

# 5 Jahre Victo- Chirurgische Konzepte im Zeitalter der Präzisionsmedizin

Walter Klepetko, MD  
Professor of Thoracic Surgery



## Vienna International Center for Thoracic Oncology

Frontline therapy for all types of thoracic malignancies. Fast and direct access to all diagnostic and therapeutic tools at the highest level of quality.



## WHO WE ARE

VICTO consists of a group of highly renowned surgeons, oncologists, and radiologists who aim to provide all the necessary services related to the treatment of thoracic malignancies at the cutting-edge of medical science.



## DIAGNOSIS

All types of bronchoscopic investigations and complete histopathological and moleculargenetic assessment.



State-of-the-art imaging techniques including:  
PET/CT, MRI, Ultrasound, Angiography





## SURGERY

VICTO offers the complete spectrum of surgical interventions, from minimal invasive to maximal radical surgery.

- Video assisted thoracic surgery
- Uniportal surgery
- Muscle sparing minithoracotomy
- Sleeve resections
- Complex resections
- Thoracic wall resections

## MEDICAL ONCOLOGY

VICTO offers the entire and most up to date medical oncology treatments.

- Personalized medicine
- Targeted therapy
- Immunotherapy
- Chemotherapy
- Various types of combinationtherapies

According to the individual situation patients are offered participation in front line studies as well as individualized forms of treatment.

# VICTO - Patient flow 2018-2023

## **Surgical admissions**

n = 950

Operative spectrum:

Mediastinoscopy/ EBUS / Videothoracoscopic Intervention

Segmental Resection / Lobectomy / Pneumonectomy

Sleeve Resection / Tracheal Resection / Carina Resection /

EPP / Superior Vena Cava Resection / Esophagectomy

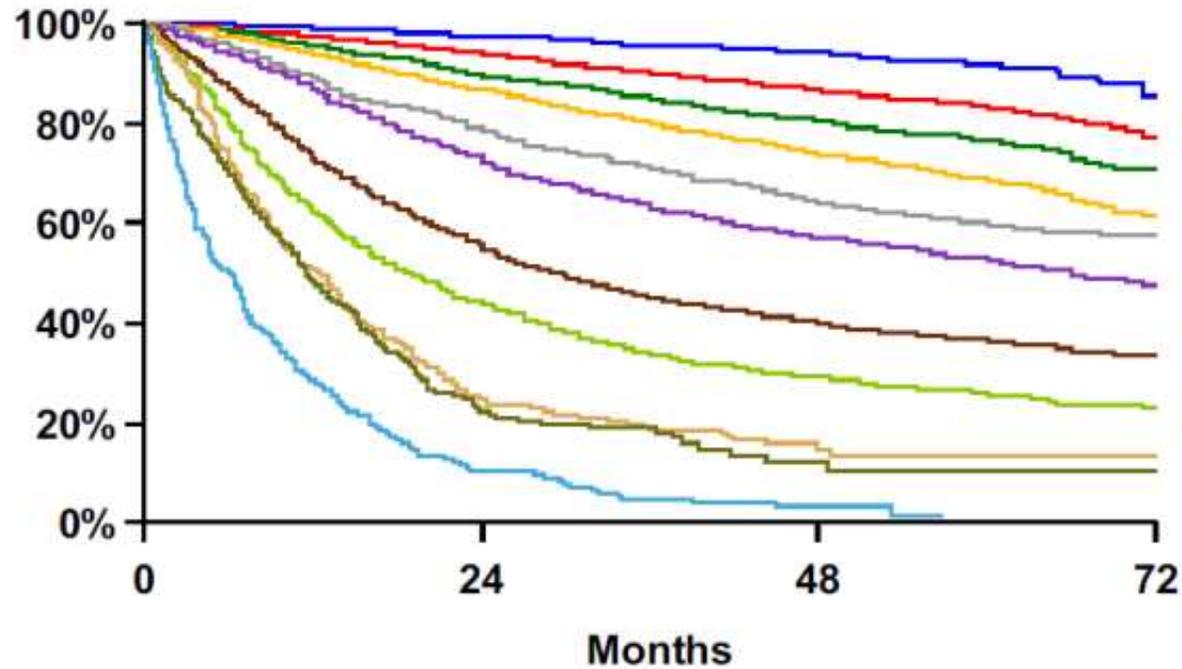
## **Medical Oncology admissions**

n = 1700

Chemo / Immuno / Targeted Therapy

Symptomatic / Palliativ Treatment

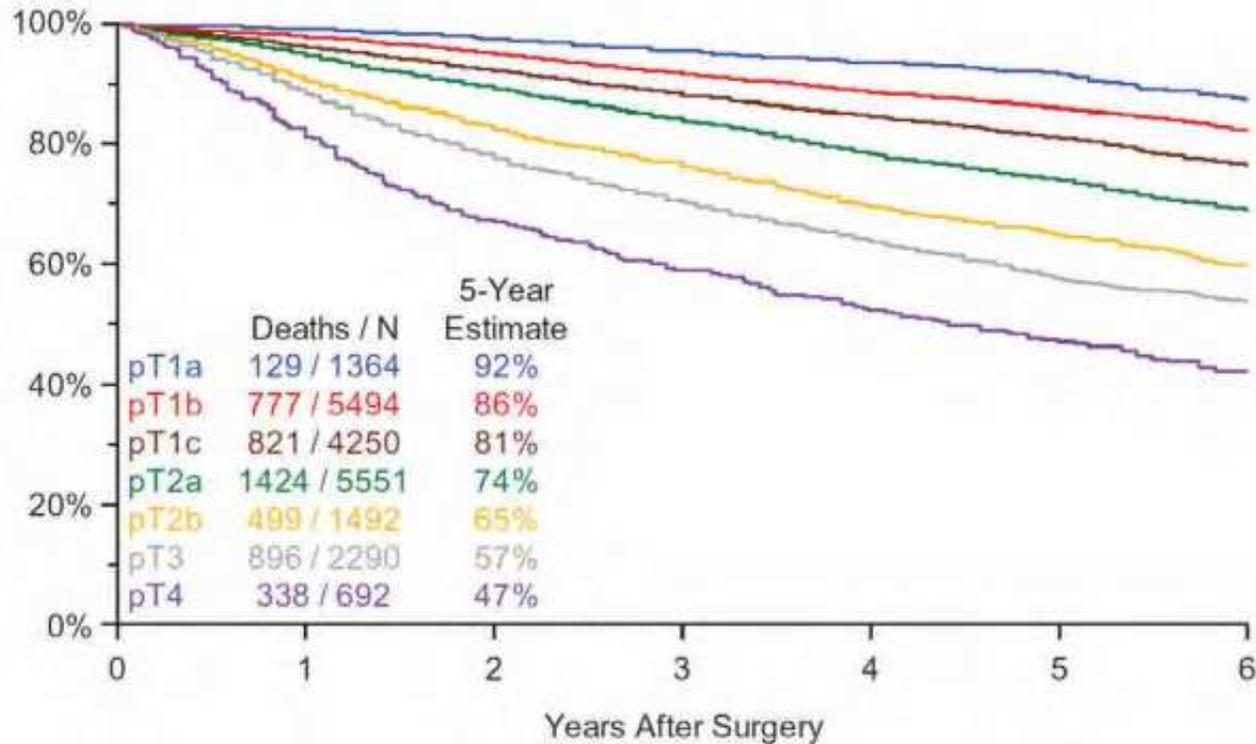
# Expected prognosis in NSCLC



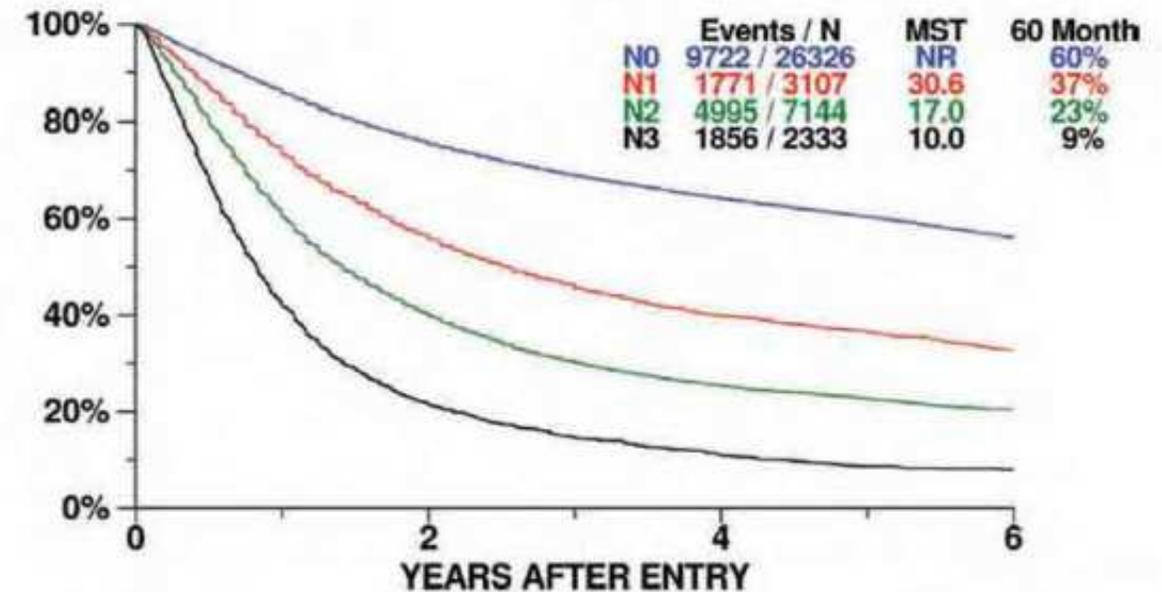
Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

TNM-8 Staging System data  
Goldstraw et al. JTO 2015

# Expected prognosis in NSCLC: Impact of T and N



TNM-8 Staging System data  
Rami-Porta et al. JTO 2015

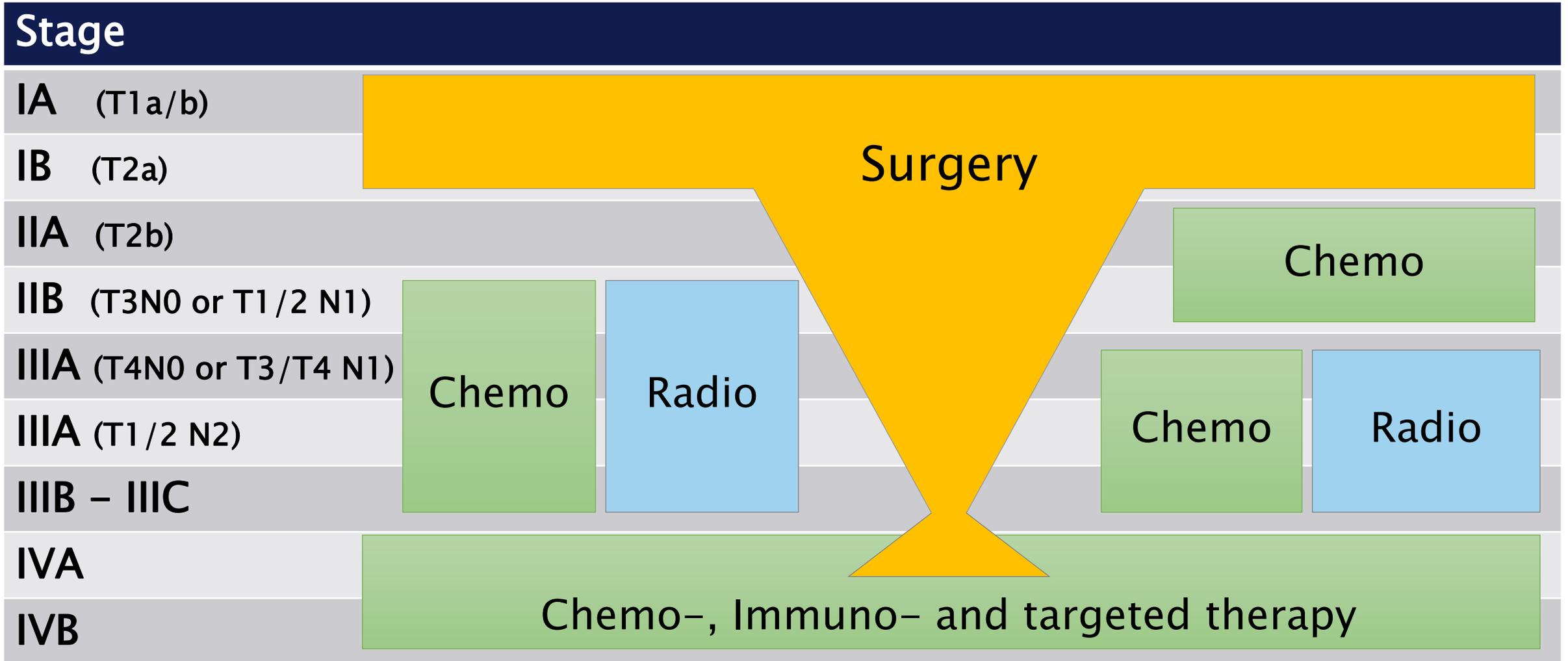


TNM-8 Staging System data  
Asamura et al. JTO 2015

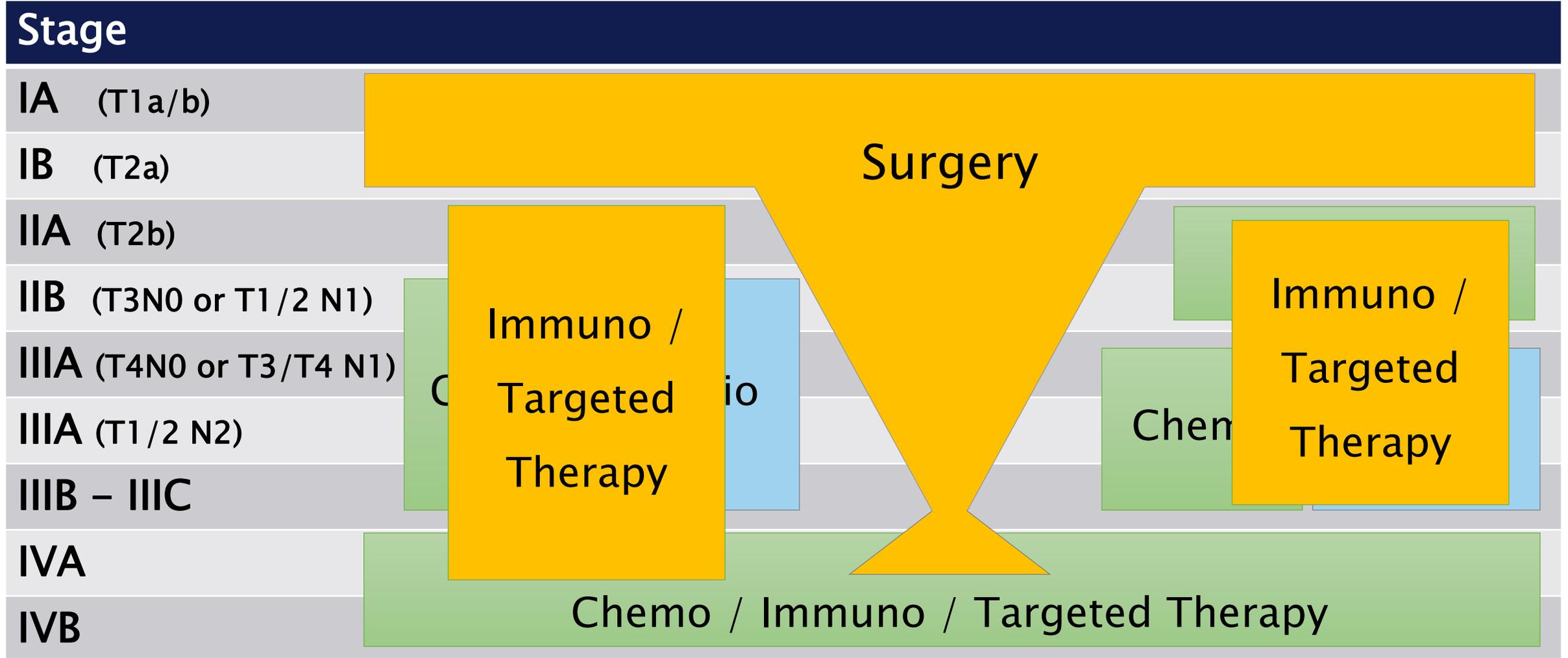
# Where we started from: Classical treatment concept for NSCLC

Stage	
I	Surgery
II	
III (T4 or N2/N3)	Chemotherapy
IV	

# Modern treatment concept



... recent changes with recent advances in targeted/ immunotherapy



**Resectable disease**

**Considerations**

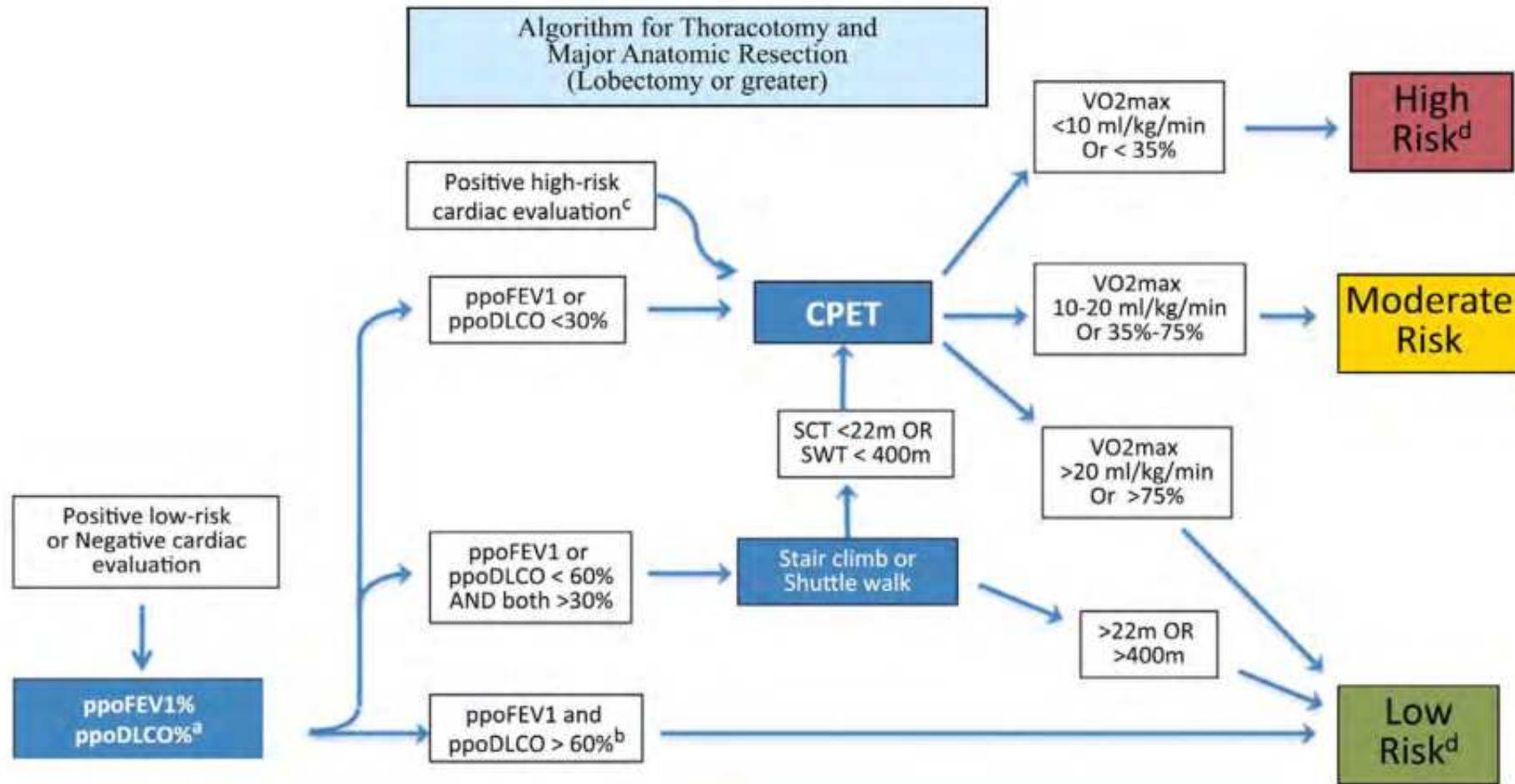
**Functional  
resectability**

**Technical  
resectability**

**Oncological  
resectability**

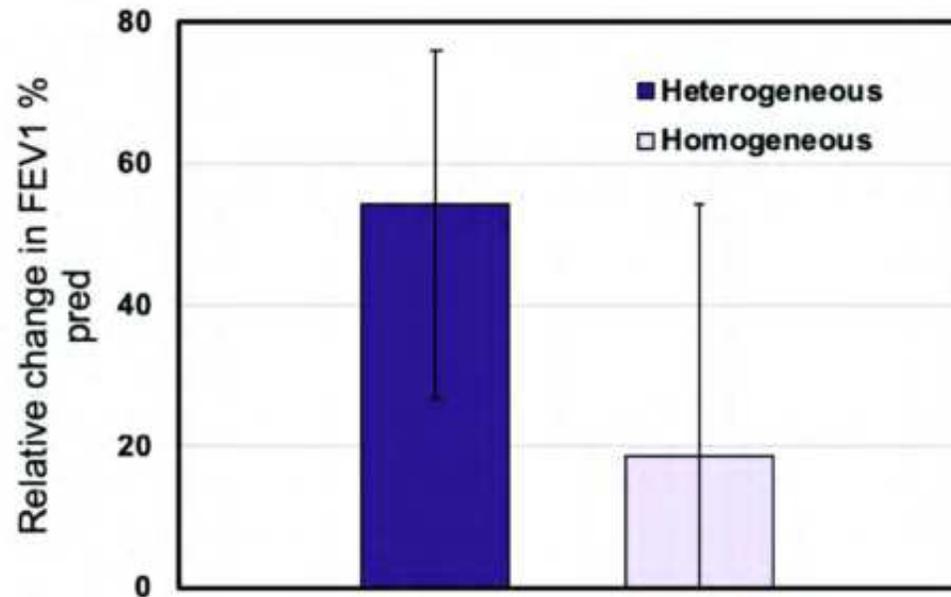
# Evaluation of functional capacity

Chest Guidelines. Brunelli et al. Chest 2013

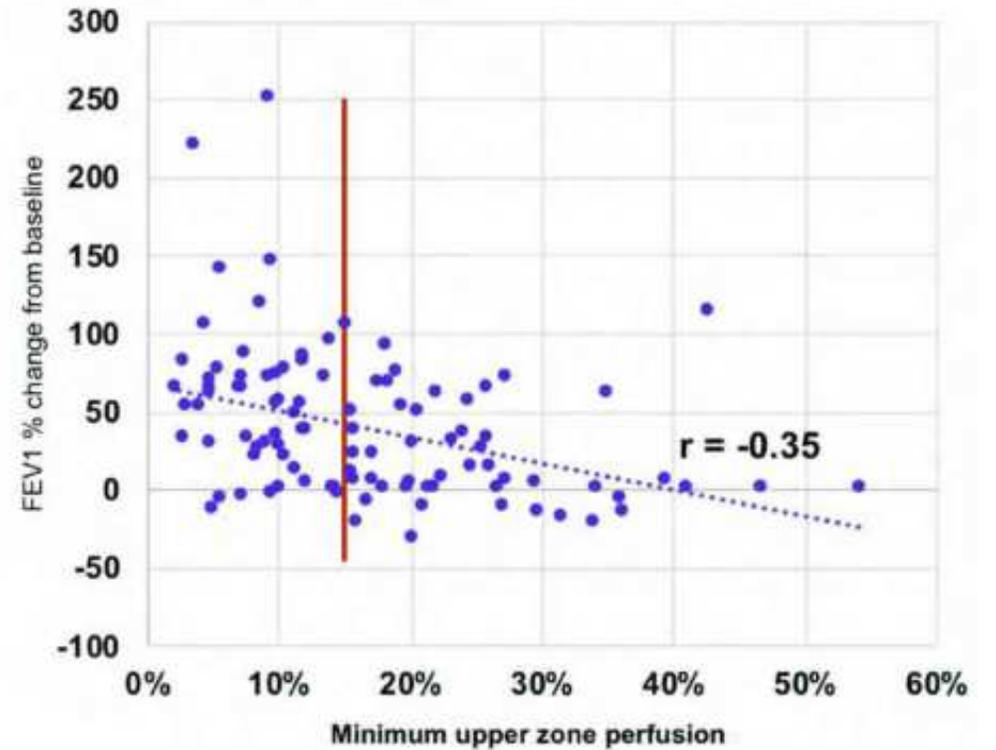


# Lung volume reduction surgery can improve functional capacity

Seadler et al. Ann Thorac Surg 2019

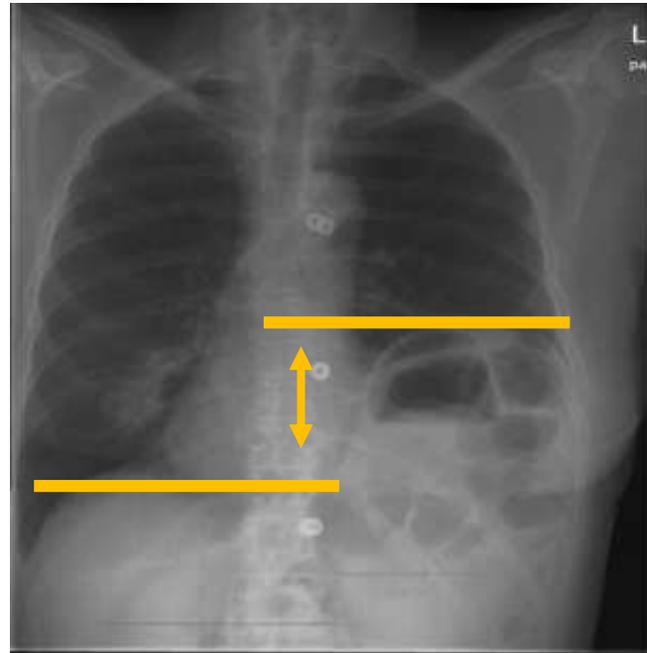
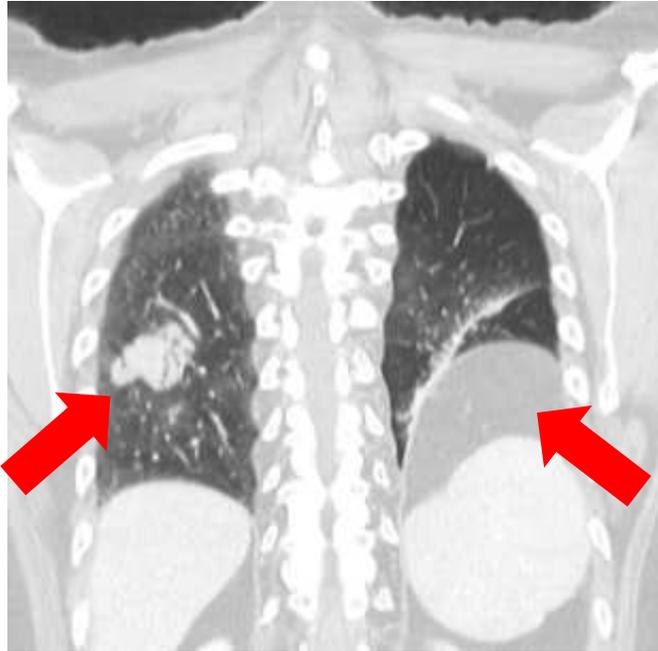


Relative change in FEV1% according to type of emphysema



Relative change in FEV1% according to upper lobe perfusion

# Adenocarcinoma RLL combined with contralateral idiopathic phrenic nerve palsy



## Spirometry

FEV1: 1,7l (78%)

FEV1 /VC max: 58,15 (74%)

VC max: 3,01 (105%)

SaO<sub>2</sub>: 93%

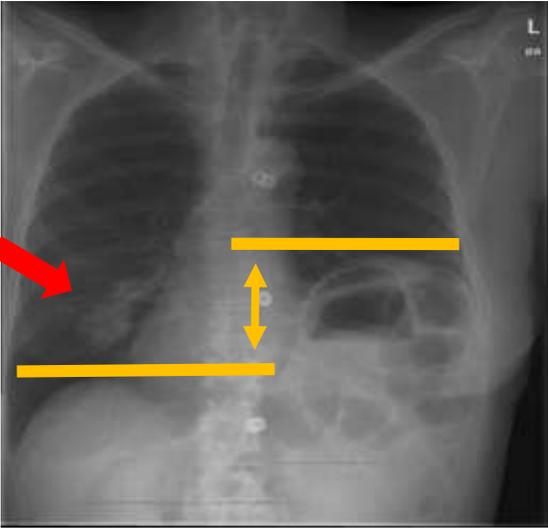
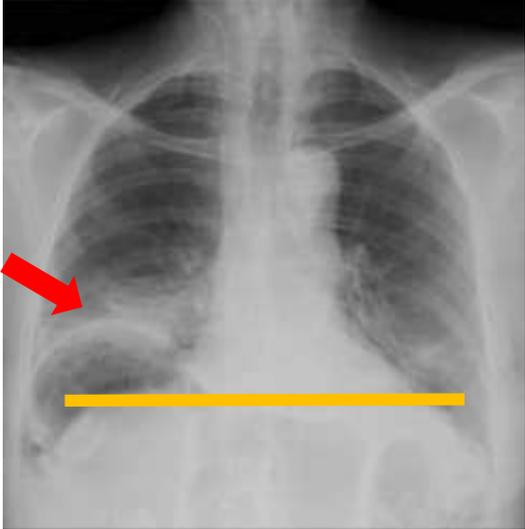
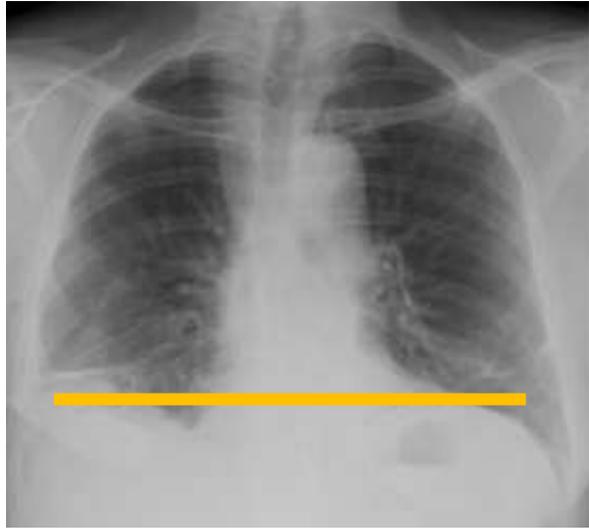
PaO<sub>2</sub>: 63 mmHG

PaCO<sub>2</sub>: 33 mmHG

## Treatment

Diaphragmatic plication followed by staged contralateral lobectomy

# Functional and oncological outcome

At diagnosis	After plication	After lobectomy	Outcome
<p>FEV1:1,75l (78%)</p> <hr/> <p>FEV1 /VC max: 58,2 (74%)</p> <p>VC max: 3,01 (105%)</p>	<p>FEV1:2,17l (96%)</p> <hr/> <p>FEV1 /VC max: 70,4 (89%)</p> <p>VC max: 3,08 (106%)</p>	<p>FEV1:1,9l (85%)</p> <hr/> <p>FEV1 /VC max: 69,8 (85%)</p> <p>VC max: 2,85 (100%)</p>	<p><b>Pathological staging</b> Adenocarcinoma pT2a pN0, R0</p> <p><b>Tumorboard</b> No adjuvant treatment</p> <p><b>Follow-up</b> Free from disease since 7 years</p>
			

Open surgery for locally advanced NSCLC

Considerations

Functional

Technical

Oncological

# Technical Resectability

## Established resectability

Stage I - IIIA

## Possible resectability

Stage IIIB IV A/B

# What determines the oncological outcome ???



Open surgery

Minimal invasive surgery



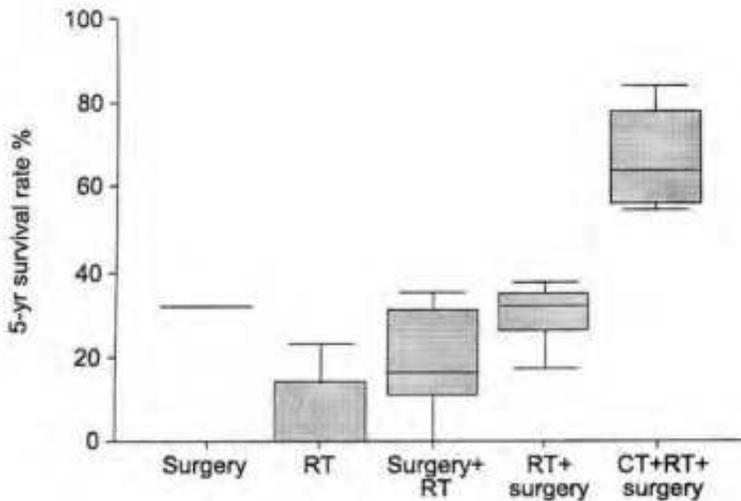
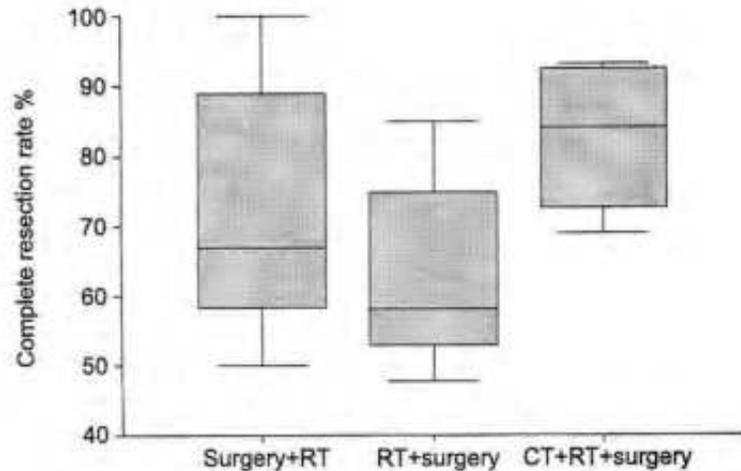
Robotic surgery



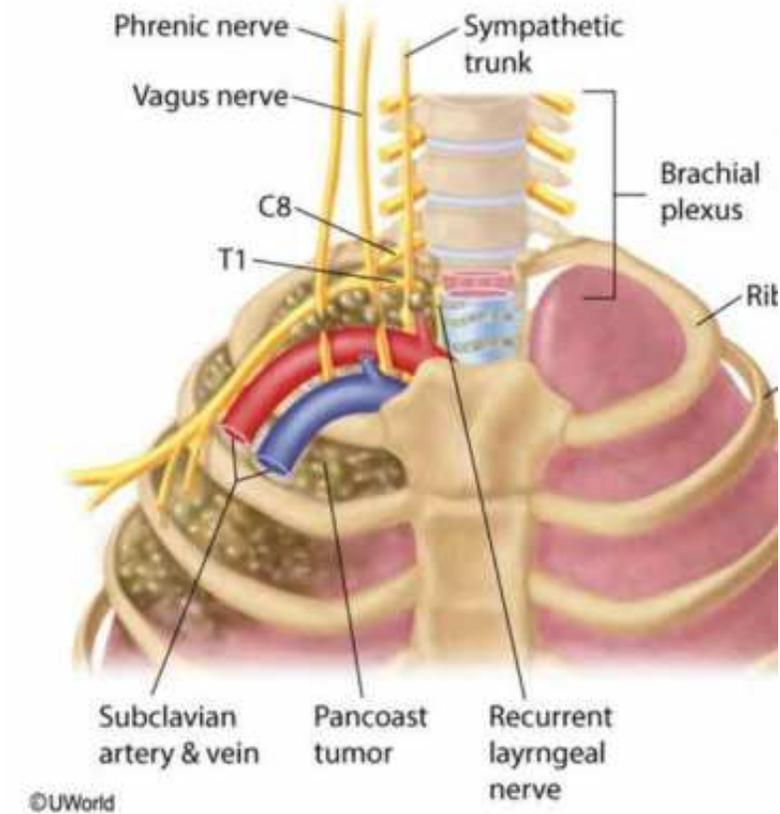
## **Radical Resection of Tumor + regional (mediastinal) Lymphadenectomy**

(regardless of surgical access)

# Advanced surgical techniques : Pancoast Tumors

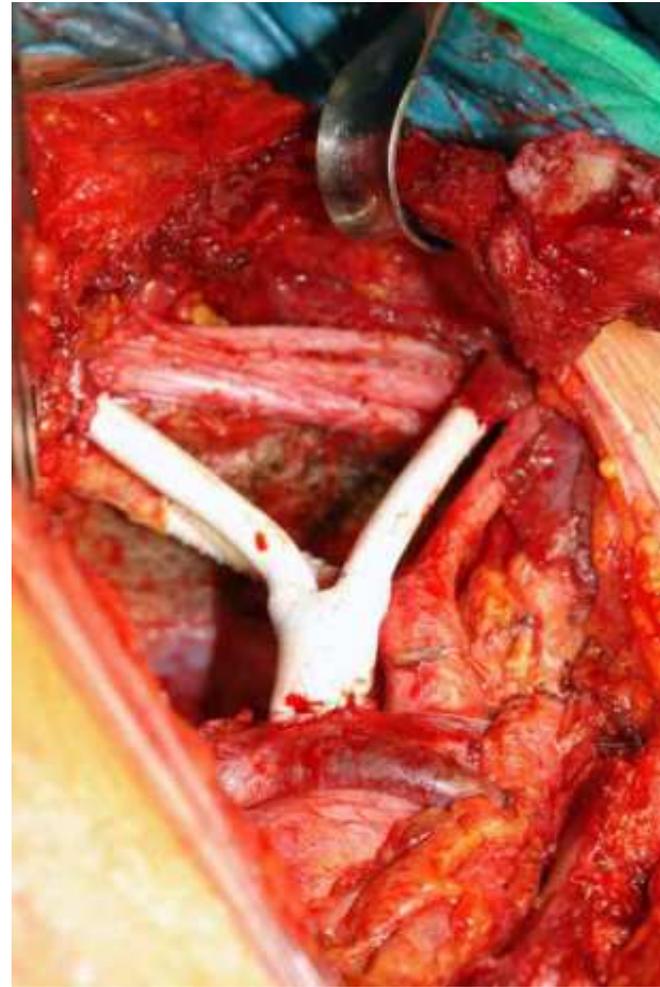
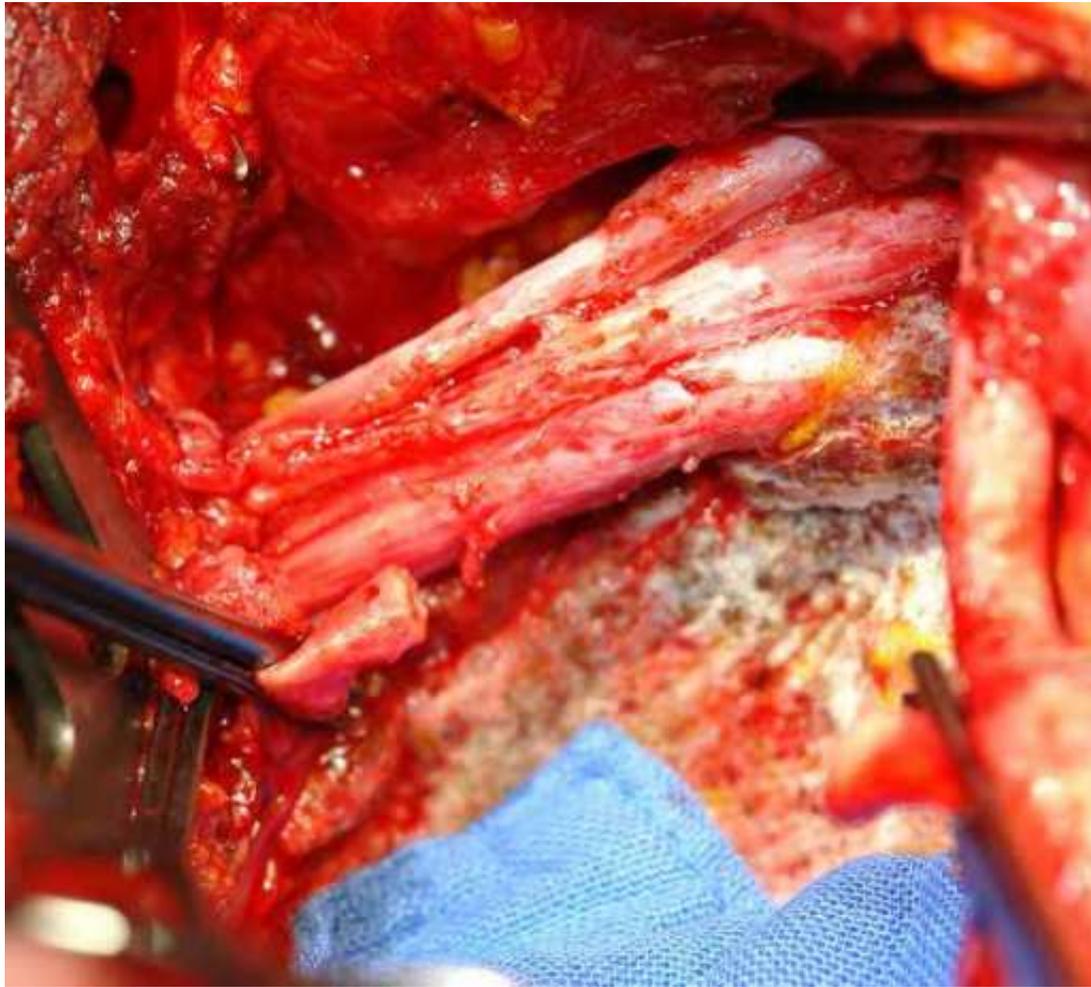


- **1930 – 1950**
  - Considered inoperable;
  - Radiotherapy only;
  - Disappointing results
- **1950 -1980**
  - Induction radiotherapy (30 Gy) +
  - “en bloc” resection;
  - R0 only in 60%
- **Late 1980 – 2000**
  - New surgical approaches
  - (*resection of vertebra, vessels, etc.*)
- **2000 -**
  - Chemo-radiotherapy + surgery;
  - R0 in > 90%

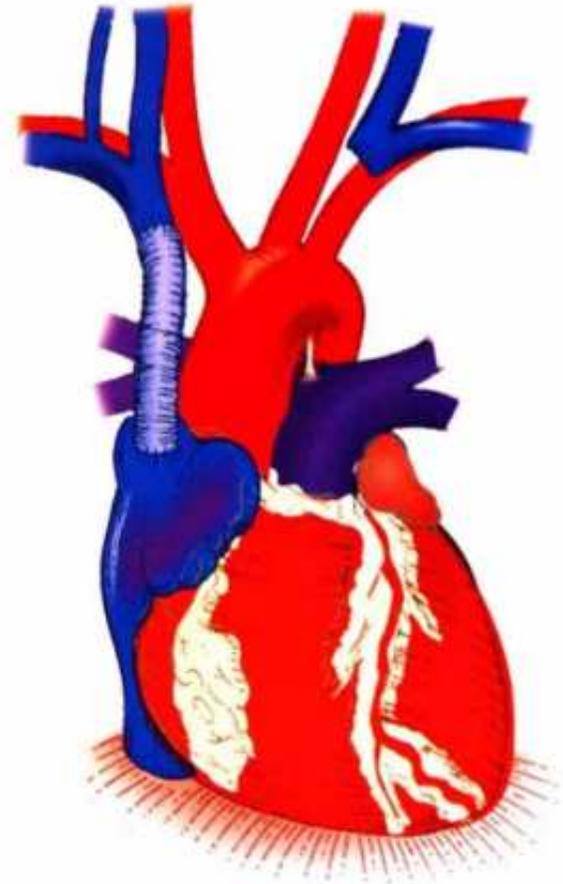
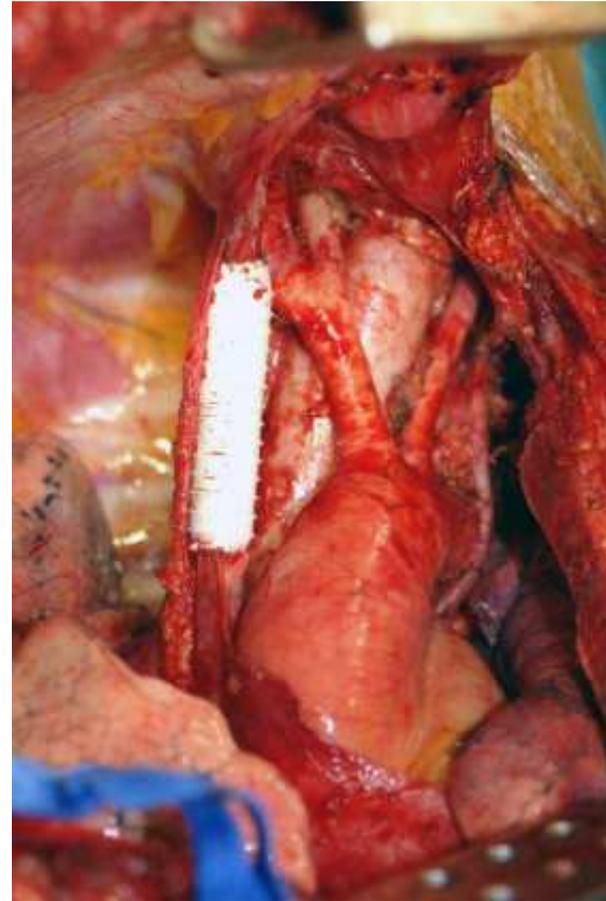
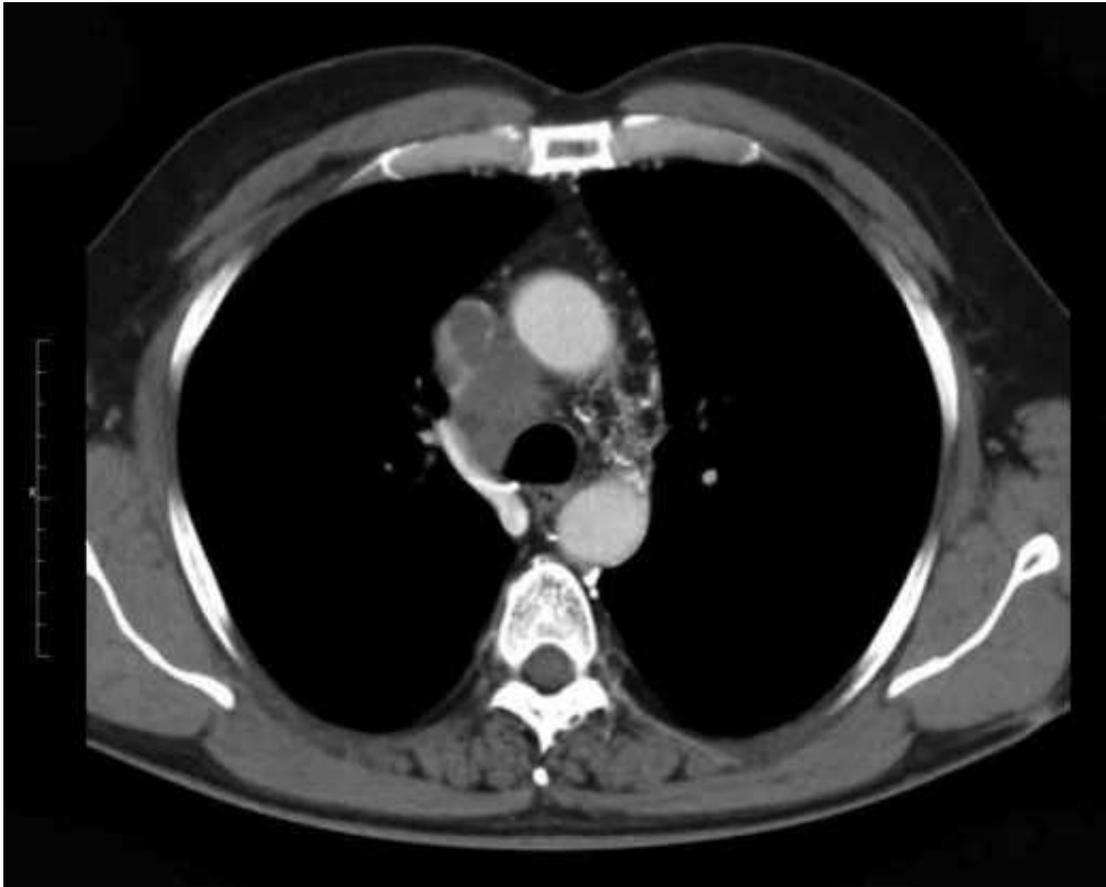


W.Eberhardt, G. Stamatidis et al. Induction chemotherapy, concurrent chemoradiation and surgery for Pancoast tumour. Eur Respir J 2007

# Combined veno/arterial reconstruction with PTFE prosthesis



# Central lung cancer with SVC infiltration



Open surgery for locally advanced NSCLC

Considerations

Functional

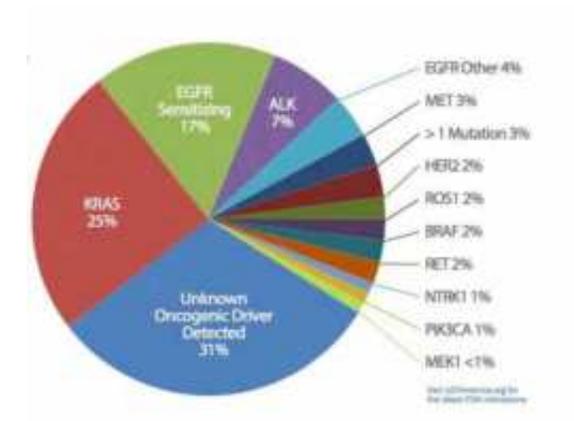
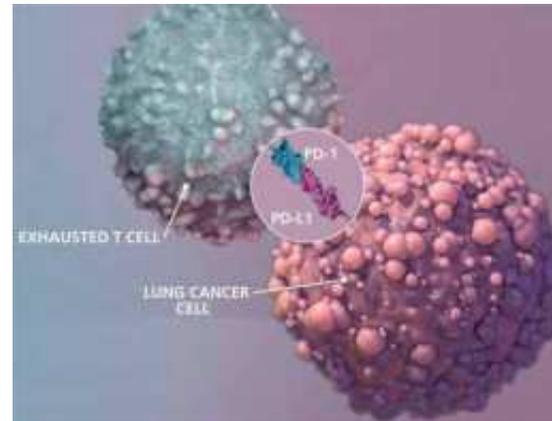
Technical

Oncological

# Oncological resectability

Only the combination of radical **local tumor control** with **effective systemic treatment** leads to success in advanced NSCLC

From the **morphological** towards the **biological** age



-> This leads to a new definition of resectability and oncological control

# Staging of NSCLC :

Based on **morphology** and not yet on **biology**

T/M	Subcategory	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
T4	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB

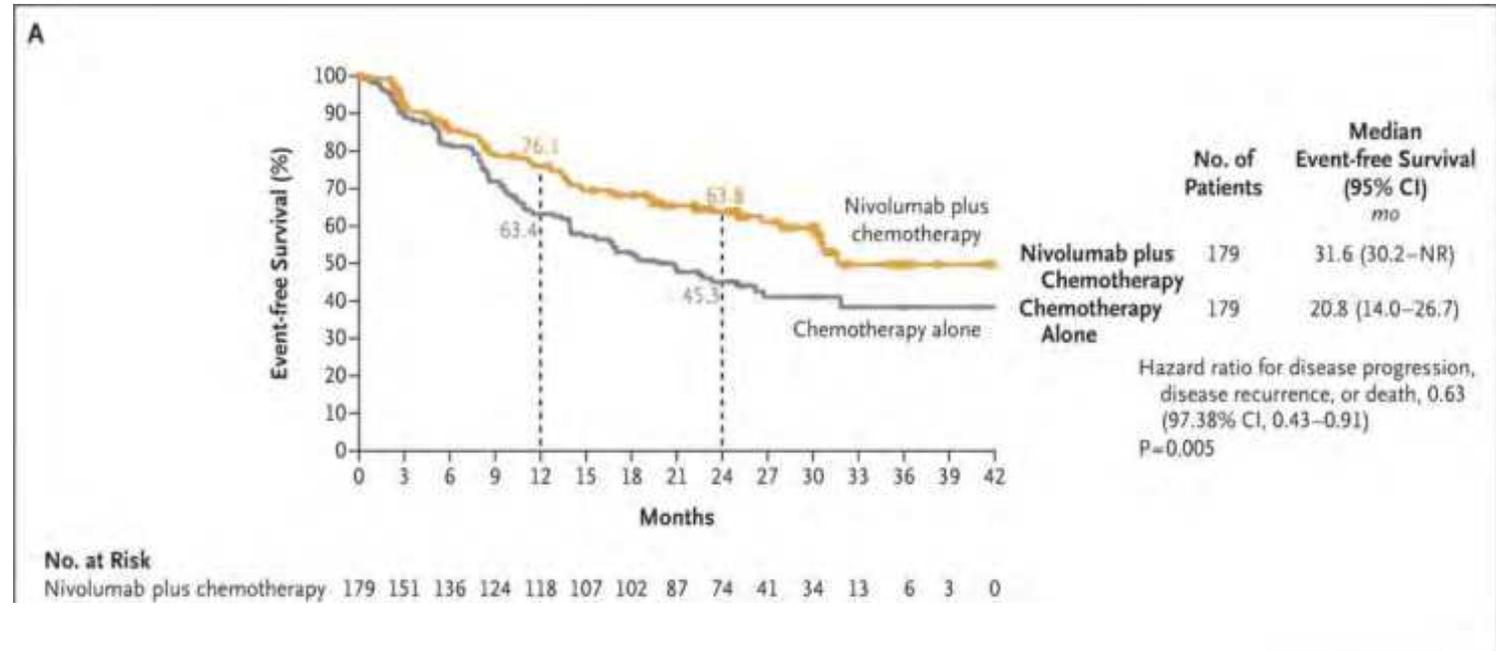
**FIGURE 1.** Lung cancer stage grouping (eighth edition).

# Questions arising from recent advances in ICPI and Targeted Therapy

- **Timing of surgical intervention:** neo? adj? Periop?

# Checkmate 816: Neoadjuvant ICI Therapy in NSCLC

NSCLC Stage IB - IIIA

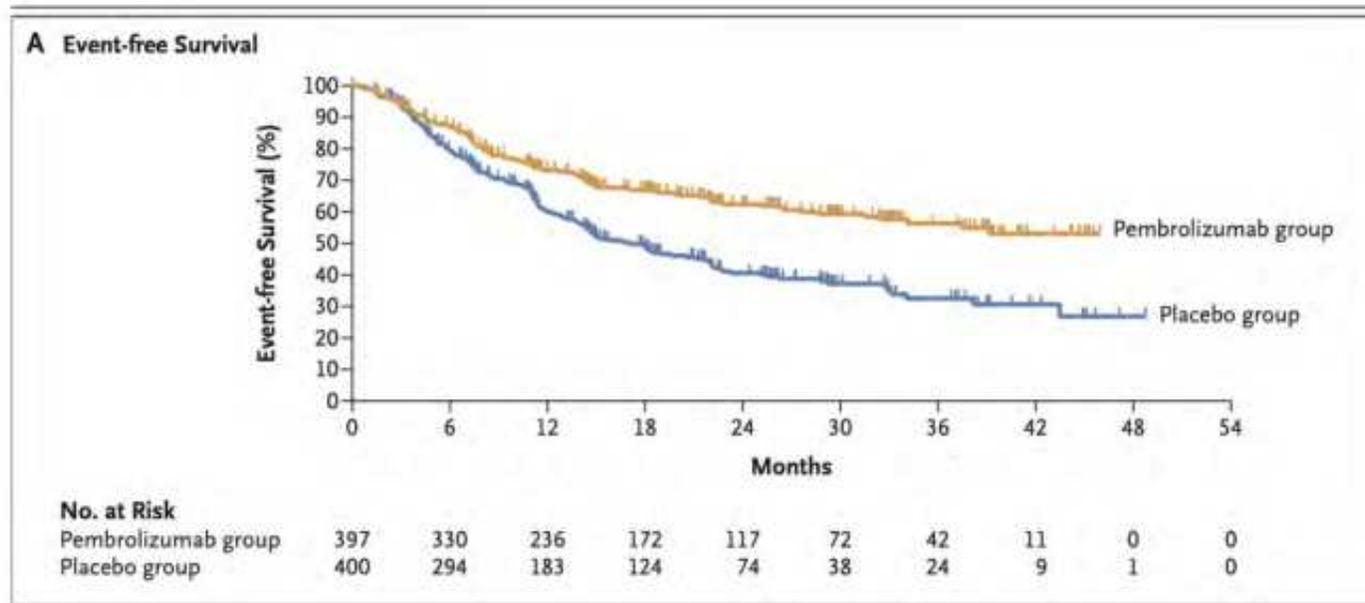


N. Girard et al., AACR Annual Meeting 2022, P. Forde et al.: N. Engl. J. Med. 386: 1973, 2022

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

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

NSCLC Stage II - IIIB



# Questions arising from recent advances in ICPI and Targeted Therapy

- Timing of surgical intervention stage II – IIIB: neo? adj? Periop

## FDA Approves Neoadjuvant/Adjuvant Pembrolizumab for Resectable NSCLC

By The ASCO Post Staff

Posted: 10/18/2023 9:26:00 AM

Last Updated: 10/18/2023 8:48:01 AM

[Get Permission](#)

On October 16, the U.S. Food and Drug Administration (FDA) approved pembrolizumab (Keytruda) with platinum-containing chemotherapy as neoadjuvant treatment, and with continuation of single-agent pembrolizumab as postsurgical adjuvant treatment, for resectable (tumors  $\geq 4$  cm or node-positive) non-small cell lung cancer (NSCLC).

KEYNOTE-671

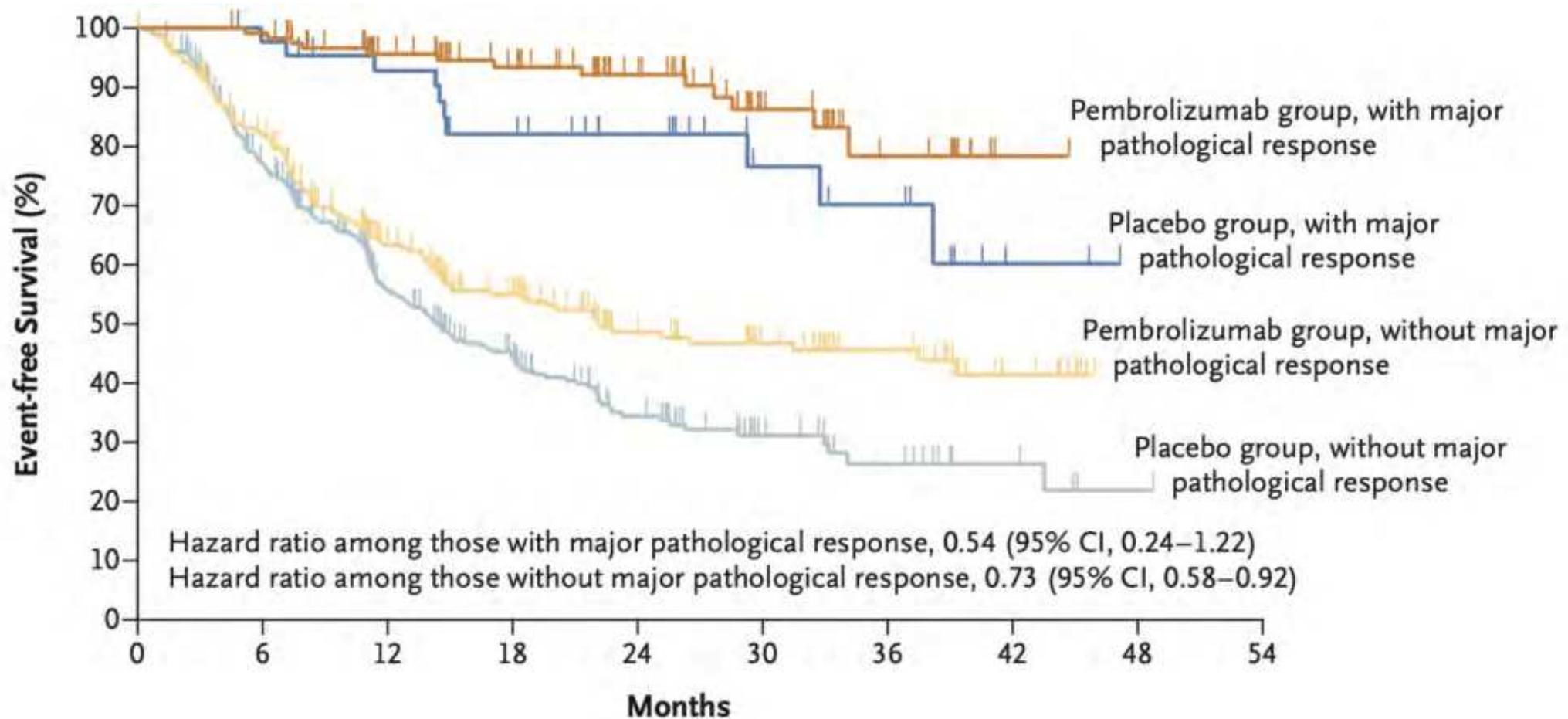
# Questions arising from recent advances in ICPI and Targeted Therapy

- **Surgery only for :**
- Major Response !!!
- Stable disease !!

Is there still a need for surgery after Radiological Complete Response

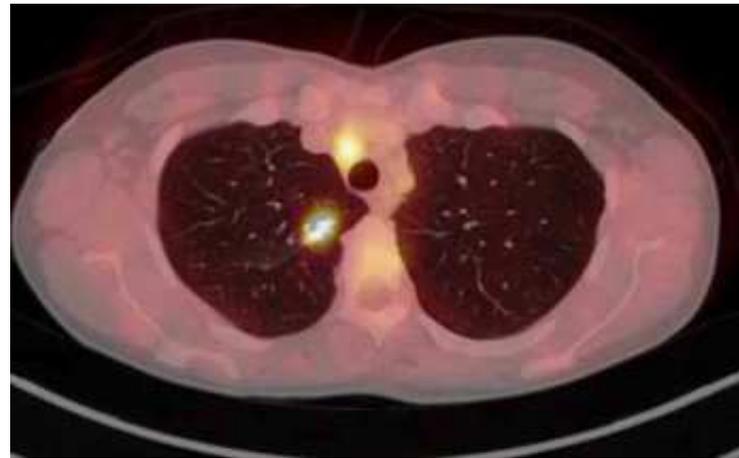
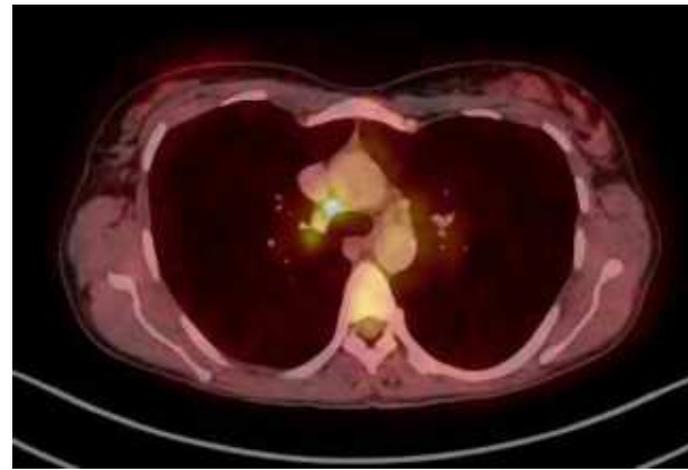
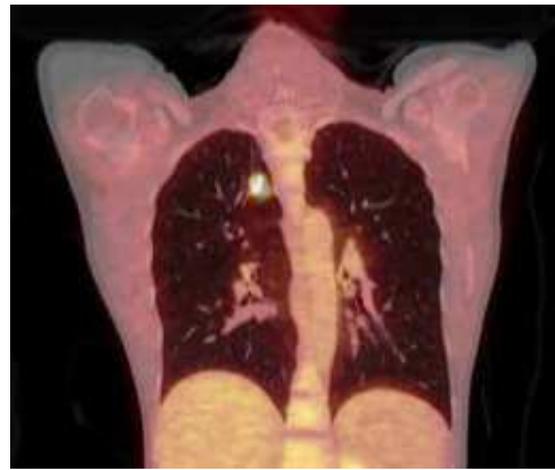
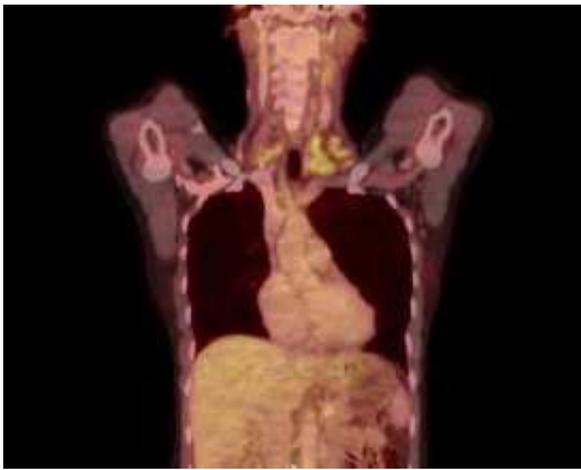
**What about disease progression ???**

# Event Free Survival with Perioperative Pembrolizumab plus 4 Neoadjuvant Courses of Chemotherapy According to Major Pathological Response



The higher the degree of response

The higher the stage for resectability



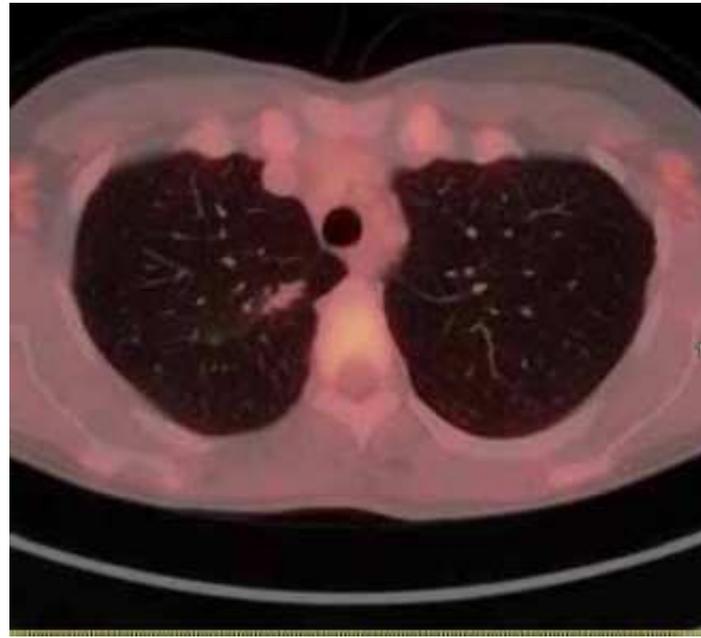
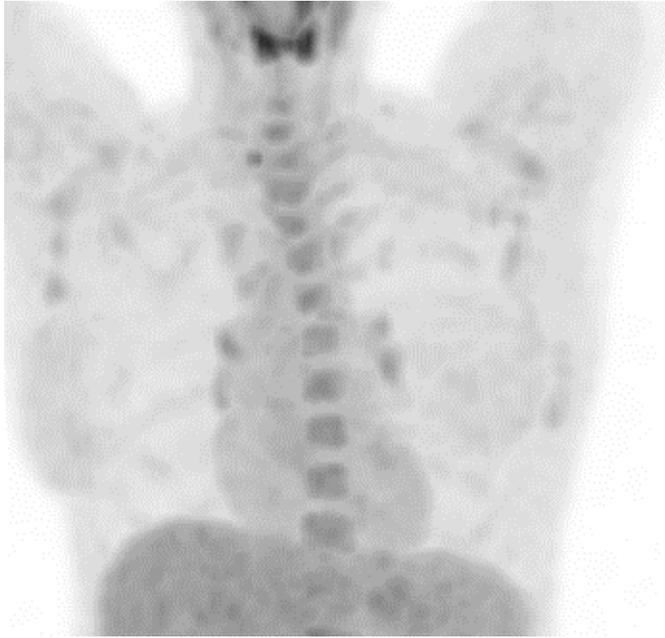
**P. C. 37y**

9/23  
Adenoca re Ol + med/cerv Lnn:

**cT2cN3 stage IIIB**

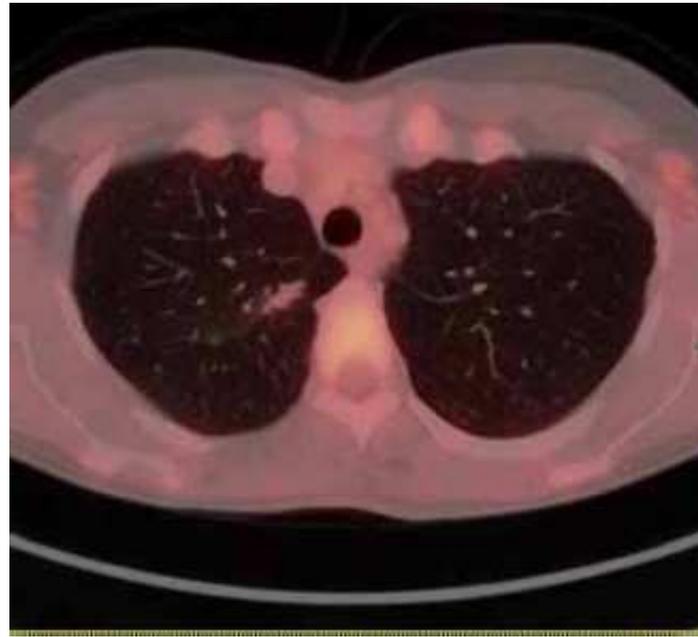
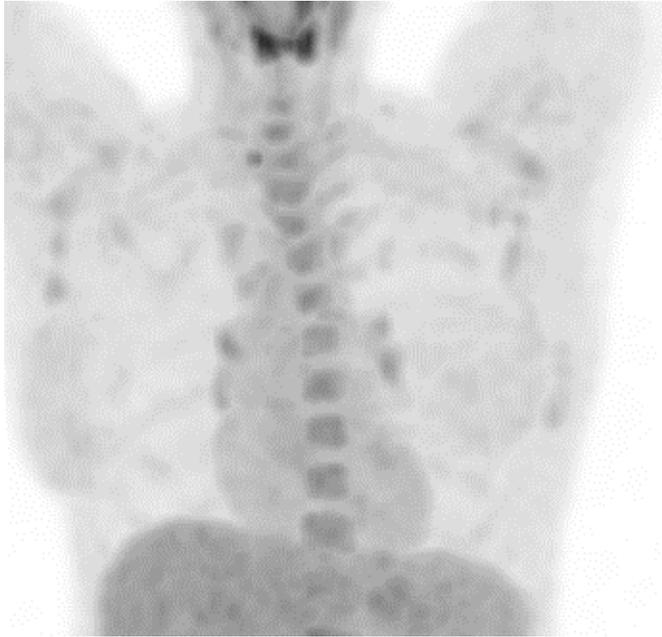
EGFR 19 mutated

Chemo/Tagrisso



**P. C. 37y**

**1/24 Complete Radiological Remission**

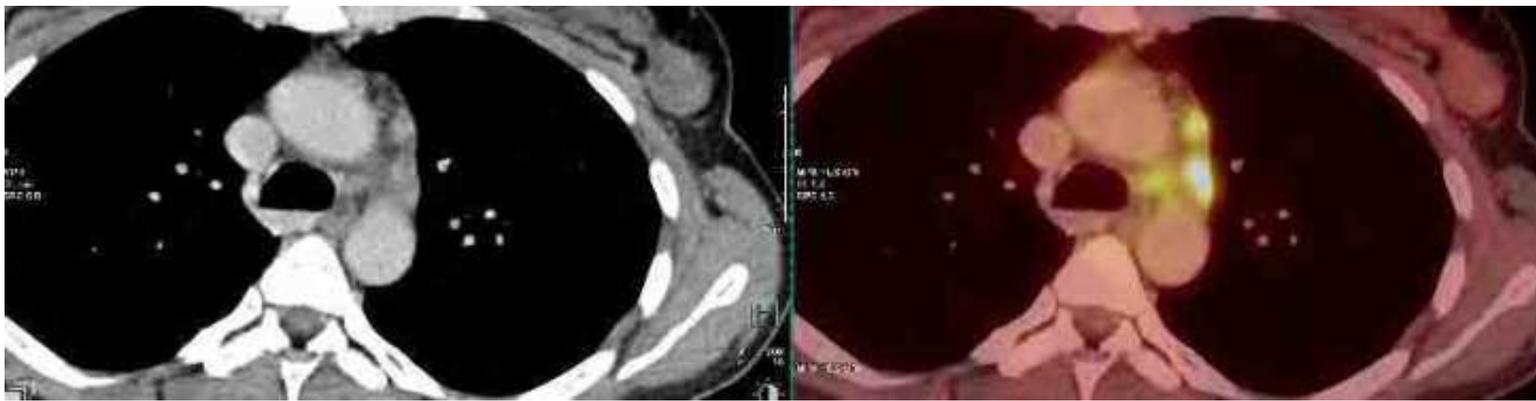


2/24  
UL Lob + med LNN

1/24 Complete Radiological Remission

P. C. 37y

Pathological Result :  
ypT1min, LOVOR0,NO



P. D. f 49 y

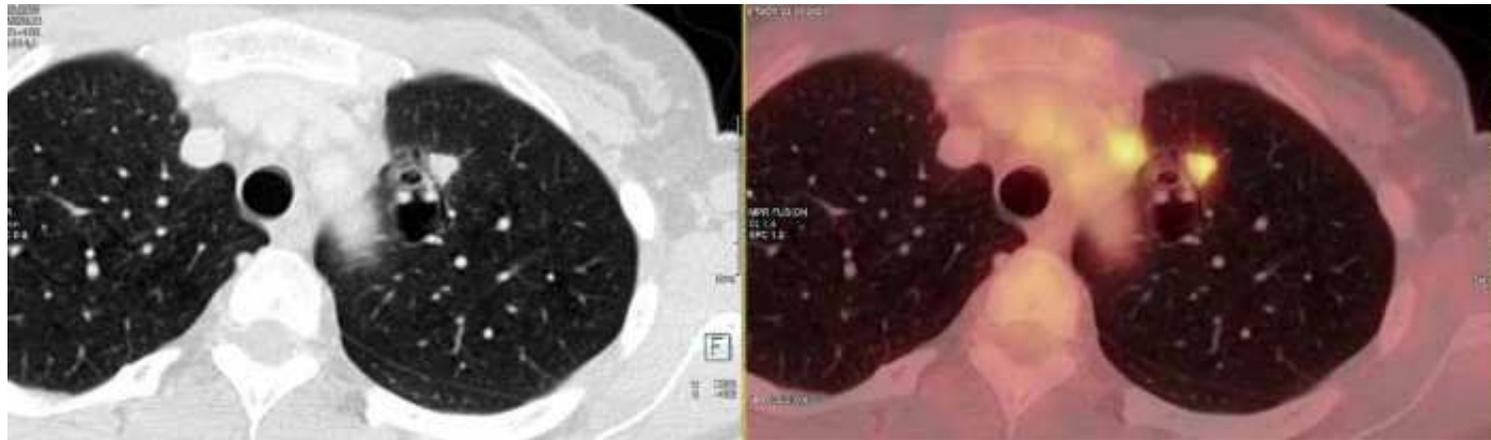
6/23

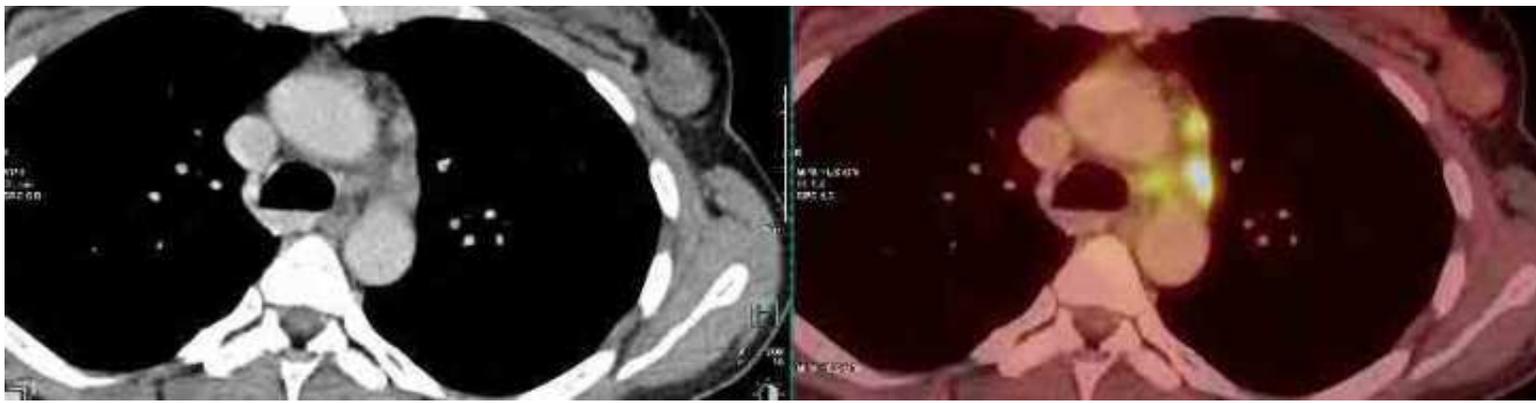
Adeno: cT1N3 (supraclav Lnn) M0

Stage IIIB

Alk pos,  
PD-L1 10%

Alectinib 600 mg/2xd





P. D. f 49 y cont.

6/23

Adeno: cT1N3M0

Stage IIIB

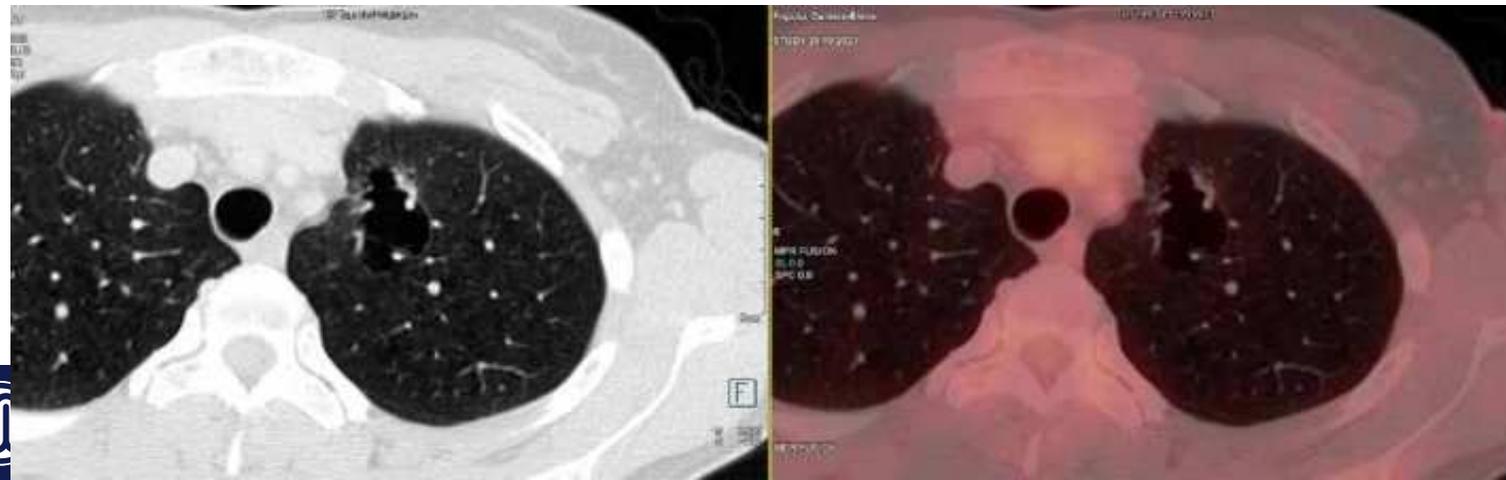
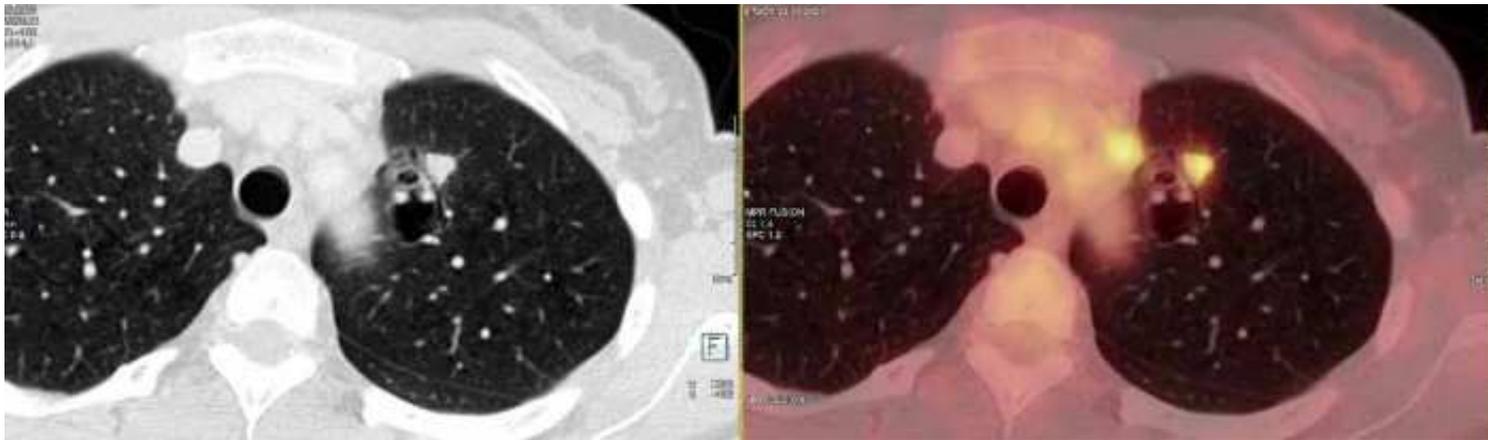
Alk pos,  
PD-L1 10%

Alectinib 600 mg/2xd

9/23 Restaging: CR

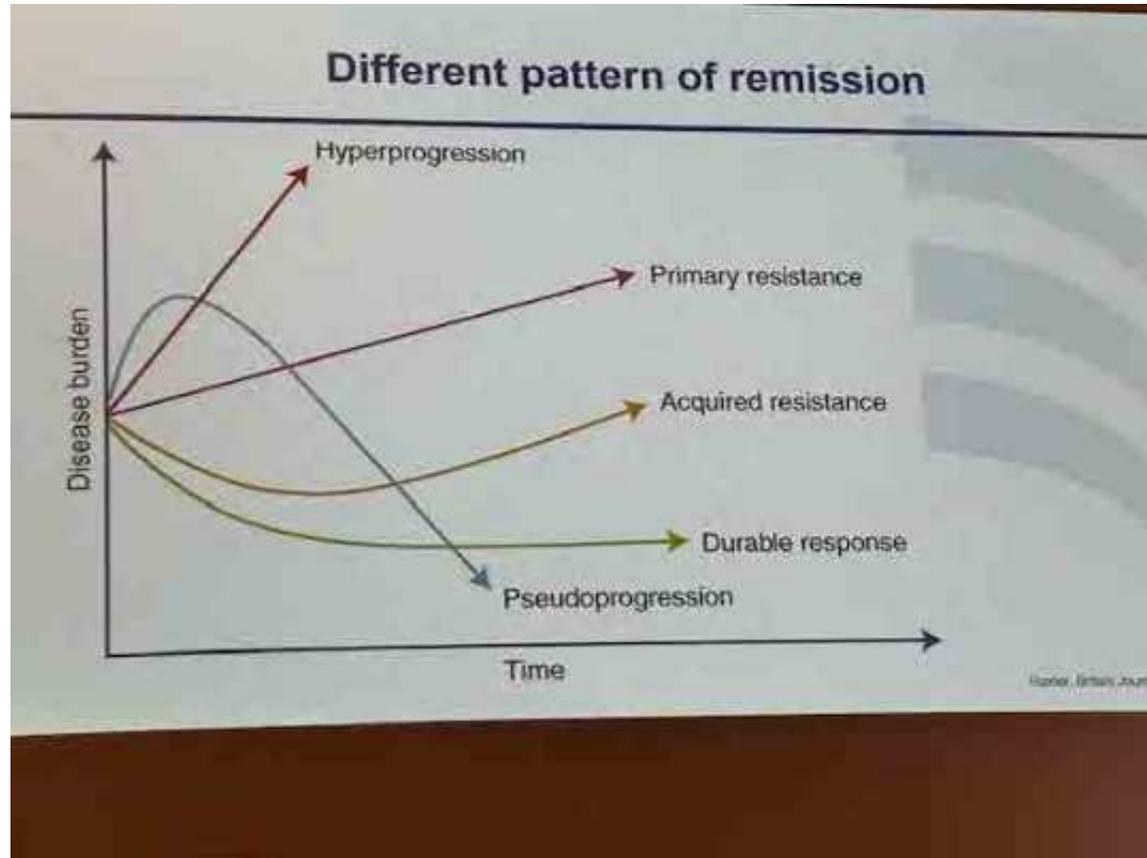
10/23 Segment res + med Lnn

Adeno ypT1mi, L0,V0,R0,N0



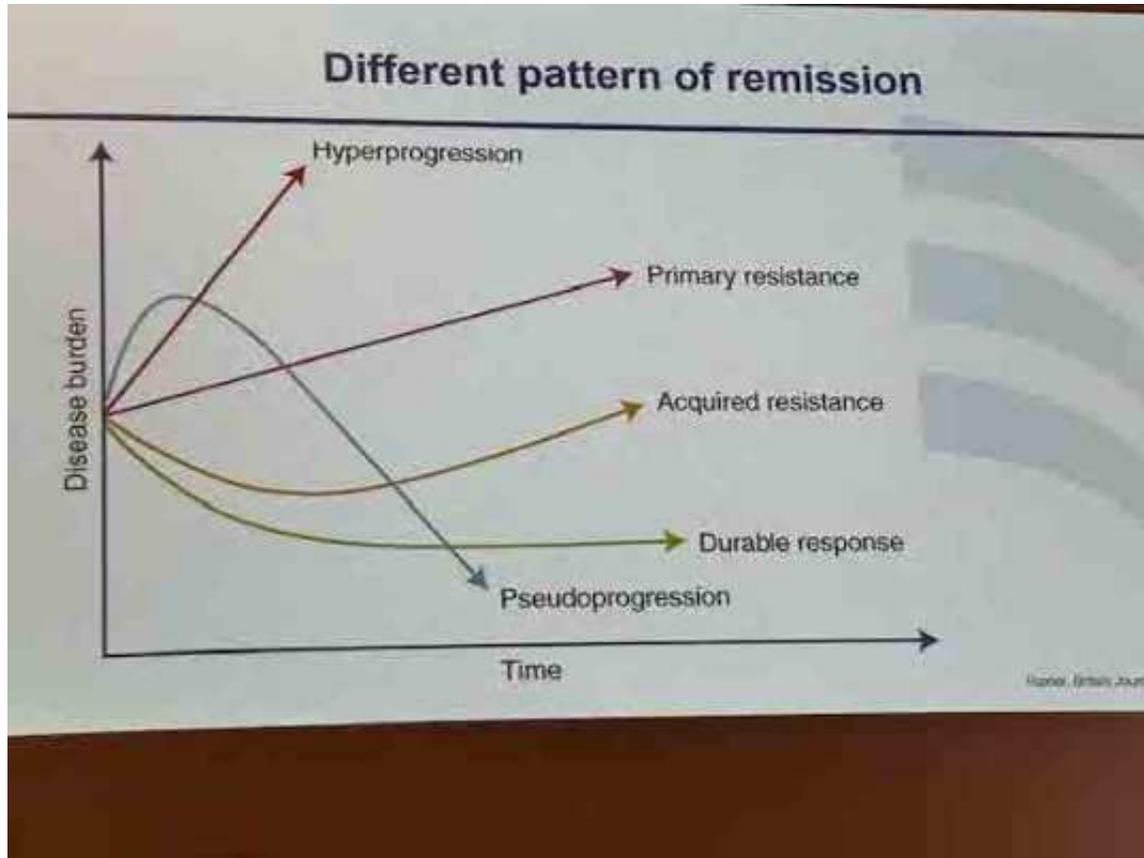
- \* Radiological complete response does not necessarily mean pathological complete response
  - \* Resection of initial tumor area remains an important part of the therapy\*
- \* Improvements in systemic control make local tumor control even more important

# Different patterns of Remission

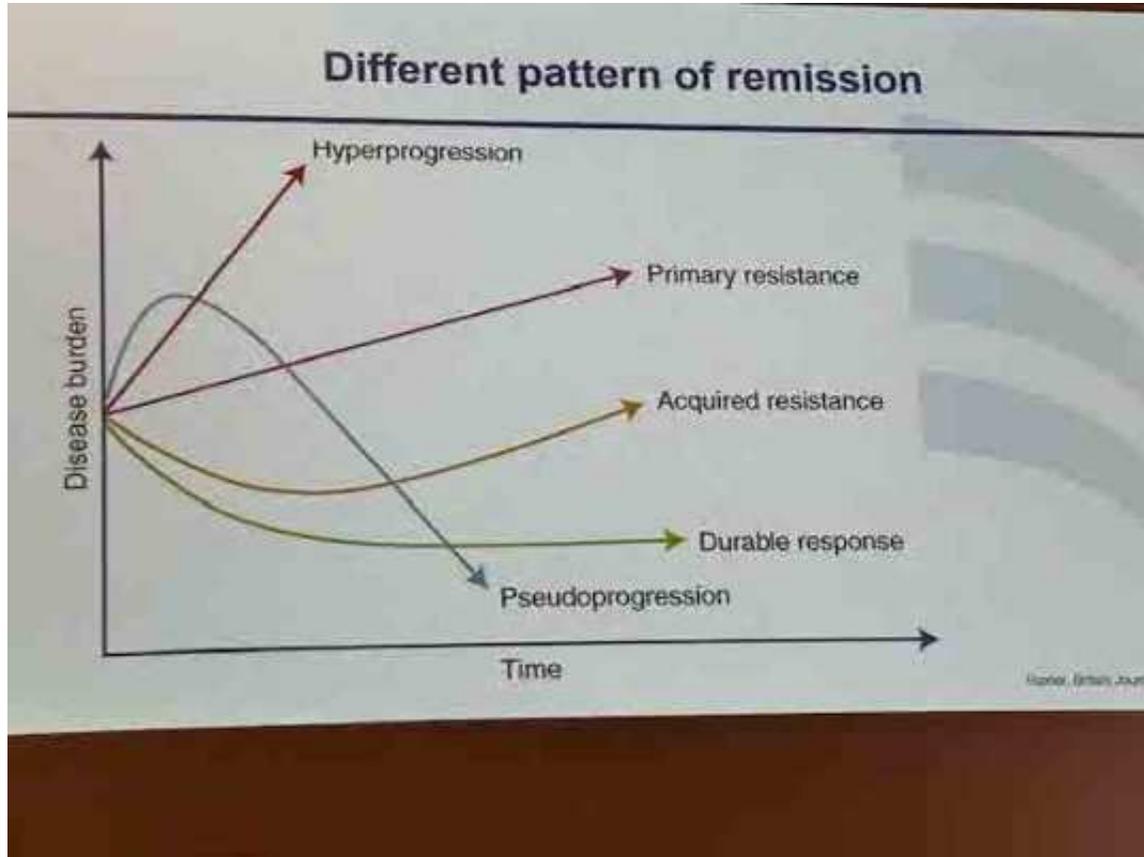


# Different patterns of Remission

- Hyperprogression

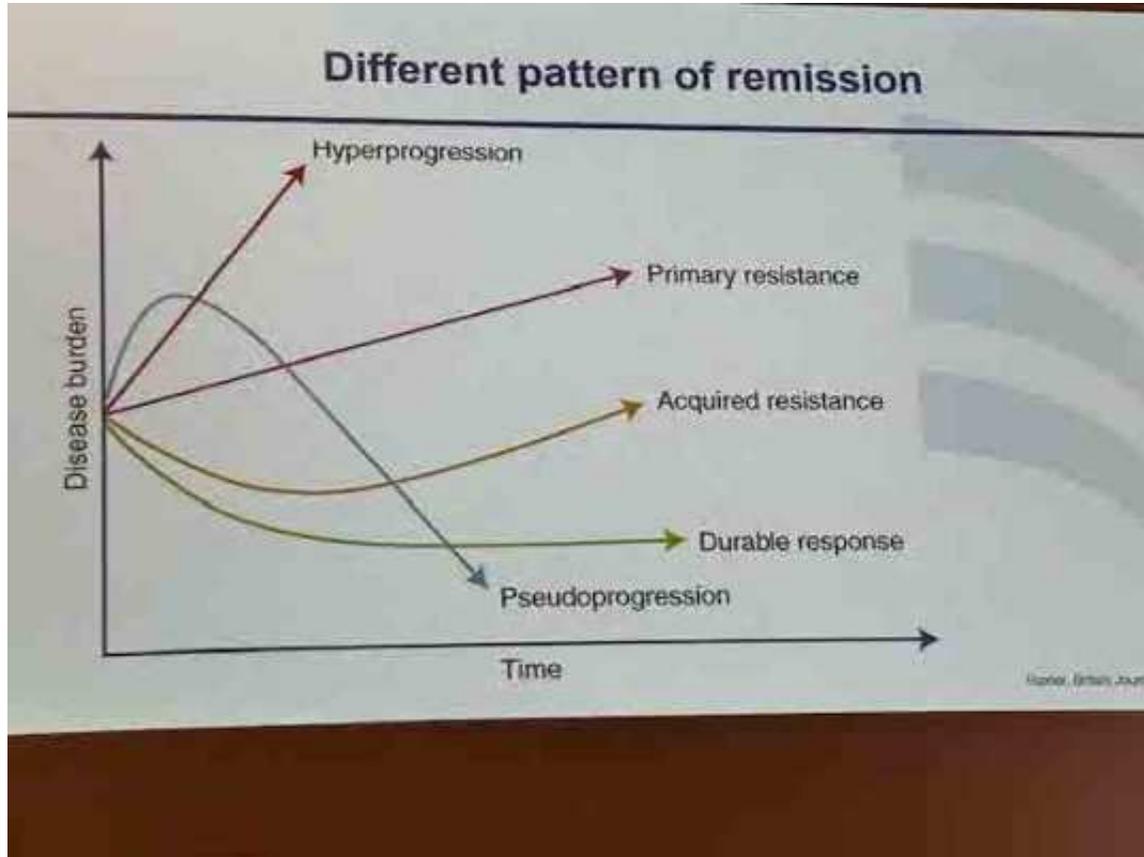


# Different patterns of Remission



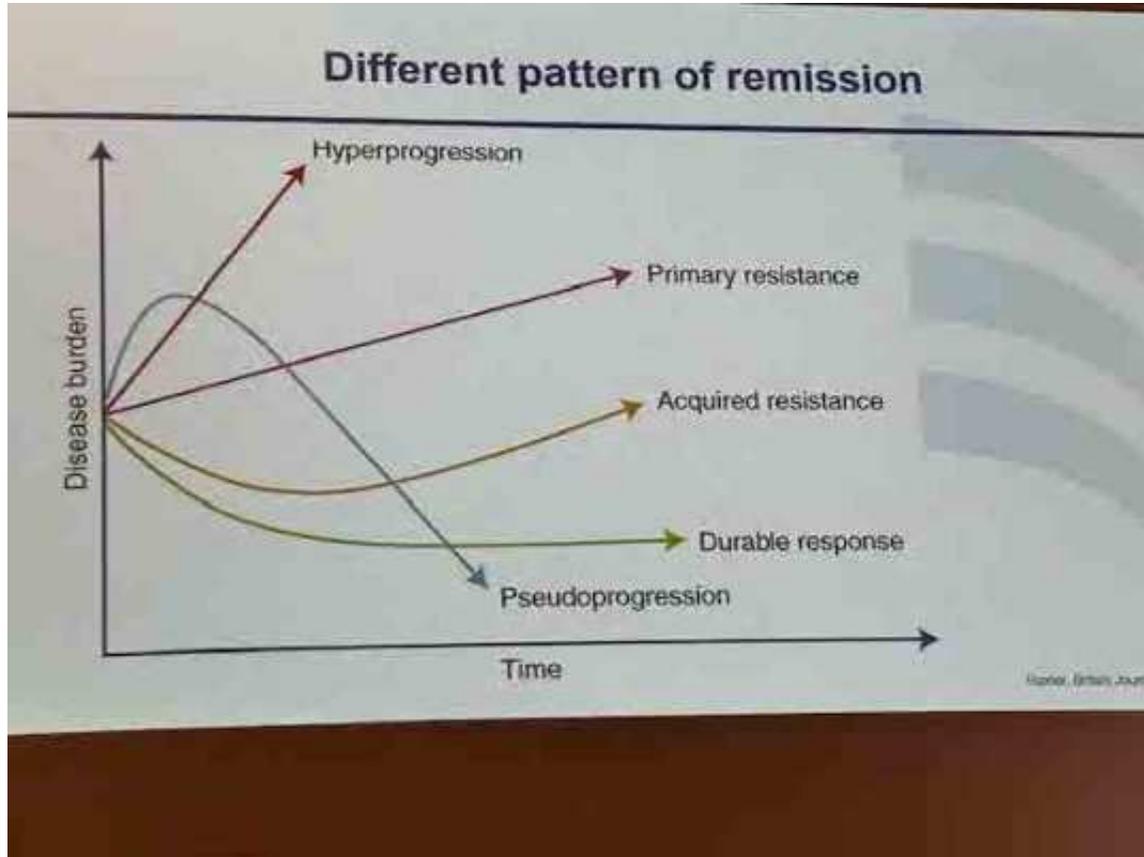
Primary Resistance

# Different patterns of Remission



Acquired resistance

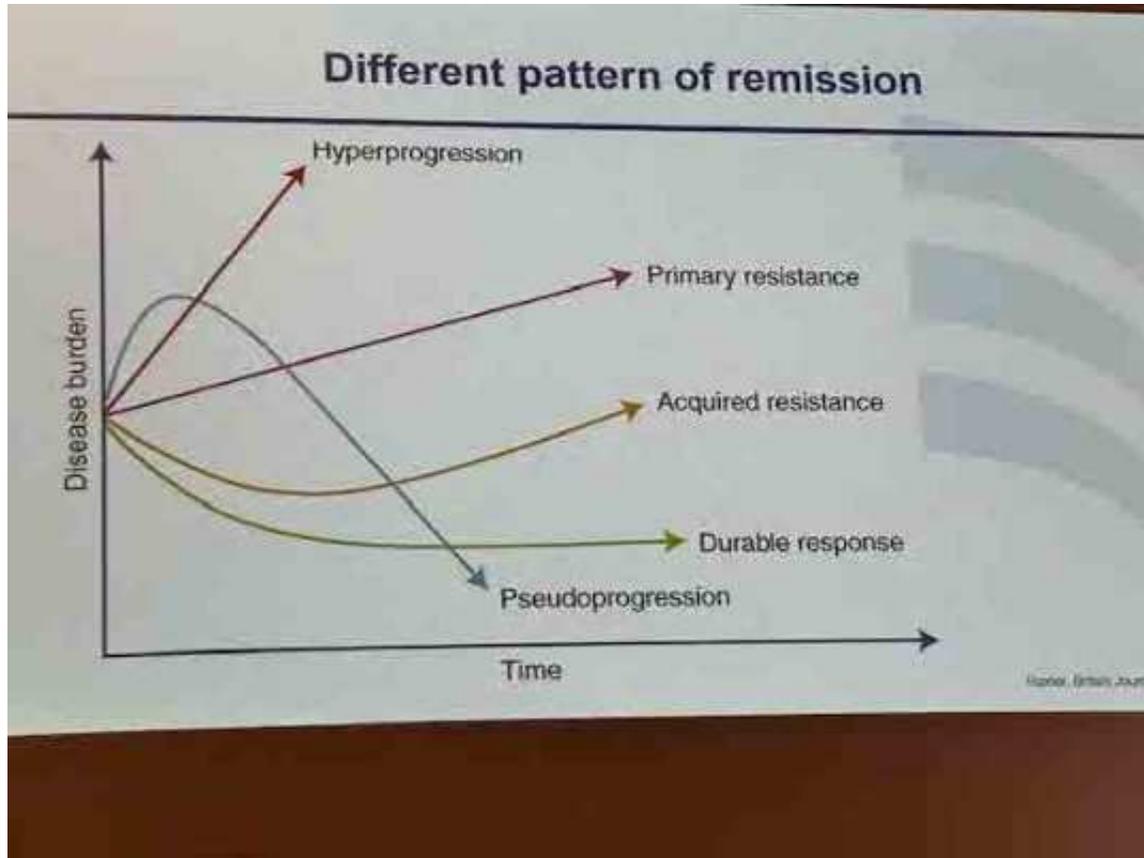
# Different patterns of Remission



Acquired resistance

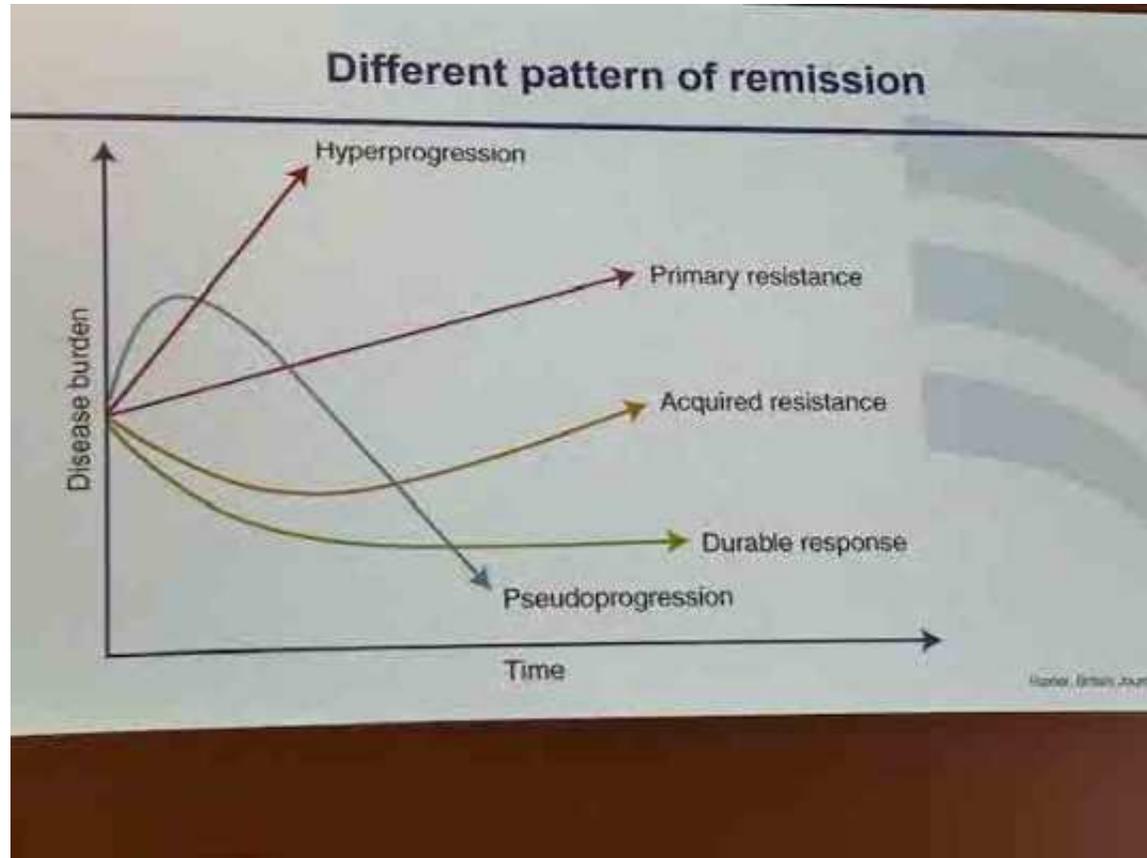
Response not necessarily lasts forever

# Different patterns of Remission



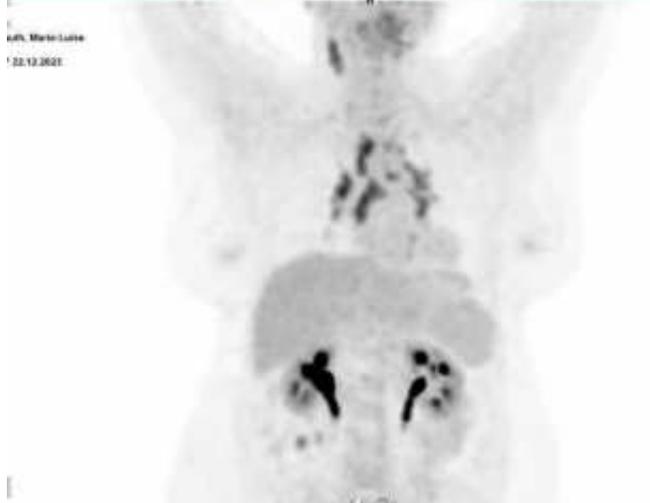
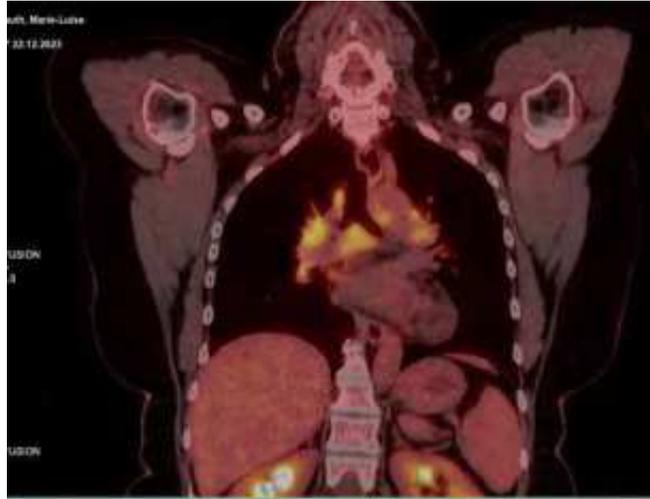
Durable response

# Different patterns of Remission



Pseudoprogession

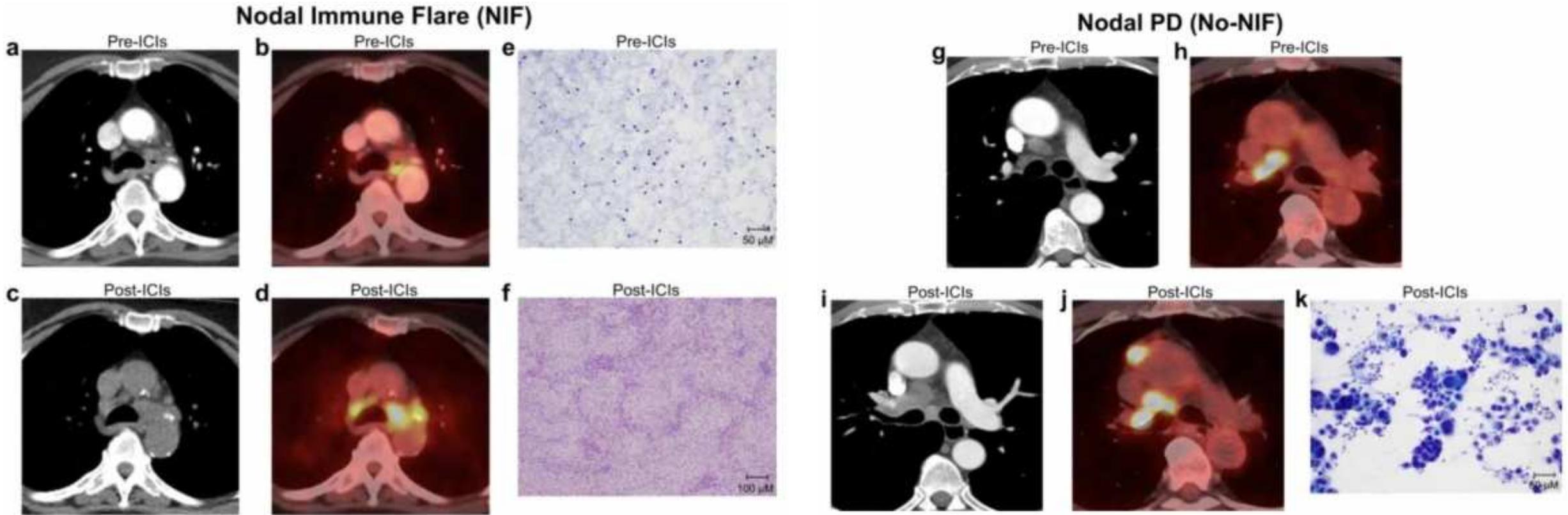
# Radiologically Progressive Disease or Pseudoprogression



## Sarcoid like reaction

- \* 63y female  
Inquinal squamous cell carcinoma
- \* multiple PET pos cervical and mediastinal lymphnodes
- \* Cervical biopsy: unspecific Lymphadenitis
- Mediastinoscopy: Sarcoidosis

# Nodal Immune Flare vs Progressive Disease

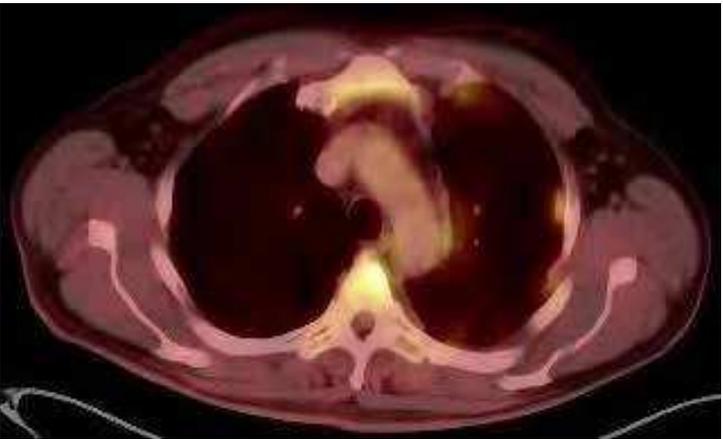


Cascone, T., Weissferdt, A., Godoy, M.C.B. *et al.* Nodal immune flare mimics nodal disease progression following neoadjuvant immune checkpoint inhibitors in non-small cell lung cancer. *Nat Commun* 12, 5045 (2021). <https://doi.org/10.1038/s41467-021-25188-0>

Clinical/morphological response # pathological response

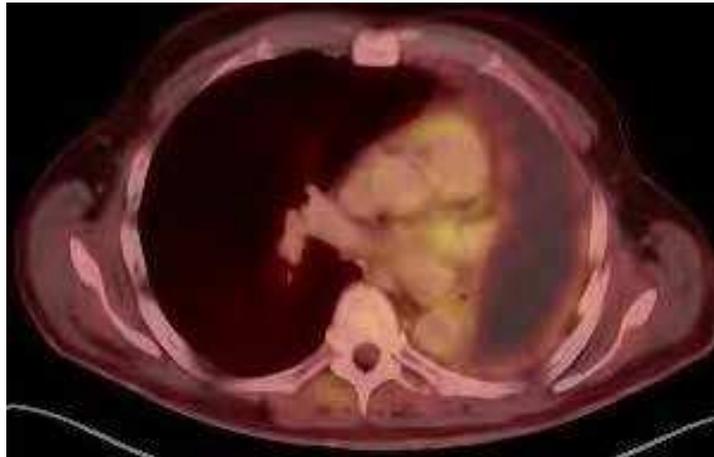
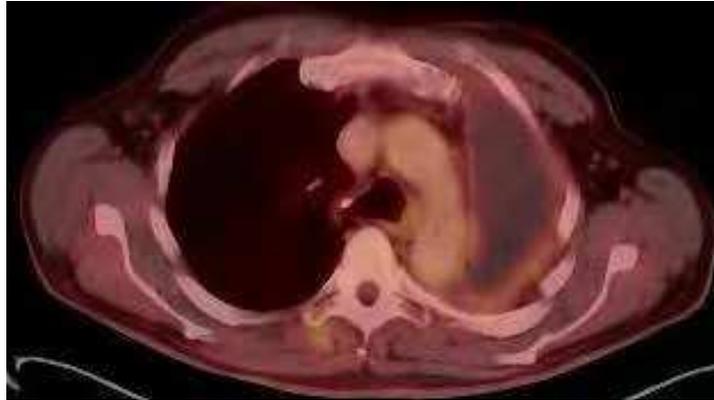
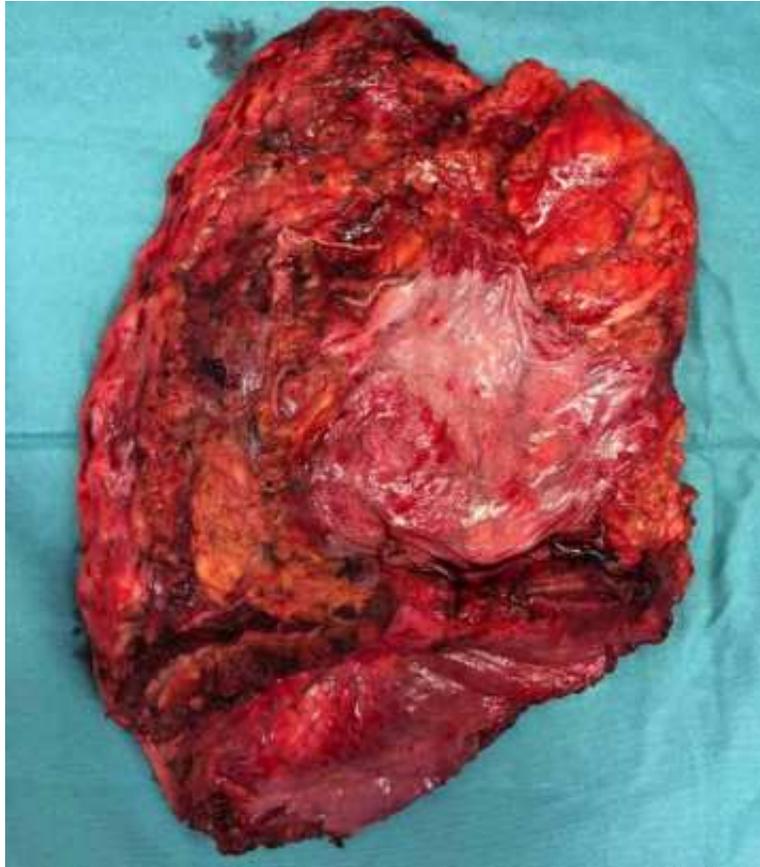
Histological confirmation mandatory

# NSCLC with pleural carcinosis : Stage IVA (M1A)



- Adenocarcinoma, T4 N0 M1a, **stage IV A(M1A)**
- EGFR, ALK, ROS1 negative
- PDL-1: 0%
- Multimodality treatment
  - 4 Cycles of chemotherapy (cisplatinum/pemetrexed)
- Stable disease after induction

# NSCLC with pleural carcinosis

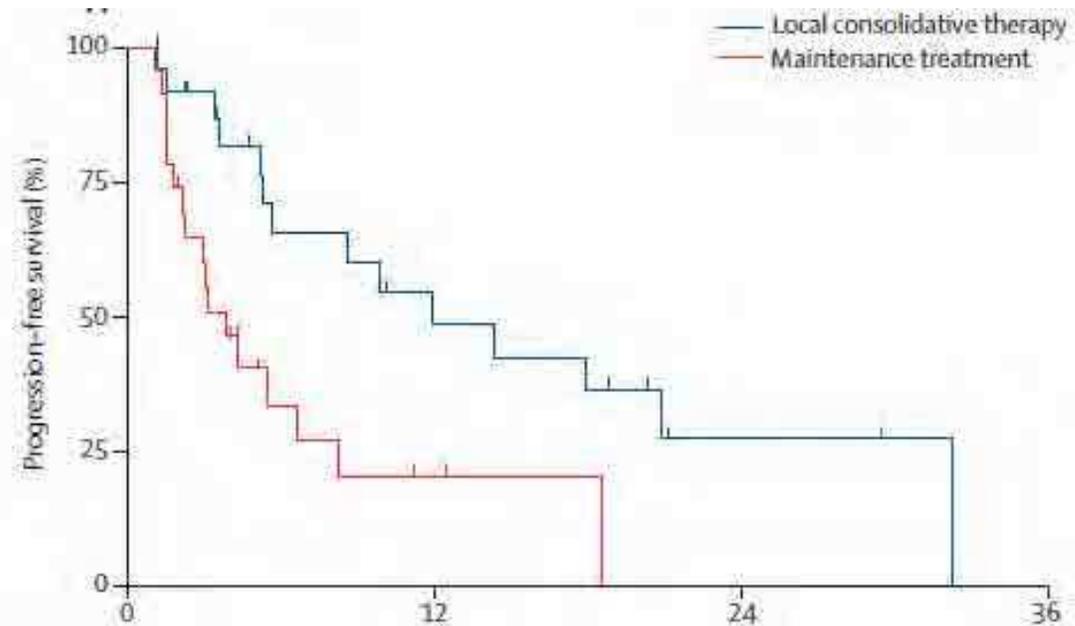


- Left sided extrapleural pneumonectomy
- Tumor-free 7 years after diagnosis

# Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study

Daniel R Gomez, George R Blumenschein Jr, J Jack Lee, Mike Hernandez, Rong Ye, D Ross Camidge, Robert C Doebele, Ferdinando Skoulidis, Laurie E Gaspar, Don L Gibbons, Jose A Karam, Brian D Kavanagh, Chad Tong, Ritsuko Komaki, Alexander V Louie, David A Palma, Anne S Tsai, Boris Sepesi, William N William, Jianjun Zhang, Qiuling Shi, Xin Shelley Wang, Stephen G Swisher\*, John V Heymach\*

- Phase II prospective randomized trial
- 49 pts w/  $\leq 3$  metastatic sites NSCLC and no progression after 1<sup>st</sup> line tx
- Local consolidative therapy vs. none
- LCT, surgery, XRT or SBRT to all sites
- Followed by maintenance tx



Number at risk (number censored)

	0	12	24	36
Local consolidative therapy	24 (0)	8 (6)	2 (3)	0 (1)
Maintenance treatment	24 (0)	2 (6)	0 (1)	0 (0)

LCT improved progression free survival (PFS) and time to development of new metastatic lesions

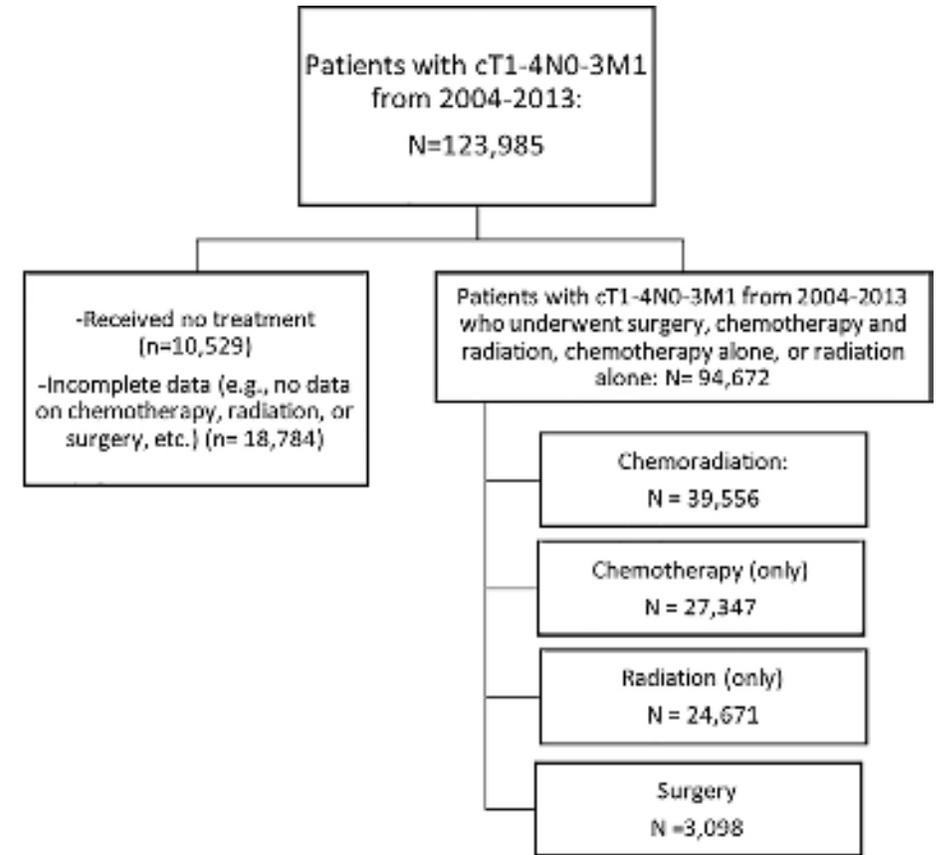
Lancet Oncol 2016; 17: 1672-82

# Long-term outcomes of surgical resection for stage IV non-small-cell lung cancer: A national analysis

Chi-Fu Jeffrey Yang<sup>a</sup>, Lin Gu<sup>b</sup>, Shivani A. Shah<sup>a</sup>, Babatunde A. Yerokun<sup>a</sup>, Thomas A. D'Amico<sup>a</sup>, Matthew G. Hartwig<sup>a</sup>, Mark F. Berry<sup>c,\*</sup>

- Outcomes and prognostic factors associated w/ resection of 1<sup>0</sup> tumor in stage IV NSCLC
- NCDB 2004–2013
- 3,098 resected M1 pts
- Subset analysis of pts w/ T1–2,N0–1,M1 and T3,N0,M1

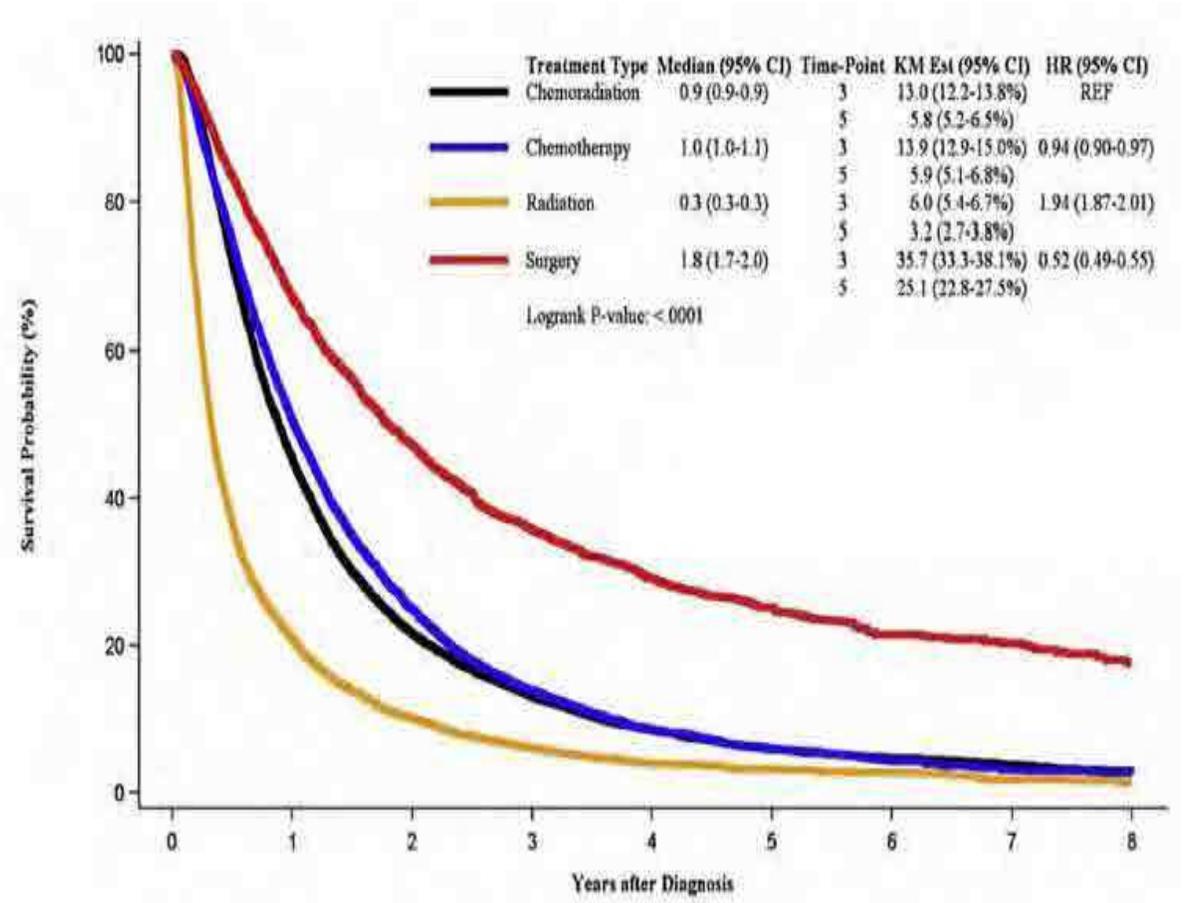
Yang C, Lung Cancer, 2018



- 5y OS in 3098 resected pts–21%
- Lower T stage, lower N–stage, lobectomy and use of chemotherapy all associated with increased survival

### Subset analysis

- 5y OS by treatment in T1–2N0–1M1 and T3N0M1 pts–25%
- significantly better than non-surgical treatments



*Yang C, Lung Cancer, 2018*

# Conclusion

**Limits for resectability of locally advanced NSCLC have been pushed further**

- Even sicker patients are undergoing more complex surgeries based on progress in perioperative management
- Complex situations can be approached surgically with advanced open surgical techniques

# Conclusion

- Clear evidence for importance of surgical resection after MR and CR
- Radiological progression of disease during immunotherapy requires histological confirmation
- Surgery for advanced NSCLC Stage IIIB and IV A (M1A/M1B) can be considered in selected patients

# Conclusion

- Recent progress in oncological therapy (ie.targeted/immunotherapy) might even widen the place for surgery in locally advanced NSCLC

Pushing to the limits .....



..but hopefully not beyond

