

ESMO Asia 2015

15-16 December 2015, Singapore

Type: Educational session

Title: Optimal therapy for earlier stages of NSCLC

# Optimal treatment of potentially resectable stage IIIA/N2 disease

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Kinki University Faculty of Medicine

# Conflicts of Interest disclosure

- **Advisor to company:** AstraZeneca, Novartis, Chugai, Boehringer-Ingelheim, Pfizer, Roche, Synta, Clovis, MSD
- **Lecture fees:** AstraZeneca, Chugai, Boehringer-Ingelheim, Pfizer, Taiho, Eli-Lilly, Daiichi-Sankyo
- **Research expenses:** AstraZeneca, Chugai, Boehringer-Ingelheim, Pfizer, Taiho, Ono, Daiichi-Sankyo, Eli-Lilly

## 2nd ESMO Consensus Conference in Lung Cancer: locally advanced stage III non-small-cell lung cancer

W. E. E. Eberhardt<sup>1</sup>, D. De Ruysscher<sup>2</sup>, W. Weder<sup>3</sup>, C. Le Péchoux<sup>4</sup>, P. De Leyn<sup>5</sup>, H. Hoffmann<sup>6</sup>,  
V. Westeel<sup>7</sup>, R. Stahel<sup>8</sup>, E. Felip<sup>9</sup>, S. Peters<sup>10</sup> & Panel Members<sup>†</sup>

incidental IIIA(N2) (unforeseen N2)



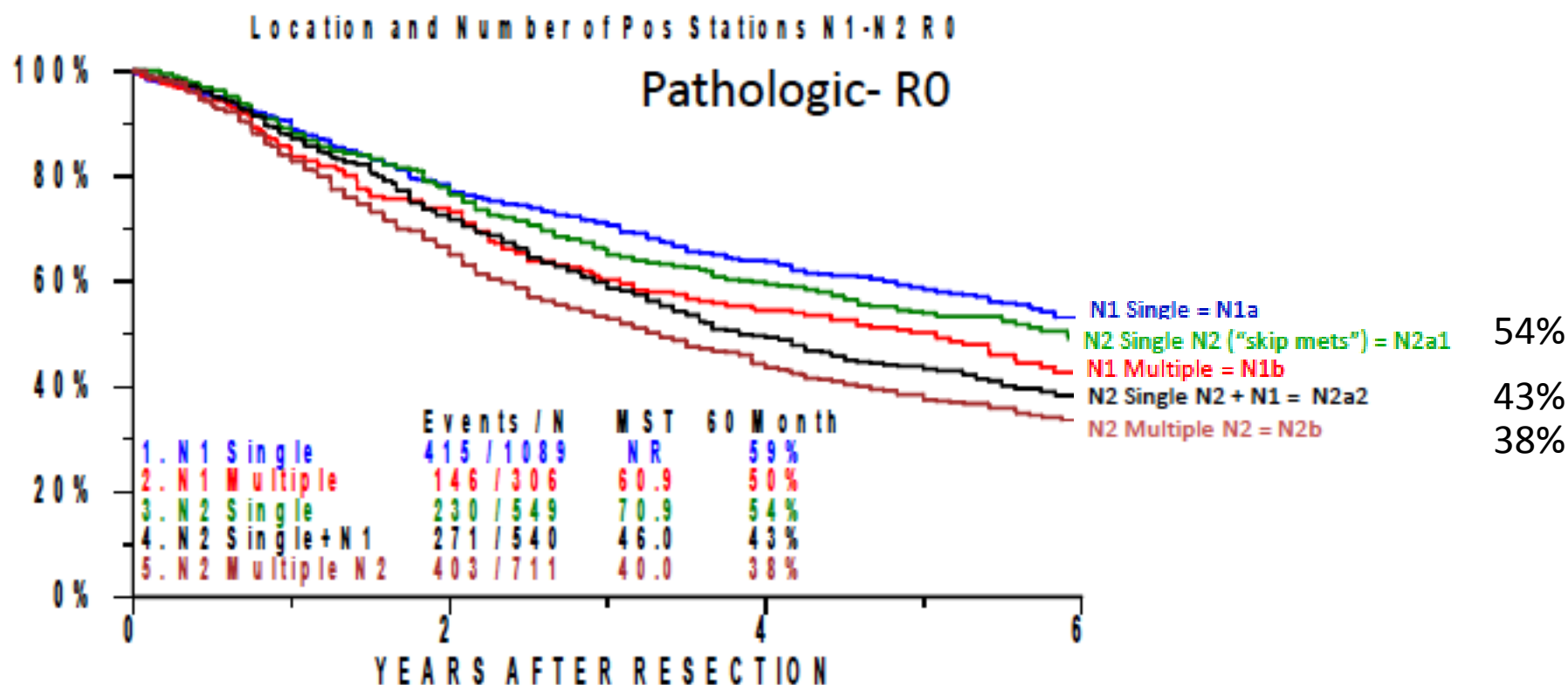
potentially resectable IIIA(N2) disease



unresectable IIIA (N2) disease and IIIB disease patients

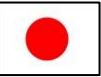





Exploratory analyses of survival for pN1 and pN2 according to the number of metastatic nodal stations (single versus multiple, skip metastasis versus non-skip metastasis) for R0

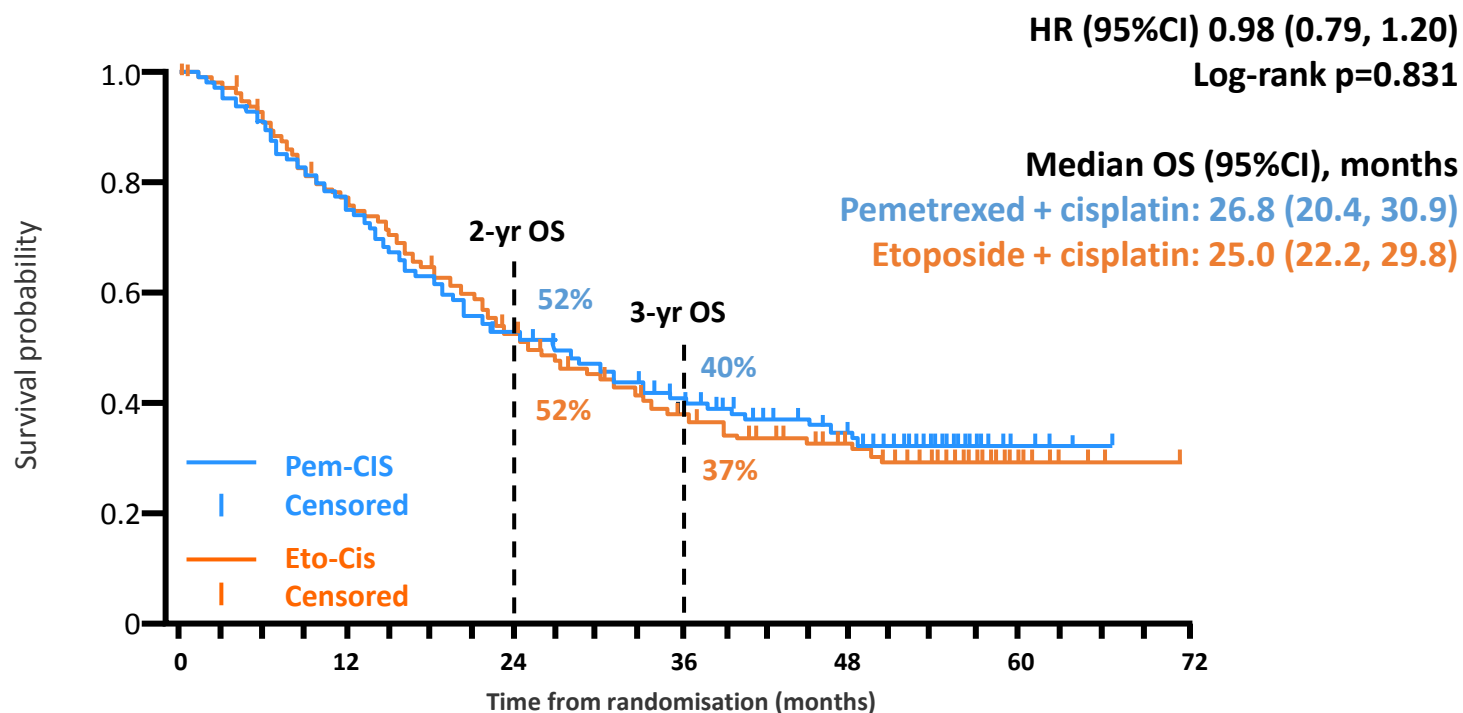


The IASLC Lung Cancer Staging Project,  
Asamura et al., JTO 2015

# State of the art: Chemoradiation for cN2

- WJTOG0105 (MVP+RT/CBDCA+PTX+RT/CDDP+CPT+RT) Yamamoto et al., JCO, 2010 
  - MST: 19.8-22mo、5YSR: ca20%
- OLCSG0007 (MVP+RT/CDDP+DTX+RT) Segawa et al., JCO, 2010 
  - MST: 23.7-26.8mo、5YSR: ca20%
  - local recurrence: 37.6-38.4%
- RTOG 0617 (CBDCA+PTX+74/60Gy、 $\pm$  Cetuximab) Bradley et al., Lancet Oncol, 2015 
  - MST: 60Gy group 28.7mo、74Gy group 19.5mo
  - local rec: 60Gy group 25%、74Gy group 34%
  - no benefit in 74Gy group
  - no benefit of addition of Cetuximab
- PROCLAIM (CDDP+PEM+RT vs. CSSP+ ETP +RT) Senan et al., ASCO, 2015 
  - MST: ETP 25.0mo、PEM 26.8mo
  - no benefit of CDDP+PEM

7506: Final overall survival (OS) results of the phase III PROCLAIM trial: Pemetrexed (Pem), cisplatin (Cis) or etoposide (Eto), Cis plus thoracic radiation therapy (TRT) followed by consolidation cytotoxic chemotherapy (CTX) in locally advanced nonsquamous non-small cell lung cancer (nsNSCLC) – Senan S et al ASCO 2015



Patients at risk:

Pemetrexed + cisplatin

Etoposide + cisplatin

301	282	268	239	221	194	178	157	145	126	98	75	67	56	46	42	33	25	19	14	10	3	1	0	0
297	278	262	232	216	201	179	164	140	113	97	82	69	56	49	46	31	26	22	16	10	6	3	1	0



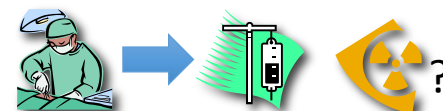
# what are the optimal multi-modality combinations for the different stage III disease sub-stages?

## 2nd ESMO Consensus Conference in Lung Cancer: locally advanced stage III non-small-cell lung cancer

W. E. E. Eberhardt<sup>1</sup>, D. De Ruyscher<sup>2</sup>, W. Weder<sup>3</sup>, C. Le Péchoux<sup>4</sup>, P. De Leyn<sup>5</sup>, H. Hoffmann<sup>6</sup>, V. Westeel<sup>7</sup>, R. Stahel<sup>8</sup>, E. Felip<sup>9</sup>, S. Peters<sup>10</sup> & Panel Members<sup>†</sup>

### incidental IIIA(N2) (unforeseen N2)

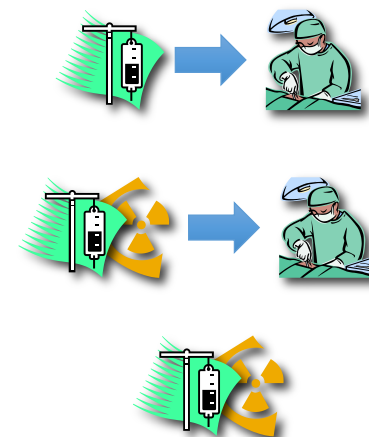
*Recommendation 4.1: If, despite adequate mediastinal staging procedures, N2 disease is only documented intra-operatively, surgery should be followed by adjuvant chemotherapy [I, A]. In case of complete resection, addition of post-operative radiotherapy is not routinely recommended, but may be an option following individual risk assessment [V, C].*



### potentially resectable IIIA(N2) disease

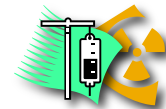
#### preoperative diagnosis of IIIA(N2)

*Recommendation 4.2.1: Possible strategies include several options: induction chemotherapy followed by surgery, induction chemoradiotherapy followed by surgery, or concurrent definitive chemoradiotherapy [I, A]. No recommendation can yet be made; however, an experienced multidisciplinary team is of paramount importance in any complex multi-modality treatment strategy decision. If induction chemotherapy alone is given preoperatively, post-operative radiotherapy is not standard treatment but may be an option based on critical evaluation of locoregional relapse risks [IV, C].*

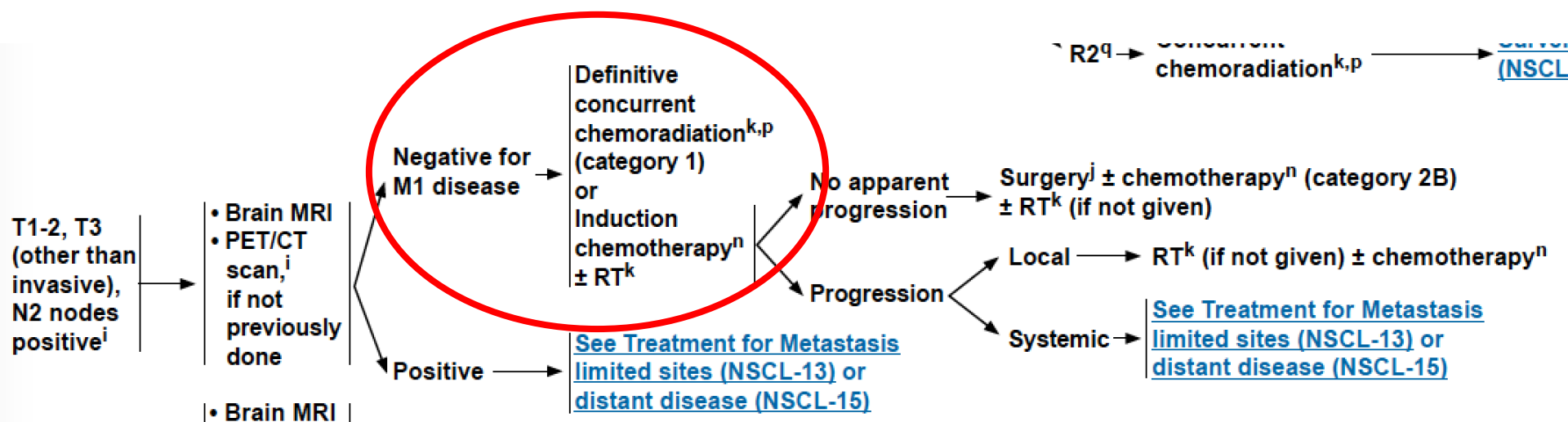


### unresectable IIIA (N2) disease and IIIB disease patients

*Recommendation 4.3: Concurrent chemoradiotherapy is the treatment of choice in patients evaluated as unresectable in stage IIIA and IIIB [I, A]. If concurrent chemoradiotherapy is not possible—for any reason - sequential approaches of induction chemotherapy followed by definitive radiotherapy represent a valid and effective alternative [I, A].*

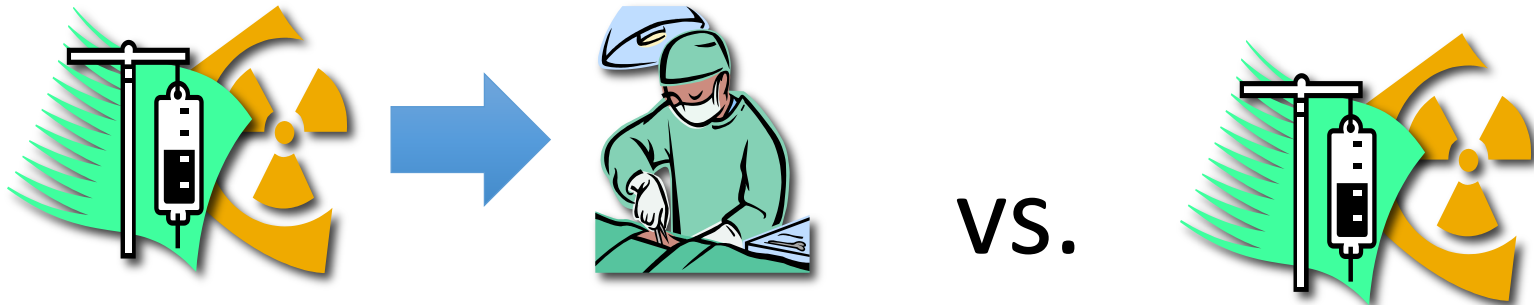


Pictures are from ACCP guideline for non-invasive mediastinal staging, 2007

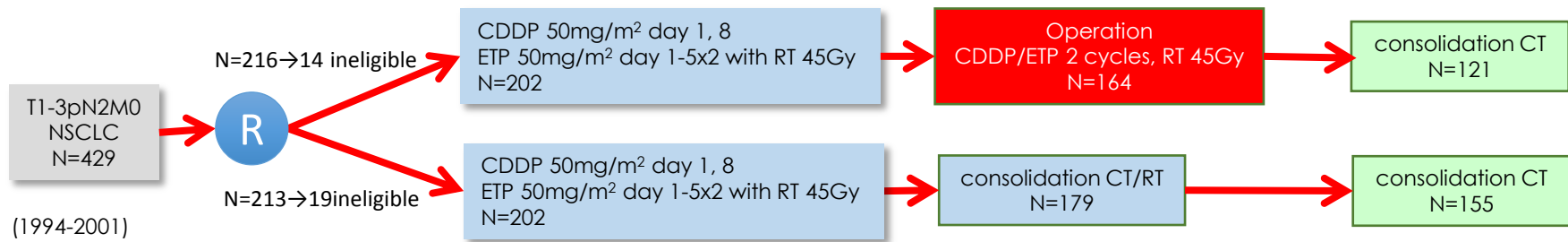




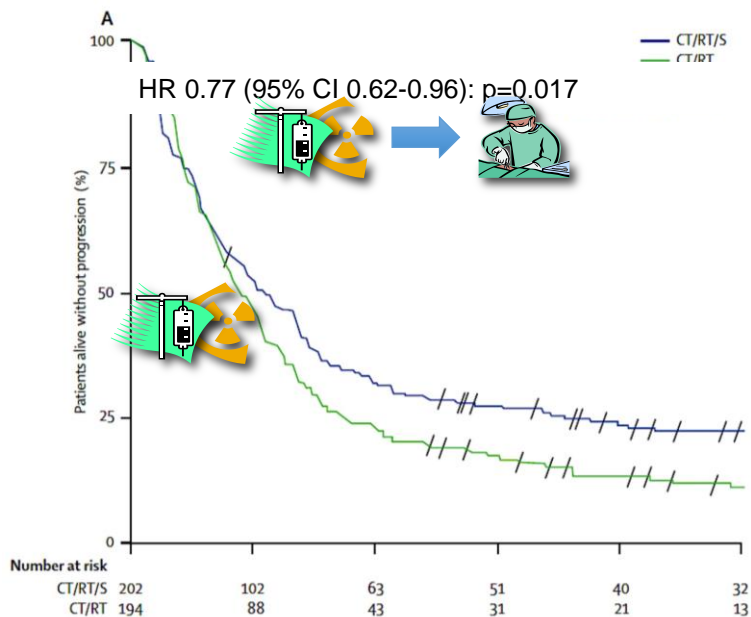
# Role of surgery ?



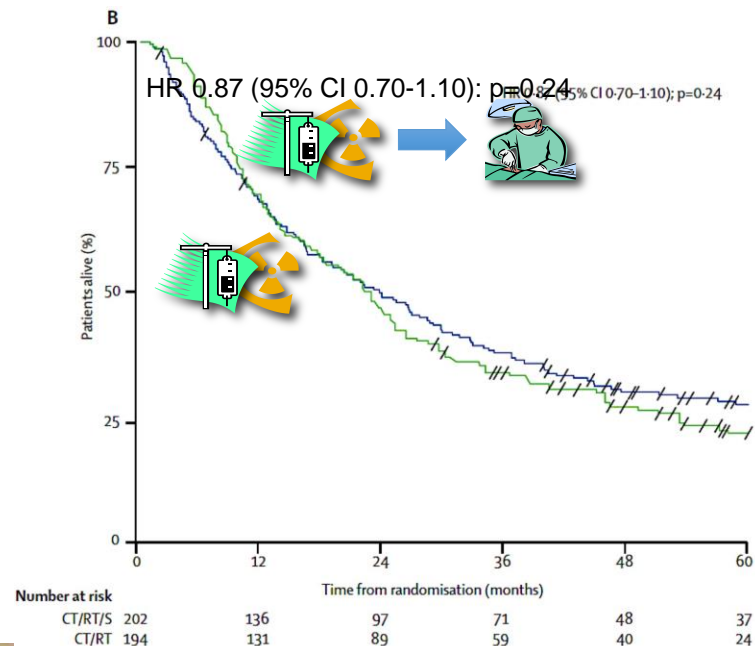
# Radiotherapy plus chemotherapy with or without surgical resection for stage III NSCLC: a phase III randomized controlled trial (INT0139) Albain et al., Lancet 2009



Progression free survival

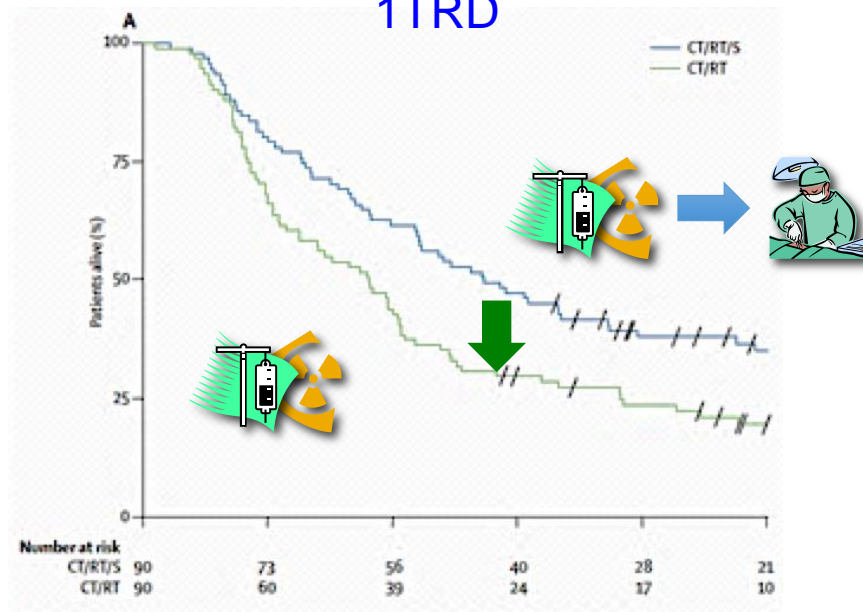


Overall survival (primary endpoint)

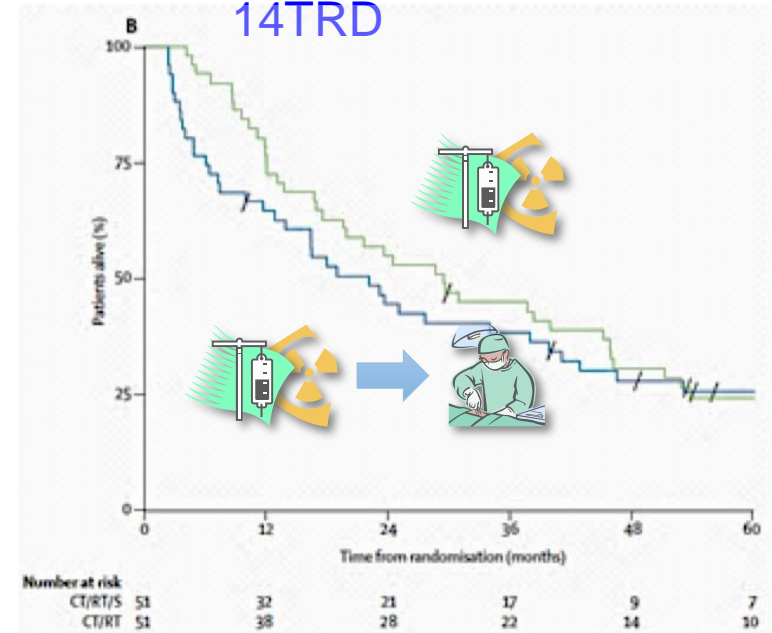


Radiotherapy plus chemotherapy with or without surgical resection for stage III NSCLC:  
a phase III randomized controlled trial (INT0139)  
Albain et al., Lancet 2009

lobectomy  
1TRD



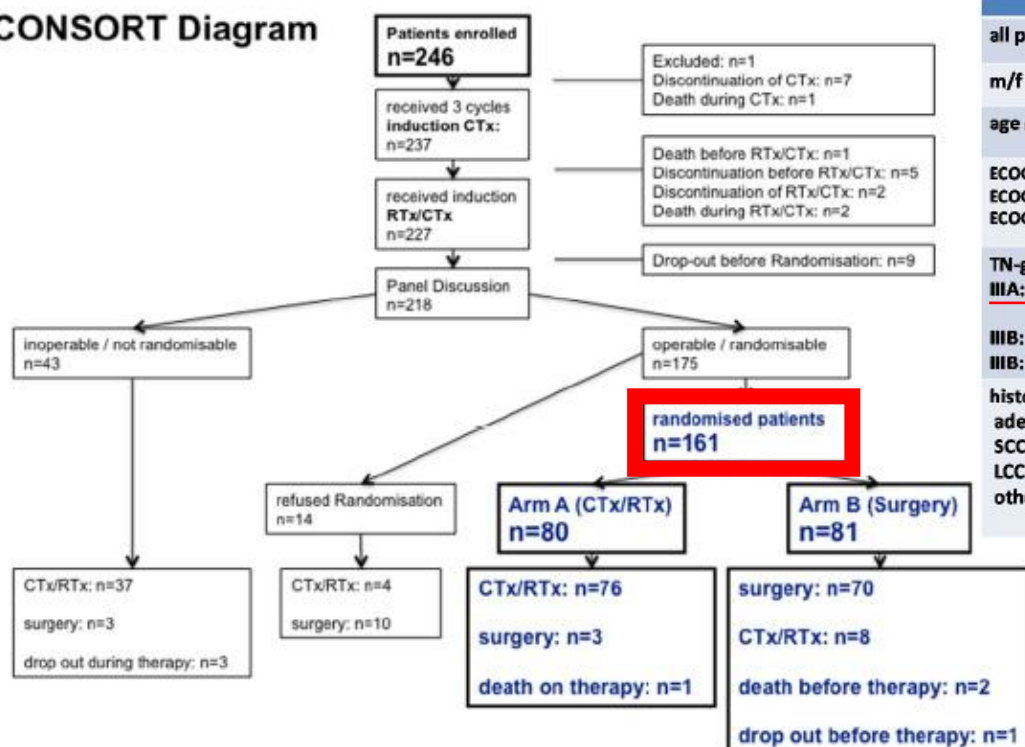
pneumonectomy  
14TRD



Phase III study of surgery vs. definitive concurrent chemoradiotherapy boost in patients with operable (stage IIIA(N2)/selected IIb (sel IIb) NSCLC following induction chemotherapy and concurrent CRTx (ESPAUE).

Eberhardt et al., Abstr 7510 et al. ASCO 2014

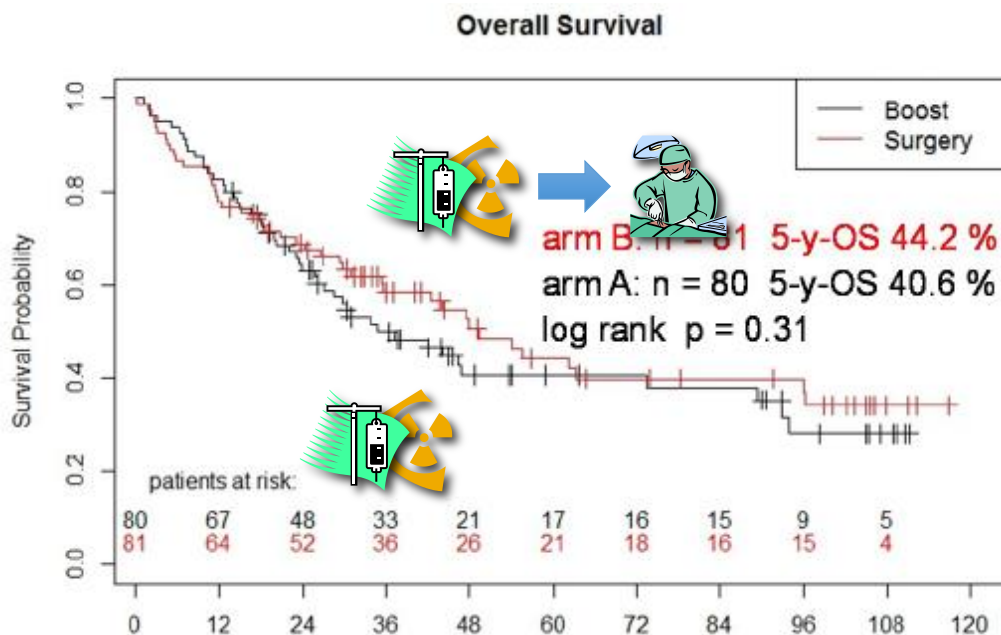
## CONSORT Diagram



Patient group	arm A def CRTx	%	arm B surgery	%	all pts INR ( n = 246 )	%
all pts	80		81		246	
m/f	53/27		56/25		176/70	
age (median; range)	59	42-74	58	33-72	59	33-74
ECOG 0	60	75	60	74	170	69.1
ECOG 1	20	25	21	26	75	30.5
ECOG 2	0	0	0	0	1	0.4
<b>TN-group</b>						
<b>IIIA: T1-3 N2</b>	26	32.5	29	35.8	75	30.5
<b>IIIB: T4 N0/1</b>	28	35	24	29.6	80	32.5
<b>IIIB: T1-4 N3 T4N2</b>	26	32.5	28	34.6	91	37
histology						
adeno ca	40	50	36	44.4	107	43.5
SCC	28	35	35	43.2	95	38.6
LCC	7	8.75	4	4.9	22	8.9
other	5	6.25	6	7.4	22	8.9

Phase III study of surgery vs. definitive concurrent chemoradiotherapy boost in patients with operable (stage IIIA(N2)/selected IIb (sel IIb) NSCLC following induction chemotherapy and concurrent CRTx (ESPATUE).

Eberhardt et al., Abstr 7510 et al. ASCO 2014



## Conclusions

- ◆ Long-term OS at 5 y in rand OP+ pts was excellent with both Tx.
- ◆ These high-volume center data confirm earlier trials: Both options are acceptable and should be discussed with individual pts.
- ◆ In the ITT population 87.8% were treated with a definitive approach. 5-y-OS of 34.1% in all 246 initially recruited patients are amongst the best published data, so far.

# Role of surgery ?



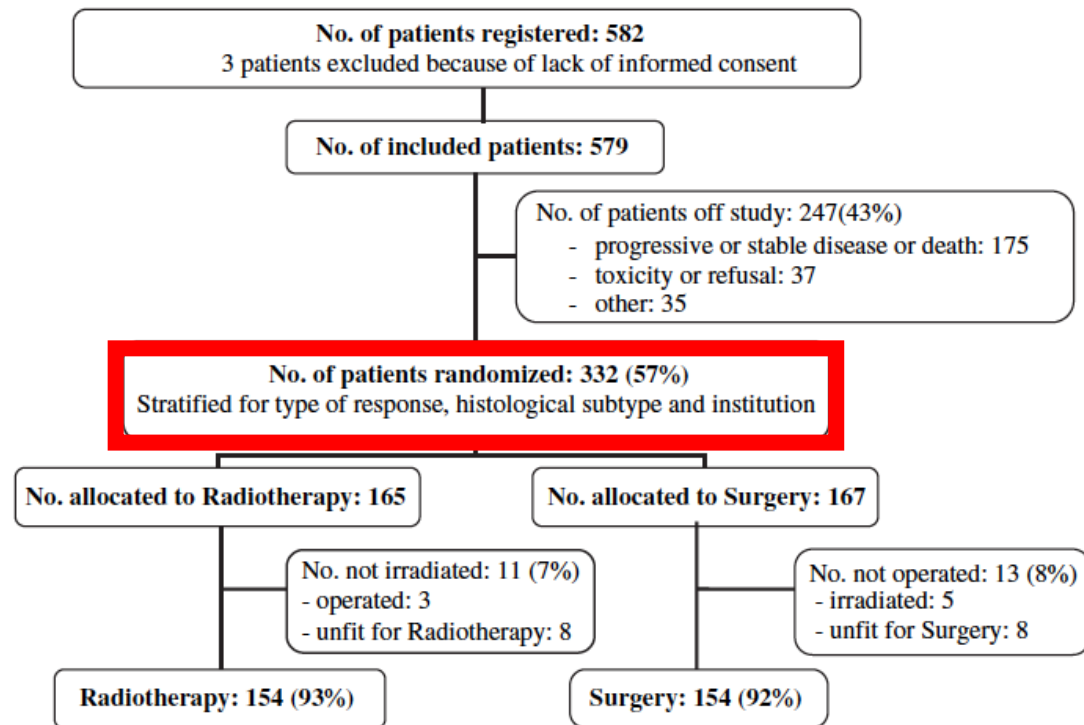


# Randomized controlled trial of resection vs. radiotherapy after induction chemotherapy in stage IIA-N2 NSCLC van Meerbeeck et al., J Natl Cancer Inst, 2007

Eligible patients  
cytologic or histologic proof of  
**unresectable** stage IIA-N2

Guidelines for unresectability

- any N2 involvement by a non-sq
- in case of sq ca, any N2 nodal involvement **exceeding level 4R** for a right-sided tumor and **level 5 and 6** for a left-sided tumor.



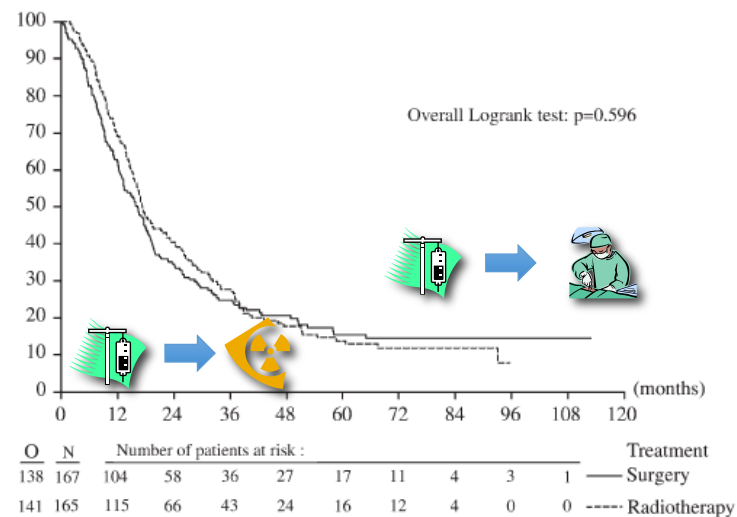
# Randomized controlled trial of resection vs. radiotherapy after induction chemotherapy in stage IIA-N2 NSCLC van Meerbeeck et al., J Natl Cancer Inst, 2007

## Overall survival

Table 5. Exploratory analyses in 154 patients in the resection surgery arm\*

Subgroup	N	Median OS, months (95% CI)	5-year OS, %	P, Univariate analysis	P, Multivariable analysis
Extent of resection				.009	.03
(Bi-)lobectomy	58	25.4 (17.7 to 48.9)	27		
Pneumonectomy	72	13.4 (11.1 to 19.5)	12		
Mediastinal status				<.001	.04
ypN0-1	64	22.7 (17.6 to 42.7)	29		
ypN2	86	14.9 (11.2 to 18.5)	7		
Type of resection				<.001	.01
Complete	77	24.1 (16.7 to 42.4)	27		
Incomplete	76	12.1 (9.5 to 17.1)	7		
No PORT	92	14.1 (11.2 to 19.9)	19	.6	.004
PORT	62	18.0 (15.0 to 25.9)	13		

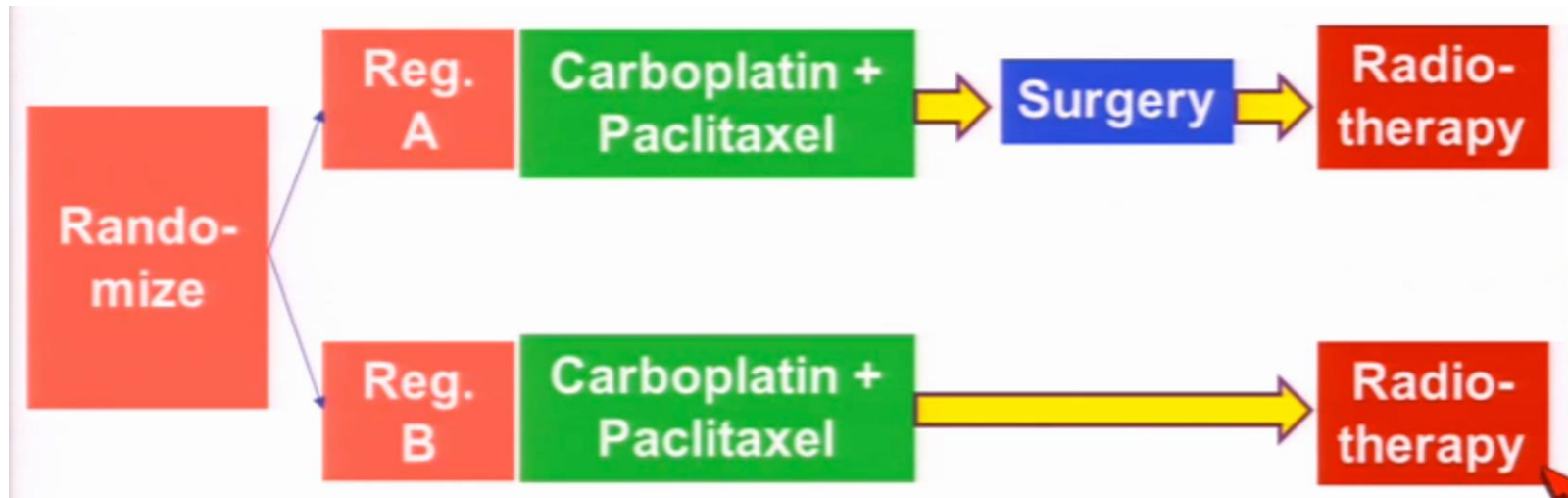
\* OS = overall survival; PORT = postoperative radiotherapy; CI = confidence interval; ypN = pathologic N after induction therapy. P values were calculated using a two-sided log-rank test.



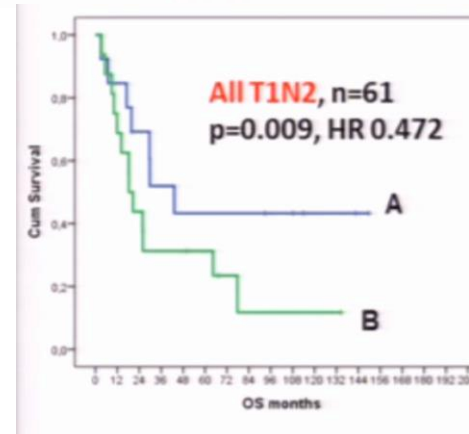
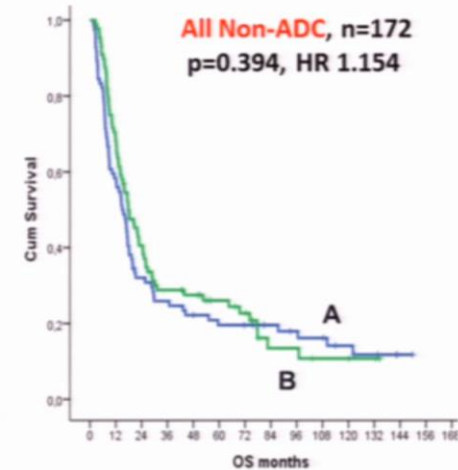
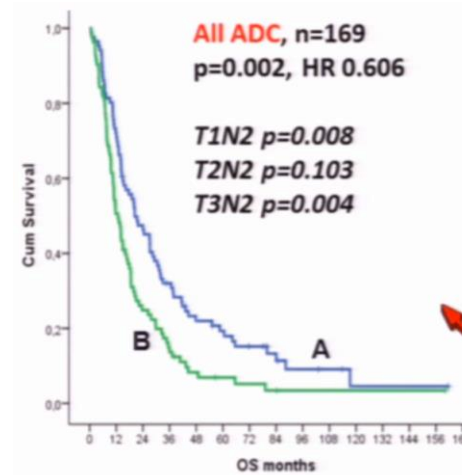
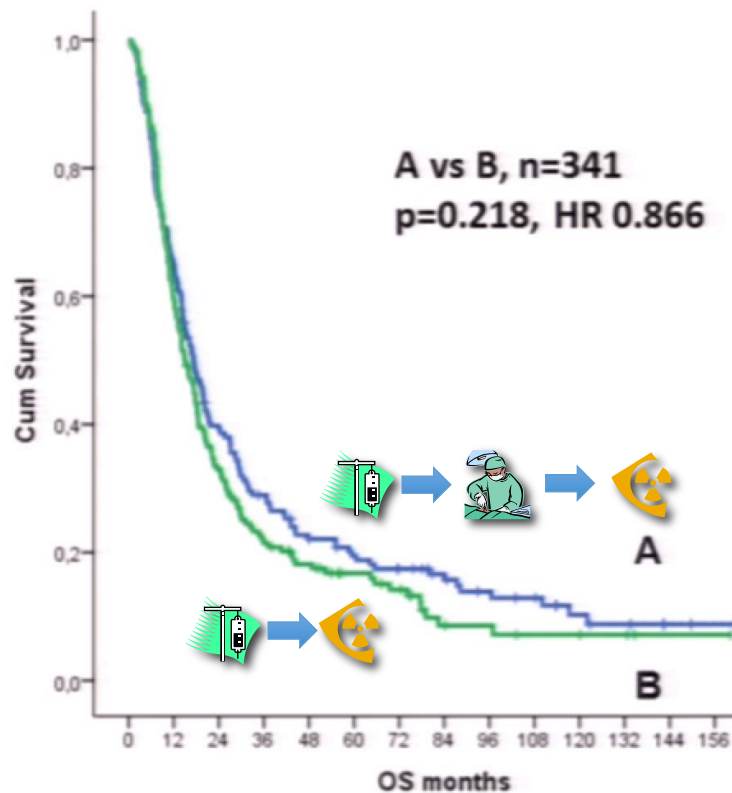
# Role of surgery ?



Surgery for NSCLC stages T1-3N2M0 having preoperative pathologically verified N2 involvement: A prospective randomized multinational phase III trial by Nordic Thoracic Oncology Group  
Sorensen, JB, et al., ASCO 2013 abstr 7504



Surgery for NSCLC stages T1-3N2M0 having preoperative pathologically verified N2 involvement: A prospective randomized multinational phase III trial by Nordic Thoracic Oncology Group  
Sorensen, JB, et al., ASCO 2013 abstr 7504



# Outcome of surgery versus radiotherapy after induction treatment in patients with N2 disease: systematic review and meta-analysis of randomised trials

Thorax 2015

P J McElnay,<sup>1</sup> A Choong,<sup>2</sup> E Jordan,<sup>3</sup> F Song,<sup>4</sup> E Lim<sup>5</sup>

Study

ID

ES (95% CI)

Weight

## Bi-modality trials

Shepherd

Johnstone

Stephens

Van Meerbeeck

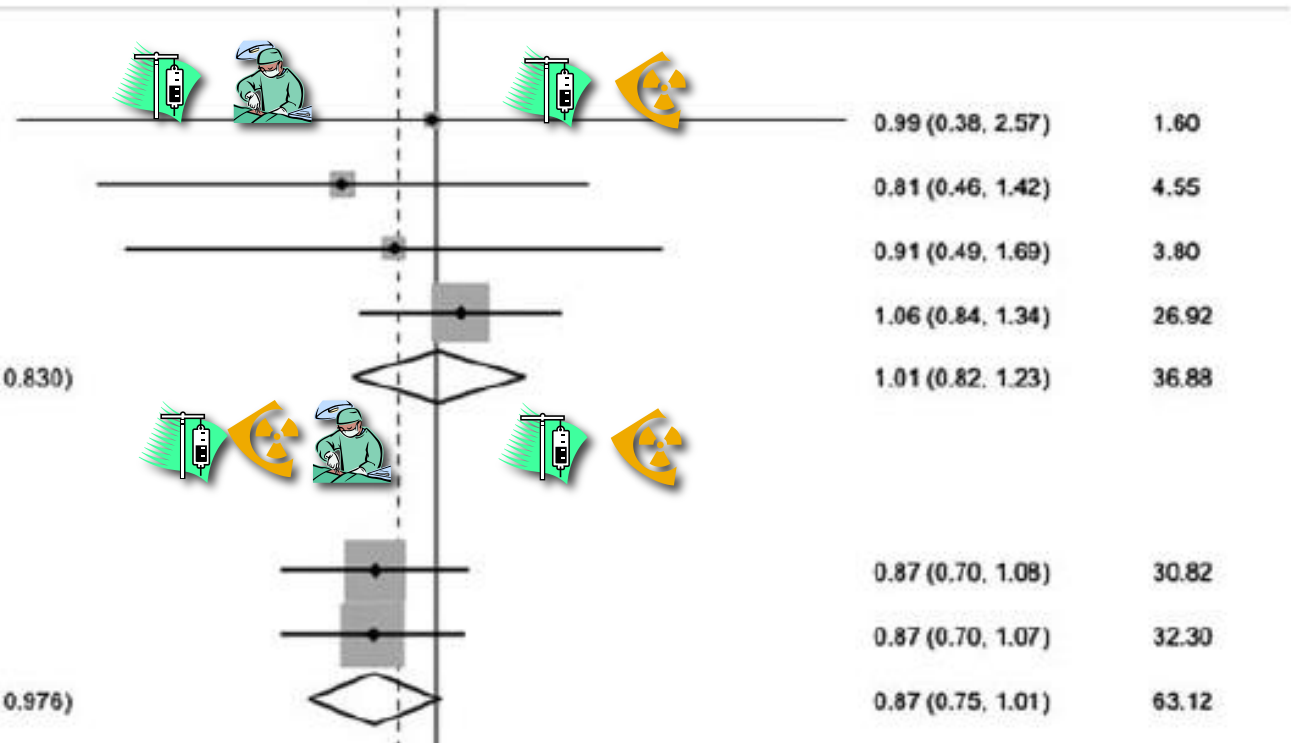
Subtotal (I-squared = 0.0%, p = 0.830)

## Tri-modality trials

Albain

Sorensen

Subtotal (I-squared = 0.0%, p = 0.976)

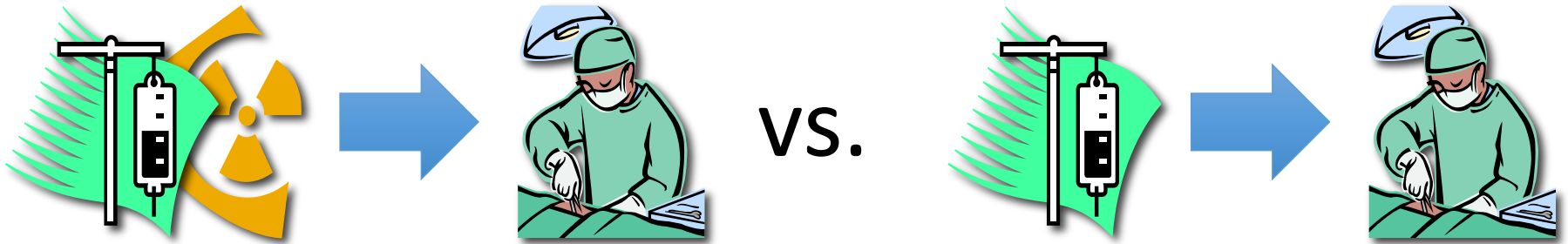


<-Favors surgery

Favors radiotherapy->

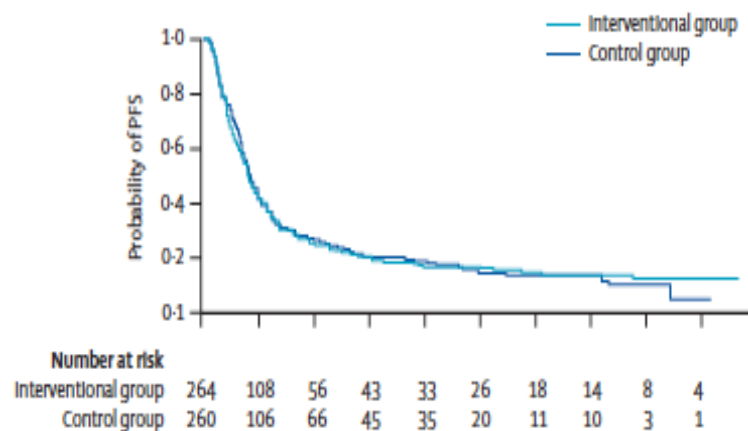
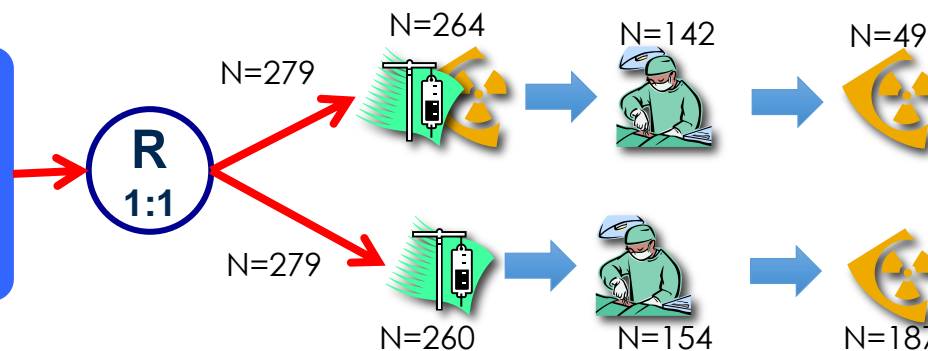


# Trimodality vs Bimodality



**Lancet Oncol 2008; 9: 636–648**

- Resectable stage IIIA/IIIB NSCLC
- PS 0–1
- Age<70
- N=558



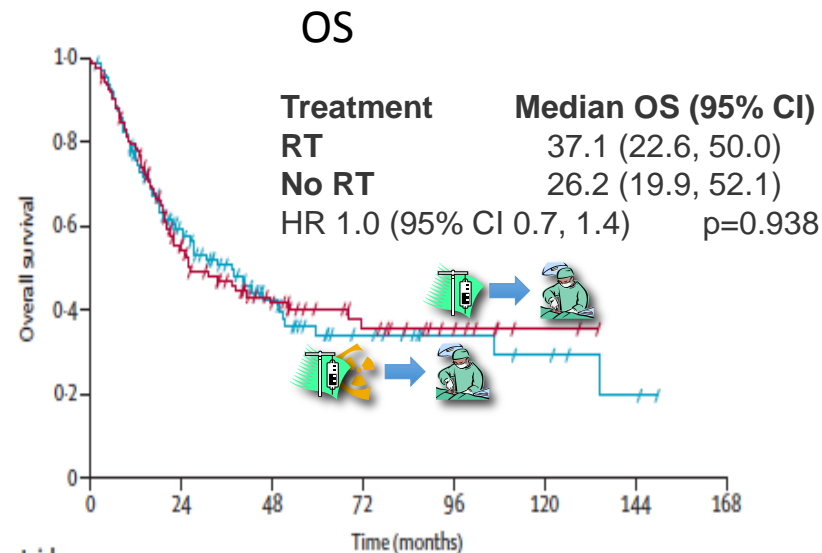
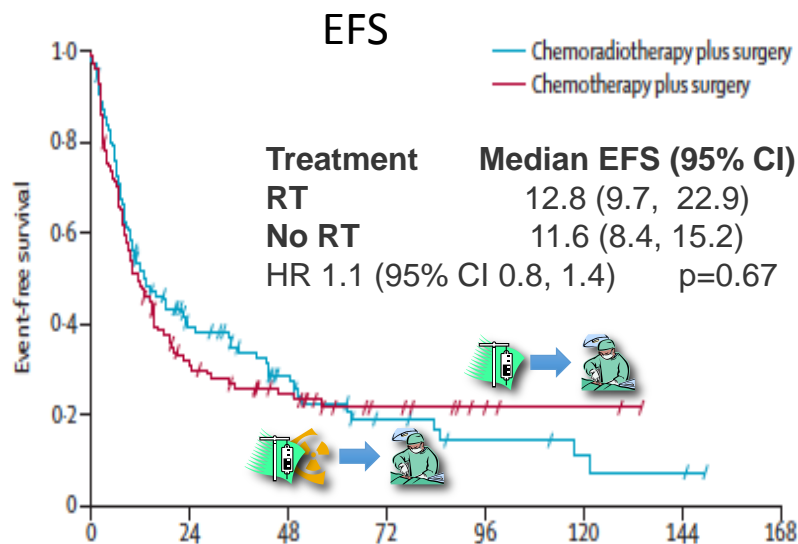
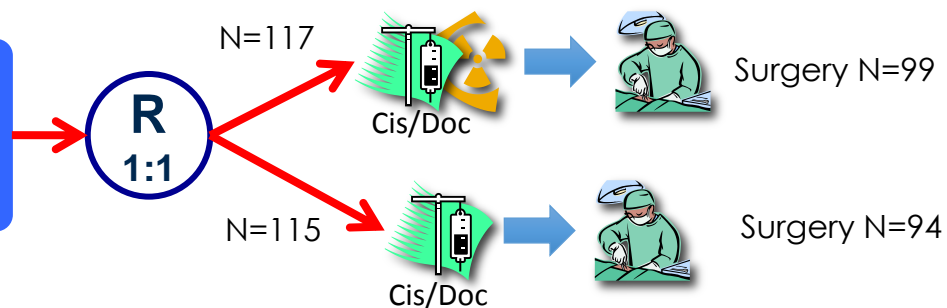
	EORTC o8941 <sup>1</sup> (stage IIIA; N2)	INT 0139 <sup>24</sup> (stage IIIA; N2)	GLCCG (stage IIIA or IIIB)		p
	CT, response, randomisation, surgery vs RT	Randomisation, CT/RT vs CT/RT, surgery, CT	Randomisation; CT, CT/RT, surgery	Randomisation; CT, surgery, RT	
Patients initially eligible, n	579	396	264	260	..
Patients initially allocated to surgery, n	..*	202	264	260	..
Patients allocated to surgery after induction, n	167	177	202	226	..
Patients undergoing surgery, n	154	164	142	154	..
Patients with negative resection margins, %	..†	88	84	77	p=0.16
Patients with complete resection¶, %	50	†	69	55	p=0.01
Patients with exploratory thoracotomy, %	14	5.5	8	8	..
Patients with lobectomy or bilobectomy, %	38	59	56	55	..
Patients with pneumonectomy, %	47	33	35	35	..
Surgical mortality, %					
Total	4	7.9	9.2	4.5	p=0.11
After lobectomy or bilobectomy	0	1	7.5	2.4	p=0.12
After pneumonectomy	7	26	14.0	5.5	p=0.14

# Induction chemoradiation in stage IIIA/N2 non-small-cell lung cancer: a phase 3 randomised trial SAKK 16/00 trial

Miklos Pless, Roger Stupp, Hans-Beat Ris, Rolf A Stahel, Walter Weder, Sandra Thierstein, Marie-Aline Gerard, Alexandros Xyrafas, Martin Fröh, Richard Cathomas, Alfred Zippelius, Arnaud Roth, Milorad Bijelovic, Adrian Ochsenbein, Urs R Meier, Christoph Mamot, Daniel Rauch, Oliver Gautschi, Daniel C Betticher, René-Olivier Mirimanoff, Solange Peters, on behalf of the SAKK Lung Cancer Project Group

Lancet 2015; 386: 1049-56

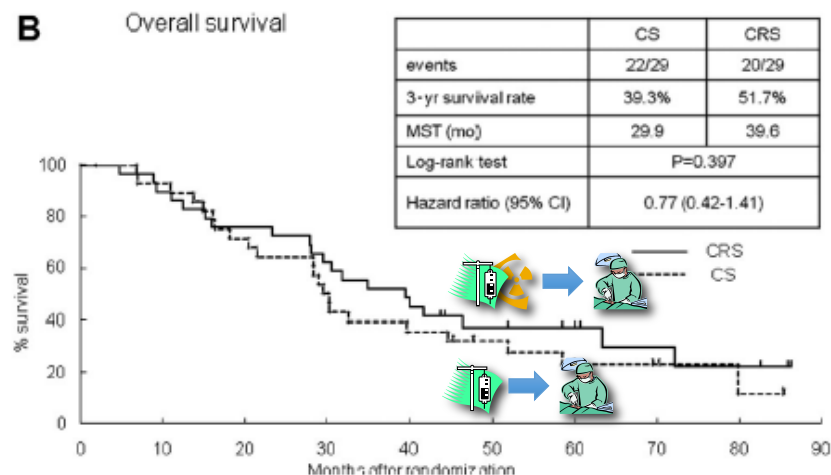
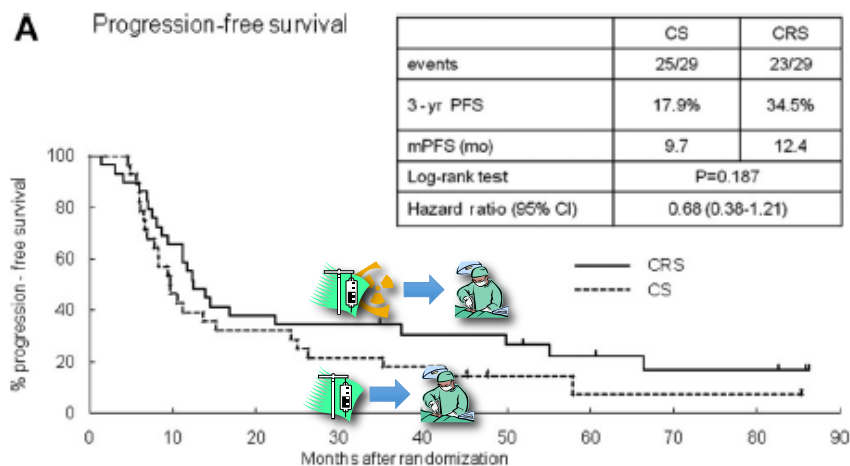
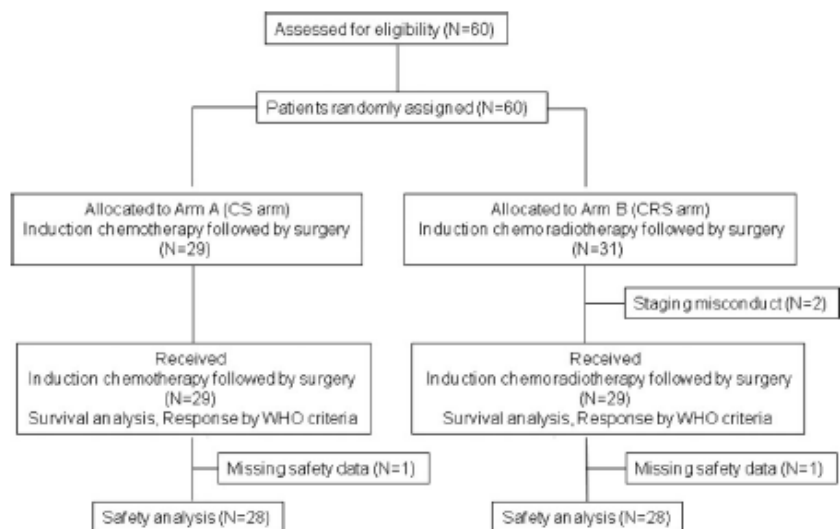
- Resectable stage IIIA/N2 NSCLC
- PS 0-1
- Adequate organ function (n=232)



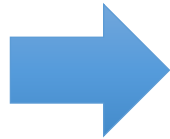
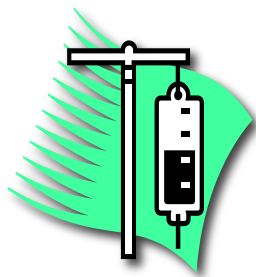
Interpretation Radiotherapy did not add any benefit to induction chemotherapy followed by surgery

# A Phase 3 Study of Induction Treatment With Concurrent Chemoradiotherapy vs Chemotherapy Before Surgery in Patients With Pathologically Confirmed N2 Stage IIIA NSCLC (WJTOG9903)

Katakami N, Tada H, Mitsudomi T, et al., Cancer 2012



# preoperative chemotherapy



VS.



Pro  
resectability  
local control  
micrometastases  
Con  
delay surgery  
increased morbidity

# The New England Journal of Medicine

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JANUARY 20, 1994

Number 3

## A RANDOMIZED TRIAL COMPARING PREOPERATIVE CHEMOTHERAPY PLUS SURGERY WITH SURGERY ALONE IN PATIENTS WITH NON-SMALL-CELL LUNG CANCER

RAFAEL ROSELL, M.D., PH.D., JOSÉ GÓMEZ-CODINA, M.D., PH.D., CARLOS CAMPS, M.D.,  
JOSÉ MAESTRE, M.D., PH.D., JOSÉ PADILLE, M.D., ANTONIO CANTÓ, M.D., JOSÉ LUIS MATE, M.D.,  
SHANRONG LI, M.D., JORGE ROIG, M.D., PH.D., ANGEL OLAZÁBAL, M.D., PH.D.,  
MERCEDES CANELA, M.D., PH.D., AURELIO ARIZA, M.D., PH.D., ZDENĚK SKÁČEL, M.D.,  
JOSÉ MORERA-PRAT, M.D., PH.D., AND ALBERT ABAD, M.D., PH.D.

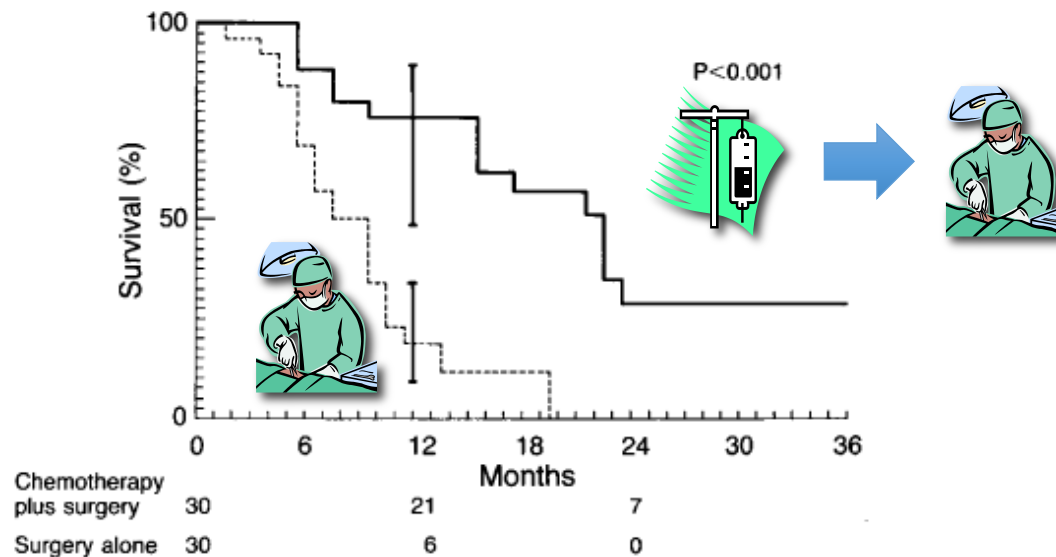


Figure 2. Kaplan-Meier Plot of Overall Survival in Patients with Stage IIIA Lung Cancer Treated with Surgery Alone (Dashed Line) or Chemotherapy plus Surgery (Solid Line).



# Preoperative chemotherapy for non-small cell lung cancer: a systematic review and meta-analysis of individual participant data

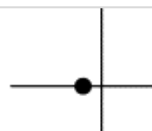
NSCLC Meta-analysis Collaborative Group\*

The Lancet, 2014; 383, 1561 - 1571

Clinical stage (IA, IB, II, III)

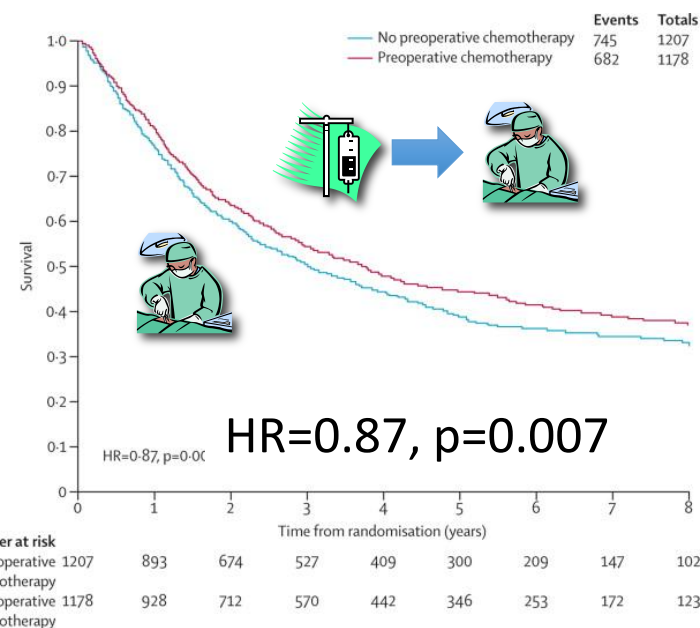
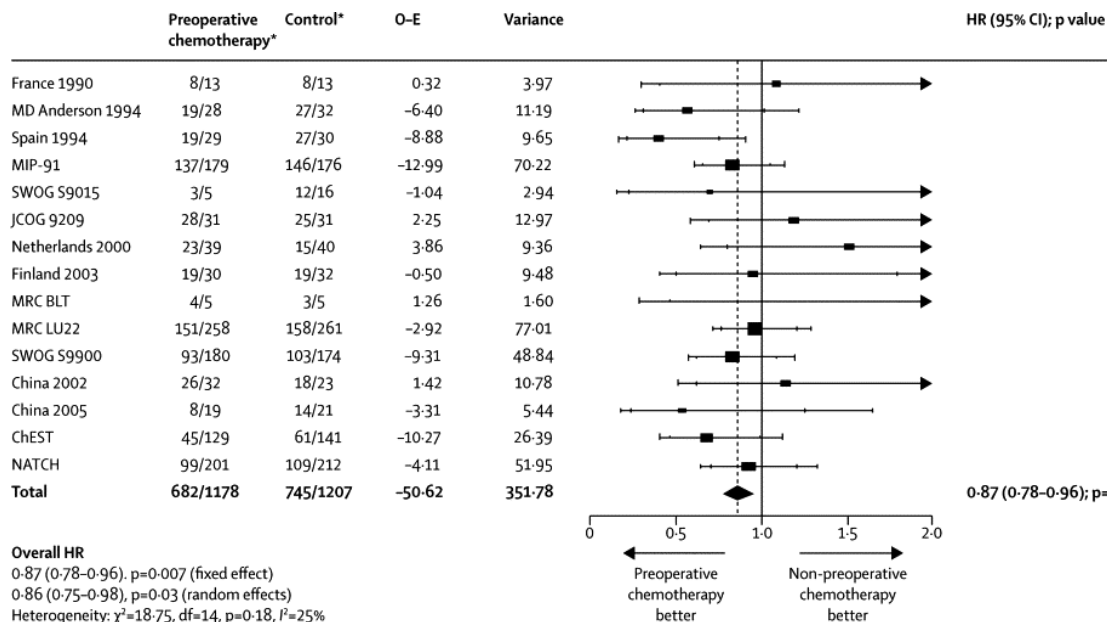
9 trials, 2171 patients

Greater treatment effect with higher clinical stage



Greater treatment effect with lower clinical stage

0.96 (0.83-1.12),  $p=0.64$ , heterogeneity  $p=0.22$





## Treatment of Stage III Non-small Cell Lung Cancer

**Diagnosis and Management of Lung Cancer,  
3rd ed: American College of Chest Physicians  
Evidence-Based Clinical Practice Guidelines**

*Nithya Ramnath, MD; Thomas J. Dilling, MD; Loren J. Harris, MD, FCCP;  
Anthony W. Kim, MD, FCCP; Gaetane C. Michaud, MD, FCCP;  
Alex A. Balekian, MD, MSHS; Rebecca Diekemper, MPH;  
Frank C. Detterbeck, MD, FCCP; and Douglas A. Arenberg, MD, FCCP*

## 2013 ACCP guidelines

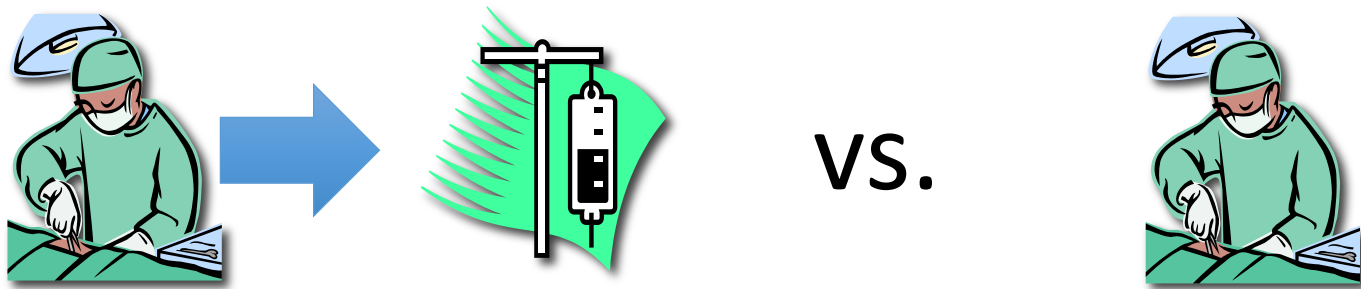
### Discrete mediastinal node involvement

In patients with discrete N2 involvement by NSCLC identified preoperatively (IIIA),

3.5.2. either definitive chemoradiation therapy or induction therapy followed by surgery is recommended over either surgery or radiation alone (Grade 1A) .

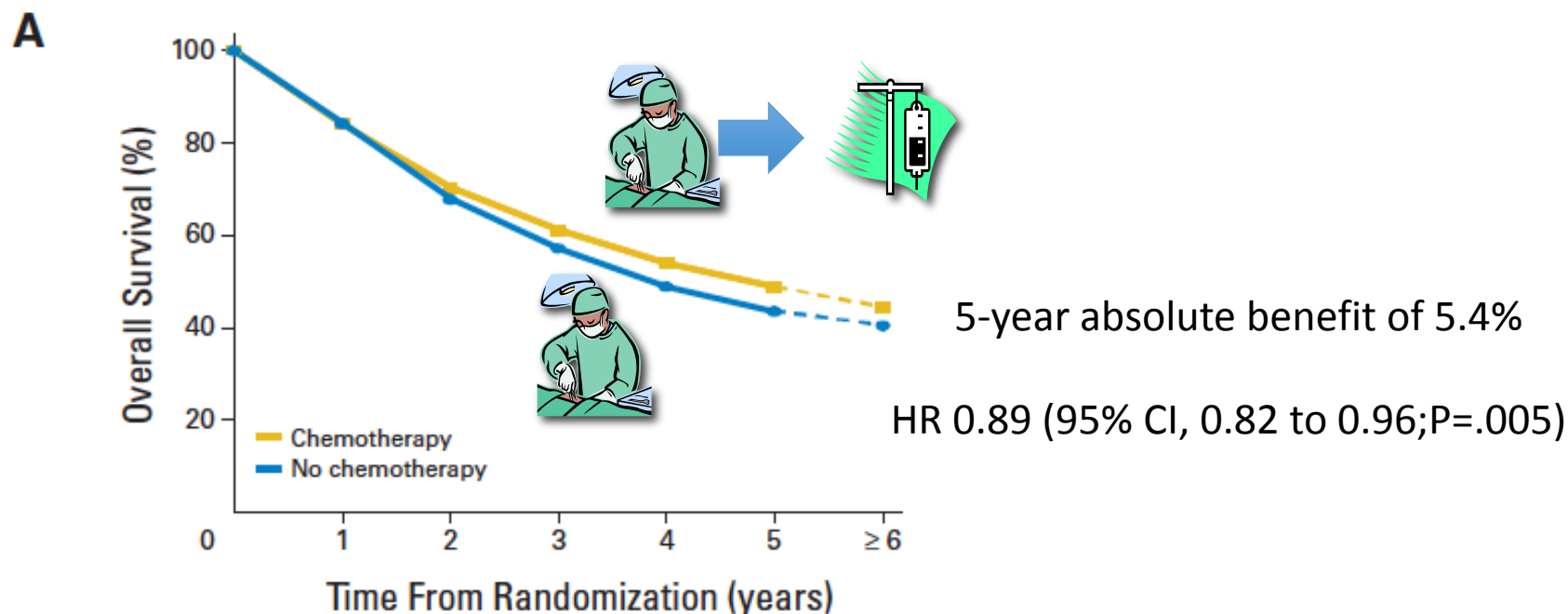
3.5.3. primary surgical resection followed by adjuvant therapy is not recommended (Grade 1C) .

# Postoperative adjuvant chemotherapy



# Lung Adjuvant Cisplatin Evaluation: A Pooled Analysis by the LACE Collaborative Group

Jean-Pierre Pignon, Hélène Tribodet, Giorgio V. Scagliotti, Jean-Yves Douillard, Frances A. Shepherd, Richard J. Stephens, Ariane Dunant, Valter Torri, Rafael Rosell, Lesley Seymour, Stephen G. Spiro, Estelle Rolland, Roldano Fossati, Delphine Aubert, Keyue Ding, David. Waller, and Thierry Le Chevalier



Deaths / person years  
by period

	Years 0-3	Years 4-5	Years ≥ 6
Control	966 / 5,155	239 / 1,668	49 / 720
Chemotherapy	857 / 5,181	203 / 1,817	76 / 790

Years 0-3

Years 4-5

Years ≥ 6

966 / 5,155

239 / 1,668

49 / 720

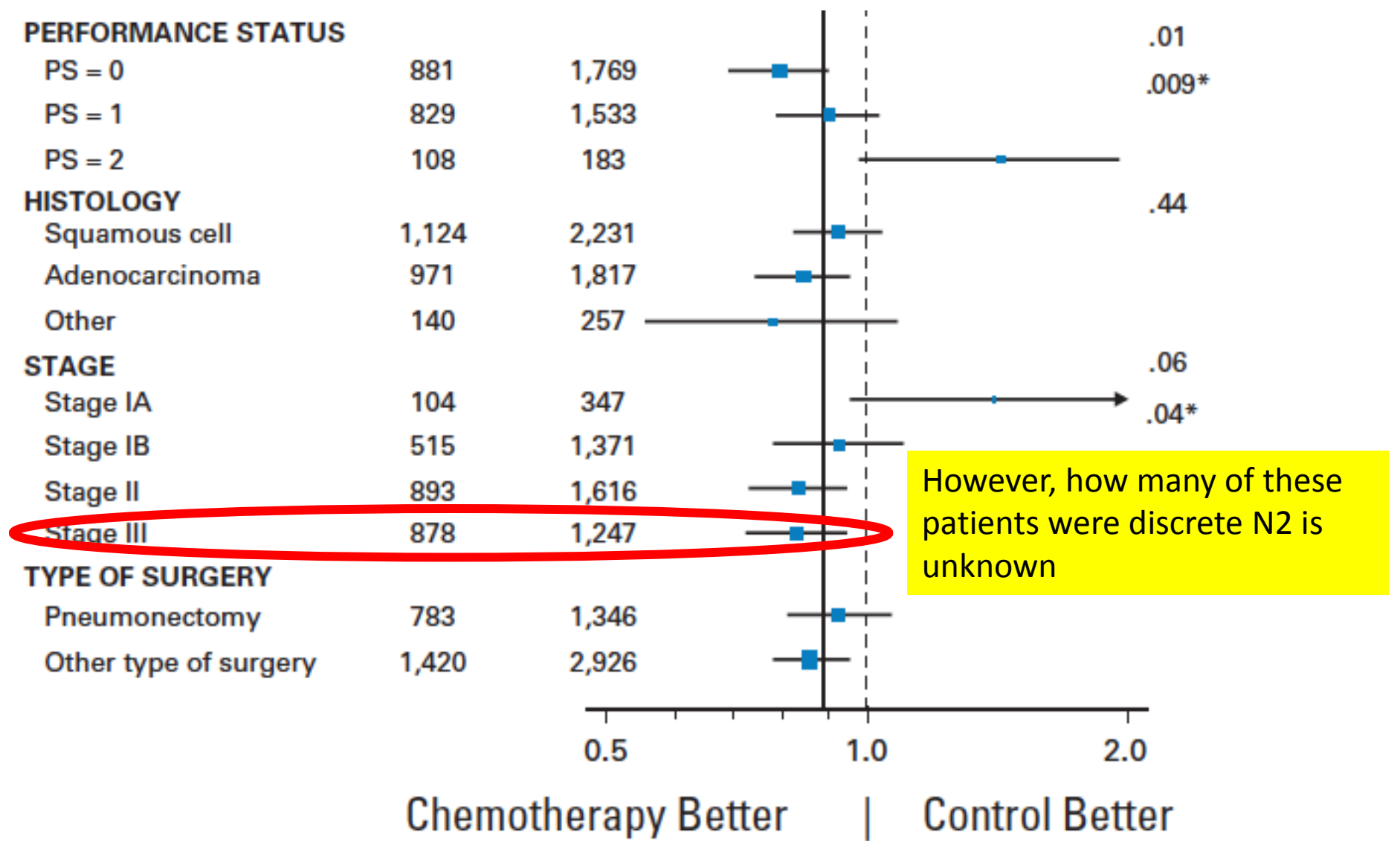
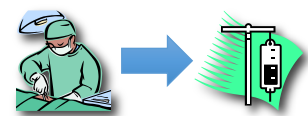
857 / 5,181

203 / 1,817

76 / 790

SINGAPORE  
2015ESMO  
ASIA18-21 DECEMBER  
SINGAPORE

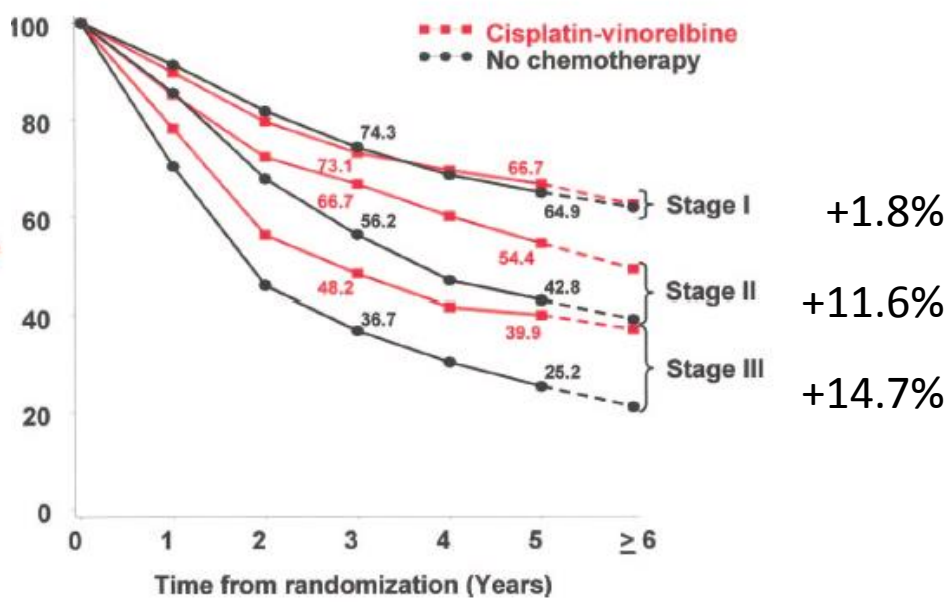
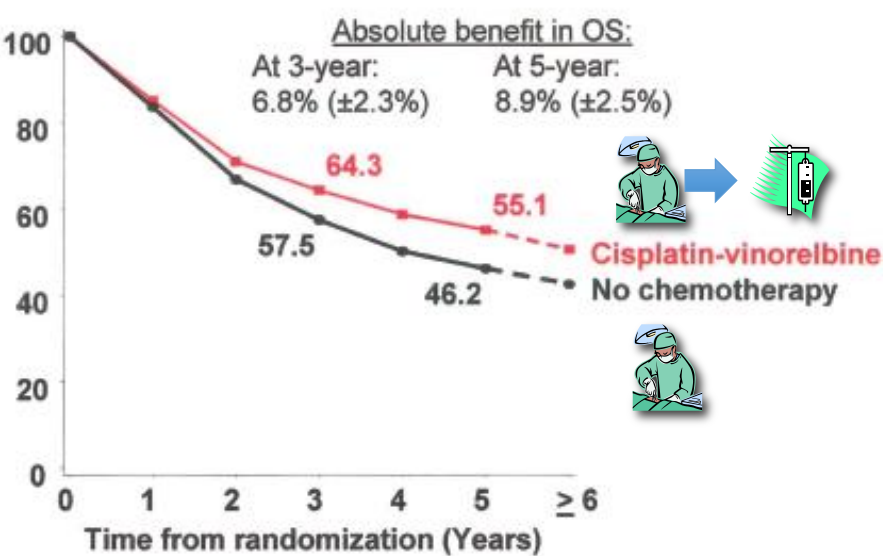
# LACE Meta-analysis (OS)



# Adjuvant Cisplatin and Vinorelbine for Completely Resected Non-small Cell Lung Cancer

## Subgroup Analysis of the Lung Adjuvant Cisplatin Evaluation

Jean-Yves Douillard, MD, PhD,\* H       Tribodet, MSc,† Delphine Aubert, MSc,‡  
 Frances A. Shepherd, MD,§ Rafael Rosell, MD, PhD,|| Keyue Ding, PhD,¶ Anne-Sophie Veillard, MSc,†  
 Lesley Seymour, PhD,¶ Thierry Le Chevalier, MD,# Stephen Spiro, MD,\*\* Richard Stephens,††  
 Jean Pierre Pignon, MD, PhD,† and on behalf of the LACE Collaborative Group





# Preop vs postop chemotherapy



## Pros

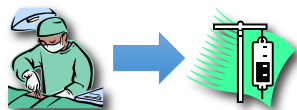
- improve resectability
- sterile micromets
- in vivo sensitivity test
- better tolerability, dose intensity

## Cons

- delay surgery
- increase morbidity?

# Preoperative vs. postoperative chemotherapy in patients with resectable NSCLC: Systematic review of indirect comparison meta-analysis of randomized trials

Lim et al., J Thorac Oncol, 4:1380-1388, 2009

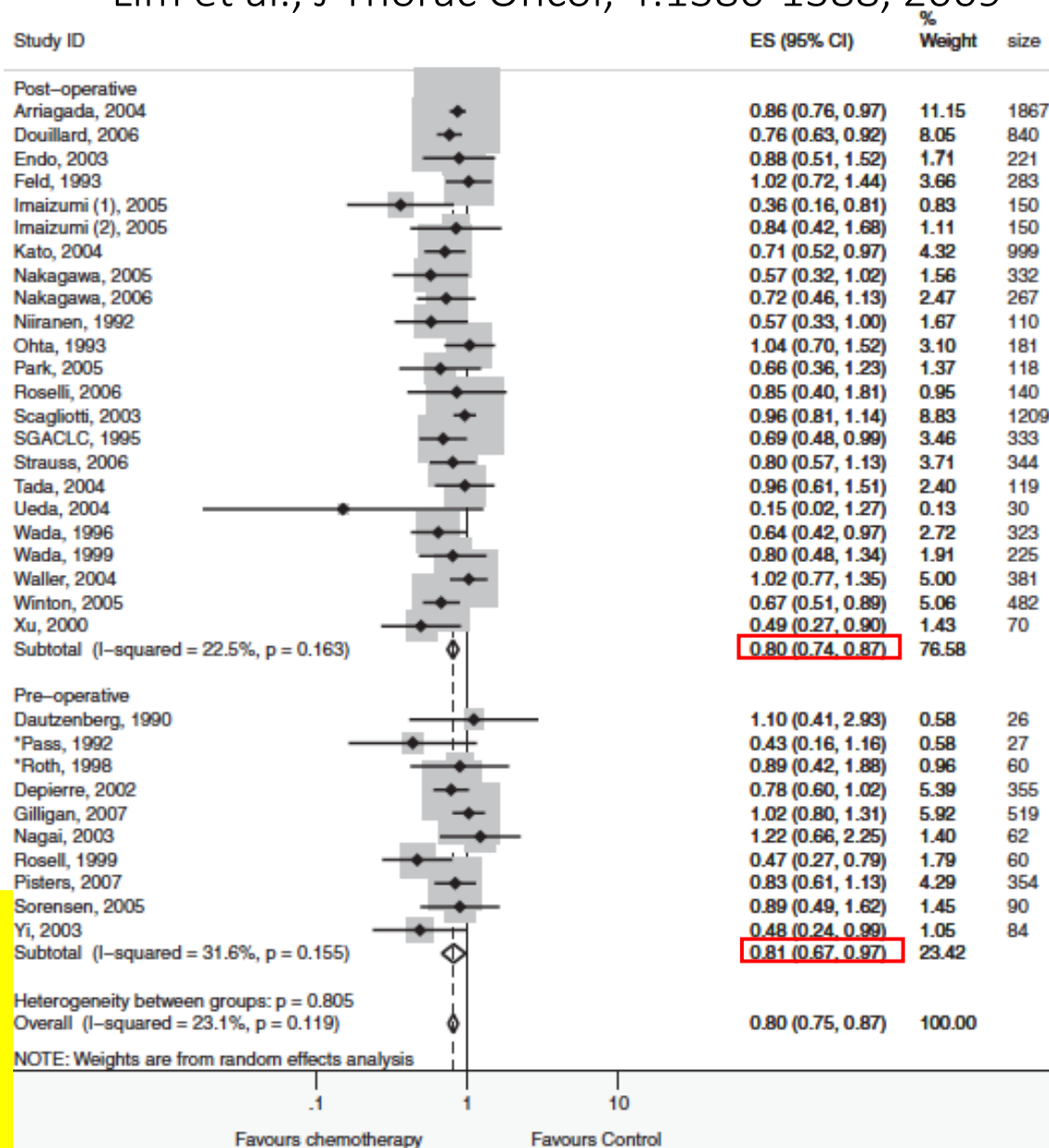


12/24 included N2



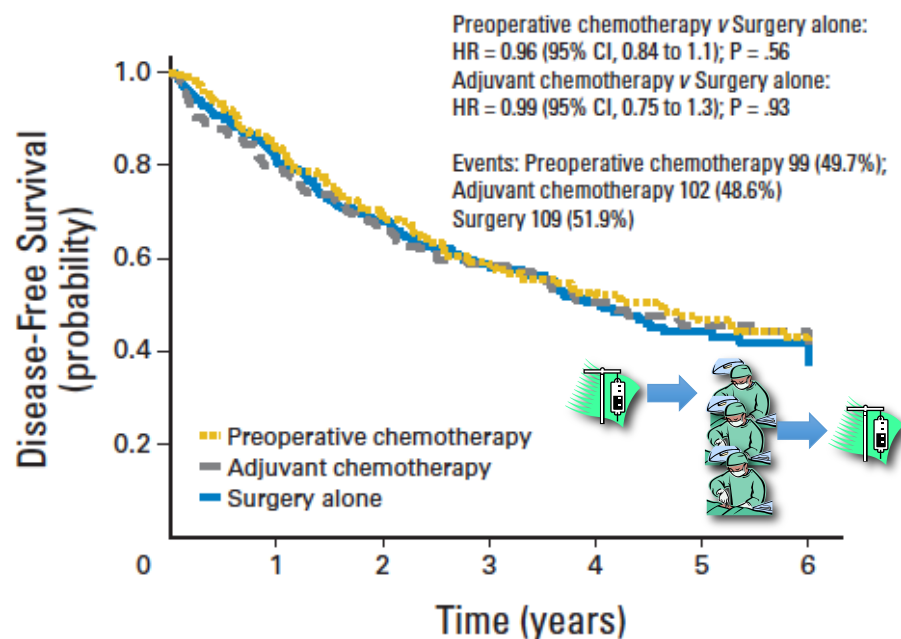
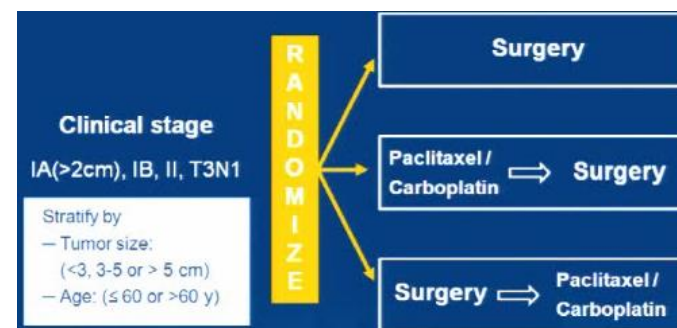
10/10 included N2

Conclusions: the relative hazards of postoperative compared with preoperative chemotherapy was 0.99 (0.81–1.21;  $p = 0.91$ ).  
In patients with resectable lung cancer, there was no evidence of a difference OS and DFS between postoperative versus preoperative CTx



# Preoperative Chemotherapy Plus Surgery Versus Surgery Plus Adjuvant Chemotherapy Versus Surgery Alone in Early-Stage Non-Small-Cell Lung Cancer

Enriqueta Felip, Rafael Rosell, José Antonio Maestre, José Manuel Rodríguez-Pantigua, Teresa Morán, Julio Astudillo, Guillermo Alonso, José Manuel Borro, José Luis González-Larriba, Antonio Torres, Carlos Camps, Ricardo Gutiérrez, Dolores Isla, Rafael Aguiló, Vicente Alberola, José Padilla, Abel Sánchez-Palencia, José Javier Sánchez, Eduardo Hermosilla, and Bartomeu Massut



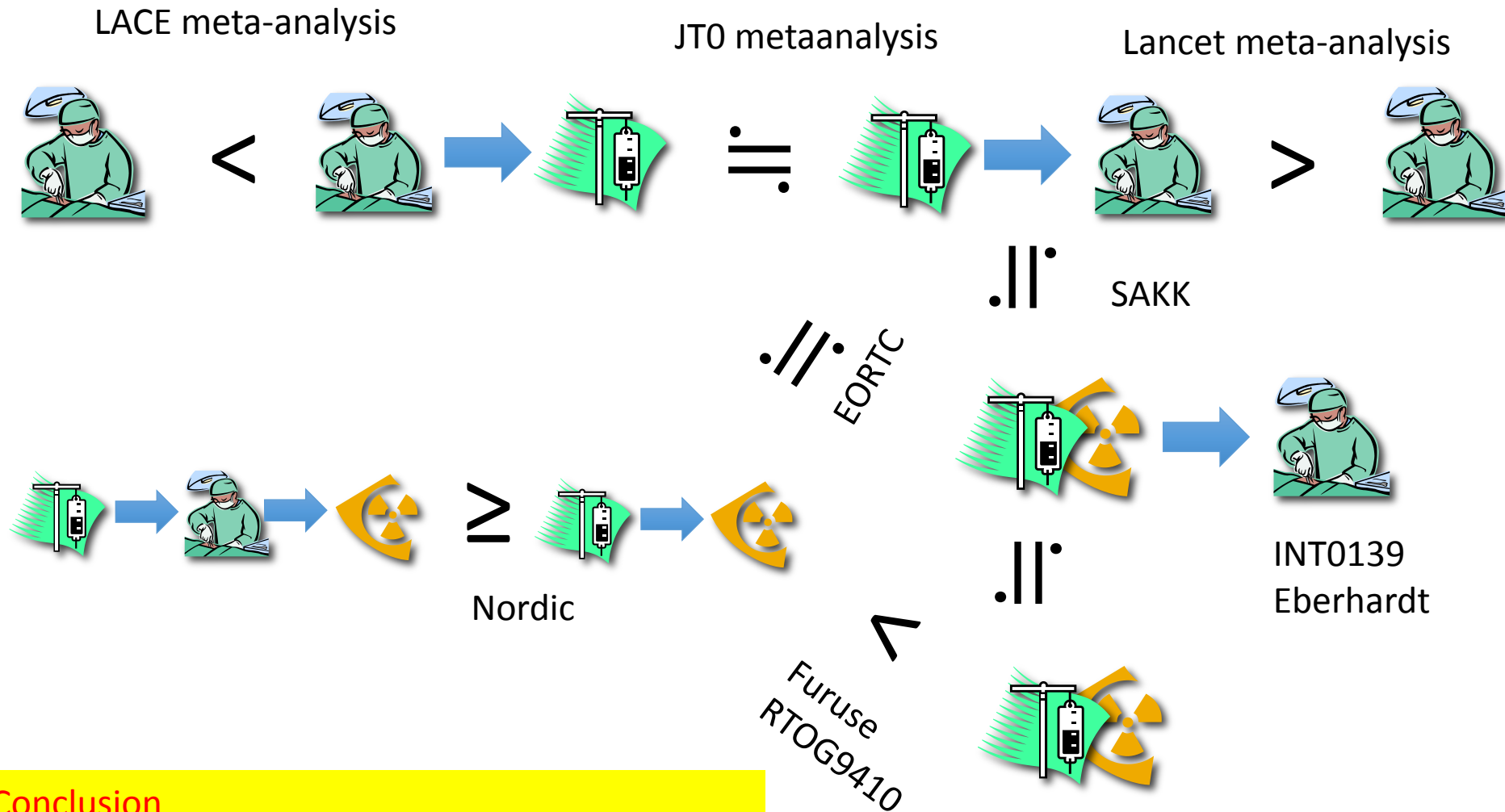
No. at risk						
Preoperative	165	131	99	71	45	31
Adjuvant	161	121	90	65	40	29
Surgery	168	131	105	72	40	27

624 patients with stage IA (tumor size 2 cm), IB, II

In early-stage patients, no statistically significant differences in disease-free survival were found with the addition of preoperative or adjuvant chemotherapy to surgery. ;

# Summary...

## Peri-operative chemo/radiotherapy for N2 disease



### Conclusion

Something is better than nothing !?

However N2 is very heterogeneous...

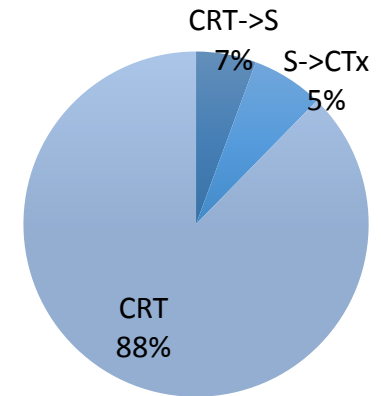
Patient subsets between the trials are not same

# Clinical practice?

# Improved Survival Associated with Neoadjuvant Chemoradiation in Patients with Clinical Stage IIIA(N2) Non-Small-Cell Lung Cancer

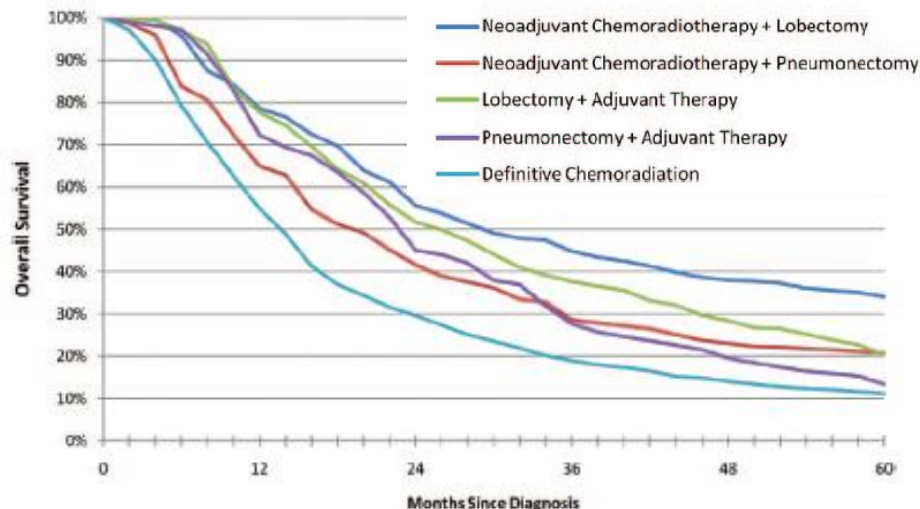
Matthew Koshy, MD,\*† Stacey A. Fedewa, MPH,‡ Renu Malik, MD,† Mark K. Ferguson, MD,§¶  
Wickii T. Vigneswaran, MD,§ Lawrence Feldman, MD,|| Andrew Howard, MD,\*† Khaled Abdelhady, MD,#  
Ralph R. Weichselbaum, MD,\*† and Katherine S. Virgo, PhD, MBA‡\*\*\*

*Journal of Thoracic Oncology® • Volume 8, Number 7, July 2013*



**TABLE 1.** Patient, Facility and Area-Level Characteristics by Treatment Type among Clinical Stage IIIA-N2 Non-Small-Cell Lung Cancer Patients, National Cancer Database (NCDB) 1998–2004

Categories	Total	Neoadjuvant Chemoradiotherapy + Lobectomy	Neoadjuvant Chemoradiotherapy + Pneumonectomy	Lobectomy + Adjuvant Therapy	Pneumonectomy + Adjuvant Therapy	Definitive Concurrent Chemoradiotherapy	p
	N = 11242	n = 564	n = 188	n = 510	n = 123	n = 9857	
	%	(4.94)	(1.65)	(4.46)	(1.08)	(86.28)	



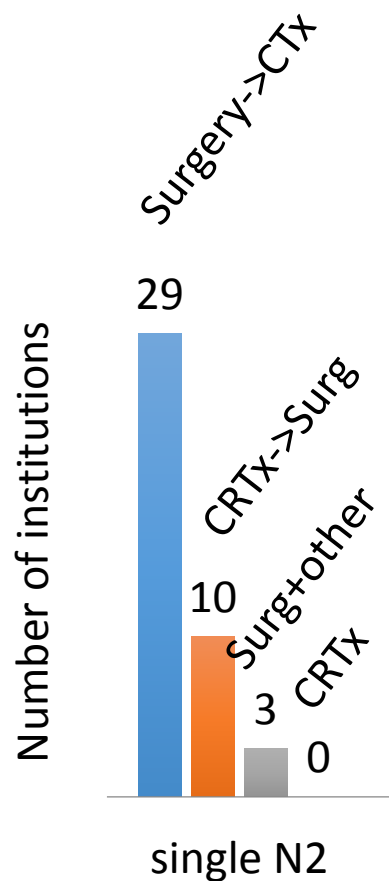
**TABLE 2.** Multivariate Cox Proportional Hazard Models Predicting 5-year Overall Survival among Clinical Stage IIIA-N2 NSCLC Patients, NCDB 1998–2004 (n = 10,058)

Parameter	5-Year Survival <sup>a,b</sup>	
	HR	95% CI
<b>Treatment</b>		
Definitive chemoradiation	1.00	
Neoadjuvant chemoradiotherapy + lobectomy	0.51	(0.45–0.58)
Neoadjuvant chemoradiotherapy + pneumonectomy	0.77	(0.63–0.95)
Lobectomy + adjuvant therapy	0.66	(0.59–0.75)
Pneumonectomy + adjuvant therapy	0.69	(0.54–0.88)

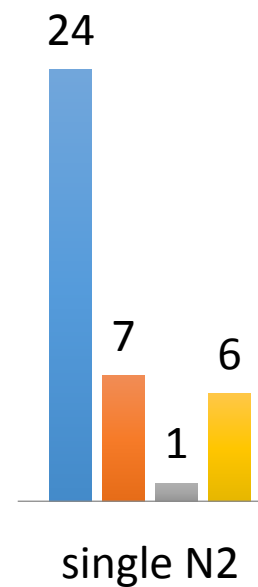


# Questionnaire survey by JCOG lung cancer surgical group (Sep, 2013)

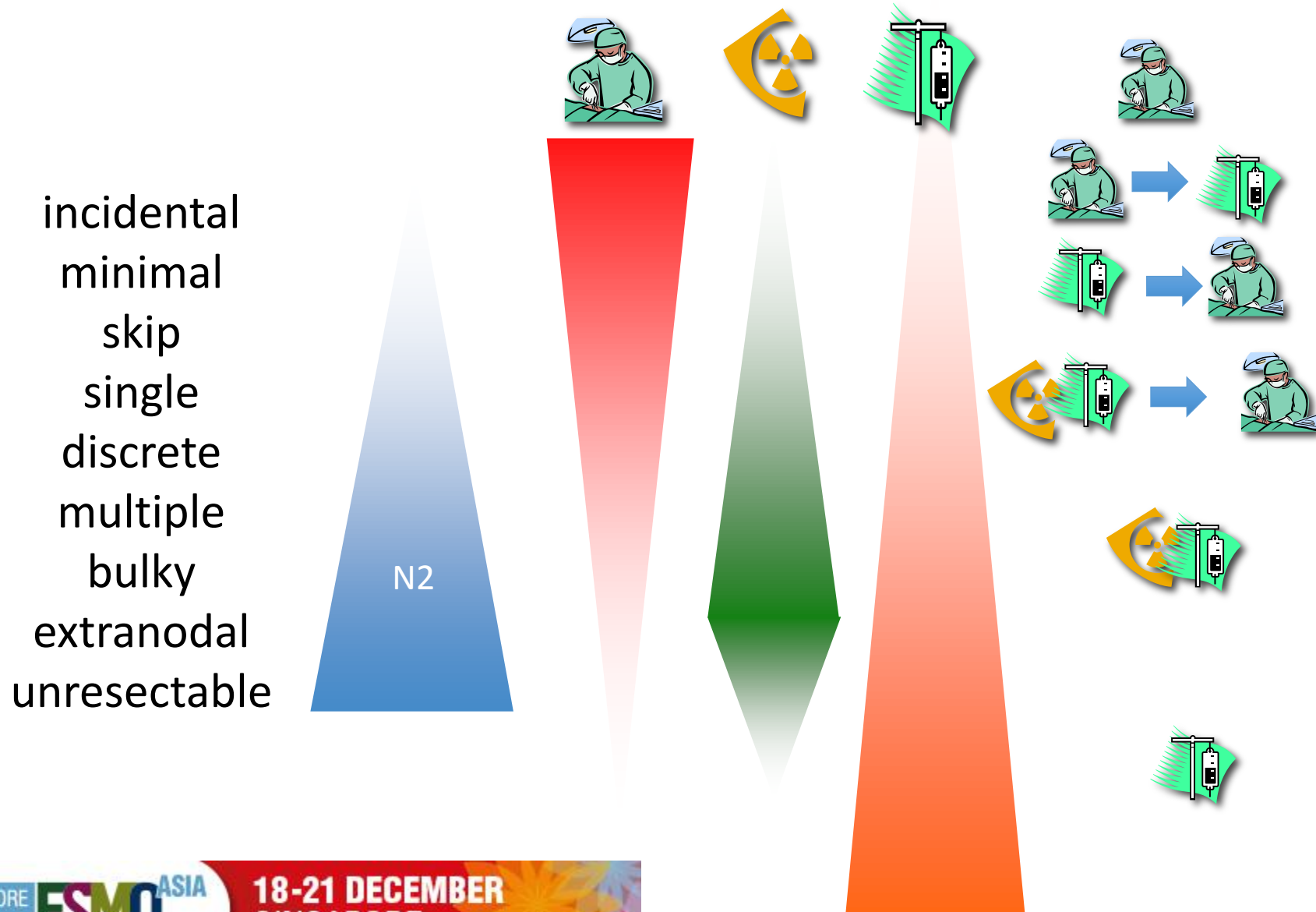
Surgeons



Medical Oncologist



# Treatment decision in the continuum of N2 disease



## 2nd ESMO Consensus Conference in Lung Cancer: locally advanced stage III non-small-cell lung cancer

W. E. E. Eberhardt<sup>1</sup>, D. De Ruyscher<sup>2</sup>, W. Weder<sup>3</sup>, C. Le Péchoux<sup>4</sup>, P. De Leyn<sup>5</sup>, H. Hoffmann<sup>6</sup>,  
V. Westeel<sup>7</sup>, R. Stahel<sup>8</sup>, E. Felip<sup>9</sup>, S. Peters<sup>10</sup> & Panel Members<sup>†</sup>



# CHEST

Supplement

DIAGNOSIS AND MANAGEMENT OF LUNG CANCER, 3RD ED: ACCP GUIDELINES

## Treatment of Stage III Non-small Cell Lung Cancer

Diagnosis and Management of Lung Cancer,  
3rd ed: American College of Chest Physicians  
Evidence-Based Clinical Practice Guidelines

Nithya Ramnath, MD; Thomas J. Dilling, MD; Loren J. Harris, MD, FCCP;  
Anthony W. Kim, MD, FCCP; Gaetane C. Michaud, MD, FCCP;  
Alex A. Balekian, MD, MSHS; Rebecca Diekemper, MPH;  
Frank C. Detterbeck, MD, FCCP; and Douglas A. Arenberg, MD, FCCP

## potentially resectable IIIA(N2) disease

### *preoperative diagnosis of IIIA(N2)*

*Recommendation 4.2.1: Possible strategies include several options: induction chemotherapy followed by surgery, induction chemoradiotherapy followed by surgery, or concurrent definitive chemoradiotherapy [I, A]. No recommendation can yet be made; however, an experienced multidisciplinary team is of paramount importance in any complex multi-modality treatment strategy decision. If induction chemotherapy alone is given preoperatively, post-operative radiotherapy is not standard treatment but may be an option based on critical evaluation of locoregional relapse risks [IV, C].*

**3.5.1. In patients with discrete N2 involvement by NSCLC identified preoperatively (IIIA), it is recommended that the treatment plan should be made with the input from a multidisciplinary team (Grade 1C).**

# Acknowledgments

Dr. Kenji Sugio, Oita University

Dr. Ichiro Yoshino, Chiba University

De. Hidehito Horinouchi, National Cancer Center, Tokyo