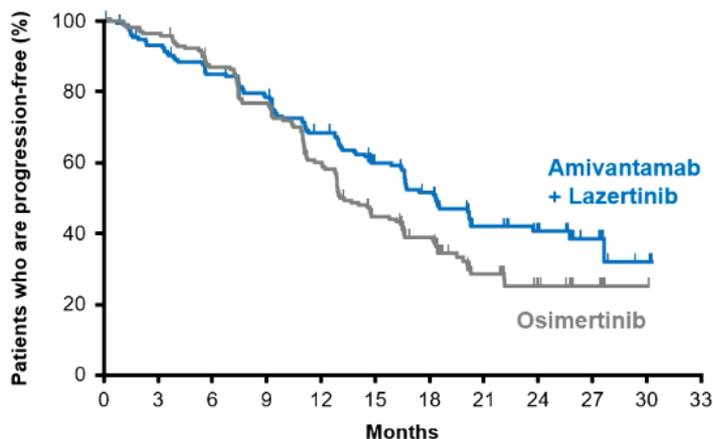
Consistent PFS with or without Brain Metastases

With History of Brain Metastases	Median PFS (95% CI)
Amivantamab + Lazertinib	18.3 mo (16.6–23.7)
Osimertinib	13.0 mo (12.2–16.4)

Without History of Brain Metastases	Median PFS (95% CI)
Amivantamab + Lazertinib	27.5 mo (22.1–NE)
Osimertinib	19.9 mo (16.6–22.9)

HR, **0.69** (95% CI, 0.53–0.92)

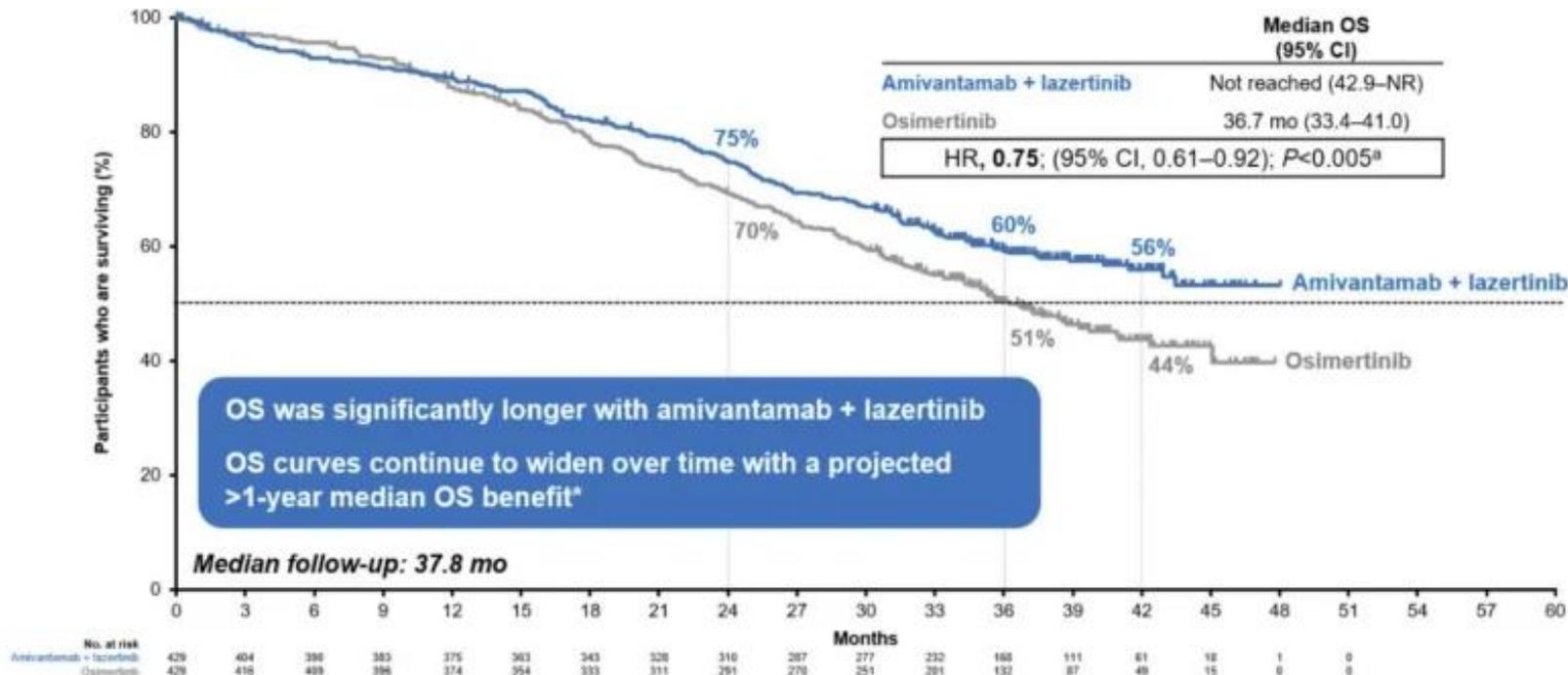
HR, **0.69** (95% CI, 0.53–0.89)



	No. at risk	0	3	6	9	12	15	18	21	24	27	30	33
Amivantamab + Lazertinib	178	162	146	134	115	92	71	34	24	12	3	0	
Osimertinib	172	164	146	126	95	64	47	21	11	6	1	0	

	No. at risk	0	3	6	9	12	15	18	21	24	27	30	33
Amivantamab + Lazertinib	251	229	211	198	176	152	123	72	36	21	5	0	
Osimertinib	257	240	212	199	171	141	113	69	37	22	9	0	

MARIPOSA: Overall Survival



OS was significantly longer with amivantamab + lazertinib
 OS curves continue to widen over time with a projected
 >1-year median OS benefit*

Median follow-up: 37.8 mo

*Based on an exponential distribution assumption of OS in both arms, the improvement in median OS is projected to exceed 1 year.

Note: Last participant was enrolled in May 2022. Clinical cutoff date was December 4, 2024. In total, 390 deaths had occurred in the amivantamab + lazertinib (173 deaths) and osimertinib (217 deaths) arms.

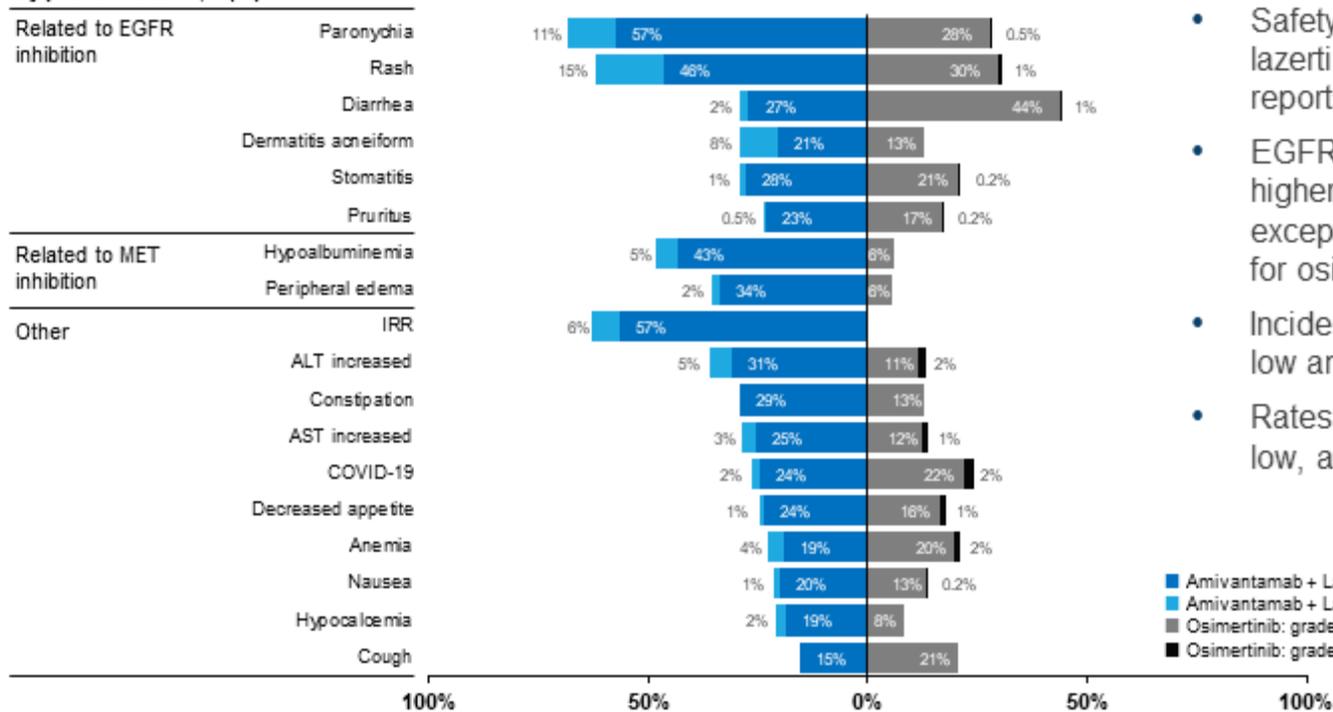
^aP-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified Cox regression model.

Yang JCH, et al. Presented at: ELCC; March 26-29, 2025; Paris, France.



Safety Profile

Most common TEAEs ($\geq 20\%$) by preferred term, n (%)



- Safety profile of amivantamab + lazertinib was consistent with prior reports, mostly grades 1-2
- EGFR- and MET-related AEs were higher for amivantamab + lazertinib except diarrhea, which was higher for osimertinib
- Incidence of grade 4-5 AEs was low and comparable between arms
- Rates of ILD/pneumonitis remained low, at $\sim 3\%$ for both arms

■ Amivantamab + Lazertinib: grade 1-2
■ Amivantamab + Lazertinib: grade ≥ 3
■ Osimertinib: grade 1-2
■ Osimertinib: grade ≥ 3

IRR = infusion-related reaction.

Cho BC, et al. Presented at: ESMO Congress; October 20-24, 2023; Madrid, Spain.



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Three Options for Adv/Met EGFRm NSCLC

	Osimertinib Monotherapy FLAURA (vs Gefitinib/Erlotinib)	Osimertinib + Chemo FLAURA2 (vs Osimertinib)	Amivantamab + Lazertinib MARIPOSA (vs Osimertinib)
PFS, Months	18.9 months (95% CI, 15.2-21.4) HR 0.46 (95% CI, 0.37-0.57)	29.4 months (95% CI, 25.1-NC) HR 0.62 (95% CI, 0.48-0.80)	23.7 months (95% CI, 19.1-27.7) HR 0.70 (0.58-0.85)
OS, Months	38.6 months (95% CI, 34.5-41.8) HR 0.80 (95% CI, 0.64-1.00)	NR HR 0.90 (95% CI, 0.65-1.24)	NR HR 0.80 (95% CI, 0.61-1.05)
Mode of Administration	PO	PO + IV	PO + IV
AE Summary	Diarrhea, rash, paronychia, stomatitis	EGFR toxicities plus... Nausea/vomiting, decreased appetite, cytopenias	EGFR toxicities plus... VTE, hypoalbuminemia, peripheral edema, IRR

VTE = venous thromboembolism.

Soria JC, et al. *N Engl J Med.* 2018;378(2):113-125. Ramalingam SS, et al. *N Engl J Med.* 2020;382(1):41-50.

Ewer MS, et al. *J Clin Oncol.* 2021;39(4):328-337. Jänne PA, et al. Presented at: WCLC; September 9-12, 2023;

Singapore. Cho BC, et al. Presented at: ESMO Congress; October 20-24, 2023; Madrid, Spain. Yang JCH, et al.

Presented at: ELCC; March 26-29, 2025; Paris, France.



Hypothetical Future Approaches for Adv/Met EGFRm NSCLC

1L

2L

FLAURA

Osimertinib (mPFS 18.9 mo)	Carbo/Pem (mPFS 4.2-5.5 mo)	Ami/Lazer (mPFS 5.1mo)
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Oral (daily)
Rash, Diarrhea, Paronychia- mainly mild

FLAURA2

Osimertinib + Carbo/Pem (mPFS 25.5 mo; HR 0.62 vs. osi)	Ami/Lazer (mPFS 5.1mo)
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Intravenous (every 3 weeks)
Hematologic toxicities, nausea
AE's greatest during first 3 months

MARIPOSA

Amivantamab + Lazertinib (mPFS 23.7 mo; HR 0.70 vs. osi)	Carbo/Pem (mPFS 4.2-5.5 mo)
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Intravenous (every 2 weeks)
Paronychia, rash, IRR, VTE
AE's likely to continue through first-line treatment

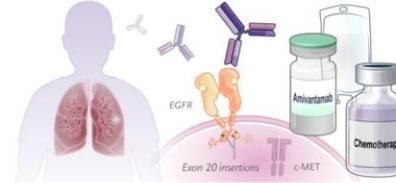
MARIPOSA 2

Osimertinib (mPFS 18.9 mo)	Carbo/Pem + Ami/Lazer (mPFS 8.3 mo, HR 0.44 vs chemo)
Osimertinib (mPFS 18.9 mo)	Carbo/Pem + Ami (mPFS 6.3 mo, HR 0.48 vs chemo)

Amivantamab plus Chemotherapy in NSCLC with EGFR Exon 20 Insertions

CLINICAL PROBLEM

In patients with non–small-cell lung cancer (NSCLC) with exon 20 insertions in the gene encoding epidermal growth factor receptor (EGFR), amivantamab — an EGFR mesenchymal–epithelial transition factor (MET) bispecific antibody with immune cell–directing activity — is approved for use after progression occurs during or after receipt of first-line platinum-based chemotherapy. A pivotal phase 1 trial also showed safety and antitumor activity of amivantamab plus carboplatin–pemetrexed chemotherapy (amivantamab–chemotherapy). More data on this combination therapy are needed.



CLINICAL TRIAL

Design: A phase 3, international, randomized trial assessed the efficacy and safety of amivantamab–chemotherapy as compared with chemotherapy alone as first-line therapy in patients with advanced NSCLC with EGFR exon 20 insertions.

Intervention: 308 adults were assigned to receive intravenous amivantamab (1400 mg weekly for the first 4 weeks; 1750 mg every 3 weeks starting at week 7 until progression occurred) plus carboplatin–pemetrexed chemotherapy or chemotherapy alone, in 21-day cycles. Patients assigned to chemotherapy alone could receive amivantamab monotherapy after disease progression was documented. The primary outcome was progression-free survival.

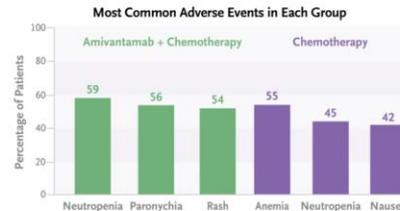
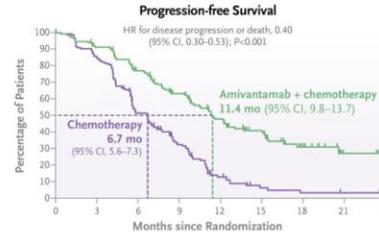
RESULTS

Efficacy: Progression-free survival was significantly longer in the amivantamab–chemotherapy group than in the chemotherapy group.

Safety: No new safety signal emerged for any agent. Discontinuation of amivantamab because of adverse reactions was reported in 7% of patients.

LIMITATIONS AND REMAINING QUESTIONS

- Blinding of treatment assignments was not possible because of differences in drug administration, pre-medication requirements, and safety profiles.
- The number of deaths in the trial was too few to provide robust conclusions regarding overall survival; an analysis is planned at approximately 4 years of follow-up.



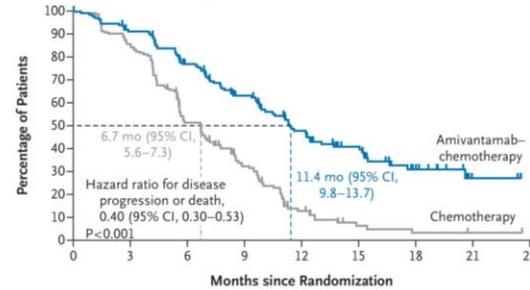
CONCLUSIONS

In patients with previously untreated, advanced NSCLC with EGFR exon 20 insertions, progression-free survival was significantly longer with combination amivantamab–chemotherapy than with chemotherapy alone.



1L Carboplatin/Pemetrexed/Amivantamab: Progression-Free Survival

A Progression-free Survival, Blinded Independent Central Review

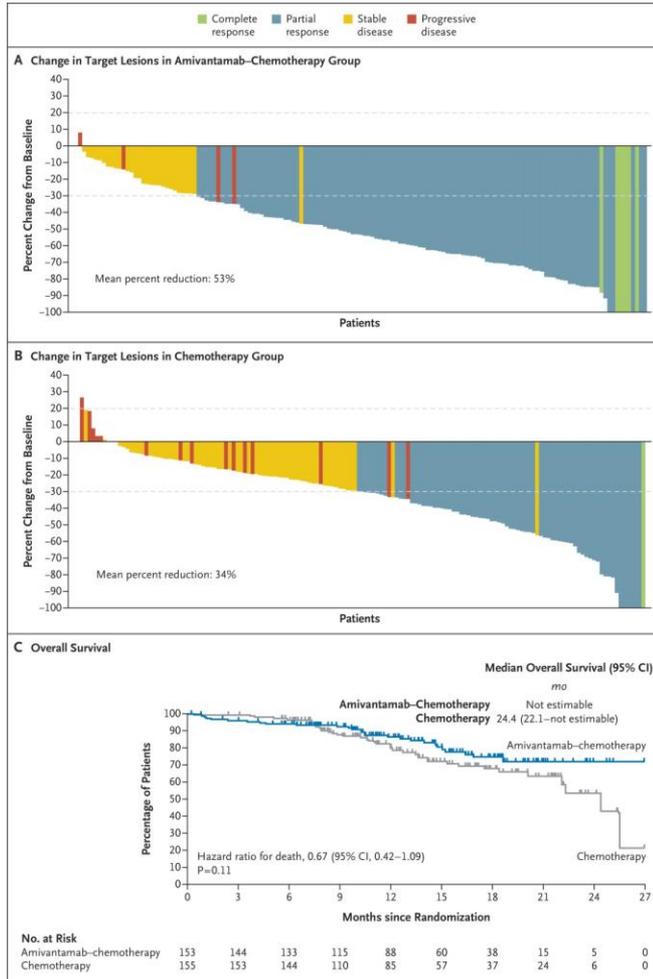


No. at Risk	153	135	105	74	50	33	15	3	0
Amivantamab-chemotherapy									
Chemotherapy	155	131	74	41	14	4	2	1	0

C Subgroup Analysis for Progression-free Survival, Blinded Independent Central Review

Subgroup	Amivantamab- Chemotherapy no. of events/total no.	Chemotherapy	Hazard Ratio for Disease Progression or Death (95% CI)
All patients	84/153	132/155	0.40 (0.30-0.53)
Age			
<65 yr	56/97	77/92	0.37 (0.26-0.53)
≥65 yr	28/56	55/63	0.44 (0.27-0.70)
Sex			
Female	41/85	81/93	0.31 (0.21-0.46)
Male	43/68	51/62	0.51 (0.34-0.78)
Race			
Asian	55/97	77/89	0.36 (0.25-0.52)
Non-Asian	27/53	51/62	0.41 (0.26-0.67)
Weight			
<80 kg	74/132	108/128	0.41 (0.31-0.56)
≥80 kg	10/21	24/27	0.26 (0.12-0.57)
ECOG score			
0	31/59	51/58	0.35 (0.22-0.55)
1	53/94	81/97	0.42 (0.29-0.61)
History of smoking			
Yes	37/65	57/64	0.45 (0.29-0.68)
No	47/88	75/91	0.37 (0.25-0.53)
History of brain metastases			
Yes	28/36	34/38	0.63 (0.38-1.06)
No	56/117	98/117	0.33 (0.23-0.46)

Best Response and Interim Overall Survival



Adverse Events

Table 3. Adverse Events.*

Adverse Events	Amivantamab+Chemotherapy (N=151)		Chemotherapy (N=155)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	<i>number of patients (percent)</i>			
Any event	151 (100)	114 (75)	152 (98)	83 (54)
Any serious event	56 (37)		48 (31)	
Any event resulting in death	7 (5)		4 (3)	
Any event leading to interruption of any agent	104 (69)		56 (36)	
Interruption in dose of amivantamab				
Any	97 (64)			
Related to amivantamab†	63 (42)			
Any event leading to reduction of any agent	73 (48)		35 (23)	
Reduction in dose of amivantamab				
Any	54 (36)			
Related to amivantamab†	54 (36)			
Any event leading to discontinuation of any agent	36 (24)		16 (10)	
Discontinuation of amivantamab				
Any	17 (11)			
Related to amivantamab†	10 (7)			
Discontinuation of all agents because of adverse events‡	12 (8)		12 (8)	
Adverse events reported in ≥15% of patients in either group§				
Neutropenia	89 (59)	50 (33)	70 (45)	35 (23)
Paronychia	85 (56)	10 (7)	0	0
Rash	81 (54)	17 (11)	12 (8)	0
Anemia	76 (50)	16 (11)	85 (55)	19 (12)
Infusion-related reaction	63 (42)	2 (1)	2 (1)	0
Hypoalbuminemia	62 (41)	6 (4)	15 (10)	0
Constipation	60 (40)	0	47 (30)	1 (1)
Leukopenia	57 (38)	17 (11)	50 (32)	5 (3)
Nausea	55 (36)	1 (1)	65 (42)	0
Thrombocytopenia	55 (36)	15 (10)	46 (30)	16 (10)
Decreased appetite	54 (36)	4 (3)	43 (28)	2 (1)
Increased alanine aminotransferase	50 (33)	6 (4)	56 (36)	2 (1)
Increased aspartate aminotransferase	47 (31)	1 (1)	51 (33)	1 (1)
Dermatitis acneiform	47 (31)	6 (4)	5 (3)	0
Peripheral edema	45 (30)	2 (1)	16 (10)	0
Stomatitis	38 (25)	2 (1)	9 (6)	0
Covid-19	36 (24)	3 (2)	21 (14)	1 (1)
Diarrhea	33 (22)	5 (3)	20 (13)	2 (1)
Hypokalemia	32 (21)	13 (9)	13 (8)	2 (1)
Vomiting	32 (21)	5 (3)	29 (19)	1 (1)
Asthenia	30 (20)	8 (5)	29 (19)	4 (3)
Pyrexia	24 (16)	0	9 (6)	0
Fatigue	23 (15)	1 (1)	32 (21)	2 (1)
Increased γ-glutamyltransferase	21 (14)	4 (3)	26 (17)	6 (4)
Cough	21 (14)	0	24 (15)	0

* The safety population included all the patients who had undergone randomization and received at least one dose of any trial treatment. Adverse events that are graded 1, 2, and 3 or higher are shown in Table S13 in the Supplementary Appendix. Covid-19 denotes coronavirus disease 2019.

† The determination of whether an event was related to amivantamab was made by the investigator.

‡ In the amivantamab+chemotherapy group, this category included patients who discontinued amivantamab, carboplatin, and pemtrexed at any time and those who discontinued amivantamab and pemtrexed after the completion of carboplatin. In the chemotherapy group, this category included patients who discontinued carboplatin and pemtrexed at any time and those who discontinued pemtrexed after the completion of carboplatin.

§ Events in this category are listed according to decreasing incidence in the amivantamab+chemotherapy group.



Multidisciplinary Supportive Care and Survivorship

- Management of toxicities with specialists
 - Dermatology referral for paronychia and dermatitis
 - Typically, topical steroids, including on scalp
 - GI referral or supportive care (loperamide) for diarrhea
 - Dexamethasone mouthwash for stomatitis
 - Medication interactions
 - In terms of differential, discuss with oncology if reason for patient being admitted may not be cancer, could be treatment effect (eg, may not be COVID-19, could be drug pneumonitis)
- Psychosocial and family support
- Given survival measured in years for patients with this disease, consideration of appropriate prevention strategies warranted, balanced with understanding of benefit of interventions with >5- and >10-year benefit
 - Non-invasive colorectal screening may be preferred



Key Learning Points



- Molecular testing crucial in workup and management of metastatic NSCLC
- For canonical EGFR mutations, osimertinib, chemotherapy + osimertinib, amivantamab + lazertinib reasonable options
- “EGFR+” is not sufficient annotation; for EGFR exon 20 insertion mutations, amivantamab (EGFR/MET bispecific antibody) is a standard of care in the 2L setting
- Carboplatin/pemetrexed/amivantamab shows improvement in clinical outcomes in 1L EGFRx20ins NSCLC

