NCCN 2025
Lung Cancer Congress

Evolving Evidence and Practical Integration of Radiation Therapy in Metastatic Non-Small Cell Lung Cancer

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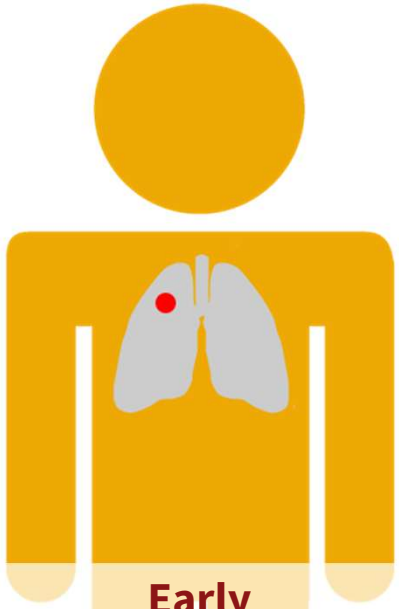
Thoracic Radiation Oncology Program
Stanford Molecular Imaging Program
Stanford Cancer Institute

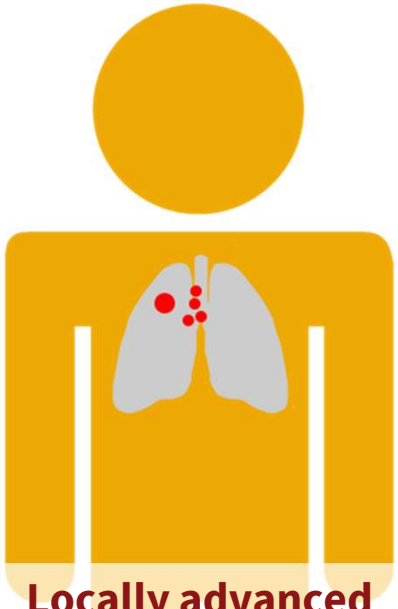
NCCN National Comprehensive Cancer Network®

Lung Cancer Stages (Classical)

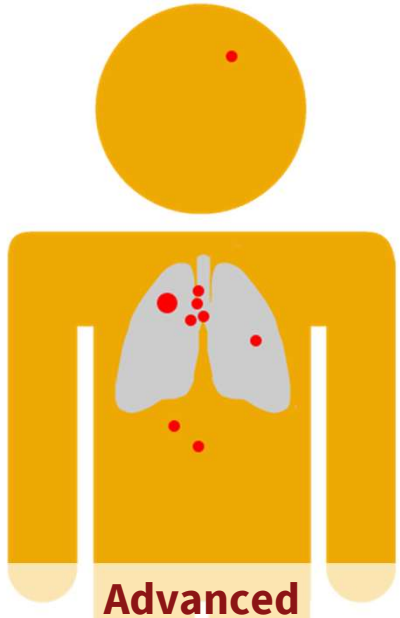
Thoracic Rad Onc @Stanford



Early (Localized)
15% of patients
55% survival @ 5yr



Locally advanced (Regional)
25% of patients
25% survival @ 5yr

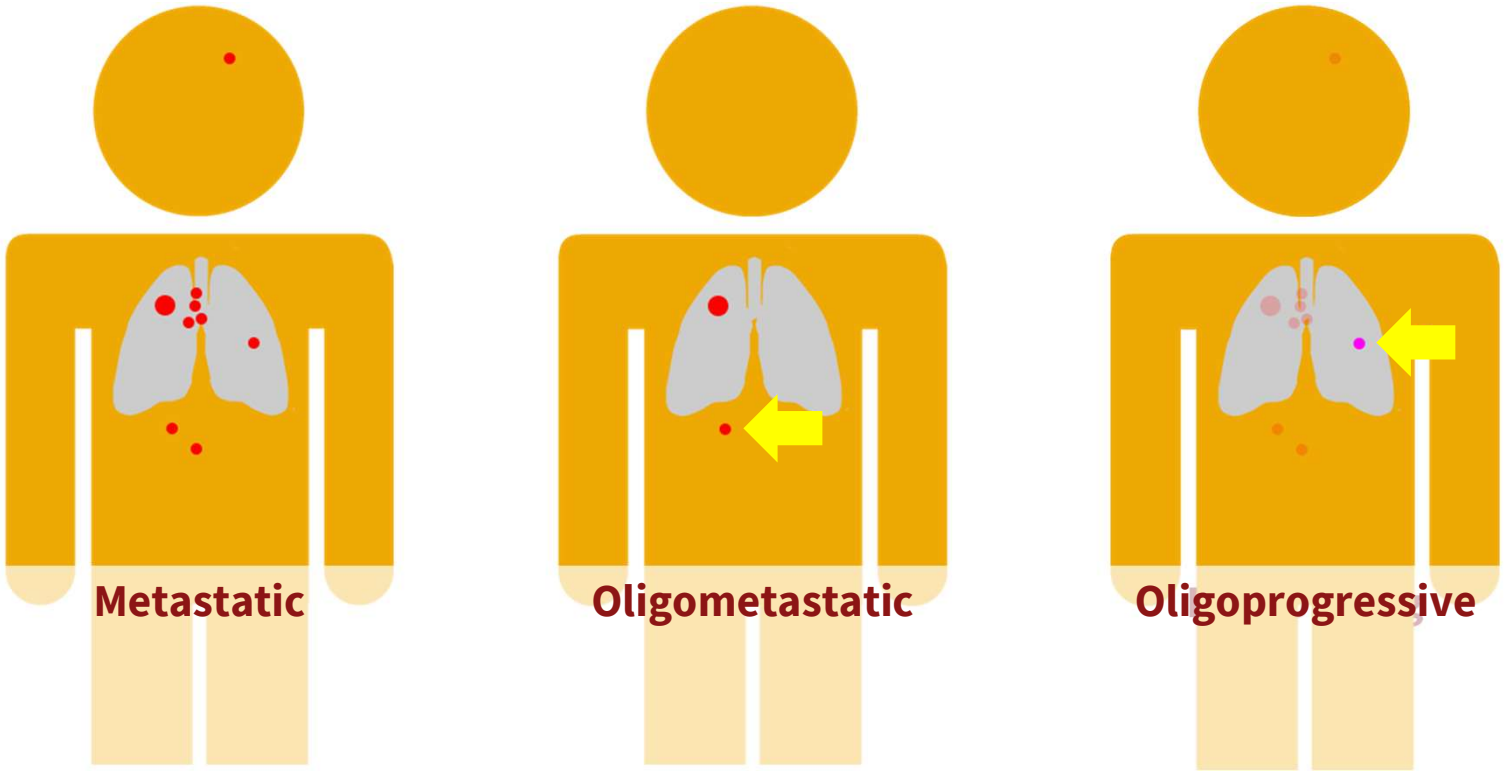


Advanced (Distant / Metastatic)
60% of patients
5% survival @ 5yr

B Loo – Stanford Radiation Oncology

Lung Cancer Stages (New concepts)

Thoracic Rad Onc @Stanford

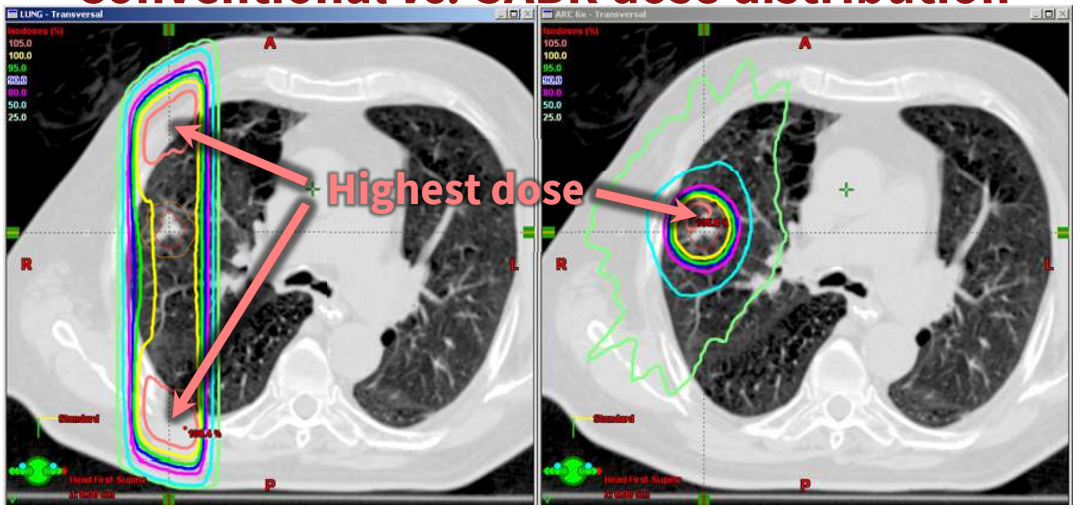


B Loo – Stanford Radiation Oncology

Precision radiotherapy

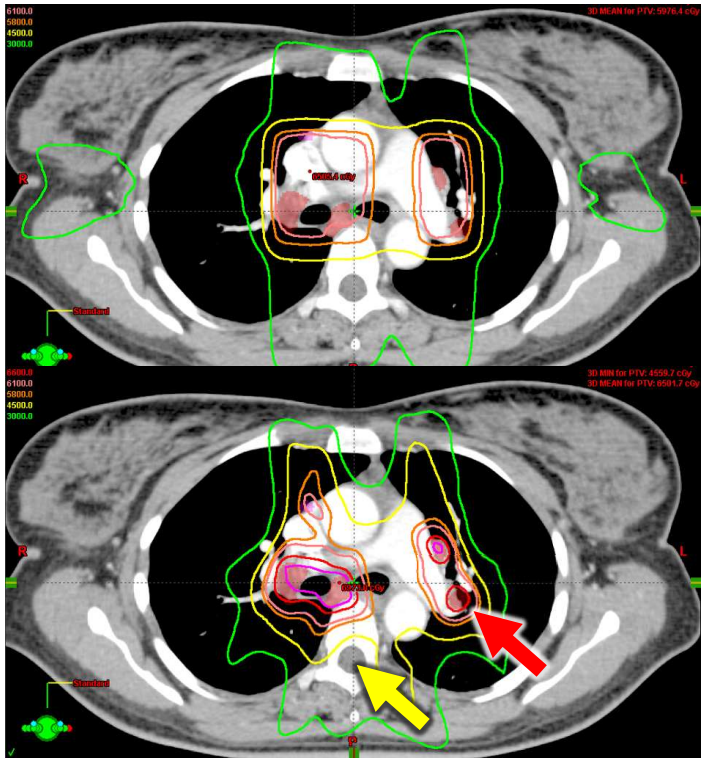
Thoracic Rad Onc @Stanford

Conventional *vs.* SABR dose distribution



! *Major improvements in **therapeutic index** through **spatial precision***

Conformal RT



Highly conformal RT

NSCLC case

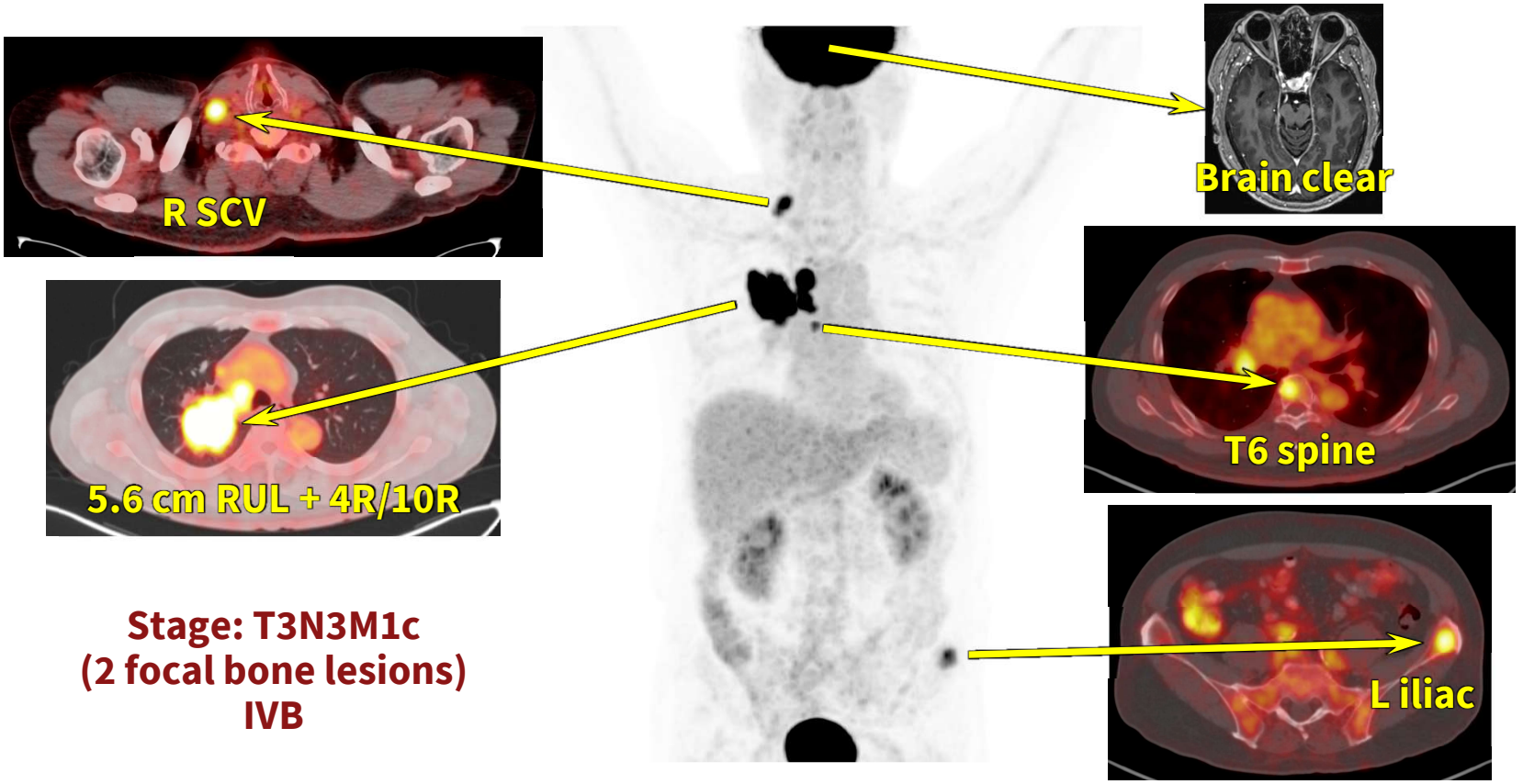
Thoracic Rad Onc @Stanford

- 60 yo Asian man, healthy never smoker
- Active with excellent performance status
- Persistent cough and RUL consolidation on CXR despite antibiotics
- CT thorax demonstrates RUL mass and mediastinal lymphadenopathy
- CBCT-guided robotic bronchoscopy & EBUS biopsies find adenocarcinoma in RUL, 4R, 10R nodes. FNA of R SCV also +

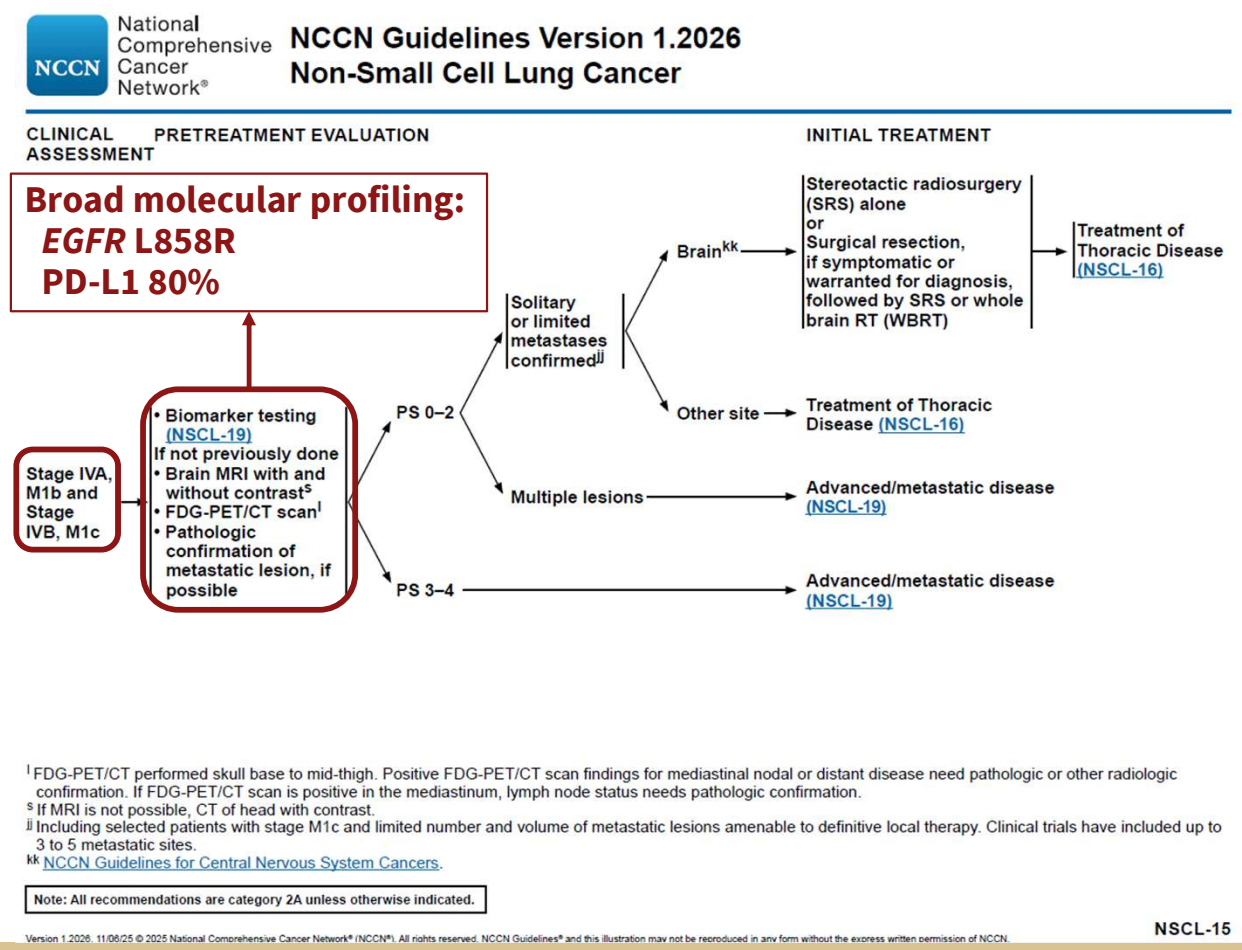
CBCT, cone beam CT; CXR, chest x-ray; EBUS, endobronchial ultrasound; FNA, fine-needle aspiration; RUL, right upper lobe; SCV, supraclavicular.

Staging

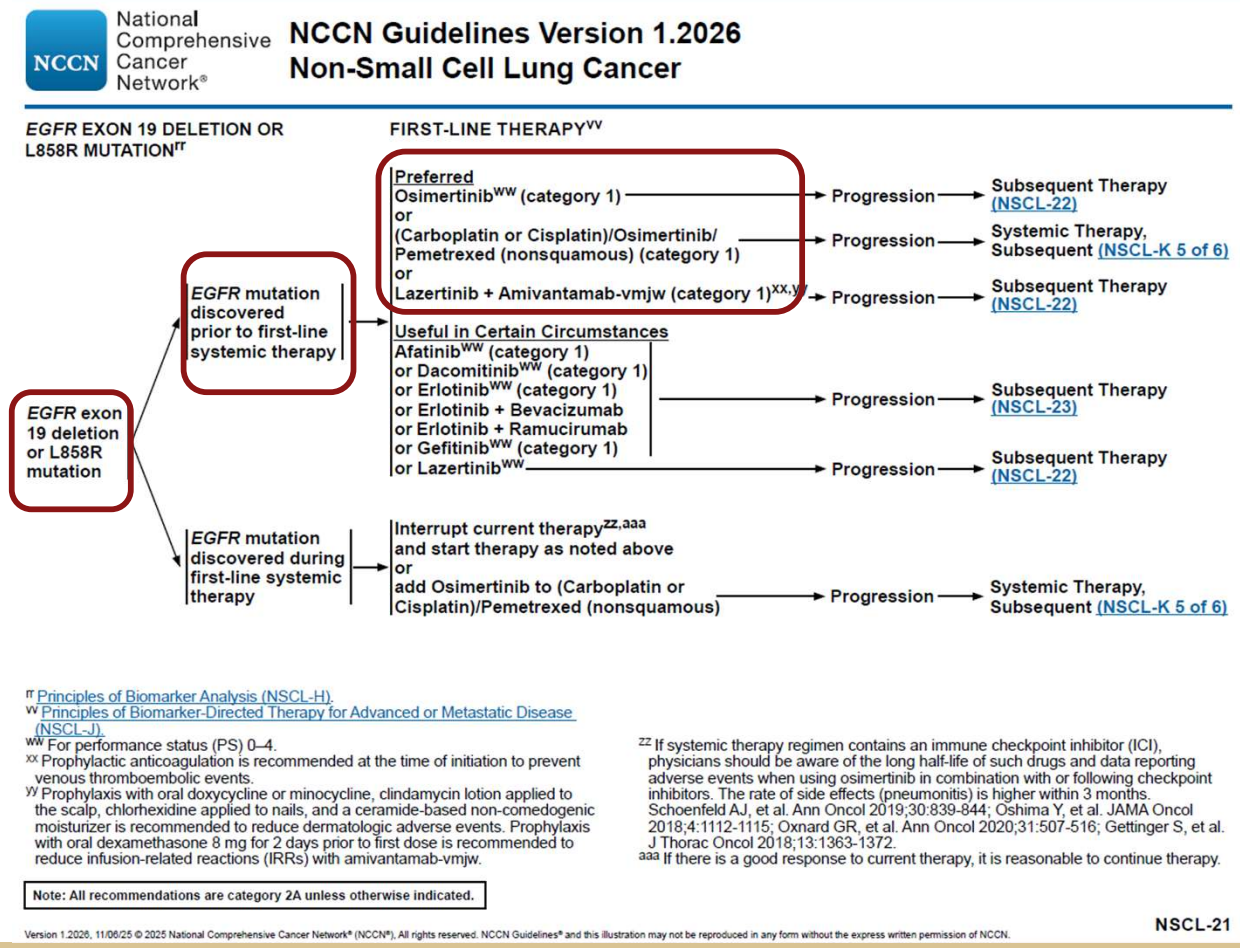
Thoracic Rad Onc @Stanford



Stage: T3N3M1c
(2 focal bone lesions)
IVB



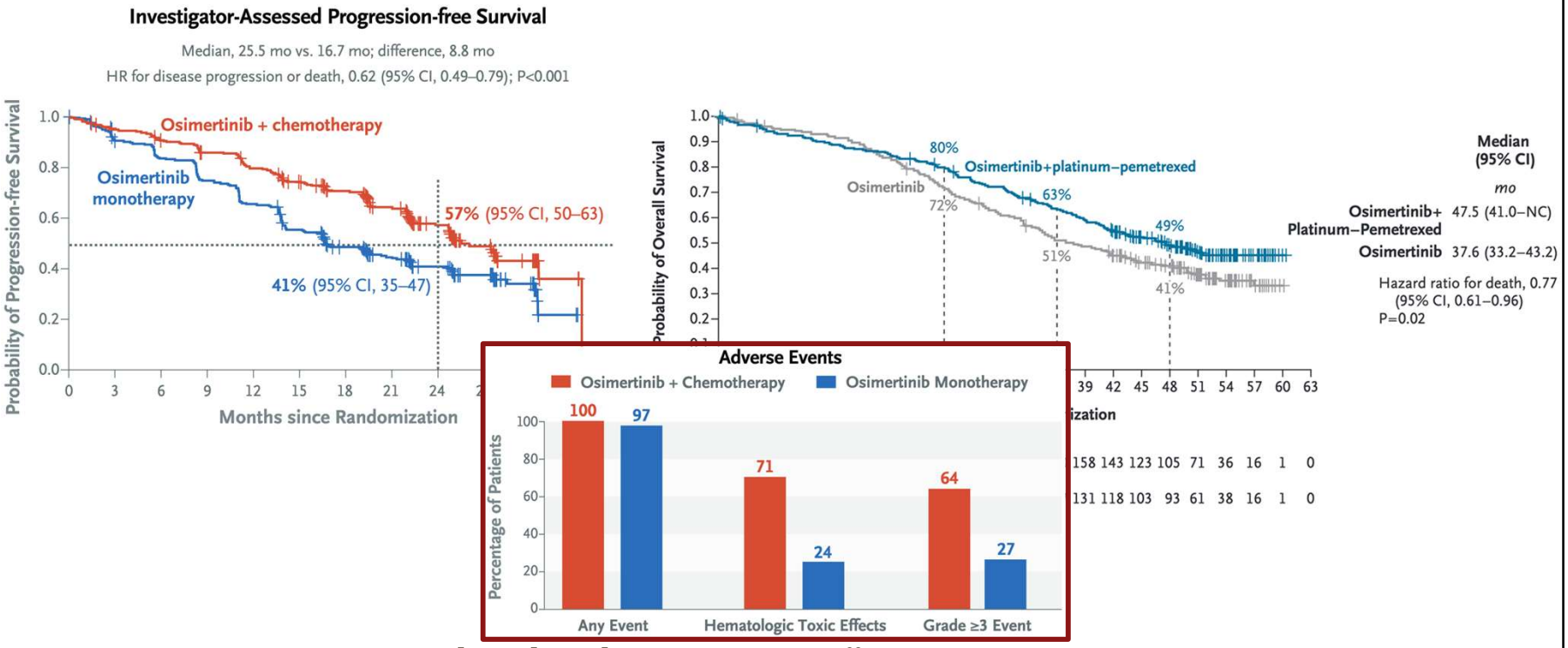
B Loo – Stanford Radiation Oncology



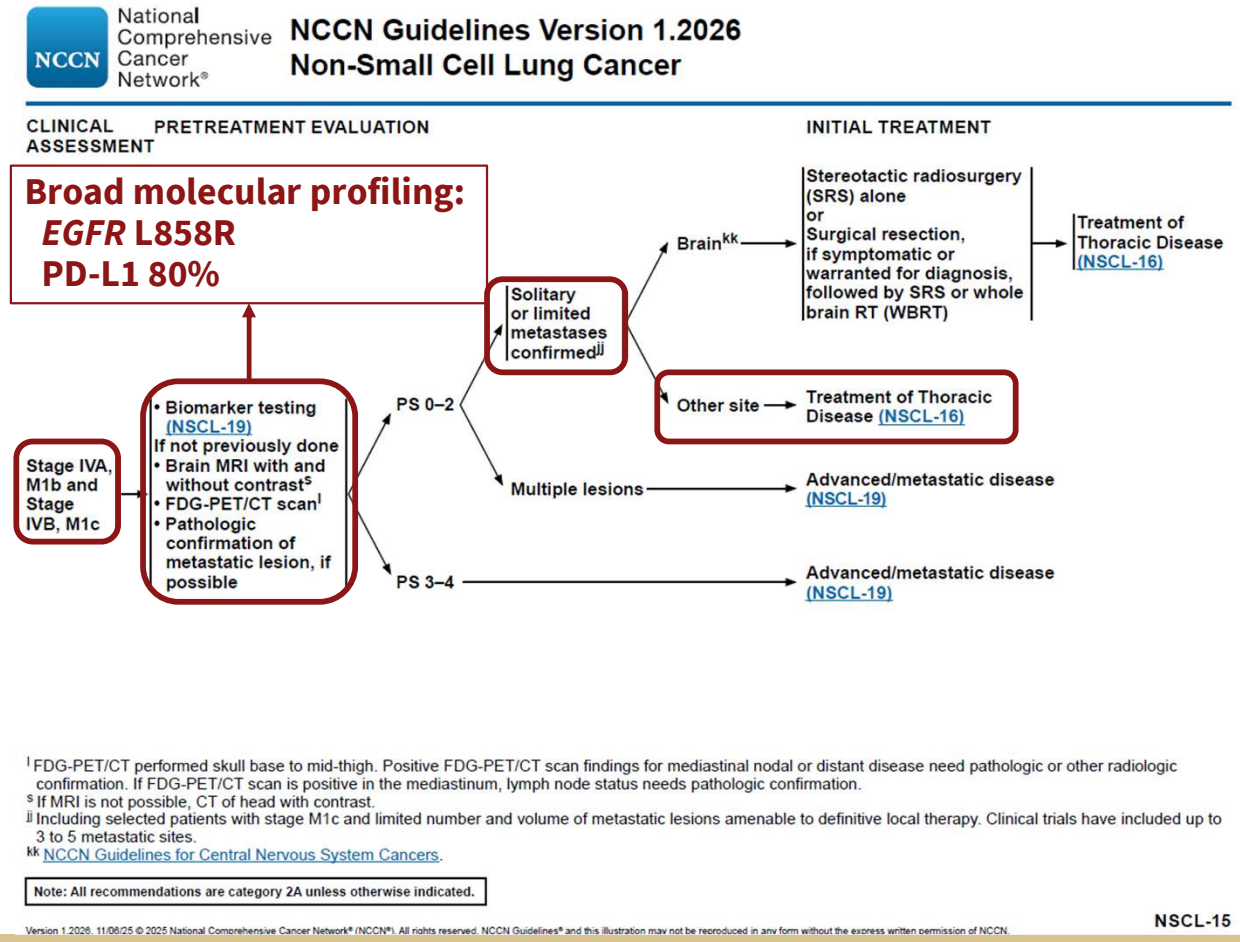
TKI ± chemo for metastatic *EGFR*m

Thoracic Rad Onc @Stanford

FLAURA2: Phase III osimertinib ± platinum/pemetrexed for metastatic *EGFR*m



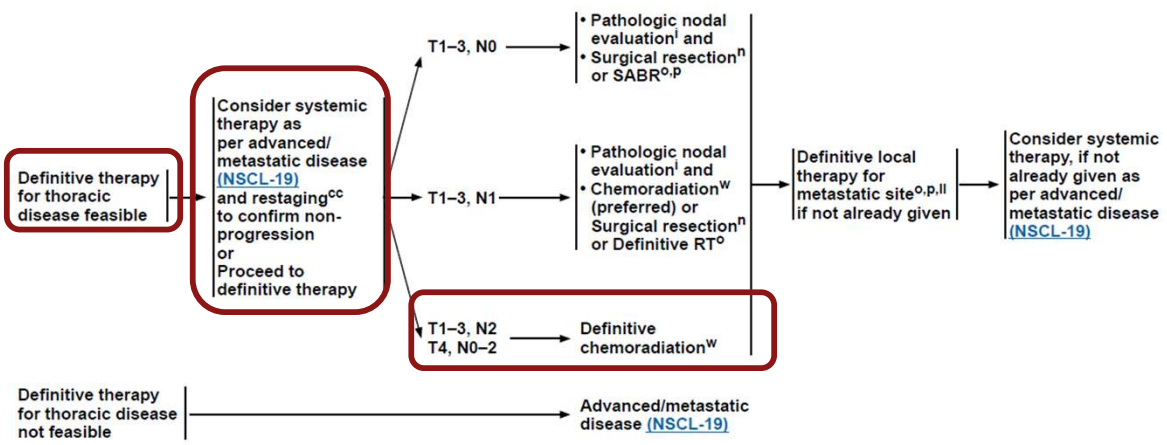
Planchard *NEJM* 2023; Jänne *NEJM 2025*



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2026
Non-Small Cell Lung Cancer

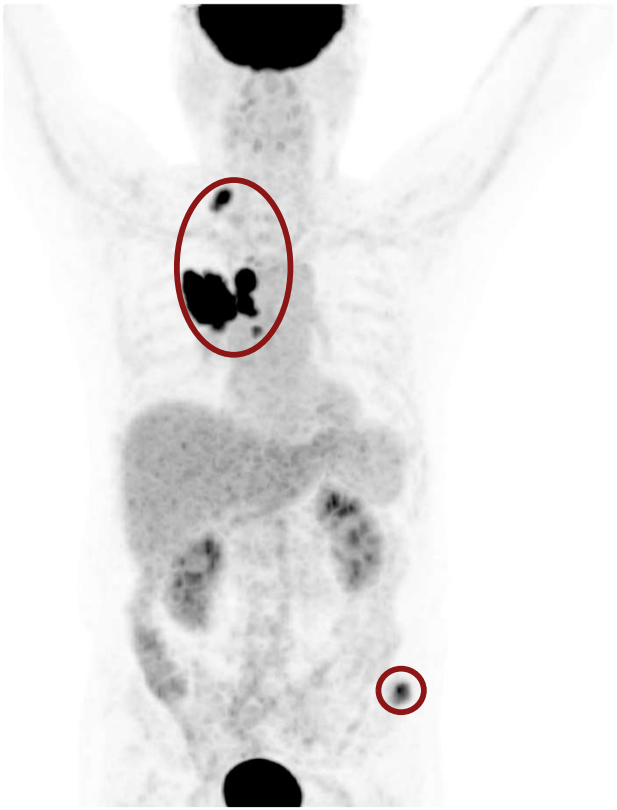
TREATMENT OF THORACIC DISEASE



[i] Methods for evaluation include mediastinoscopy, mediastinotomy, EBUS, EUS, and CT-guided biopsy. An EBUS-TBNA negative for malignancy in a clinically (FDG-PET/CT and/or CT) positive mediastinum should undergo subsequent mediastinoscopy prior to surgical resection.
[n] Principles of Surgical Therapy (NSCL-B).
[o] Principles of Radiation Therapy (NSCL-C).
[p] IGTA therapy (eg, cryotherapy, microwave, radiofrequency) may be an option for select patients. Principles of Image-Guided Thermal Ablation Therapy (NSCL-D).
[w] Concurrent Chemoradiation Regimens (NSCL-F).
[cc] Chest CT with contrast and/or FDG-PET/CT to evaluate progression.
[ll] Typically, RT (including SABR) or surgical resection.

Note: All recommendations are category 2A unless otherwise indicated.

NSCL-16



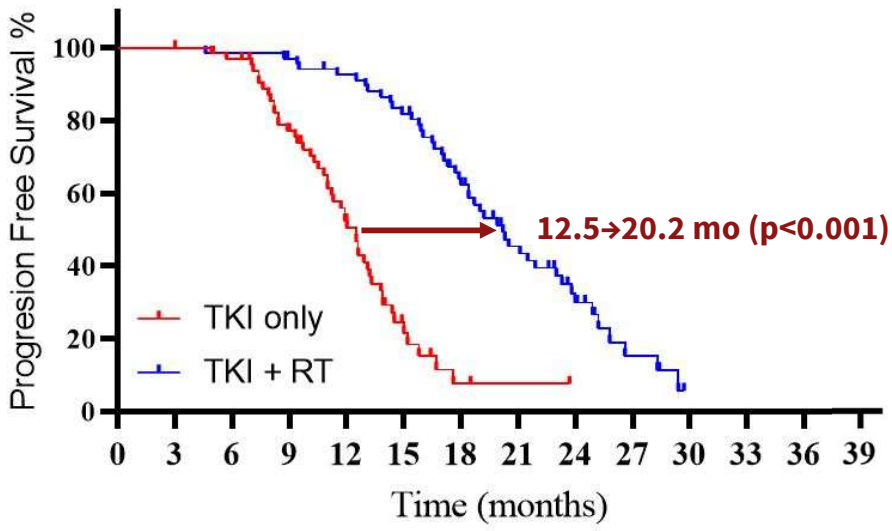
B Loo – Stanford Radiation Oncology

Radical RT for oligometastatic *EGFR*m

Thoracic Rad Onc @Stanford

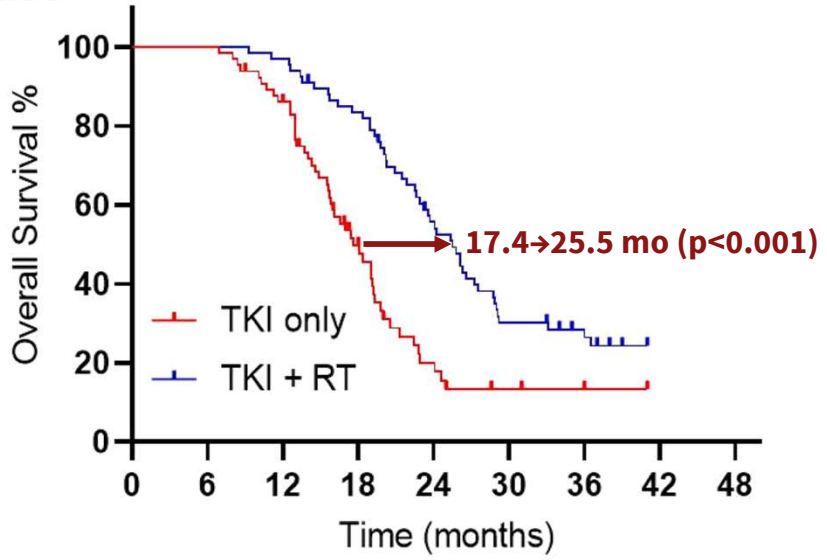
SINDAS: Phase III TKI ± up front SABR for synchronous oligometastatic *EGFR*m

Figure 2



TKI only	65	65	62	48	28	8	3	2	1	0	0
TKI + RT	68	67	67	65	60	51	37	22	12	5	1

Figure 3



TKI only	65	65	55	26	9	5	3	2
TKI + RT	68	68	66	56	36	20	14	9

SABR, stereotactic ablative radiotherapy; TKI, tyrosine kinase inhibitor; RT, radiation therapy.

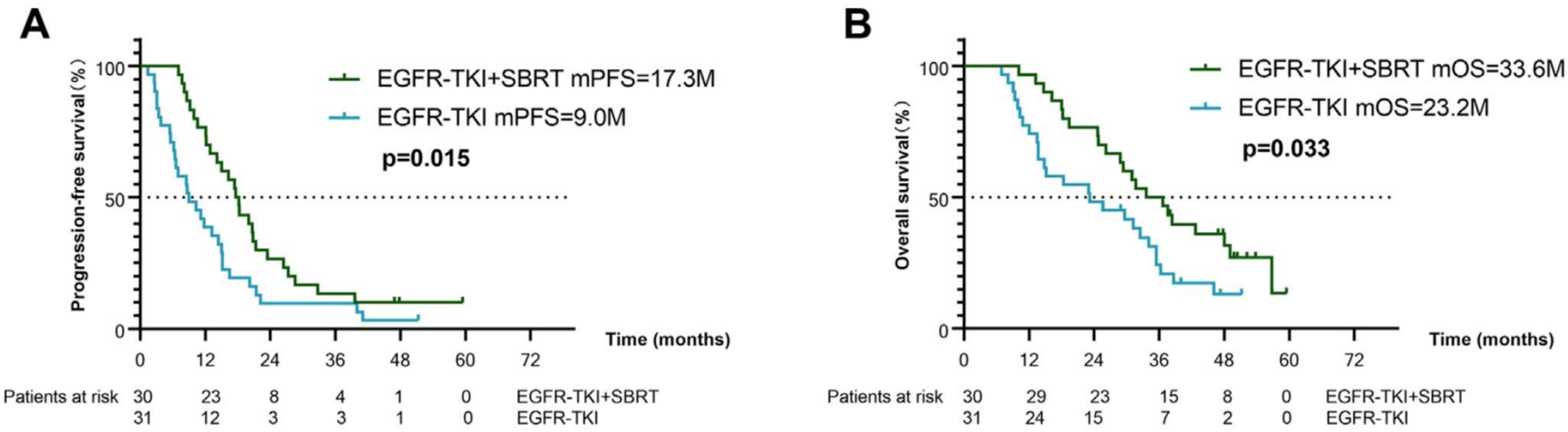
Wang *JNCI* 2022

Radical RT for oligometastatic *EGFR*m

Thoracic Rad Onc @Stanford

Wuhan: Phase IIR TKI ± SABR* for synchronous oligometastatic *EGFR*m

***after 3 mo PR/SD on TKI**



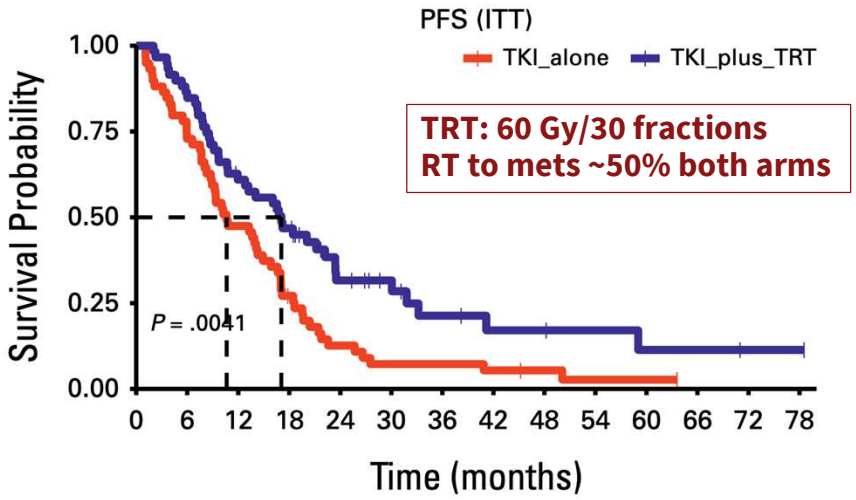
PR, partial response; SBRT, stereotactic body radiation therapy; SD, stable disease.

Peng *Radiother Oncol* 2023

Thoracic RT for oligo-organ *EGFR*m

Thoracic Rad Onc @Stanford

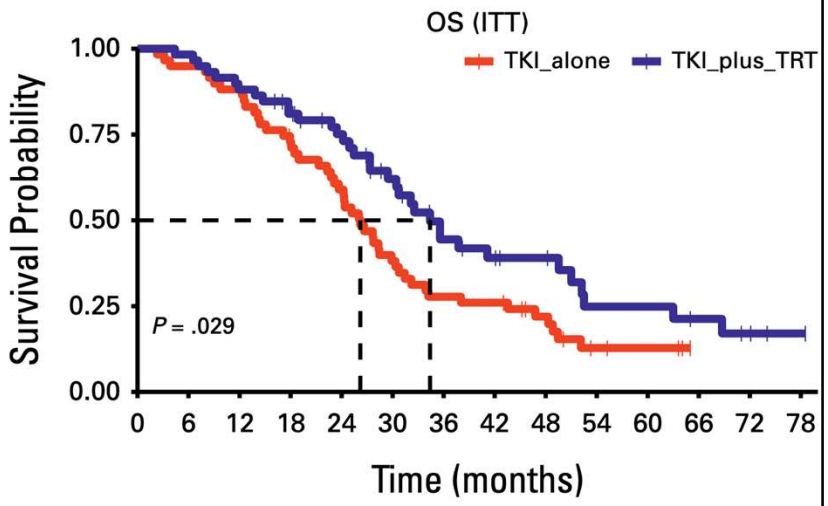
Northern Radiation Oncology Group of China 002 Trial: Phase III TKI ± thoracic RT (TRT) for synchronous *oligo-organ* metastatic *EGFR*m



TRT: 60 Gy/30 fractions
RT to mets ~50% both arms

Number at risk

TKI_alone	59	43	28	15	7	4	4	3	2	1	1	0	0	0
TKI_plus_TRT	59	51	35	26	14	10	6	4	4	3	2	2	1	1



Number at risk

TKI_alone	59	56	52	42	34	22	16	15	10	4	3	0	0	0
TKI_plus_TRT	59	58	51	45	37	26	17	14	12	7	7	5	3	1

Sun *J Clin Oncol* 2025

Treatment plan

Thoracic Rad Onc @Stanford

(Caveat: the 3 trials above used 1st gen EGFR TKIs)

- Definitive thoracic RT with concurrent platinum/pemetrexed
  - 60-66 Gy to RUL mass, involved mediastinal & SCV nodes
  - Include T6 metastasis in thoracic treatment volume
- Stereotactic ablative radiotherapy (SABR) to L iliac bone metastasis
- Adjuvant/maintenance Osimertinib

Takeaway: radical RT has the potential to improve survival in oligometastatic NSCLC in addition to systemic therapy

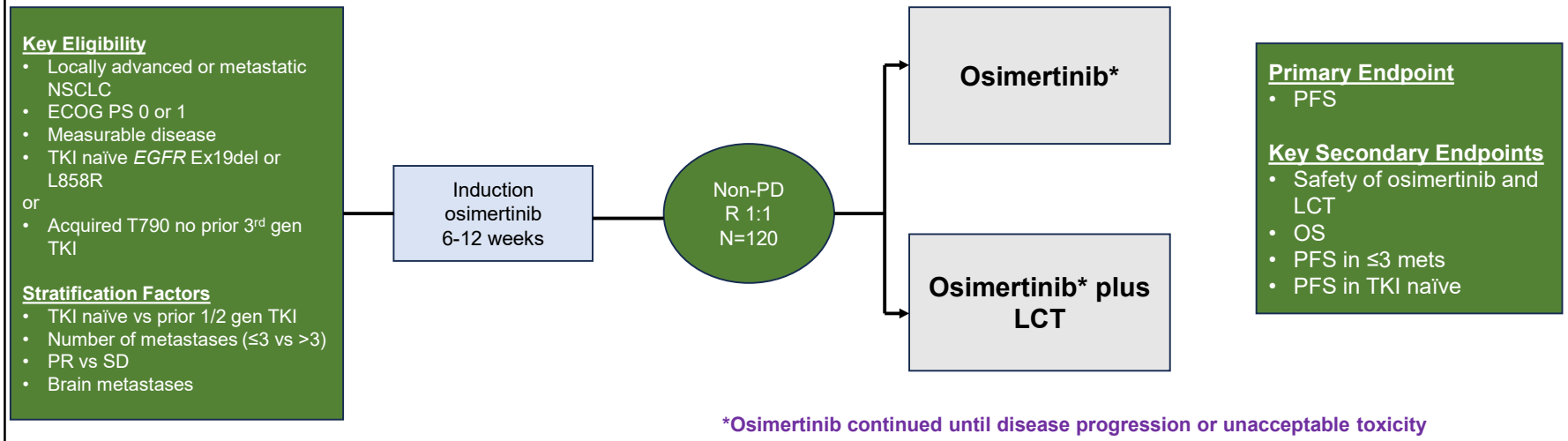
NorthStar: A Phase II Randomized Study of Osimertinib (OSI) With or Without Local Consolidative Therapy (LCT) for Metastatic EGFR-Mutant Non-Small Cell Lung Cancer (NSCLC)

Yasir Y. Elamin, Saumil J. Gandhi, Mara B. Antonoff, Enoch Chang, George Blumenschein Jr, Zhongxing Liao, Daniel R. Gomez, Joe Y. Chang, Steven H. Lin, Tina Cascone, Carl Gay, Janet Tu, Xiuning Le, Anne Tsao, Michael S. O'Reilly, Matthew S. Ning, Collin Blakely, Chad G. Rusthoven, Jia Wu, Ara A. Vaporciyan, Stephen G. Swisher, John V. Heymach

Courtesy J Chang MDACC

NorthStar Study Design

Randomized, multicenter, phase II trial, NCT03410043

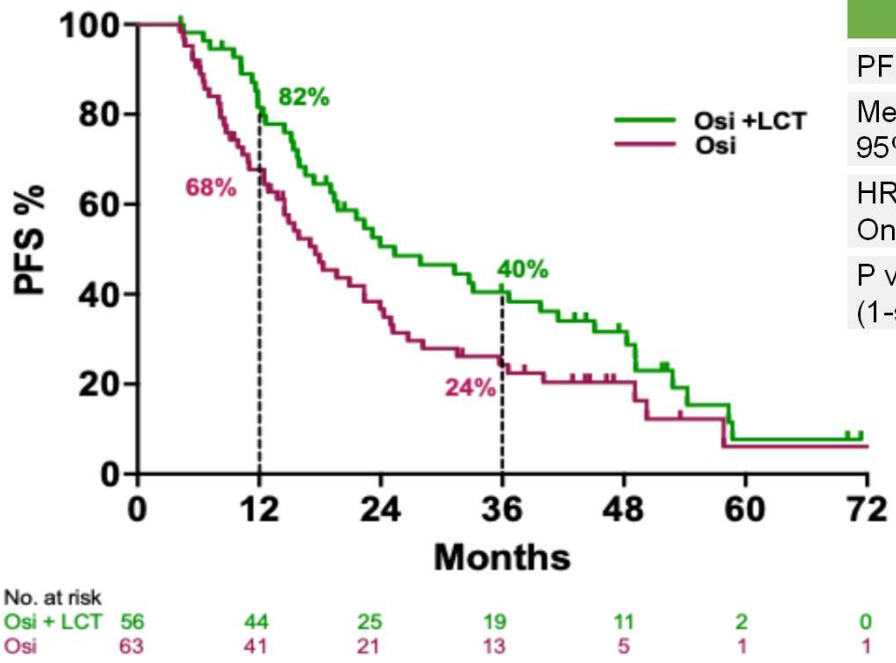


*Osimertinib continued until disease progression or unacceptable toxicity

Yasir Elamin, MD

Courtesy J Chang MDACC

Progression-Free Survival



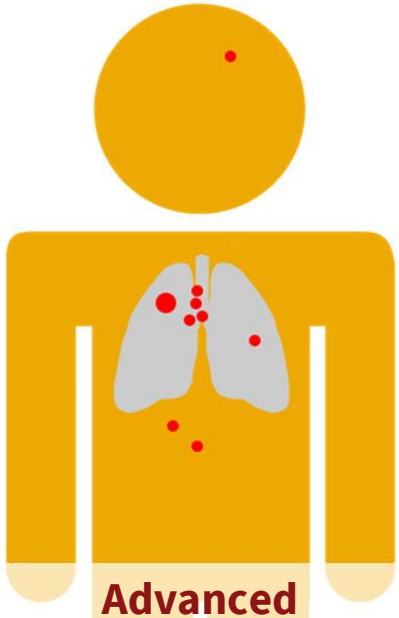
	Osimertinib (n=63)	Osimertinib plus LCT (n=56)
PFS events, n (%)	50 (79.3%)	42 (75%)
Median PFS month 95% CI	**17.5** (14.5, 24.3)	**25.3** (19.4, 45.0)
HR One-sided 90% CI	**0.66** 0.50 - 0.87	
P value (1-sided log rank)	0.025	

Yasir Elamin, MD

Courtesy J Chang MDACC

Advanced lung cancer

Thoracic Rad Onc @Stanford



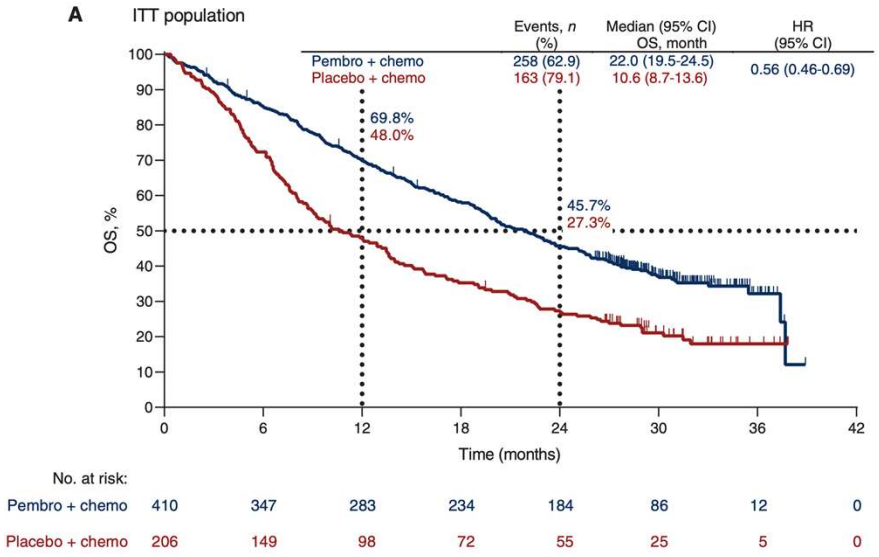
Advanced
(Distant / Metastatic)
Oligometastatic
Oligoprogressive

- Standard treatment is systemic drugs: chemo, mutation targeted, immunotherapy
- More focused radiation allows safe ablation of more tumors
- More effective drug therapy **increases** the potential of effective local therapy to achieve cures or improve survival

Standard: chemo and/or immuno

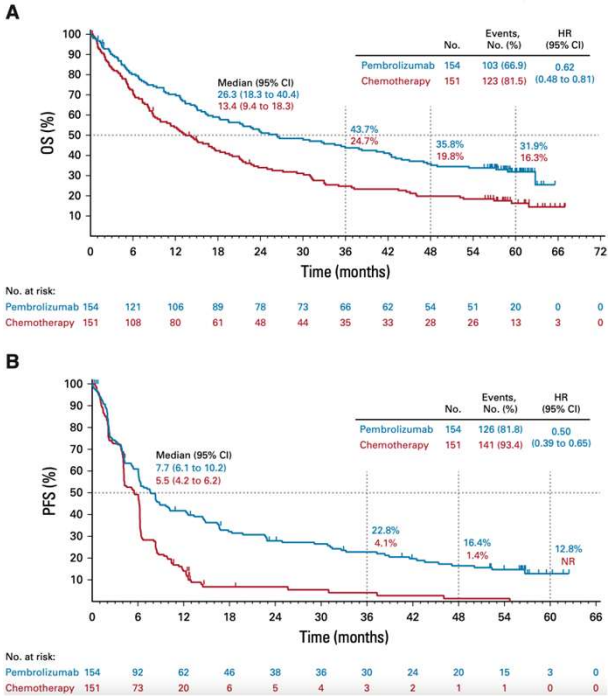
Thoracic Rad Onc @Stanford

KEYNOTE-189: chemo ± pembro



Rodriguez-Abreu *Ann Oncol* 2021

KEYNOTE-024: pembro vs. chemo, PD-L1 50%



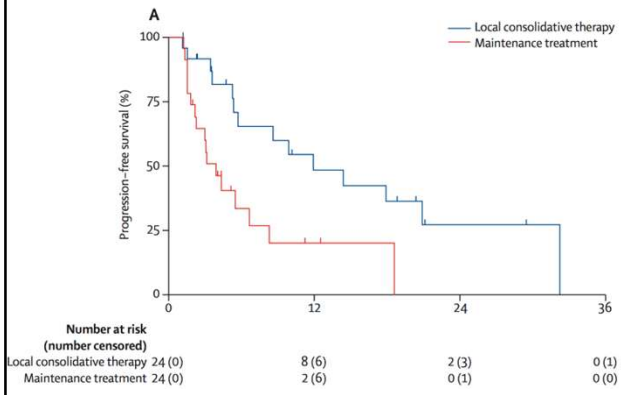
Reck *J Clin Oncol* 2021

Randomized data for oligometastasis

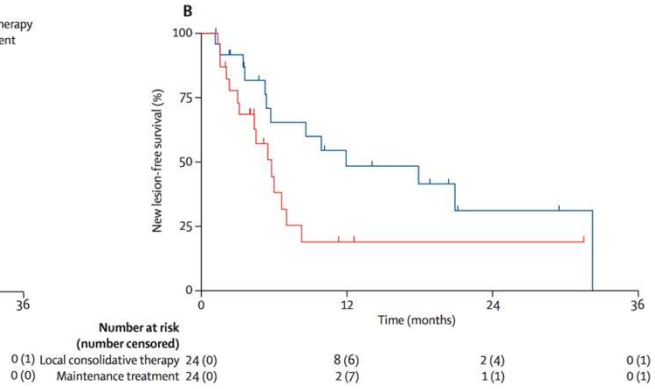
Thoracic Rad Onc @Stanford

Consolidative ablation of synchronous oligometastases extends progression free survival (Phase IIR)

PFS

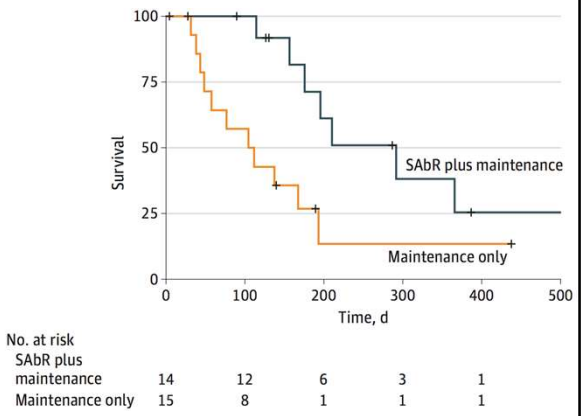


New lesions



Gomez *Lancet Oncol* 2016

PFS

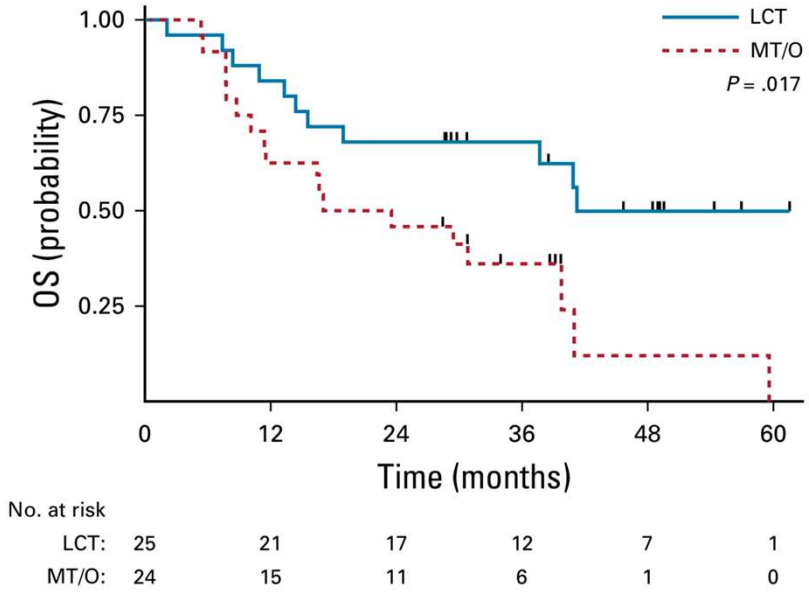


Iyengar *JAMA Oncol* 2017

Radical RT for oligometastatic cancer

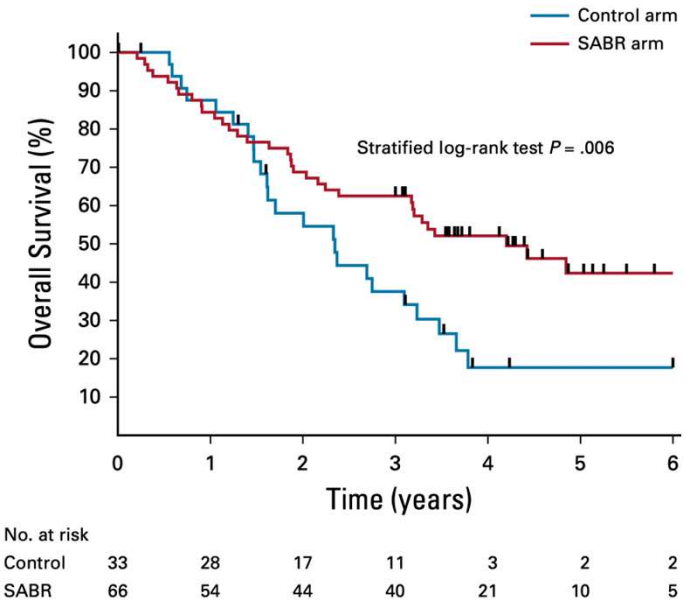
Thoracic Rad Onc @Stanford

LCT *vs*. maintenance/obs for synchronous oligometastatic lung cancer ("OliGomez")



Gomez *J Clin Oncol* 2019

SABR *vs*. SOC for metachronous oligometastatic cancer (SABR-COMET)



Palma *J Clin Oncol* 2020

NRG ONCOLOGY

Advancing Research. Improving Lives.™

NRG-LU002: *Randomized Phase II/III Trial Of Maintenance Systemic Therapy Versus Local Consolidative Therapy (LCT) Plus Maintenance Systemic Therapy For Limited Metastatic Non-Small Cell Lung Cancer (NSCLC)*

Puneeth Iyengar, MD, PhD, Chen Hu, PhD, Daniel Gomez, MD, Robert Timmerman, MD, Charles Simone, MD, Clifford Robinson, MD, David Gerber, MD, Saiama N Waqar, MBBS, MSCI, Jessica S Donington, MD, Stephen G Swisher, MD, Michael Weldon, MSc, Jackie Wu, PhD, Bryan Faller, MD, Sawsan Rashdan, MD, Kevin L Stephans, MD, Pamela Samson, MD, Kristin A Higgins, MD, Ryan Nowak, MD, Jessica A Lyness, MS, Jeffrey D Bradley, MD

Puneeth Iyengar, MD, PhD; Attending and Director, Metastatic Service,
Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center

@IyengarPuneeth

@NRGonc

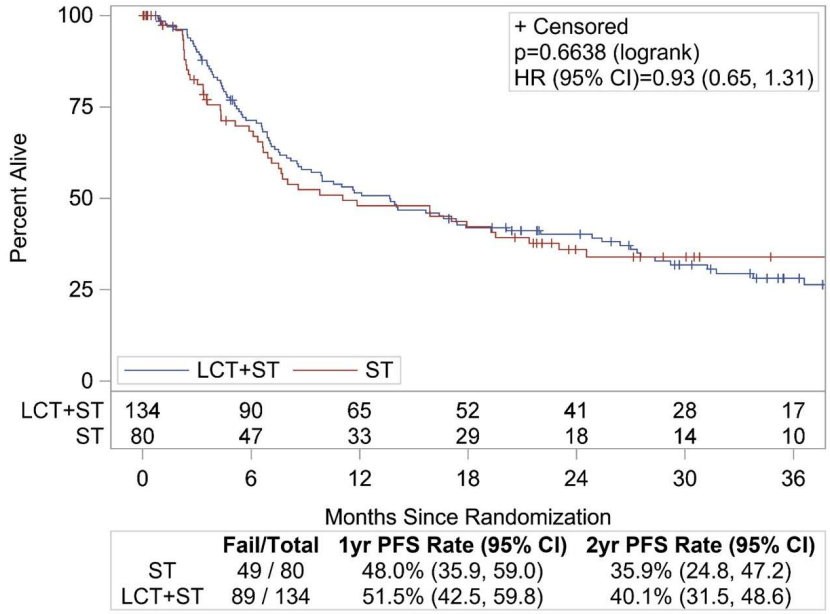
ASCO 2024

NCI National Clinical Trials Network — a National Cancer Institute program

NCI Community Oncology Research Program — A program of the National Cancer Institute of the National Institutes of Health

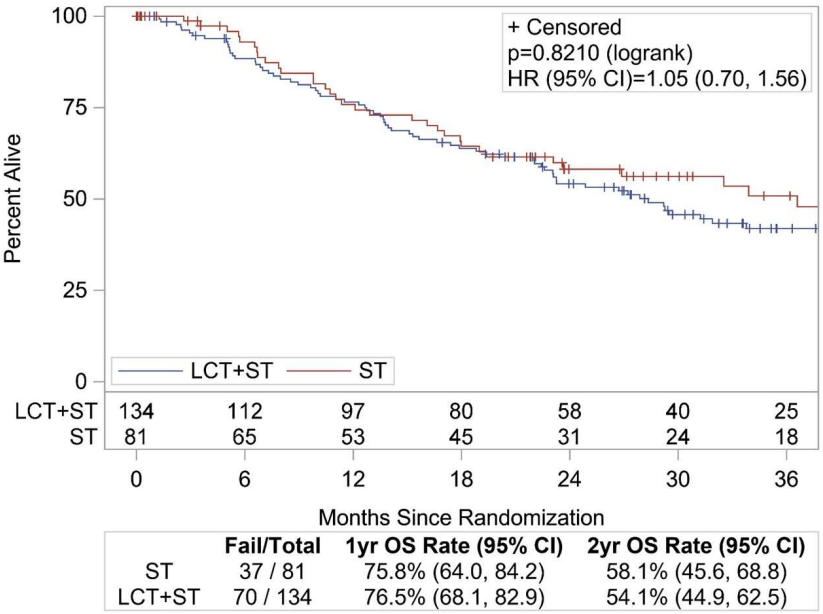
NRG LU002

PFS



	Fail/Total	1yr PFS Rate (95% CI)	2yr PFS Rate (95% CI)
ST	49 / 80	48.0% (35.9, 59.0)	35.9% (24.8, 47.2)
LCT+ST	89 / 134	51.5% (42.5, 59.8)	40.1% (31.5, 48.6)

OS



	Fail/Total	1yr OS Rate (95% CI)	2yr OS Rate (95% CI)
ST	37 / 81	75.8% (64.0, 84.2)	58.1% (45.6, 68.8)
LCT+ST	70 / 134	76.5% (68.1, 82.9)	54.1% (44.9, 62.5)

Median Follow-up:

All patients – 21.9 mo

Surviving patients – 29.4 mo

Of 185/215 patients treated with IO-containing systemic therapy regimens, the PFS HR was 0.90 (95% CI: 0.61, 1.32).

Iyengar *ASCO* 2024

Of 185/215 patients treated with IO-containing systemic therapy regimens, the OS HR remained 1.05 (95% CI: 0.68, 1.63).

RT enhances immunotherapy

Thoracic Rad Onc @Stanford

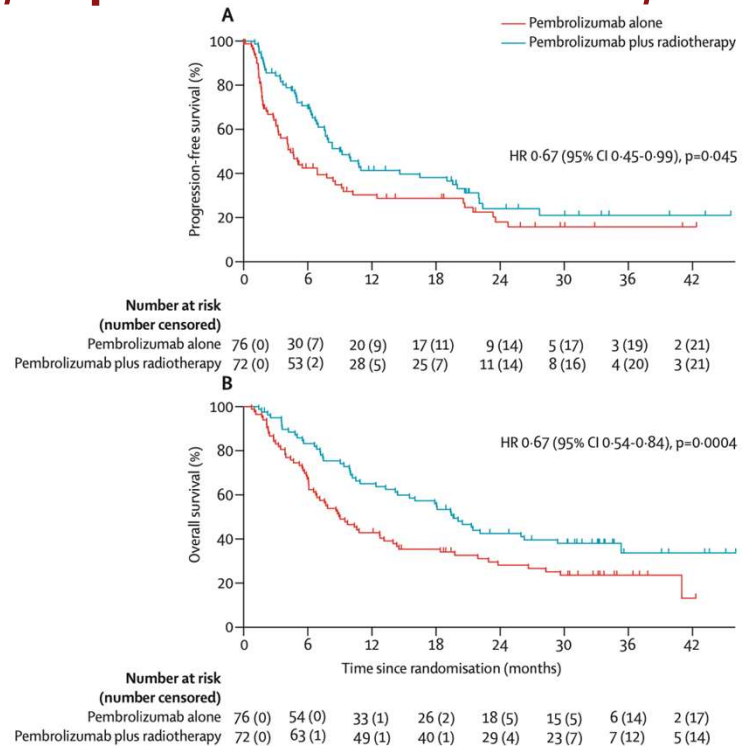
Pooled PEMBRO-RT & MDACC: Phase 1/2R pembro ± accelerated RT/SABR

Abscopal effects

	Pembrolizumab alone (n=76)	Pembrolizumab plus radiotherapy (n=72)	Number needed to treat	Odds ratio (95% CI)	p value
Best overall response					
Abscopal response rate	15/76 (19·7%)	30/72 (41·7%)	2·00	2·96 (1·42–6·20)	0·0039
Abscopal control rate	33/76 (43·4%)	47/72 (65·3%)	4·58	2·51 (1·28–4·91)	0·0071
PD-L1 status					
<1%	6/36 (16·7%)	11/29 (37·9%)	4·69	3·00 (0·96–10·00)	0·080
1–49%	3/14 (21·4%)	9/19 (47·4%)	3·85	3·30 (0·96–16·70)	0·16
≥50%	5/15 (33·3%)	6/13 (46·2%)	16·13	1·72 (0·37–7·69)	0·70
Objective response at 12 weeks					
Abscopal response rate	14/76 (18·4%)	25/72 (34·7%)	5·26	1·95 (0·91–4·20)	0·086
Abscopal control rate	29/76 (38·2%)	45/72 (62·5%)	4·09	2·71 (1·39–5·28)	0·0033

Data are n (%), unless otherwise stated.

Table 2: **Response to treatment**



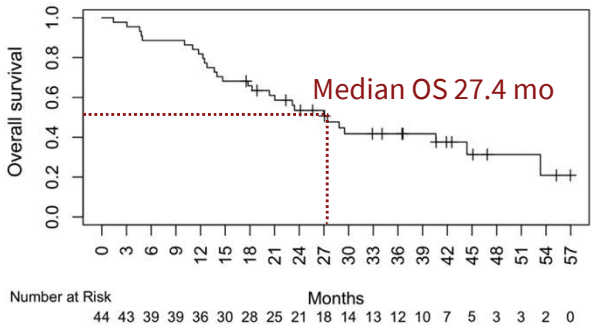
Theelen/Chen *Lancet Respir Med* 2020

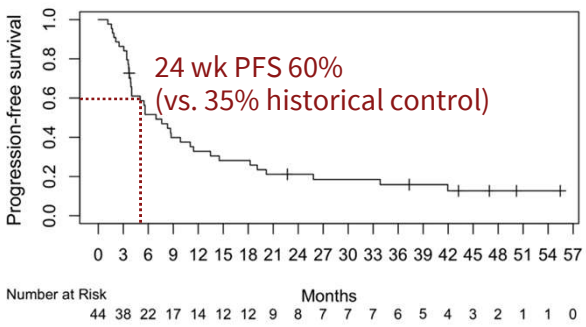
RT enhances immunotherapy

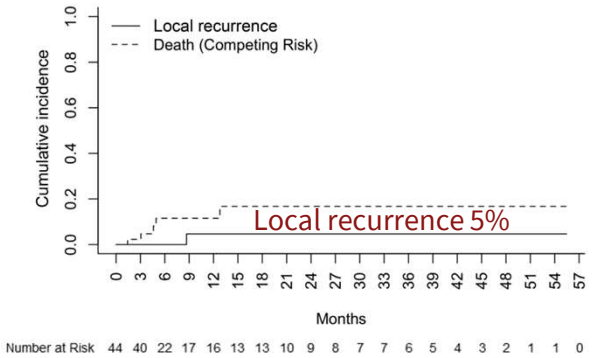
Thoracic Rad Onc @Stanford

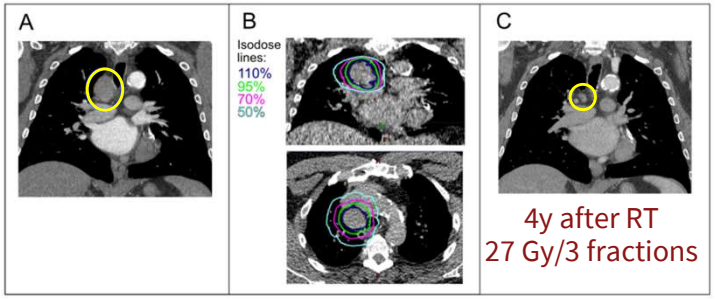
Stanford Radical RADiotherapy and Immunotherapy for metastatic CAncer of the Lung (RRADICAL) trial

Radical dose radiotherapy to 1-4 extracranial tumors in patients with metastatic NSCLC responding to or mildly progressing on ICI, with goal of maximal cytoreduction









Gensheimer *IJROBP* 2025

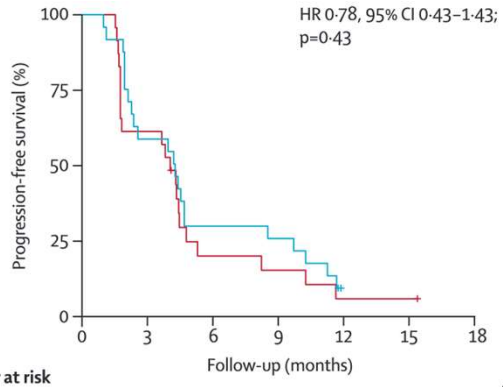
SABR for oligo*progressive* cancer

Thoracic Rad Onc @Stanford

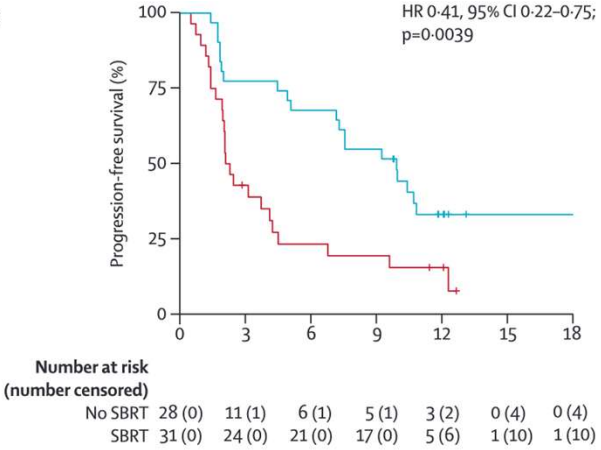
CURB: Phase IIR SOC systemic ± SABR* for oligoprogressive breast/lung cancer

***to all progressive sites (up to 5), no limit on total # non-progressing metastases**

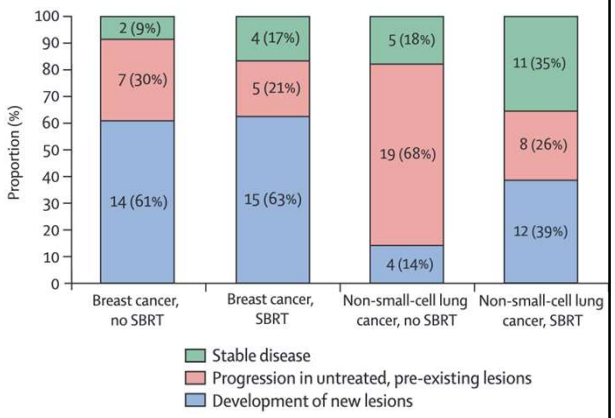
Progression-free survival (breast cancer)



Progression-free survival (lung cancer)



Patterns of recurrence



Tsai *Lancet* 2024

Phase II individualized SABR (iSABR)

Thoracic Rad Onc @Stanford

Tumor volume/location/histology adapted dosing

A Small tumor (≤10 cm^3)

Peripheral: 25 Gy in 1 fx (BED_{10}=87.5)
Central: 40 Gy in 4 fx (BED_{10}=80)
Colorectal: 50 Gy in 4 fx (BED_{10}=112.5)

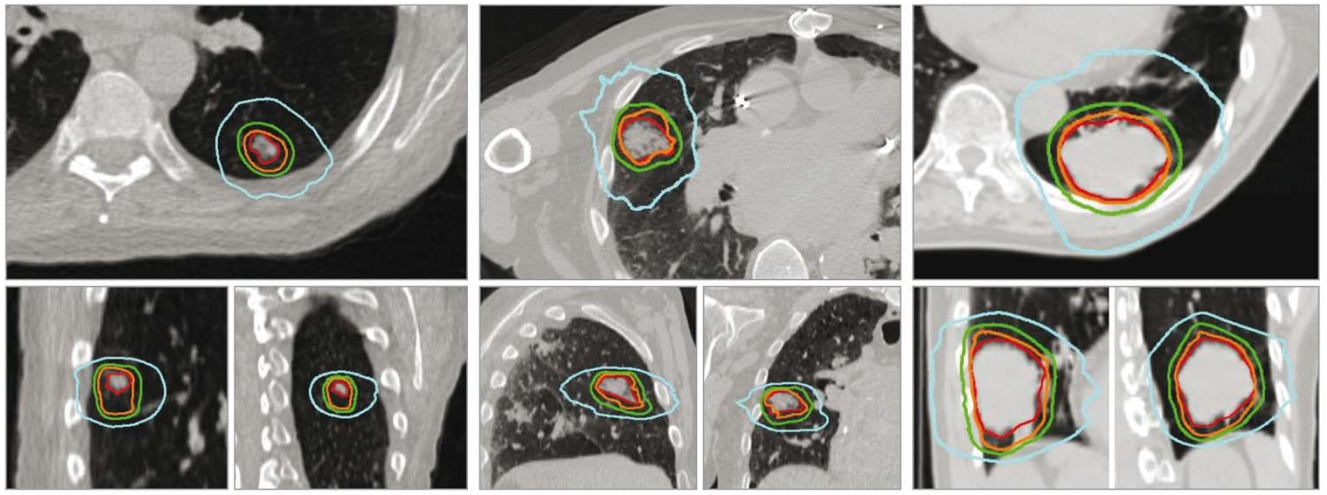
B Medium tumor (>10 cm^3 and ≤30 cm^3)

Peripheral: 50 Gy in 4 fx (BED_{10}=112.5)
Central: 50 Gy in 4 fx (BED_{10}=112.5)

C Large tumor (>30 cm^3)

Peripheral: 54 Gy in 3 fx (BED_{10}=151.2)
Central: 60 Gy in 8 fx (BED_{10}=105)

Gross tumor volume — 110% IDL — 95% IDL — 50% IDL



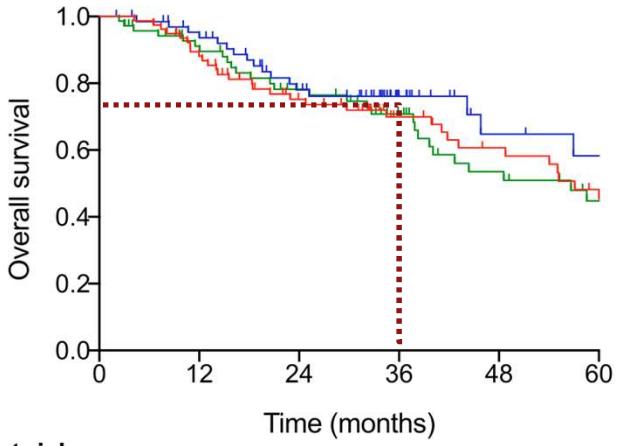
1-cm^3 tumor | 15-cm^3 tumor | 43-cm^3 tumor

Gensheimer *JAMA Oncol* 2023

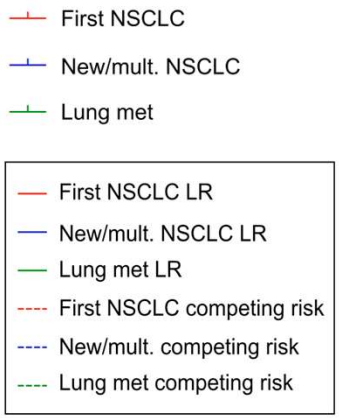
Phase II individualized SABR (iSABR)

Thoracic Rad Onc @Stanford

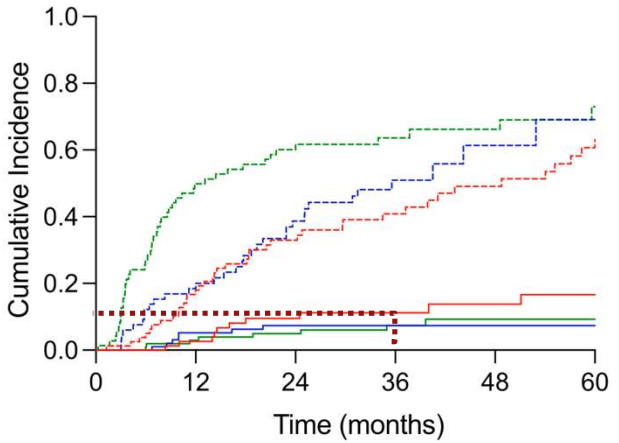
Overall survival



No. at risk						
First NSCLC	79	66	48	33	26	18
New/mult. NSCLC	67	60	44	24	12	10
Lung met	71	59	45	34	22	15



Local recurrence (LR)



No. at risk						
First NSCLC	79	59	39	25	18	13
New/mult. NSCLC	103	70	50	22	12	10
Lung met	103	53	37	24	13	11

Gensheimer *JAMA Oncol* 2023

2025 ASCO ANNUAL MEETING

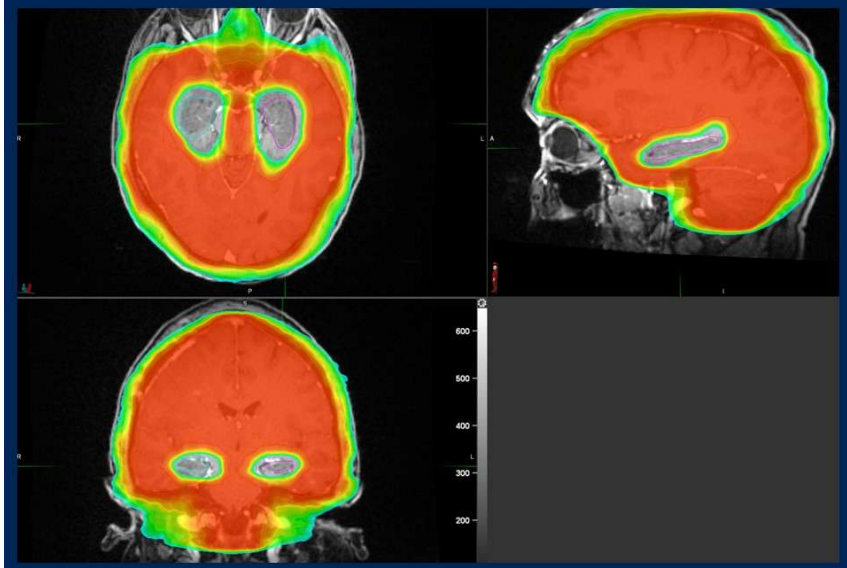
Stereotactic radiation (SRS/SRT) versus hippocampal avoidance whole brain radiation (HA-WBRT) in patients with 5-20 brain metastases: A multicenter, phase 3 randomized trial

Ayal Aizer MD MHS, Shyam Tanguturi MD, Grant Benham, Paul Brown MD, Daniel Cagney MD, Paul Catalano ScD, Fallon Chipidza MD, Daphne Haas-Kogan MD, Jaroslaw Hepel MD, Monica Krishnan MD, Marciana Johnson BA MPH, Nayan Lamba MD, Jennifer Nosker PhD, Michael Parsons PhD, Luke Peng MD ScM, Ivy Ricca BA, Diana Shi MD, Kee-Young Shin MS, Patrick Wen MD, Rifaquat Rahman MD

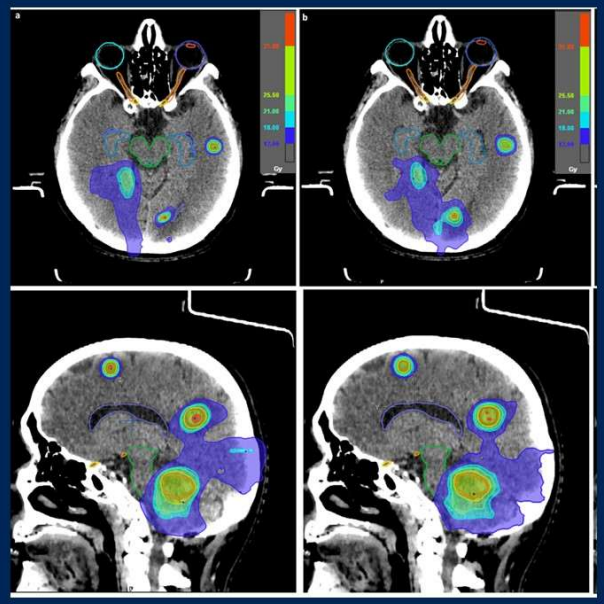
Ayal Aizer MD, MHS
Director of Central Nervous System Radiation Oncology
Brigham and Women's Hospital / Dana-Farber Cancer Institute
Associate Professor, Harvard Medical School

Conclusion: SRS is standard of care

Is LESS MORE?

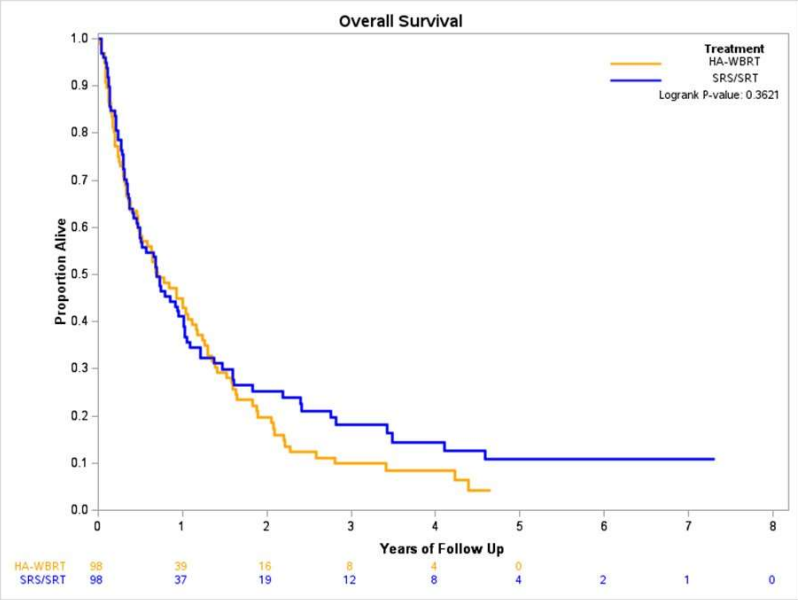


Ayer, A



Cancers **2021**, *13*(14), 3458

Overall Survival



	SRS/SRT	HA-WBRT
Median Survival, mo (95% CI)	8.3 (5.9 -12.3)	8.5 (5.9 - 13.9)
12 Month Survival (95% CI)	41.1% (31.3% - 50.7%)	42.8% (32.7% - 52.6%)
Median # brain mets	15	13
% NSCLC	47%	43%

Primary Outcome

MDASI-BT Symptom Severity			
	SRS/SRT	HA-WBRT	p
Baseline (mean)	2.19	1.90	0.20
Post baseline minus baseline (weighted, mean)	-0.03	0.59	
Difference	**-0.62**		**<0.001**

MDASI-BT Symptom Interference			
	SRS/SRT	HA-WBRT	p
Baseline (mean)	3.49	3.18	0.40
Post baseline minus baseline (weighted, mean)	-0.62	0.89	
Difference	**-1.50**		**<0.001**

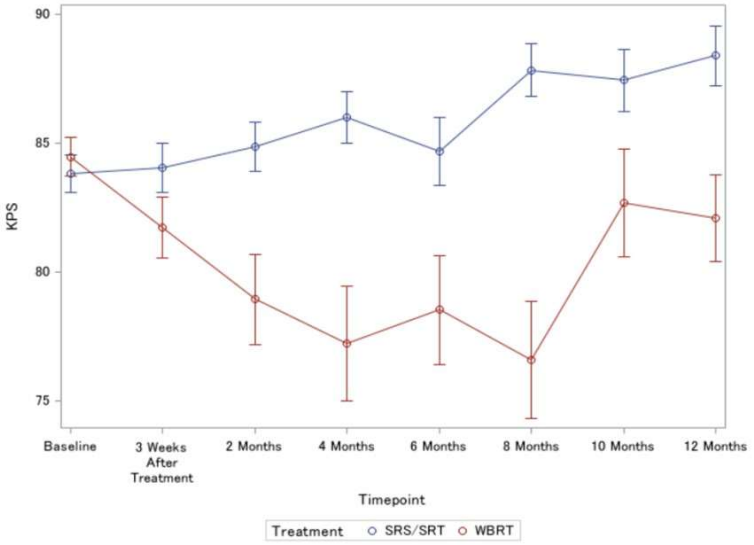
Averaged Severity + Interference (N=172): -1.06 (95% CI -1.54, -0.58), indicating lower symptom burden and interference with daily function with SRS/SRT (p<0.001)

2025 ASCO ANNUAL MEETING #ASCO25

PRESENTED BY: Ayal Aizer MD, MHS

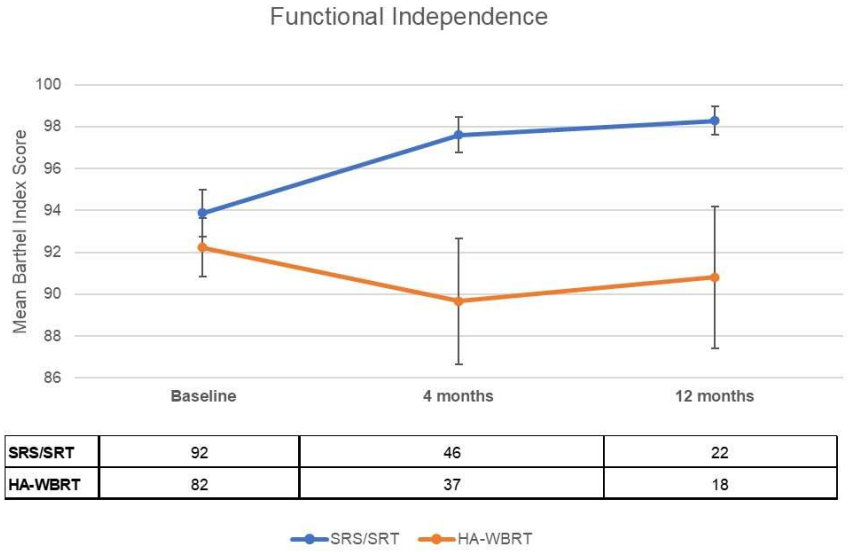
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Performance Status



	BL	3 wk	2 mo	4 mo	6 mo	8 mo	10 mo	12 mo
SRS/SRT	97	79	70	55	45	37	35	31
HA-WBRT	92	76	65	50	47	35	30	29

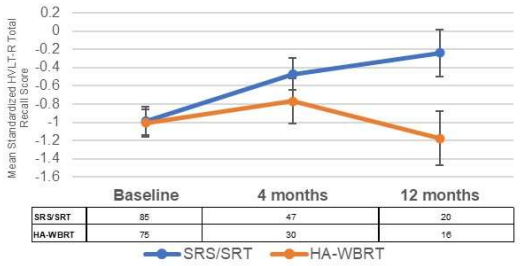
Functional Independence



SRS/SRT	92	46	22
HA-WBRT	82	37	18

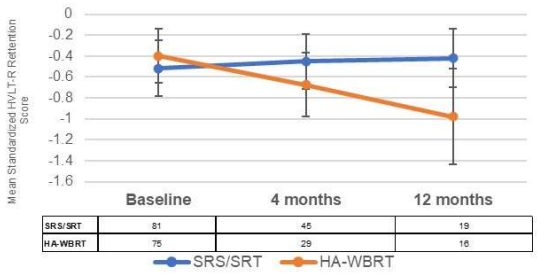
Neurocognitive Testing - HVLT

HVLT-R Total Recall



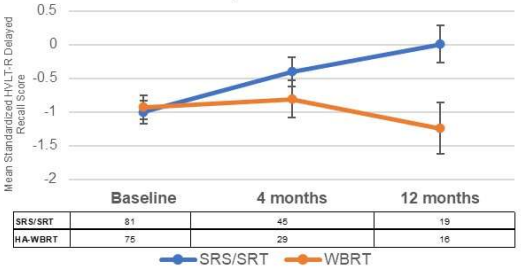
Timepoint	p
Baseline	0.39
4 Months	0.20
12 Months	0.03

Retention



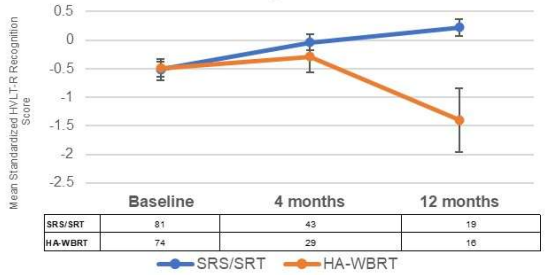
Timepoint	p
Baseline	0.77
4 Months	0.69
12 Months	0.31

Delayed Recall



Timepoint	p
Baseline	0.82
4 Months	0.19
12 Months	0.01

Recognition



Timepoint	p
Baseline	0.91
4 Months	0.43
12 Months	0.004

Take-home points

Thoracic Rad Onc @Stanford

- Systemic therapies for NSCLC are (finally) becoming more effective
- Ablative local therapy has an emerging role in metastatic lung cancer
- Radical RT has the potential to improve survival in oligometastatic or oligoprogressive NSCLC, and even polymetastatic NSCLC, in addition to systemic therapy
- As systemic therapies improve, the impact of effective local therapies is likely to increase

Stanford MEDICINE

Thoracic Rad Onc @Stanford

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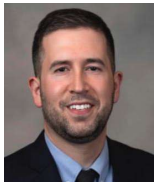
Max Diehn, MD PhD
Professor

Alex Chin, MD
Assistant Professor

Lucas Vitzthum, MD
Associate Professor



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B Loo – Stanford Radiation Oncology

National Comprehensive Cancer Network®

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An alliance of leading cancer centers devoted to patient care, research, and education

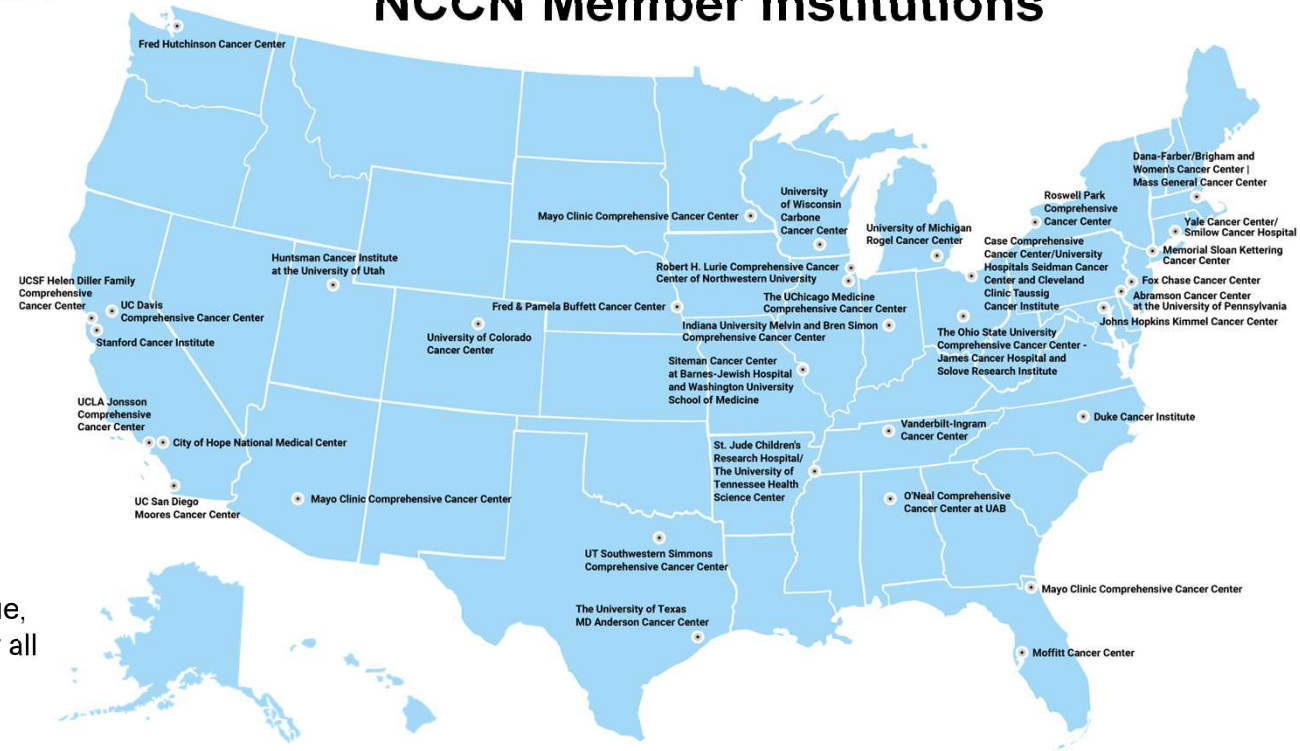
Our Mission

To define and advance quality, effective, equitable, and accessible cancer care and prevention so all people can live better lives

Our Vision

Access to high-quality, high-value, patient-centered cancer care for all people globally

NCCN Member Institutions



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