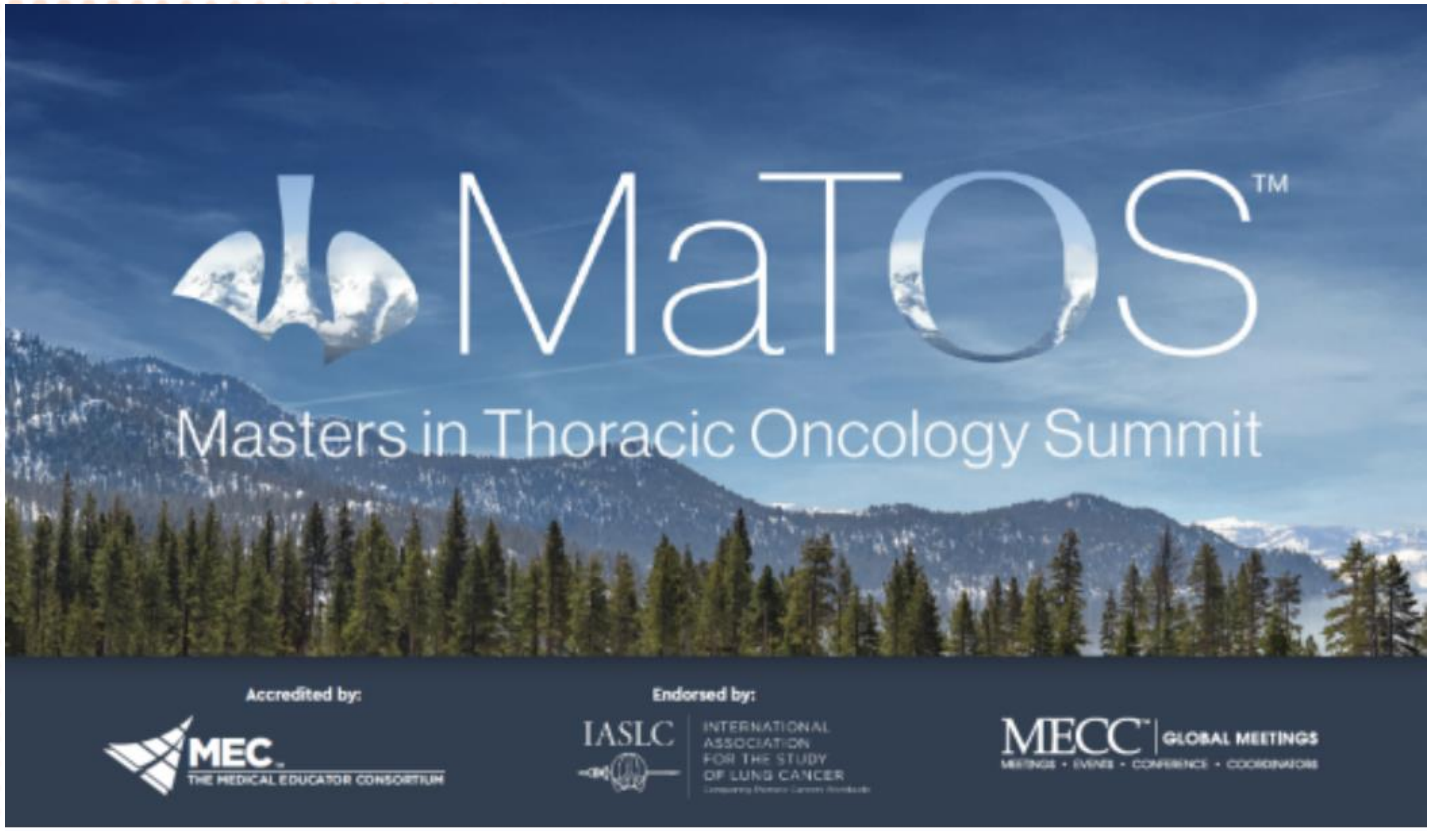
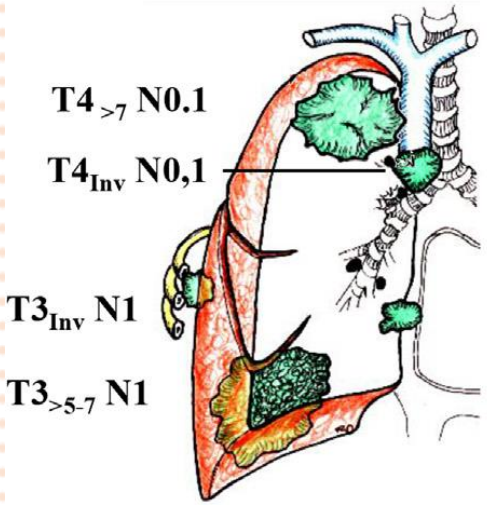
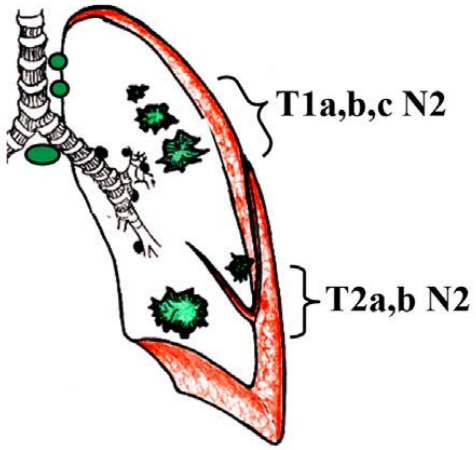
ASSESSING RESECTABILITY IN STAGE III LUNG CANCER

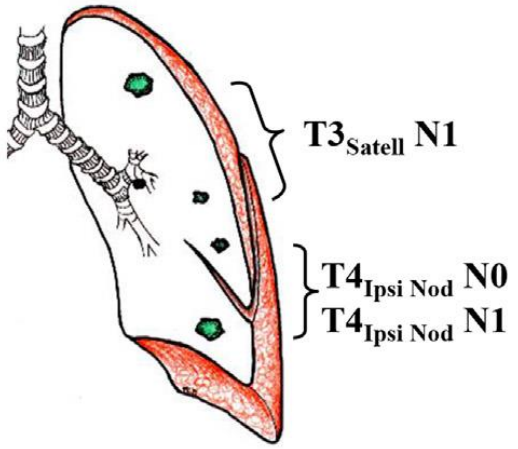


Linda W. Martin, MD, MPH
Professor and Chief,
Thoracic Surgery
University of Virginia

Stage IIIA







Specific Notes:

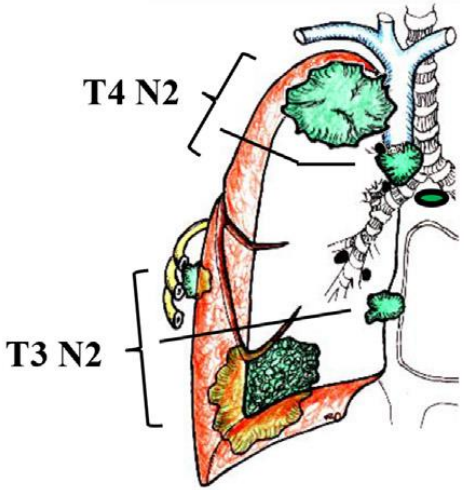
Tumor size defined as largest dimension of the solid (imaging, c-stage) or invasive (p-stage) component

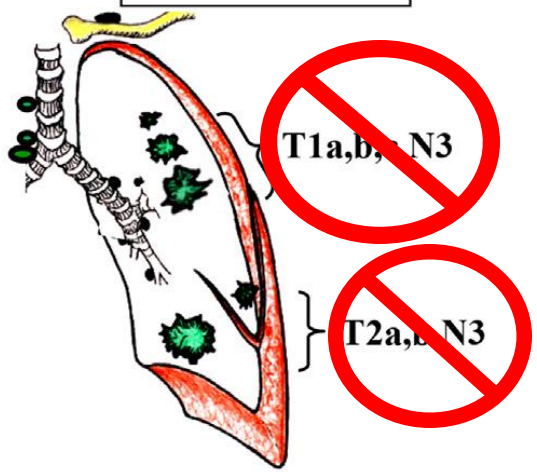
Direct extension of the primary tumor into an adjacent node counts as nodal involvement

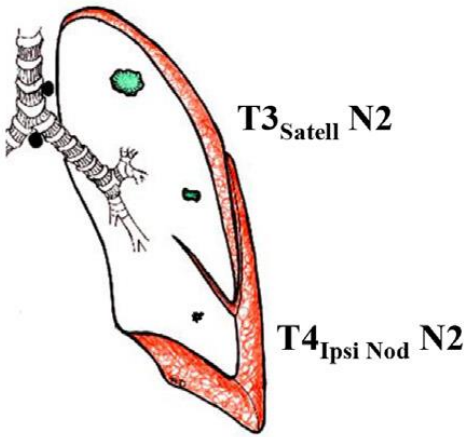
Extension of a nodal metastasis into a T structure does not count for the T category

The highest T category is used when there is a discrepancy between T by size or by other factors

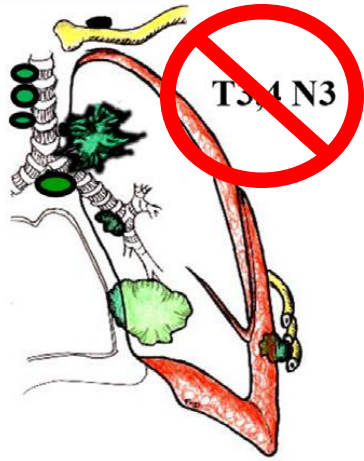
Stage IIIB







Stage IIIC



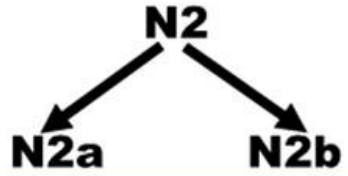
AJCC 8th edition: CHEST 2017; 151(1):193-203

The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groups in the Forthcoming (Ninth) Edition of the TNM Classification for Lung Cancer

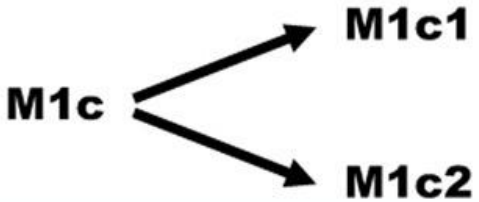
Journal of Thoracic Oncology

Changes in the 9th Edition

N2 involvement is split into:
N2a (single station)
N2b (multiple stations)



M1c involvement is split into:
M1c1 (single organ system)
M1c2 (multiple organ systems)



T/M category	Subcategory, Descriptor	N0	N1	N2		N3
				N2a	**N2b**	
T1	T1a T1b T1c	IA	**IIA**	**IIB**	**IIIA**	IIIB
T2	T2a	IB	?IIIB	**IIIA**	**IIIB**	IIIB
	T2b	IIA				
T3	Size Invasion Nodule	IIB	IIIA	**IIIA**	**IIIB**	IIIC
T4	Size Invasion Nodule	IIIA	IIIA	**IIIB**	**IIIB**	IIIC
M1	M1a, M1b	IVA				
	M1c1, M1c2	**IVB**				

CONCLUSION: The proposed changes improve the granularity of nomenclature of anatomic extent that has benefits as treatment becomes increasingly differentiated and complex.

IASLC

Rami-Porta et al. *J Thorac Onc* (2024)

enter
Center

RESECTABILITY

Can we agree on a definition?

WHEN should it be decided? Before any therapy, or based on response?

RESECTABILITY DEFINITIONS– AUDIENCE RESPONSE

A. A carefully guarded secret of thoracic surgeons
B. Can be determined from imaging studies
C. Can be determined with the right application of artificial intelligence
D. Is uniform regardless of practice setting and surgical expertise
E. None of the above

RESECTABILITY DEFINITIONS– AUDIENCE RESPONSE

A. A carefully guarded secret of thoracic surgeons
B. Can be determined from imaging studies
C. Can be determined with the right application of artificial intelligence
D. Is uniform regardless of practice setting and surgical expertise
E. None of the above

BINIAM KIDANE'S RULES OF RESECTABILITY

Three intersecting domains:

- Oncologic
- Technical
- Physiologic

BINIAM KIDANE'S RULES OF RESECTABILITY

- Technical Resectability:
  - Can you achieve R0 resection?
  - Subjective
  - **Can vary based on local resources**
  - **Can change with potent induction strategy…**

OPEN SURGERY IS NOT A BAD THING

THORACIC: LUNG CANCER

Is less really more? Reexamining video-assisted thoracoscopic versus open lobectomy in the setting of an enhanced recovery protocol

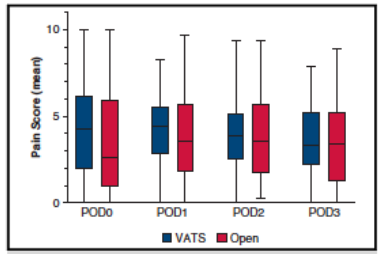
Check for updates

Elizabeth D. Krebs, MD, MSc,[a] J. Hunter Mehaffey, MD, MSc,[a] Bethany M. Sarosiek, MSN, MPH,[a] Randal S. Blank, MD, PhD,[b] Christine L. Lau, MD, MBA,[a] and Linda W. Martin, MD, MPH[a]

ABSTRACT

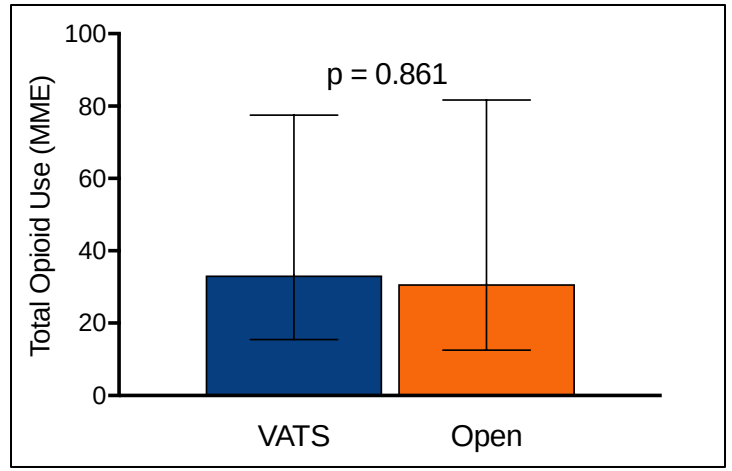
Objectives: Video-assisted thoracoscopic surgery lobectomy has been associated with improved pain, length of stay, and outcomes compared with open lobectomy. However, enhanced recovery protocols improve outcomes after both procedures. We aimed to compare video-assisted thoracoscopic surgery and open lobectomy in the setting of a comprehensive enhanced recovery protocol.

Methods: All patients undergoing lobectomy for lung cancer at a single institution since the adoption of an enhanced recovery protocol (May 2016 to December 2018) were stratified by video-assisted thoracoscopic surgery versus open status and compared. Demographics and outcomes, including length of stay, daily pain scores, and short-term operative complications, were compared using stan-

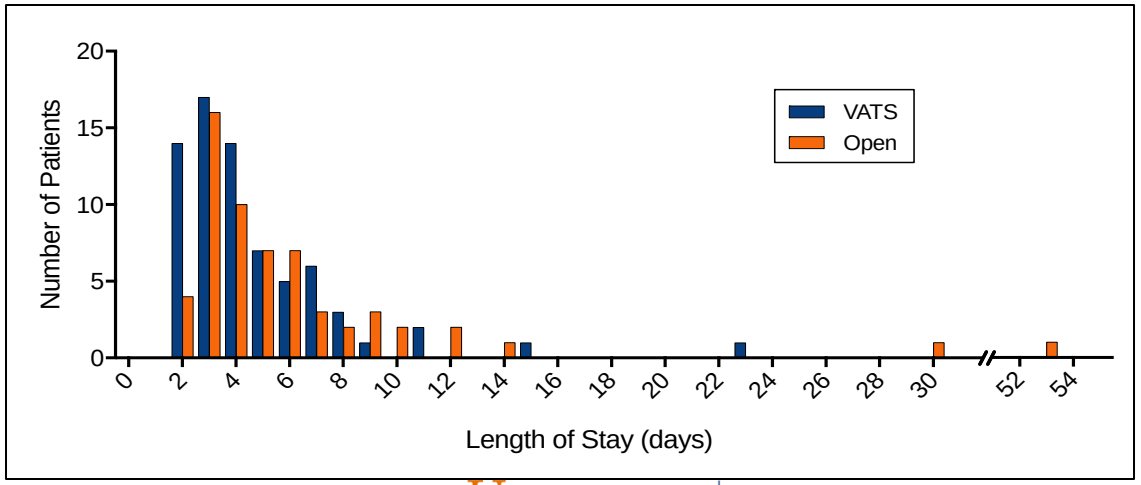


Distribution of mean daily pain scores for patients undergoing VATS lobectomy and open lobectomy.

(J Thorac Cardiovasc Surg 2020;159:284-94)



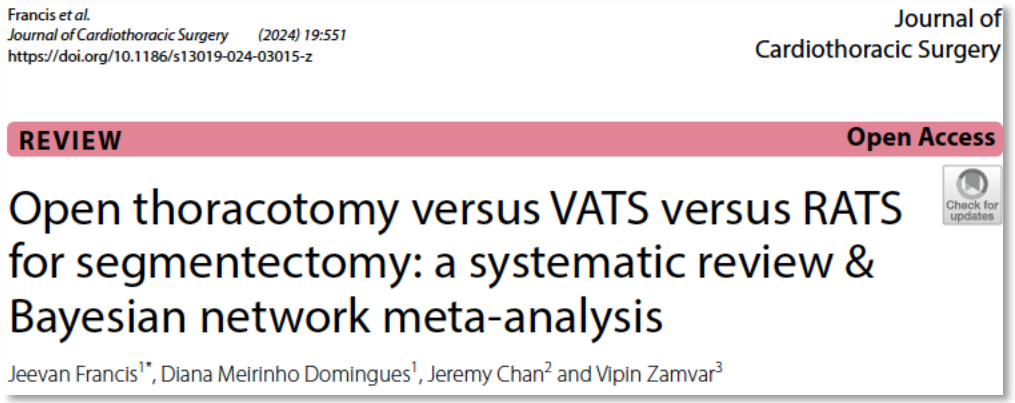
mg morphine equivalents (MME) 33 and 31, the equivalent of 4 – 4.5 oxycodone tablets



@LindaMThoracic

UNIVERSITY of VIRGINIA HEALTH SYSTEM | UVA Cancer Center An NCI-Designated Cancer Center

COMPARISON OF SURGICAL INCISIONS



Francis et al.
Journal of Cardiothoracic Surgery (2024) 19:551
https://doi.org/10.1186/s13019-024-03015-z

Journal of Cardiothoracic Surgery

REVIEW Open Access

Open thoracotomy versus VATS versus RATS for segmentectomy: a systematic review & Bayesian network meta-analysis

Jeevan Francis[1*], Diana Meirinho Domingues[1], Jeremy Chan[2] and Vipin Zamvar[3]

- 30 day mortality
- Readmission
- Pneumonia
- airleak

11 studies
7700 patients

Conclusion There are no significant differences between the three approaches in the clinical outcomes measured. While our analysis demonstrates the potential benefits of RATS, it is important to note that the steep learning curve associated with this technique may impact its wider adoption and efficacy in the community. Further randomised control studies are required to compare the short and long terms results of VATS and RATS approaches.

BINIAM KIDANE'S RULES OF RESECTABILITY

- Physiologic Resectability
  - Can the patient in front of me tolerate this surgery safely?
  - Some objective measures, some subjectivity
    - Grit, mental toughness

MOST OF OUR PATIENTS DO NOT LOOK LIKE THIS…

What Is a Cardiopulmonary Stress Test?

@LindaMThoracic

University of Virginia Health System | UVA Cancer Center
An NCI-Designated Cancer Center

Frailty

ECOG

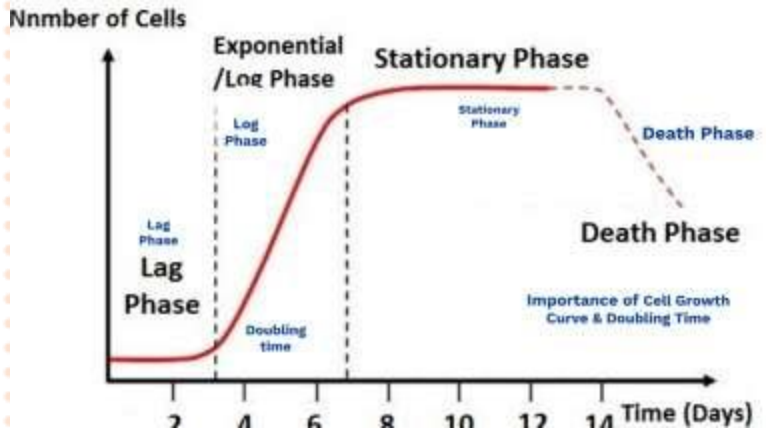
@LindaMThoracic

https://doi.org/10.1016/j.eclinm.2021.101260 eClinical Medicine Jan 2022

BINIAM KIDANE'S RULES OF RESECTABILITY

Oncologic Resectability:

- Can this disease be controlled by surgery?
- That is, what's the tumor biology?
  - small cell=extreme example
  - Bulky, invasive N2
  - Doubling time, SUV



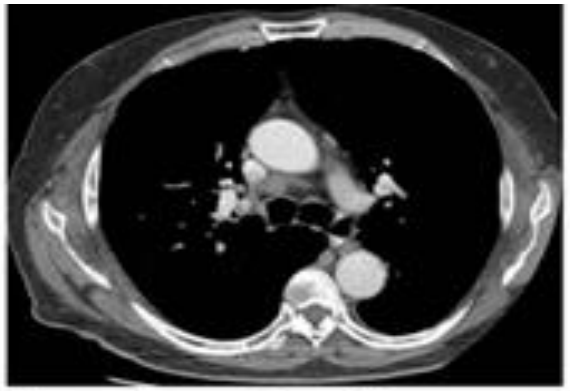
Is this tumor spreading like wildfire?

@LindaMThoracic

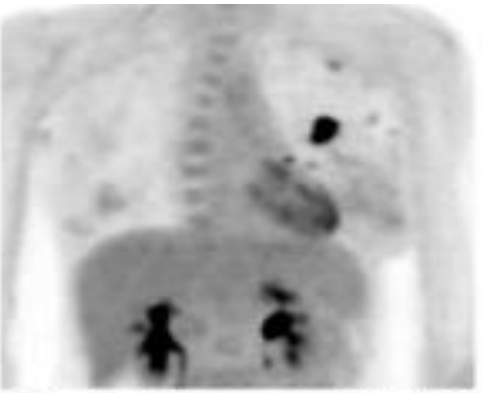
University of Virginia Health System | UVA Cancer Center
An NCI-Designated Cancer Center

CLASSIFICATION SCHEME

Mediastinal Infiltration

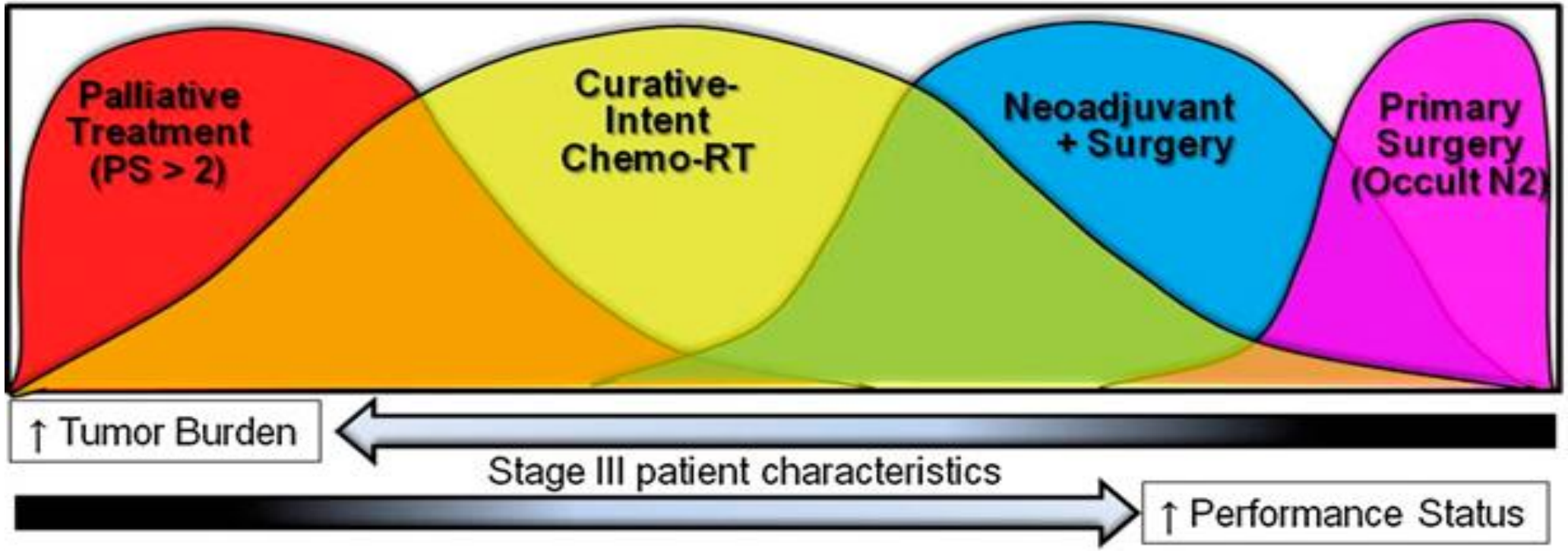


Discrete node enlargement



Clinically occult N2

chematic of types of patients included in studies using different treatment approaches



CHEST 2013; 143(5)(Suppl):e314S–e340S

IASLC 2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE

Consensual definition of stage III NSCLC Resectability:

EORTC-Lung Cancer Group initiative with other scientific societies

A-M. Dingemans[1], J. Remon[2], L. Hendriks[3], J. Edwards[4], C. Faivre-Finn[5], N. Reguart[6], E. Smit[7], A. Levy[8], D. Sanchez[9], J.C. Trujillo[10], A. Filippi[11], K. Stathopoulos[12], T.G. Blum[13], M. Guckenberger[14], S. Popat[15], I. Opitz[14], A. Brunelli[16], R. De Angelis[12], P. Hofman[17], K. Hartemink[18], RH. Petersen[19], E. Ruffini[20], C. Dickhoff[21], E. Prisciandaro[22], J. Derks[3], I. Bahce[21], A. Mariolo[23], E. Xenophontos[24], N. Giaj Levra[25], I. Houda[21], M. Brandão[12], T. Berghmans[12]

[1]Erasmus MC, Rotterdam/NL,[2]IGR, Paris/FR, [3]MUMC, Maastricht/NL ,[4]Sheffield Teaching Hospitals NHS Foundation Trust - Weston Park Hospital, Sheffield/GB, [5]The Christie NHS Foundation Trust, Manchester/GB, [6]Hospital Clinic de Barcelona, Barcelona/ES, [7]LUMC, Leiden/NL, [8]Gustave Roussy, Paris/FR, [9]Hospital Clinic of Barcelona, Barcelona/ES, [10]Hospital de la Santa Creu i Sant Pau, Barcelona/ES, [11]Fondazione IRCCS - Policlinico San Matteo, Pavia/IT, [12]Institut Jules Bordet, Brussels/BE, [13]HELIOS Klinikum Berlin, Berlin/DE, [14]UniversitaetsSpital Zurich, Zurich/CH, [15]Royal Marsden Hospital, London/GB, [16]St. James's University Hospital, Leeds/GB, [17]CHU de Nice - Hopital Pasteur, Nice/FR, [18]NKI-AVL, Amsterdam/NL, [19]Copenhagen University Hospital, Rigshospitalet, Denmark/DK, [20]Universita Di Torino - San Giovanni Battista, Torino/IT, [21]AmsterdamUMC, Amsterdam/NL, [22]U.Z. Leuven - Campus Gasthuisberg, Leuven/BE, [23]Institute Mutualiste Montsouris - Institut du Thorax Curie Montsouris, Paris/FR, [24]EORTC, Brussels/BE, [25]IRCCS Ospedale Sacro Cuore Don Calabria, Verona/IT

EORTC
The future of cancer therapy

In abstract form only:
https://doi.org/10.1016/j.jtho.2023.09.046

	N0	N1	N2 SINGLE (non-bulky, non-invasive)	N2 MULTI (non-bulky, non-invasive)	N2 BULKY¶	N2 INVASIVE	N3
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE	RESECTABLE	POTENTIALLY RESECTABLE*	UNCLEAR	UNRESECTABLE	UNRESECTABLE
T3 size / satellite / invasion	NOT STAGE III DISEASE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 size / satellite	RESECTABLE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 invasion	POTENTIALLY RESECTABLE§	POTENTIALLY RESECTABLE§	POTENTIALLY RESECTABLE§	POTENTIALLY RESECTABLE*§	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE

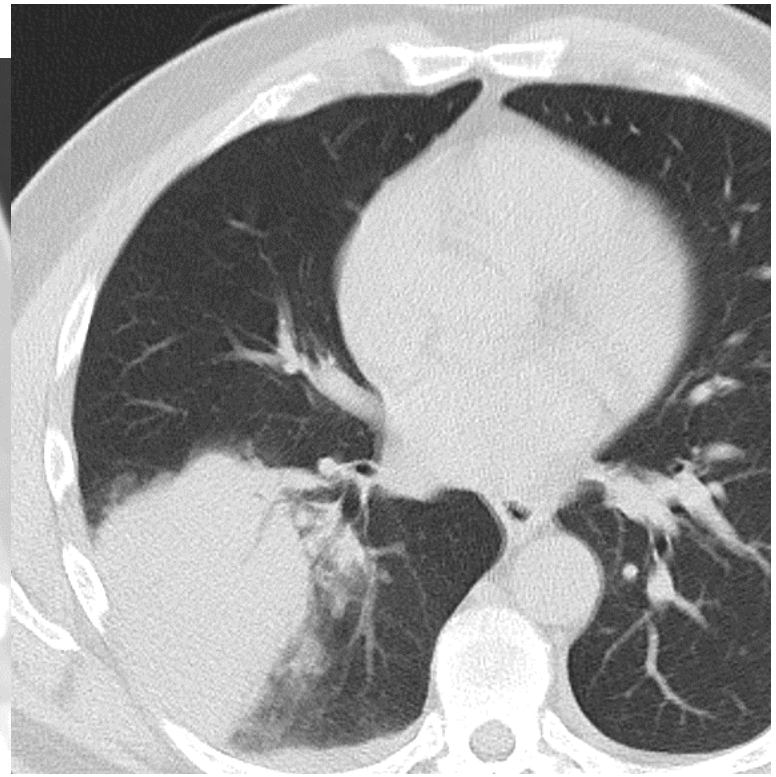
***Multiple station N2**: case-by-case discussion; the exact number of nodes/stations cannot be defined

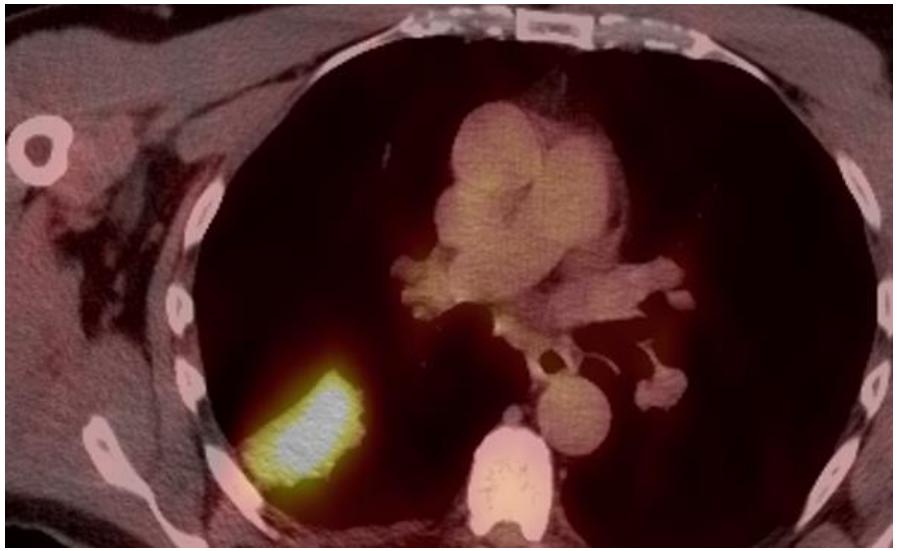
¶**Bulky N2**: lymph nodes with a short-axis diameter >2.5-3 cm; in specific situations of *highly selected patients*, including those patients in multidisciplinary trials with surgery as local therapy can be discussed

§Some **T4 tumours by infiltration of major structures** are potentially resectable – see Table 1

WHEN TO DECIDE ON RESECTABILITY: CONSIDER THE FOLLOWING…

BORDERLINE RESECTABILITY – BY STAGE





PET showing NEGATIVE subcarinal space

CASE PRESENTATION 1

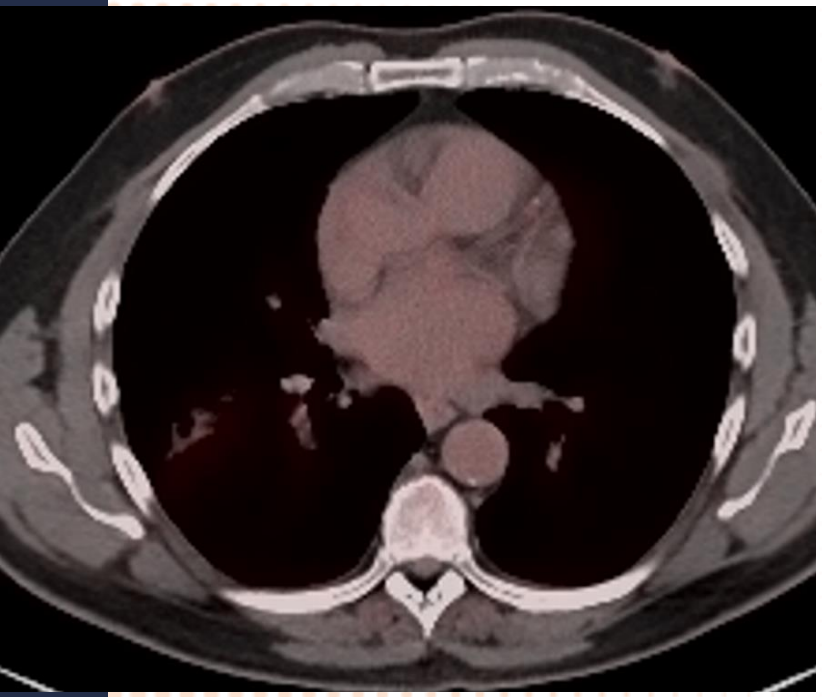
- cT4N0M0
- Upfront surgery planned (predated CM816 approval)
- No mediastinal staging – planned for EBUS, ROSE, then proceed

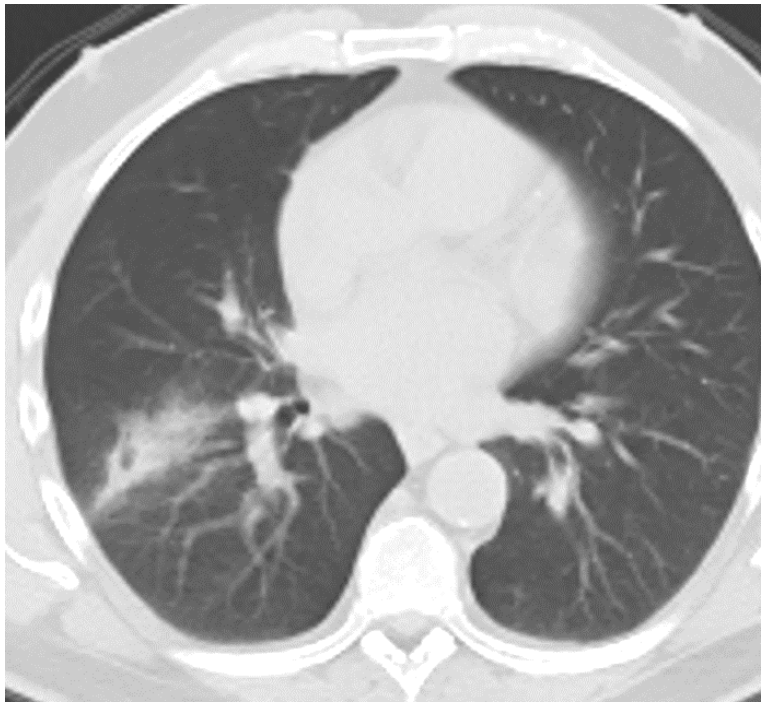
- Level 7 was POSITIVE intraoperatively
- Now T4N2M0…

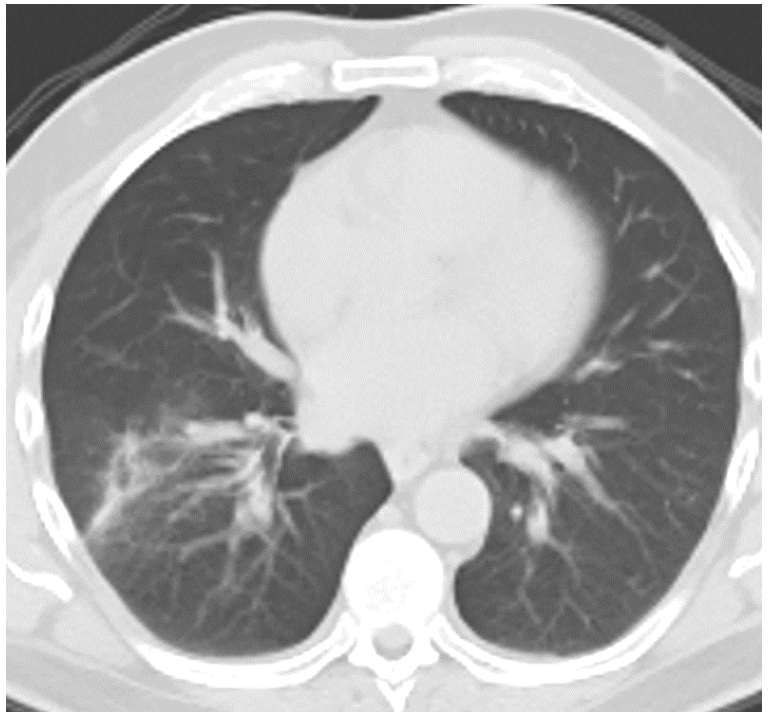
AUDIENCE RESPONSE:
T4 BY SIZE, SINGLE/OCCULT N2
HEALTHY PATIENT – WHAT NEXT?

A. ChemoRT -> durvalumab (PACIFIC)
B. Proceed with lobectomy ->adjuvant chemo/CPI
C. Chemo/CPI x 3 cycles -> lobectomy
D. Chemo/CPI x 3 cycles -> lobectomy -> PORT

FOLLOWING CHEMO/CPI X 3 CYCLES:



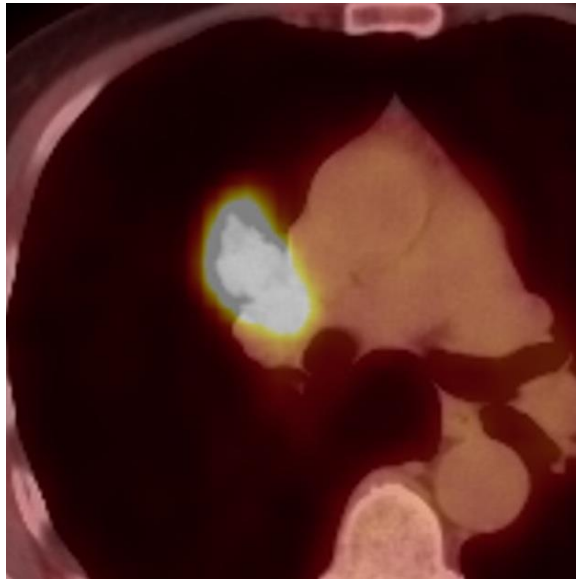




SURGERY

- Open RLL
- Home in 2 days, no pain, took about 2 oxy 5 mg
- Pathology: ypT3N0 (a bit surprising), R0
- So “borderline resectable” T4N2 was resectable

Case 2 – can we enhance resectability?



RUL SCCA

PDL1 80%

Lung function would not allow for right pneumonectomy

Clinical T2N1

@LindaMThoracic

University of Virginia Health System | UVA Cancer Center
An NCI-Designated Cancer Center

RIGHT PNEUMONECTOMY REQUIRED

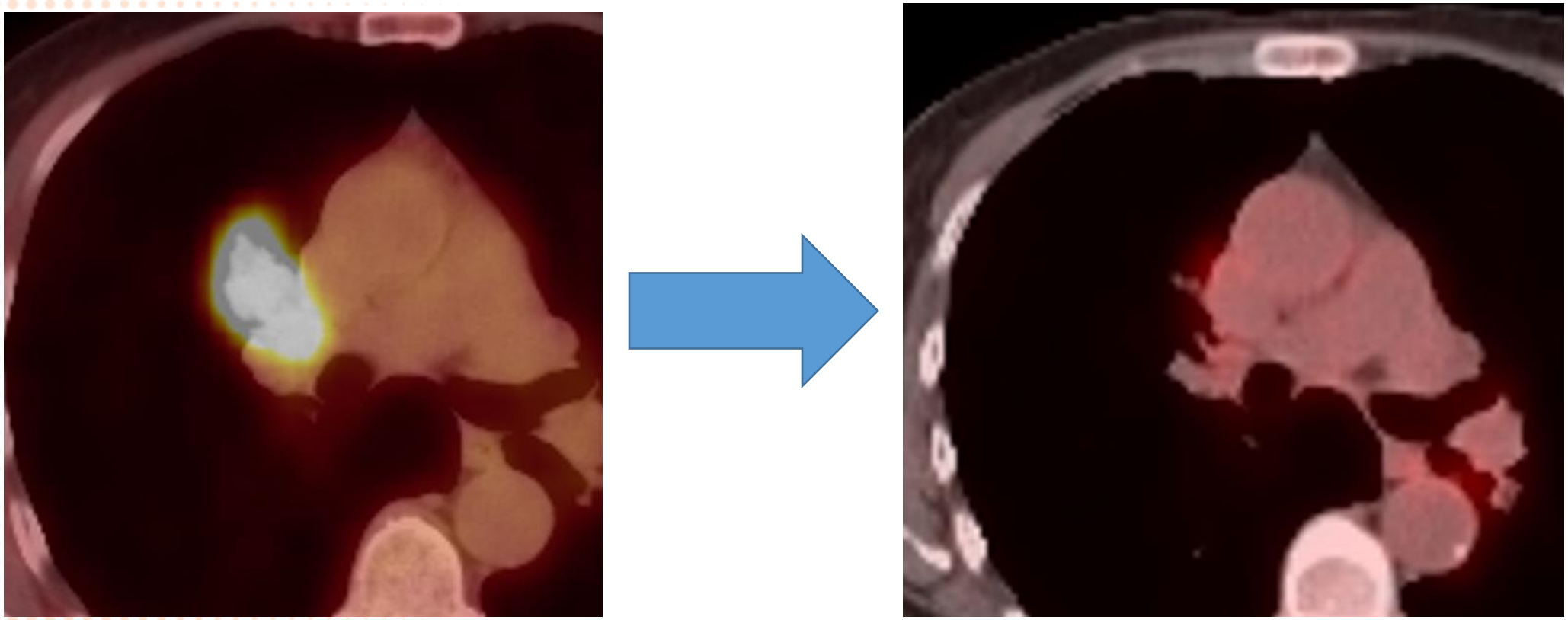
- Oncologically, technically resectable
- But PFT's very borderline – would be just under 30% FEV1 and DLCO with right pneumonectomy

AUDIENCE RESPONSE:
RIGHT HILAR TUMOR, T2N1 PHYSIOLOGICALLY UNRESECTABLE

A. ChemoRT -> durvalumab (PACIFIC)
B. Proceed with pneumonectomy ->adjuvant chemo/CPI 
C. Chemo/CPI x 3 cycles -> MDT reassessment

CM816 STRATEGY: 3 CYCLES PLATINUM DOUBLET + NIVO

IMPRESSIVE RESPONSE!



pre

post

@LindaMThoracic

UNIVERSITY of VIRGINIA HEALTH SYSTEM | UVA Cancer Center
An NCI-Designated Cancer Center

SURGERY

- Open Right upper lobectomy – NO PNEUMONECTOMY NEEDED!
- Path: ypT0N0M0
- Returned to work, respiratory status excellent
- NED 18 months postoperatively

OPINION: RESECTABILITY SHOULD BE RESPONSE-BASED

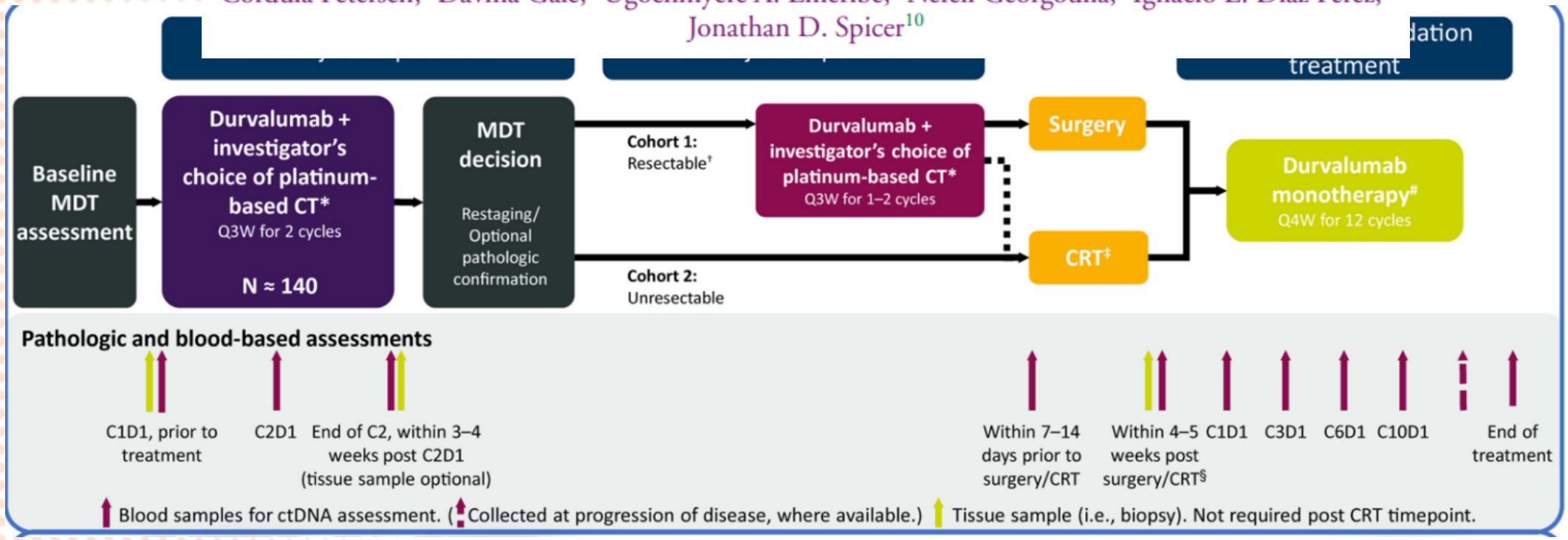
Two examples of oncologically and physiologically marginal patients getting to surgery

@LindaMThoracic

University of Virginia Health System | UVA Cancer Center
An NCI-Designated Cancer Center

MDT-BRIDGE: Neoadjuvant Durvalumab Plus Chemotherapy Followed by Either Surgery and Adjuvant Durvalumab or Chemoradiotherapy and Consolidation Durvalumab in Resectable or Borderline-resectable Stage IIB–IIIB NSCLC

Martin Reck,[1] Ernest Nadal,[2] Nicolas Girard,[3] Andrea R. Filippi,[4] Linda W. Martin,[5] Carl M. Gay,[6] Cordula Petersen,[7] Davina Gale,[8] Ugochinyere A. Emeribe,[9] Nefeli Georgoulia,[9] Ignacio E. Diaz Perez,[9] Jonathan D. Spicer[10]



Clinical Lung Cancer July 2024

CONCLUSIONS/SUMMARY

- **Resectability is subjective** – need MDT and/or surgeon to evaluate
- You will give more people with lung cancer a chance at resection if assessed *during* and *after* neoadjuvant
- Unanswered – can we safely salvage with CRT if surgery not possible