

Surgery Should be a Component of Multimodality Treatment for all Fit Stage IIIA NSCLC Patients: Pro

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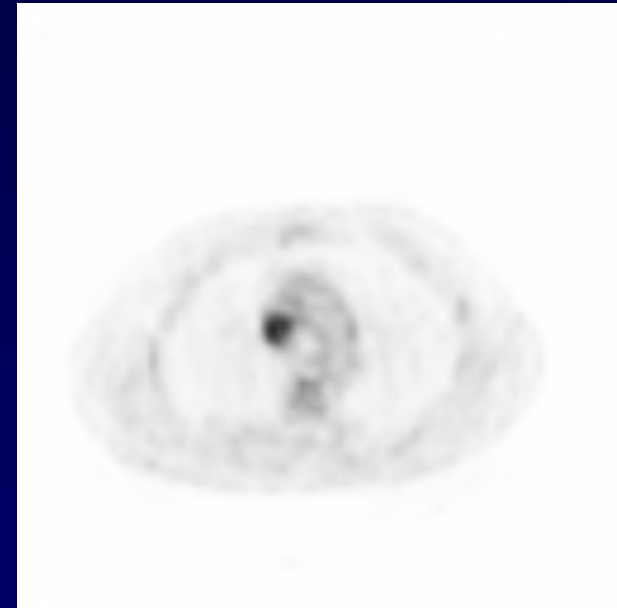
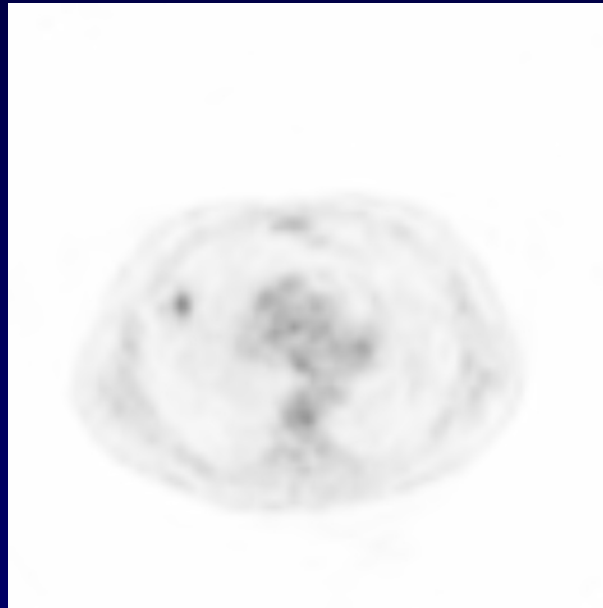
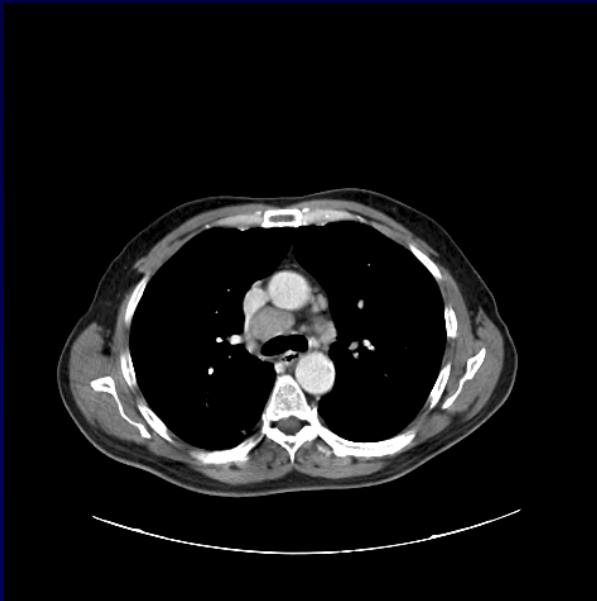
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N2 NSCLC

- Heterogenous group
 - Symptomatic Bulky N2 (unresectable)
 - Radiological enlarged LN (potentially resectable)
 - Radiological normal sized LN (potentially resectable)
 - Unforeseen N2 disease (resectable)
- No role for single modality treatment (Surgery or RT)

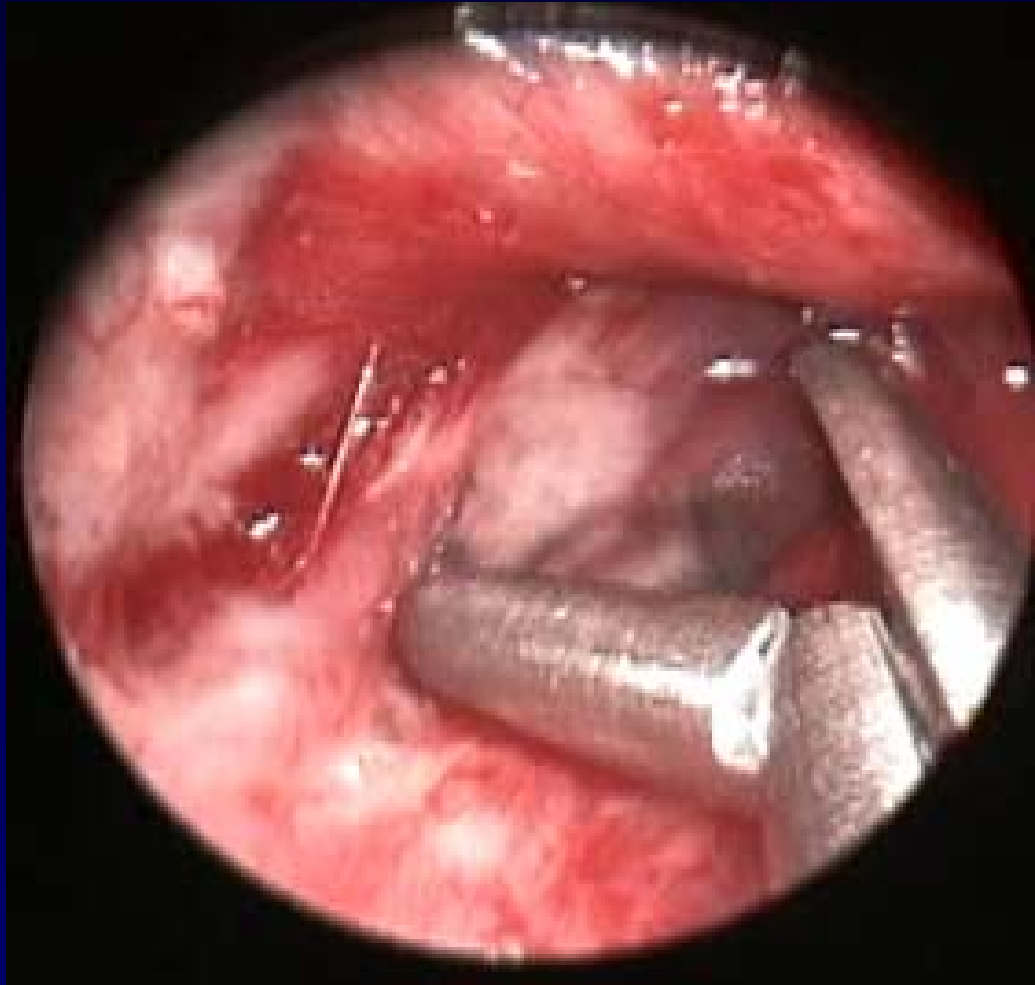
Potentially Resectable N2 Disease (after induction treatment)



**Multilevel bulky N2 disease
(Unresectable N2 disease)**



Extensive extracapsular spread (Unresectable N2 disease)



N2 NSCLC

Surgical Multimodality Treatment

- Evidence from (small) randomised studies
- Large evidence from single centre studies
- Response rate of 50%-70%
- Complete resectability : 50%-90%
- Surgery after induction chemotherapy is feasible with acceptable mortality and morbidity
- Median 5-yr survival : 20%-30%

N2 NSCLC

Surgical Multimodality Treatment

Prognostic factors

- Completeness of surgical resection
- Extent of resection (pneumonectomy < lobectomy)
- Downstaging of mediastinal LN's
- Lower T stage
- Single LN station involvement
- Degree of pathologic response in the primary tumour

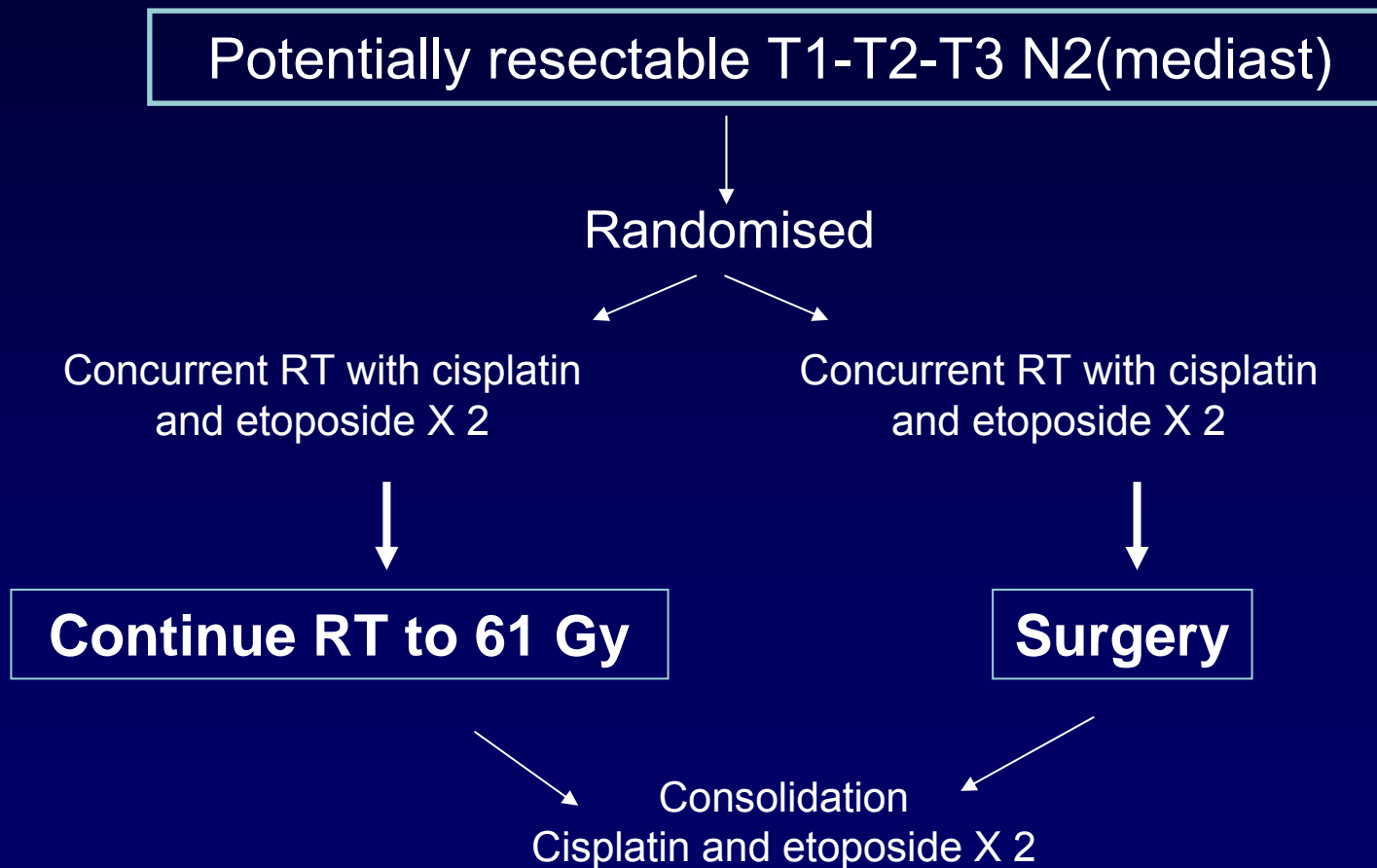
N2 NSCLC

Surgical Multimodality vs CT+RT?

- Lung Intergroup Trial R0139
- EORTC Trial 08941

IIIA-N2: T1-3 N2

Lung Intergroup Trial R0139

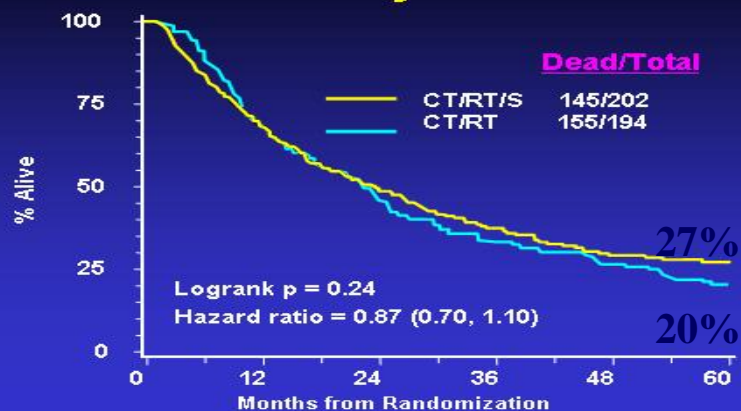


Intergroup trial

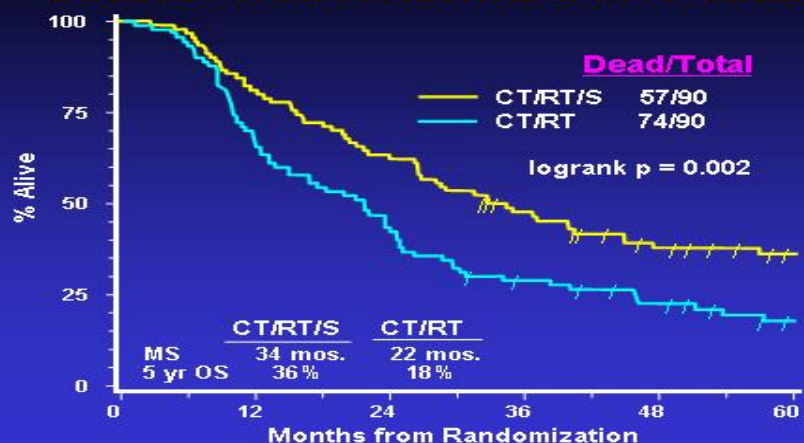
Albain et al., ASCO 2005

	CT+S	CT+ RT	
pNO	46%		
R0	88%		
Overall survival (5 year)	27%	20%	p=NS
Progression-free survival (2 year)	22%	11%	P=0.017
Lobectomy subset versus matched CT/RT subset (5 year survival)	36%	18%	P=0.002

Intergroup 0139/RTOG 9309 Overall Survival by Treatment Arms



INT0139 Overall Survival of the Lobectomy Subset versus Matched CT/RT Subset

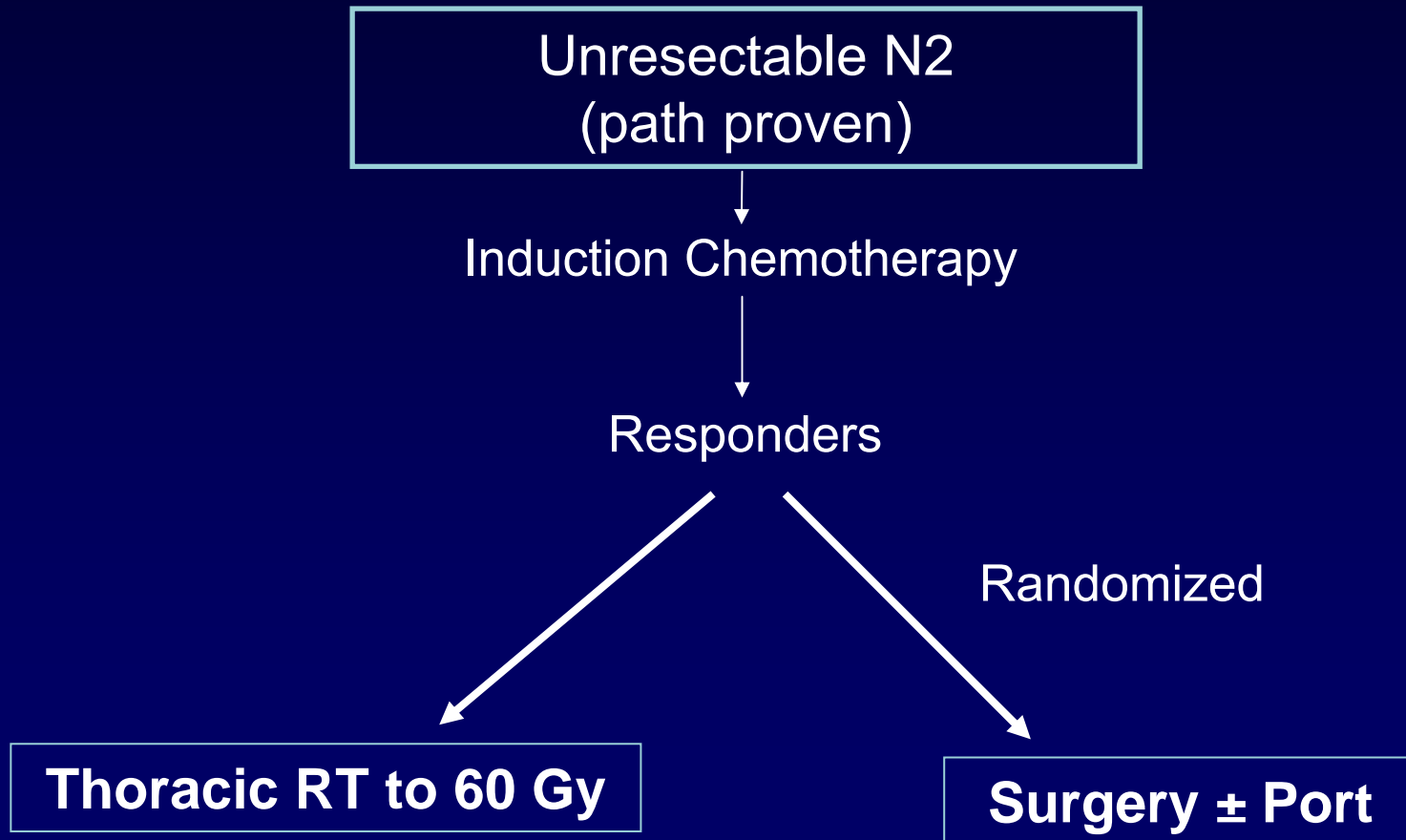


Intergroup Trial

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pNO	46%		
R0	88%		
Overall survival (5 year)	27%	20%	p=NS
Progression-free survival (2 year)	22%	11%	P=0.017
Treatment related mortality	7% Lobect : 1% Pneum : 26% R Pneum : 38%	1.6%	

IIIA-N2: T1-3 N2

EORTC 8947



EORTC 08941

	CT+S (± Port)	CT+ RT	
pNO	42%		
R0	50%		
Overall survival (5 year)	16%	14%	p=NS
Progression-free survival (2 year)	26.5%	24.2%	P=NS
Treatment related mortality	6%	NA	

EORTC Trial 1994 – 2002

Unresectable N2 disease was initially poorly defined (1994-2000)

Definition of unresectable tumor was left to the judgment of local surgeon
Amended in September 2000

Experience of center and thoracic surgeon?

41 centres randomised 331 patients in 8 years

13 centres randomised ≥ 10 patients

5 centres randomised 4 – 9 patients

23 centres randomised ≤ 3 patients

Surgery Following Induction Therapy in Stage IIIA-N2

EORTC trial : Unresectable disease. No conclusion can be made for resectable N2 disease

Uncommon. Complex and difficult. (Staging, restaging, treatment)

Experience of multidisciplinary team is very important

Effect of Preoperative Chemoradiation in Addition to Preoperative Chemotherapy in Stage III NSCLC

Prospective randomised trial

German Lung Cancer Cooperative Group (26 institutions)

October 1995 – July 2003

Effect of induction chemoradiotherapy compared with induction chemotherapy

Inclusion : Stage III NSCLC (marginally resectable and unresectable)
67% had IIIB
22% had pathological confirmed N3 nodes

Effect of Preoperative Chemoradiation in Addition to Preoperative Chemotherapy in Stage III NSCLC

	Interventional group (264)	Control group (260)	
Surgery (%)	54%	59%	
Complete resection	37%	32%	
Histopathological response (>90%)	60%	20%*	
% nodal downstaging (pN0-1) after complete resection	46%	29%*	
5-yr overall survival	21%	18%	
5-year PFS	16%	14%	* : < 0;05

Effect of Preoperative Chemoradiation in Addition to Preoperative Chemotherapy in Stage III NSCLC

Mortality After Surgery

	Interventional group (142)	Control group (154)
Overall	9%*	5%
Lobectomy or bilobectomy	7.5%	2.3%
Pneumonectomy	14%	6%

* 40% : BP fistulae

UZ Leuven Data 2000-2006

Surgical Multimodality Treatment for IIIA N2 NSCLC

- N=92
- Retrospective consecutive study 2000-2006
- Prospective surgical database
- NSCLC
- Histologically proven N2 disease
- Responder or stable disease after induction chemotherapy
- Surgical exploration
- If pN2 adjuvant radiotherapy

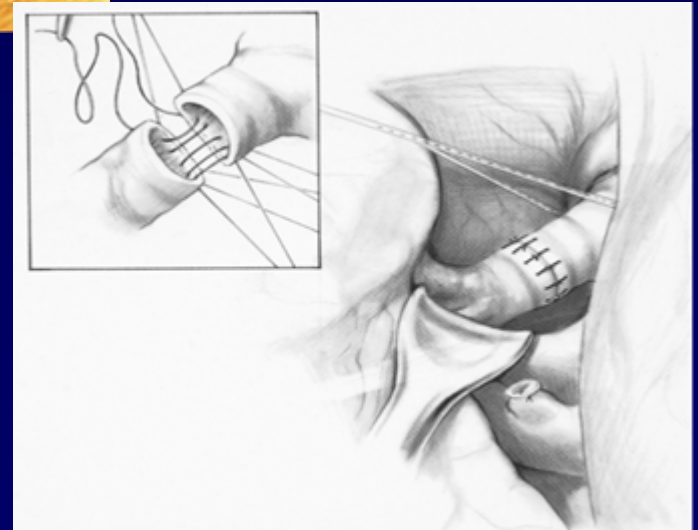
UZ Leuven Data 2000-2006

Surgical Multimodality Treatment for IIIA N2 NSCLC

In-hospital mortality

2.3%

- Intercostal muscle flap
- Sleeve lobectomy
- Fluid restriction perioperative



UZ Leuven Data 2000-2006

Surgical Multimodality Treatment for IIIA N2 NSCLC

	5 Yrs Survival
Overall survival after resection	37%
R0	43%
pT0-1	65%
Single level positive at initial mediastinoscopy	43%
pN0-1	49%
pN2	27%

Survival in persistent N2 disease

- Survival is worse compared with nodal downstaging
- BUT, subgroup of patients with persistent N2 after induction chemotherapy with good prognosis

Author	No of patients	5-year in pN2
Albain (2005)	88	24% (pN1, pN2)
Dooms (2008)	16	19%
Van Schil (2008)	17	30% (negative resected)
Cerfolio (2008)	14	42%
Decaluwé (2008)	47	27%

Albain, *Lung Cancer* 2005;23:165

Dooms, *J Clin Oncol* 2008;26:1128-34

Van Schil, *Europ J Cardiothorac Surg* 2008, 33:824-28

Cerfolio, *Ann Thorac Surg* 2008,86:912-20

Decaluwé, *Europ J Cardiothorac Surg*, submitted

Conclusions

- Marked heterogeneity in stage IIIA(N2) NSCLC
- Improved progression free survival in Intergroup trial and survival obtained in fase II studies favor surgical approach in selected group of patients with resectable IIIA (N2 disease)
- For N2 disease, there is no advantage of induction chemoradiotherapy over chemotherapy
- Surgery following induction chemotherapy is possible with acceptable mortality and morbidity in experienced centers

Conclusions

- Mainly patients with evidence of mediastinal downstaging and/or response in primary tumor benefit from surgical multimodality treatment. However, restaging is not yet optimal.
- R pneumonectomy should be avoided
- Baseline staging and restaging are of paramount importance



Thank you!

**K.U. Leuven, Belgium
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