

16th
CONGRESS
Lung **ON**
CANCER

BARCELONA
27 / 28
NOVEMBER 2025

LYMPH NODE MANAGEMENT IN THE Ch-IO ERA

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Spanish Regent in European Society of Thoracic Surgery (ESTS)
International Relations Representative of Spanish Society of Thoracic Surgery (SECT)
Editor of Video-Atlas of VATS Sublobar Resections



CONFLICT OF INTEREST



- Advisory: Astrazeneca, Touch Surgery (Medtronic)
- Proctorship: Medtronic
- Lectures and travels: Medtronic, Johnson&Johnson, Aldimesa, Acuña Fombona, Rivolution GmbH, Meril, BMS, Intuitive.
- Autorship: Video-Atlas of VATS Pulmonary Sublobar Resections (Springer)

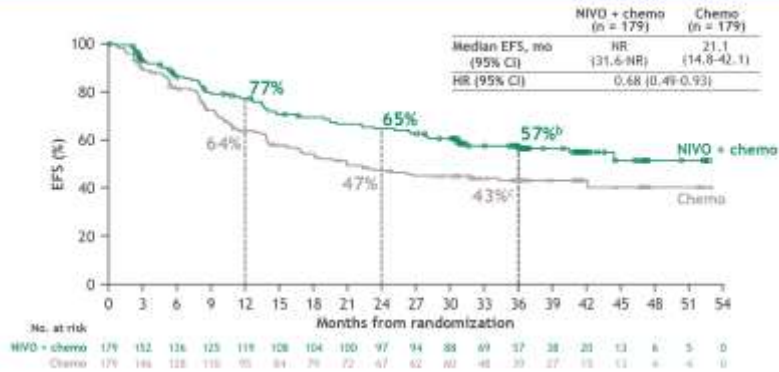
Induction Ch-IO provides better EFS

CheckMate816

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

P.M. Forde, J. Spicer, S. Lu, M. Provencio, T. Mitsudomi, M.M. Awad, E. Felip, S.R. Broderick, J.R. Brahmer, S.J. Swanson, K. Kerr, C. Wang, T.-E. Culeanu, G.B. Saylor, F. Tanaka, H. Ito, K.-N. Chen, M. Liberman, E.E. Vokes, J.M. Taube, C. Dorange, J. Cal, J. Fiore, A. Jarkowski, D. Balli, M. Sausen, D. Pandya, C.Y. Calvet, and N. Girard, for the CheckMate 816 Investigators*

EFS with neoadjuvant NIVO + chemo vs chemo: 3-year update*

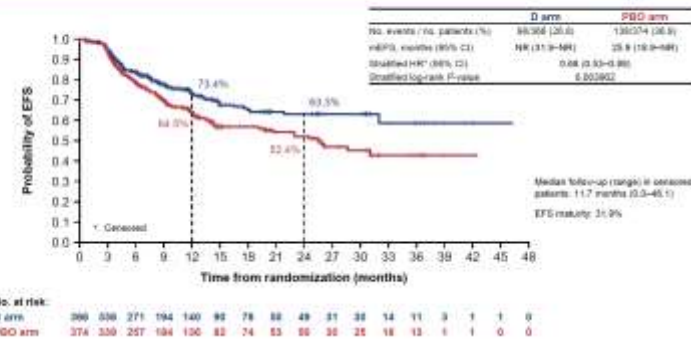


AEGEAN

Perioperative Durvalumab for Resectable Non-Small-Cell Lung Cancer

J.V. Heymach, D. Hargak, T. Mitsudomi, J.M. Taube, G. Calif, M. Hochman, T. Winder, B. Zukow, C. Carlson, S. Gan, H. Kurada, C. Ohtsuka, T.M. Tran, J. Yoo, K.-T. Im, J. Antonuzzi, Z. Papp, G. Golecki, H. Akamatsu, S. Bressan, A. Sprinz, J. Crawford, M.T. Sa, M. Apantaku, G.J. Dalbey, H. Stern, T.M. Fouad, and M. Reck, for the AEGEAN Investigators*

EFS using RECIST v1.1 (BICR) (mITT) First planned interim analysis of EFS

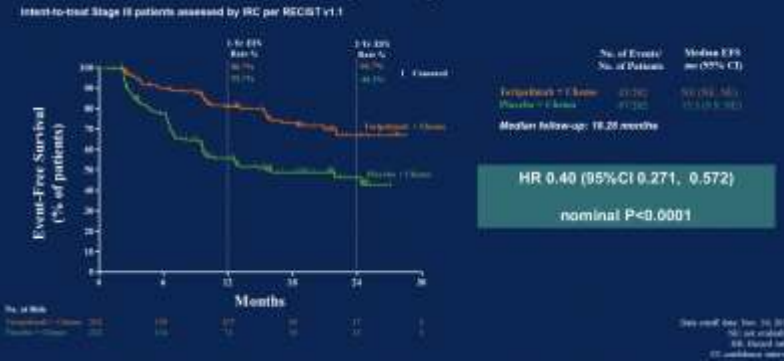


NEOTORCH

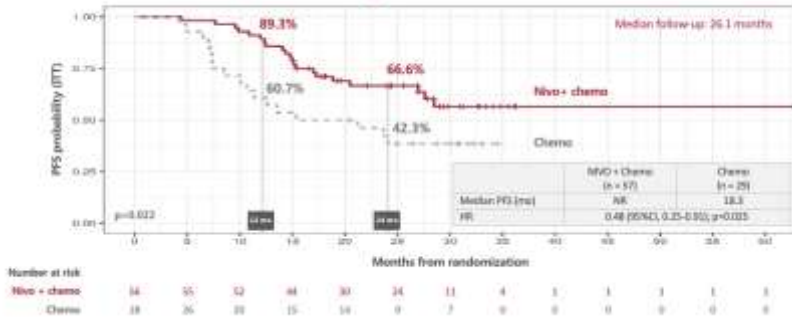
Perioperative Toripalimab Plus Chemotherapy for Patients With Resectable Non-Small Cell Lung Cancer The Neotorch Randomized Clinical Trial

Wenbiao Mo, Wei Zhang, Ping Li, Yan Peng, Peng Zhang, Peng Zhang, Peng Zhang, and the Neotorch Investigators*

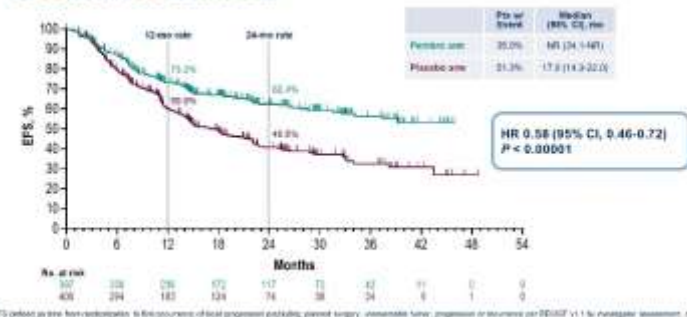
Event-Free Survival Analysis by IRC



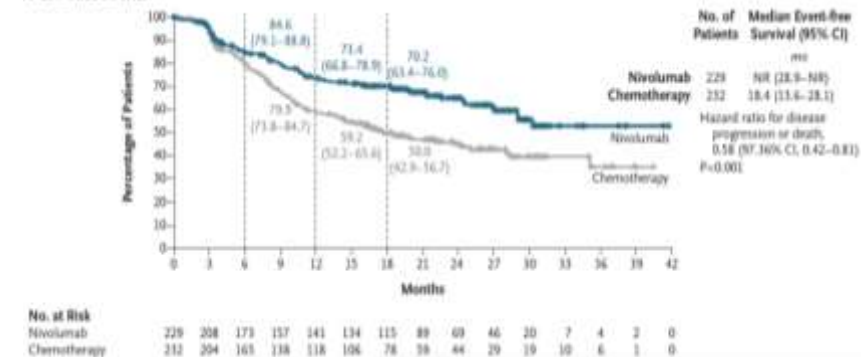
SECONDARY ENDPOINTS – Progression-free survival



Event-Free Survival



A Event-free Survival



NADIM 2

Perioperative Nivolumab and Chemotherapy in Stage III Non-Small-Cell Lung Cancer

M. Provencio, E. Hjalte, J.L. Gonzalez Garcia, A. Martinez-Marti, R. Bernabé, J. Bosch-Barrera, J. Catal-Rubio, V. Calvo, A. Ima, S. Ponce, R. Reguart, J. de Castro, J. Mosquera, M. Cobos, A. Aguiló, C. Lopez-Vivanco, C. Camps, R. López-Castro, T. Mosquera, I. Barrios, D. Rodríguez-Alonso, E. Serra-Rosell, R. Barrios, C. Aguado de la Rosa, R. Palmero, F. Hernández-Trancho, J. Martín-López, D. Bernárdes, S. Masot, and A. Barrios

Keynote671

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

H. Wakelee, M. Lippman, T. Kubo, M. Tachibana, S. H. Lee, S. Gan, C.-R. Chen, C. Doonan, M. Miyazaki, E. Eggebo, G.L. Marshall, D. Bellizzi, D. Rodriguez-Alonso, J. Chab, S. Sawada, J. Yang, S.M. Taylor, A. Santoni, and J.C. Sprinz, for the KEYNOTE-671 Investigators*

CheckMate 77T

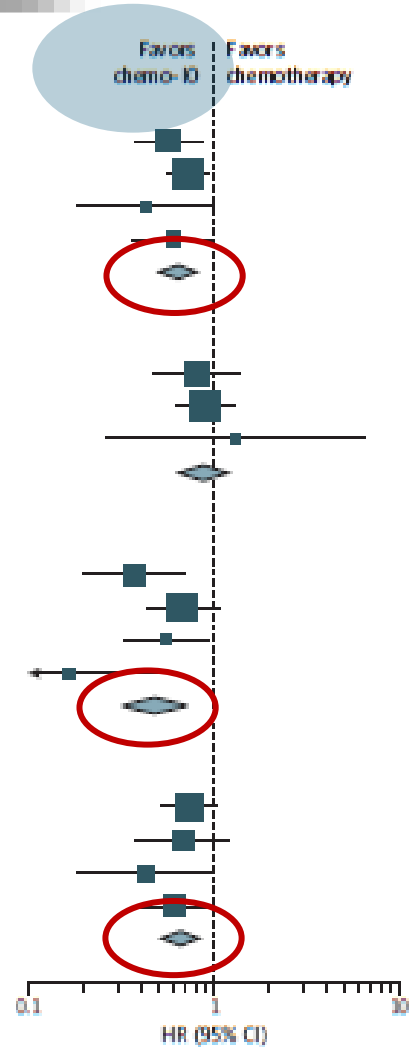
Perioperative Nivolumab in Resectable Lung Cancer

T. Cassaro, M.M. Awad, J.D. Spicer, J. Ho, S. Lu, B. Sapiro, F. Tanaka, J.M. Taube, B. Camilleri, L. Wang, N. Karimova, J. Kuznetsov, L.B. Petruzzella, L. Wu, J.-I. Fujita, H. Ito, T.-E. Culeanu, L. de Oliveira Moura-Roch, A. Jankovic, A. Alcantara, S. Barlow, T.V. Mousavizadeh, Y. Guo, Y. Wu, C. Comandini Edelman, P. Sathyanarayanan, S. Shrestha, Shreyashris, S.I. Barlow, and M. Provencio-Puig, for the CheckMate 77T Investigators*

OS data in Chemo-Immuno trials



Study	Patients, No.		HR (95% CI)
	Chemo-IO	Chemotherapy	
All patients			
Forde et al, ⁸ 2022; Forde et al, ^{9,4} 2023; Provencio Pulla et al, ⁶⁵ 2023; Provencio Pulla et al, ⁶⁶ 2023	179	179	0.57 (0.38-0.87)
Wakelee et al, ¹⁰ 2023; Spicer et al, ¹¹ 2023; Spicer et al, ^{6,7} 2023	397	400	0.72 (0.56-0.93)
Provencio et al, ⁷¹ 2023	57	29	0.43 (0.19-0.98)
Lu et al, ⁶⁷ 2023; Lu et al, ⁶⁸ 2023	202	202	0.62 (0.38-1.00)
Random-effects model	835	810	0.65 (0.54-0.79)
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0.1$; $P = .57$			
PD-L1 <1%			
Forde et al, ⁸ 2022; Forde et al, ^{9,4} 2023; Provencio Pulla et al, ⁶⁵ 2023; Provencio Pulla et al, ⁶⁶ 2023	78	77	0.81 (0.48-1.36)
Wakelee et al, ¹⁰ 2023; Spicer et al, ¹¹ 2023; Spicer et al, ^{6,7} 2023	138	151	0.91 (0.63-1.32)
Provencio et al, ⁷¹ 2023	20	8	1.31 (0.27-6.41)
Random-effects model	236	236	0.89 (0.66-1.19)
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0.1$; $P = .83$			
PD-L1 ≥1%			
Forde et al, ⁸ 2022; Forde et al, ^{9,4} 2023; Provencio Pulla et al, ⁶⁵ 2023; Provencio Pulla et al, ⁶⁶ 2023	89	89	0.38 (0.20-0.71)
Wakelee et al, ¹⁰ 2023; Spicer et al, ¹¹ 2023; Spicer et al, ^{6,7} 2023 ^a	127	115	0.69 (0.44-1.07)
Wakelee et al, ¹⁰ 2023; Spicer et al, ¹¹ 2023; Spicer et al, ^{6,7} 2023 ^b	132	134	0.55 (0.33-0.93)
Provencio et al, ⁷¹ 2023	30	15	0.17 (0.05-0.57)
Random-effects model	378	353	0.49 (0.33-0.73)
Heterogeneity: $I^2 = 48.5\%$; $\tau^2 = 0.1$; $P = .12$			
Stage III			
Wakelee et al, ¹⁰ 2023; Spicer et al, ¹¹ 2023; Spicer et al, ^{6,7} 2023 ^c	217	224	0.74 (0.53-1.03)
Wakelee et al, ¹⁰ 2023; Spicer et al, ¹¹ 2023; Spicer et al, ^{6,7} 2023 ^d	62	55	0.69 (0.39-1.22)
Provencio et al, ⁷¹ 2023	57	29	0.43 (0.19-0.98)
Lu et al, ⁶⁷ 2023; Lu et al, ⁶⁸ 2023	202	202	0.62 (0.38-1.00)
Random-effects model	538	510	0.67 (0.53-0.85)
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0.1$; $P = .67$			



Better OS in all patients, PD-L1>1% and stage III with chemo-IO compared to conventional chemo

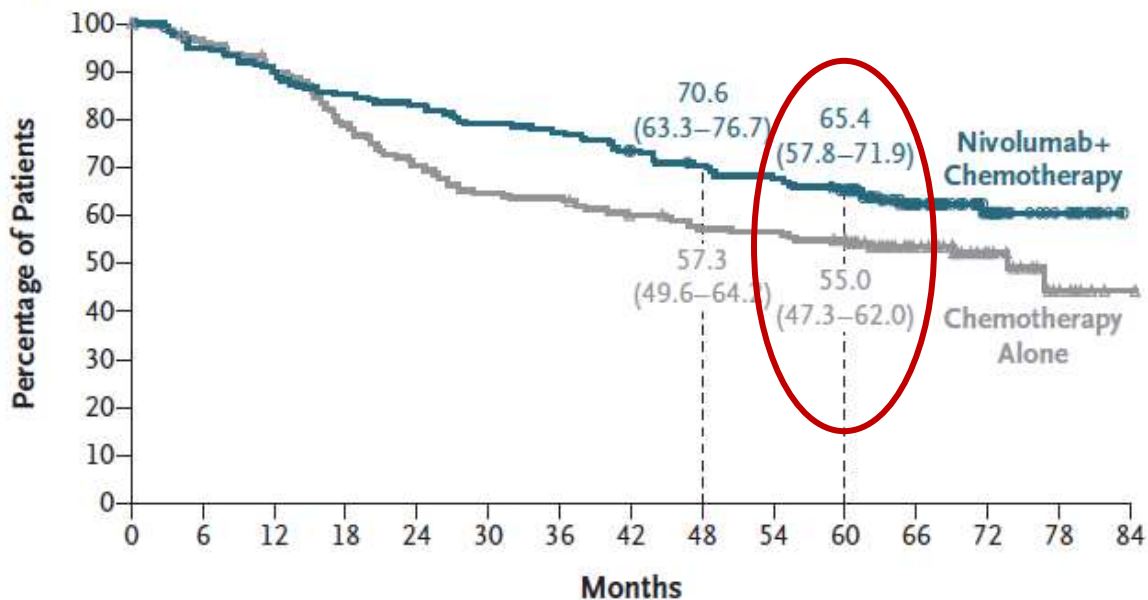
Overall Survival with Neoadjuvant Nivolumab plus Chemotherapy in Lung Cancer



Patrick M. Forde, M.B., B.Ch., Ph.D.,¹ Jonathan D. Spicer, M.D., Ph.D.,⁴ Mariano Provencio, M.D., Ph.D.,³ Tetsuya Mitsudomi, M.D., Ph.D.,² Mark M. Awad, M.D., Ph.D.,² Changli Wang, M.D.,² Shun Lu, M.D., Ph.D.,² Enriqueta Felip, M.D., Ph.D.,² Scott J. Swanson, M.D.,² Julie R. Brahmer, M.D.,¹⁰ Keith Kerr, M.B., Ch.B.,¹¹ Janis M. Taube, M.D.,¹² Tudor-Eliade Ciuleanu, M.D., Ph.D.,¹³ Fumihiko Tanaka, M.D., Ph.D.,¹⁴ Gene B. Saylor, M.D.,¹⁵ Ke-Neng Chen, M.D., Ph.D.,¹⁶ Hiroyuki Ito, M.D., Ph.D.,¹⁷ Moishe Liberman, M.D., Ph.D.,¹⁸ Claudio Martin, M.D.,¹⁹ Stephen Broderick, M.D.,²⁰ Lily Wang, M.D.,²¹ Junliang Cai, M.D.,²² Quyen Duong, Ph.D.,²³ Stephanie Meadows-Shropshire, Ph.D.,²⁴ Joseph Fiore, Pharm.D.,²⁵ Sumeena Bhatia, Ph.D.,²⁶ and Nicolas Girard, M.D., Ph.D.,¹¹ for the CheckMate 816 Investigators⁴

CheckMate816

A Overall Survival



	Median Overall Survival (95% CI) mo
Nivolumab+Chemotherapy (N=179)	NR (NR-NR)
Chemotherapy Alone (N=179)	73.7 (47.3-NR)

Hazard ratio for death, 0.72 (95% CI, 0.523-0.998)
P=0.048

No. at Risk

Nivolumab+chemo-therapy	179	168	159	151	147	140	137	129	122	117	111	67	29	9	0
Chemotherapy alone	179	170	159	139	124	114	112	104	98	97	91	58	29	6	1

Earliest data from phase III RCT shows 5y-OS benefit from Ch-IO

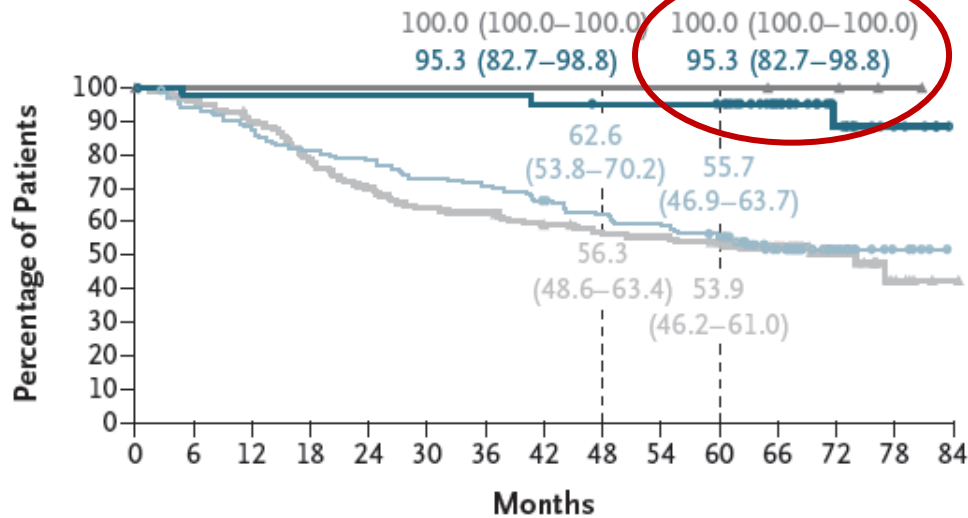
Overall Survival with Neoadjuvant Nivolumab plus Chemotherapy in Lung Cancer



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CheckMate816

Overall Survival in Patients with or without a Pathological Complete Response (pCR)



Median Overall Survival (95% CI) mo

Nivolumab+Chemotherapy

— pCR (N=43) NR (NR–NR)
 — No pCR (N=136) NR (53.9–NR)

Hazard ratio for death, 0.11 (0.04–0.36)

Chemotherapy Alone

— pCR (N=4) NR (NR–NR)
 — No pCR (N=175) 73.7 (46.7–NR)

No. at Risk

Pathological complete response

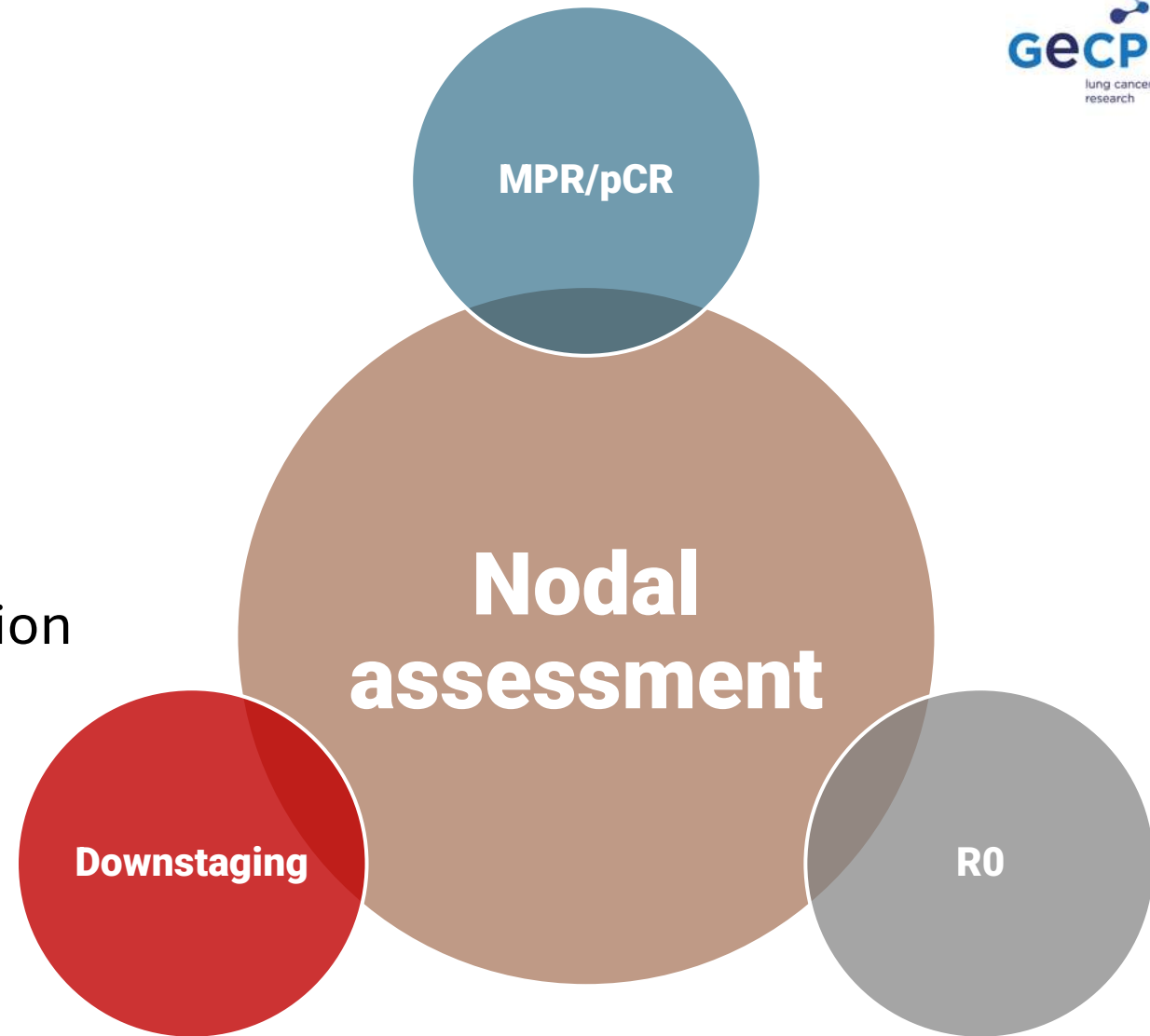
Nivolumab+chemotherapy	43	42	42	42	42	42	42	41	40	40	39	25	13	4	0
Chemotherapy alone	4	4	4	4	4	4	4	4	4	4	4	3	3	1	0

No pathological complete response

Nivolumab+chemotherapy	136	126	117	109	105	98	95	88	82	77	72	42	16	5	0
Chemotherapy alone	175	166	155	135	120	110	108	100	94	93	87	55	26	5	1

When there is no residual disease regardless of the treatment, patients live longer

- Main goals are EFS and OS
- Predictors:
 - Pathological response (MPR, pCR)
 - Downstaging
 - R0
- All these predictors require LN evaluation
 - Quality
 - Accomplishment



“In the absence of distant metastasis, nodal involvement leads prognosis”

Rami-Porta, R. 2021

- What has been done on RCT's?
- Why is LN evaluation important?
- Extent of LN evaluation



- What has been done on RCT's?
- Why is LN evaluation important?
- Extent of LN evaluation



Study (year)	n	cTNM	Response assesment	INVASIVE Restaging LN's
CheckMate816 (2022)	35 8	IB-III A	PET/CT within 7d prior to surgery (RECIST v1.1)	None
CTONG1103 (2022)	72	III A N2	Chest-enhanced CT scan or PET/CT (RECIST v1.1)	None
AEGEAN (2023)	80 2	II-III B	Chest-enhanced CT scan or PET/CT (RECIST v1.1)	Only if radiological progression suggesting pseudoprogression or NIF

DECISION WHETHER PROCEEDING TO SURGERY HAS BEEN BASED ON IMAGING CRITERIA (RECIST)

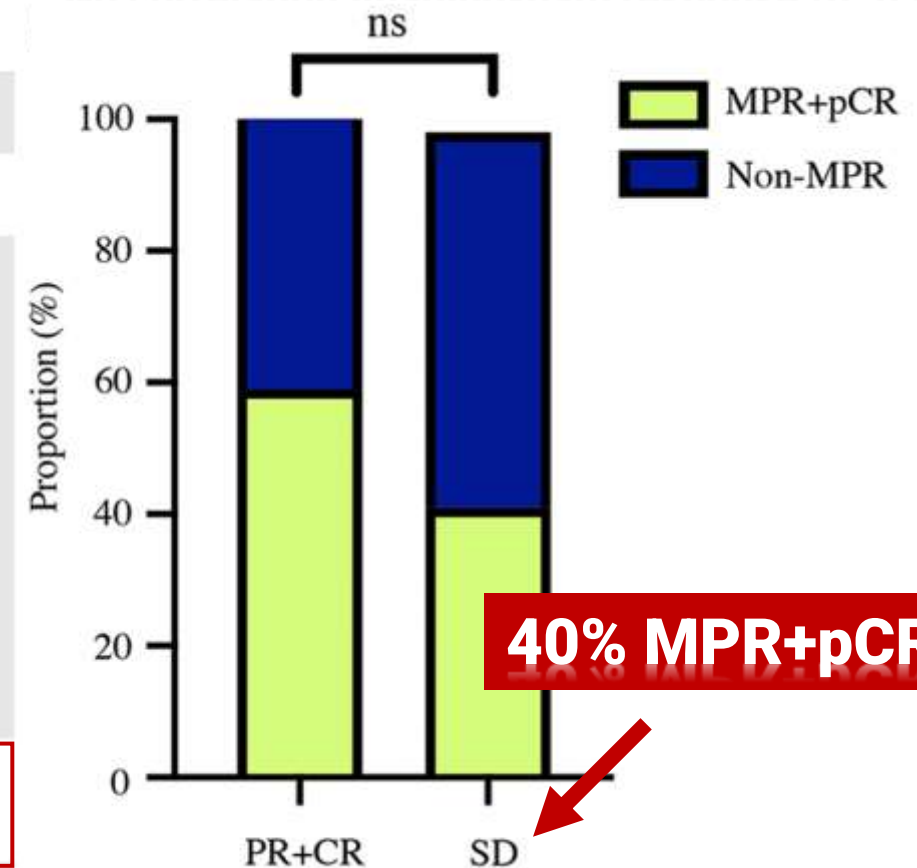
			(RECIST v1.1)	
NEOSTAR (2023)	42	IB-III A	Chest-enhanced CT scan or PET/CT (RECIST v1.1)	None
Keynote 671 (2023)	79 7	II-III B	Chest-enhanced CT scan or PET/CT (RECIST v1.1)	None
Neotorch (2024)	40 4	II A-III B	Chest-enhanced CT scan or PET/CT (RECIST v1.1)	None

Rui Han¹ | Yimin Zhang¹ | Tianhu Wang² | Huallang Xiao¹ | Zhilin Luo² | Cheng Shen³ | Jianghua Li¹ | Chenglong Zhao¹ | Li Li¹ | Mengxiao Zhu¹ | Haiwei Du⁴ | Huan Tang¹ | Zheng Ma⁵ | Yubo Wang¹ | Yong He¹

TABLE 1 Characteristics of NSCLC patients with major, complete, and non-major pathological response to neoadjuvant immunotherapy.

Characteristics	Category	Pathological response (pCR, N = 12)	Major pathological response (MPR, N = 4)	Non-MPR (N = 13)	p-value
Age (years)	Median (IQR)	62.50 (59.25, 65.00)	67.50 (66.00, 71.25)	63.00 (57.00, 65.50)	0.058
Gender, n (%)	Male	10 (83.3%)	2 (50%)	9 (69.2%)	0.472
	Female	2 (16.4%)	2 (50%)	4 (30.8%)	
Smoking status, n (%)	Former or current	10 (83.3%)	2 (50%)	9 (69.2%)	0.472
	Never	2 (16.4%)	2 (50%)	4 (30.8)	
Histology, n (%)	Squamous	8 (66.6%)	1 (25%)	10 (76.9%)	0.181
	Adenocarcinoma	4 (33.4%)	3 (75%)	3 (23.1%)	
Stage, n (%)	III	8 (66.6%)	2 (50%)	13 (100%)	0.017
	IV	4 (33.4%)	2 (50%)	0	
Neoadjuvant immunotherapy, n (%)	Pembrolizumab combined with Pemetrexed + Lobaplatin	2 (16.4%)	1 (25%)	0	0.001
	Pembrolizumab combined with Taxol + Lobaplatin	1 (8.3%)	1 (25%)	1 (7.7%)	
	Nivolumab combined with Taxol + Lobaplatin	5 (41.7%)	0	0	
	Sintilimab combined with Taxol + Lobaplatin	1 (8.3%)	0	7 (53.8%)	
	Sintilimab combined with Pemetrexed + Lobaplatin	0	1 (25%)	2 (15.4%)	
	Tislelizumab combined with Pemetrexed + Lobaplatin	0	1 (25%)	0	
	Tislelizumab combined with Taxol + Lobaplatin	3 (25%)	0	3 (23.1%)	
Radiological response, n (%)	PR	9 (75%)	3 (75%)	9 (69.2%)	0.97
	SD	3 (25%)	0	4 (30.8%)	
	CR	0	1 (25%)	0	
Treatment cycles, n (%)	<4	4 (33.4%)	1 (25%)	7 (53.8%)	0.511
	≥4	8 (66.6%)	3 (75%)	6 (46.2%)	

No correlation imaging-path response (p=0.667)



With RECIST, we can be missing responders

Association between pathologic response and survival after neoadjuvant therapy in lung cancer

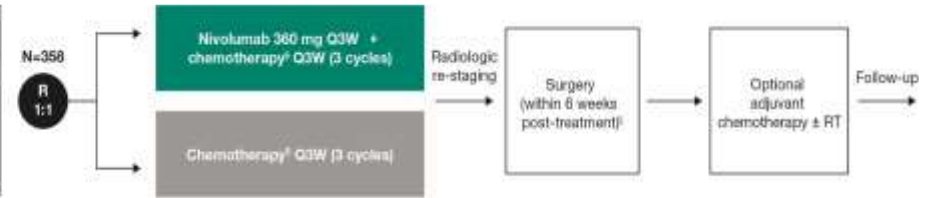


CheckMate816

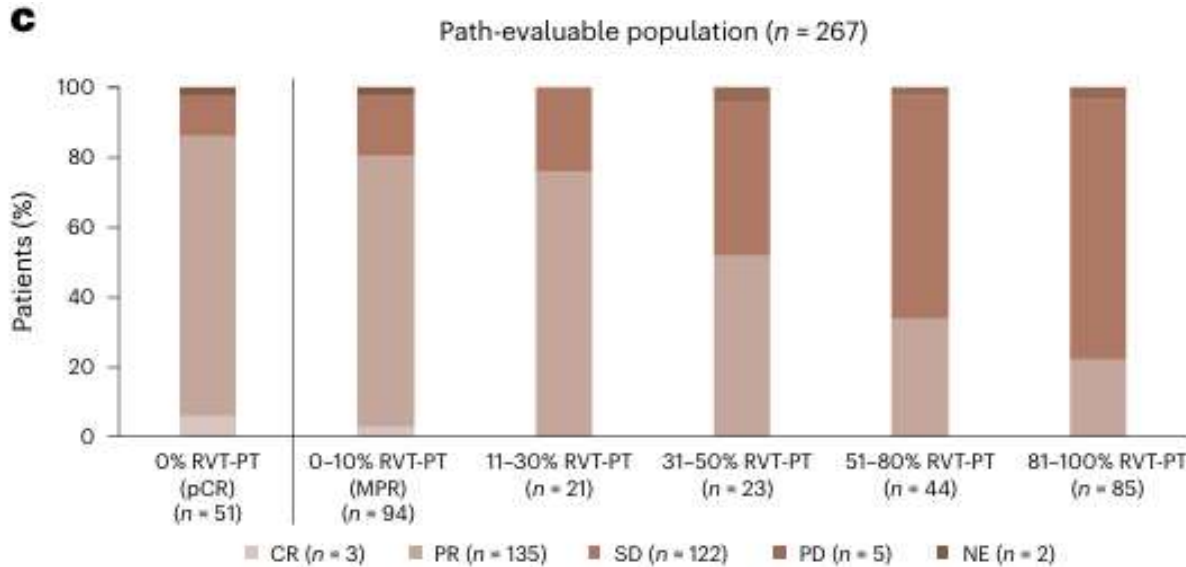
Key Eligibility Criteria

- Newly diagnosed, resectable, stage IB (≥ 4 cm)-IIIA NSCLC (per TNM 7th edition)
- ECOG PS 0-1
- No known sensitizing EGFR mutations or ALK alterations

Stratified by stage (IB/II vs. IIIA), PD-L1[†] (≥1% vs. <1%), and sex



RECIST



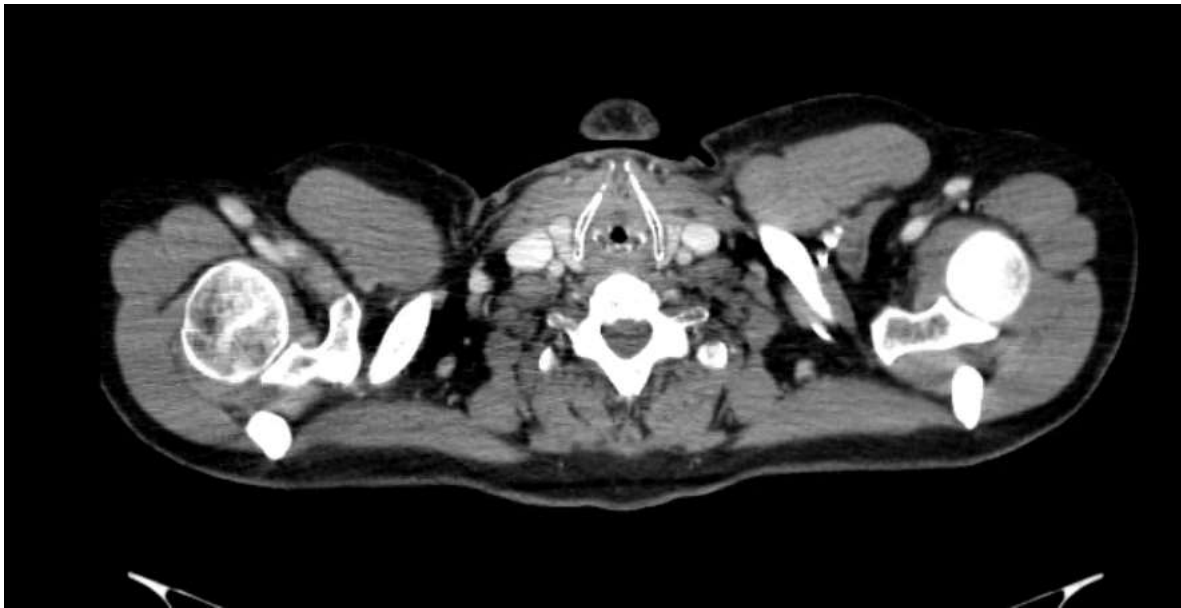
Survival surrogate	No.	HR (EFS)	95% CI
Radiographic response by RECIST1.1: responders versus nonresponders ^c	84 (responders) 56 (nonresponders)	0.32	0.17-0.58
Pathologic response: pCR-PT versus no pCR-PT ^d	46 (pCR-PT) 95 (no pCR-PT)	0.18	0.07-0.46
Pathologic response: MPR-PT versus no MPR-PT	72 (MPR-PT) 69 (no MPR-PT)	0.26	0.14-0.50
Each additional 1% increase in %RVT-PT as a continuous variable	141	1.017	1.010-1.025
ctDNA clearance ^e : with versus without ctDNA CL	17 (with ctDNA CL) 16 (without ctDNA CL)	0.66	0.26-1.67

Pathological response better predicted EFS than RECIST

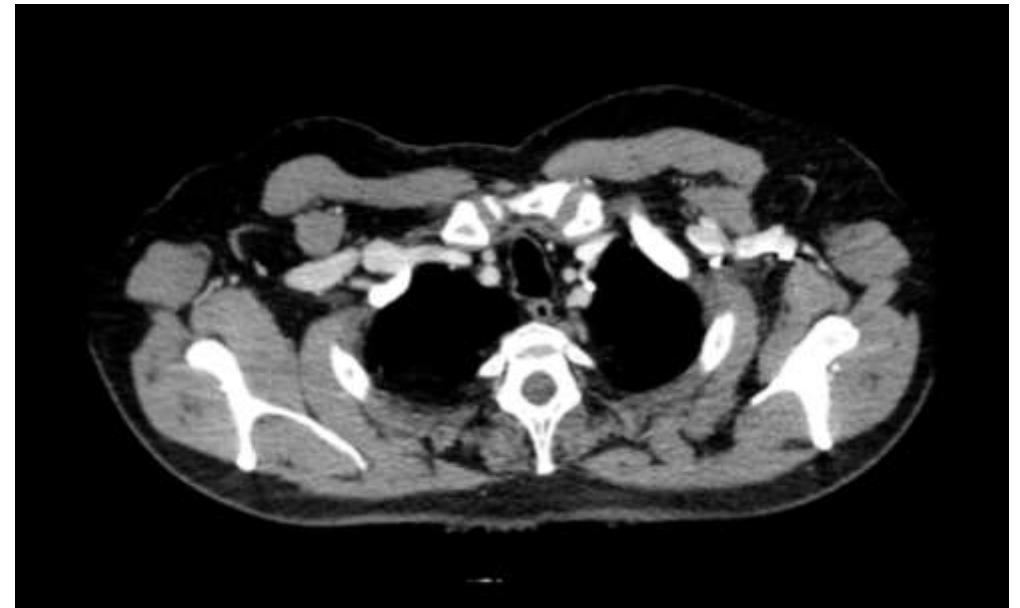
- LLL cT1bN1 ADC (EBUS #7 neg, #11 pos) – *3 cycles Carbo-Paclitaxel-Nivolumab*
- Restaging: **SD RECIST** (no suspicion of N2 involvement)

Ch-IO → Surgery

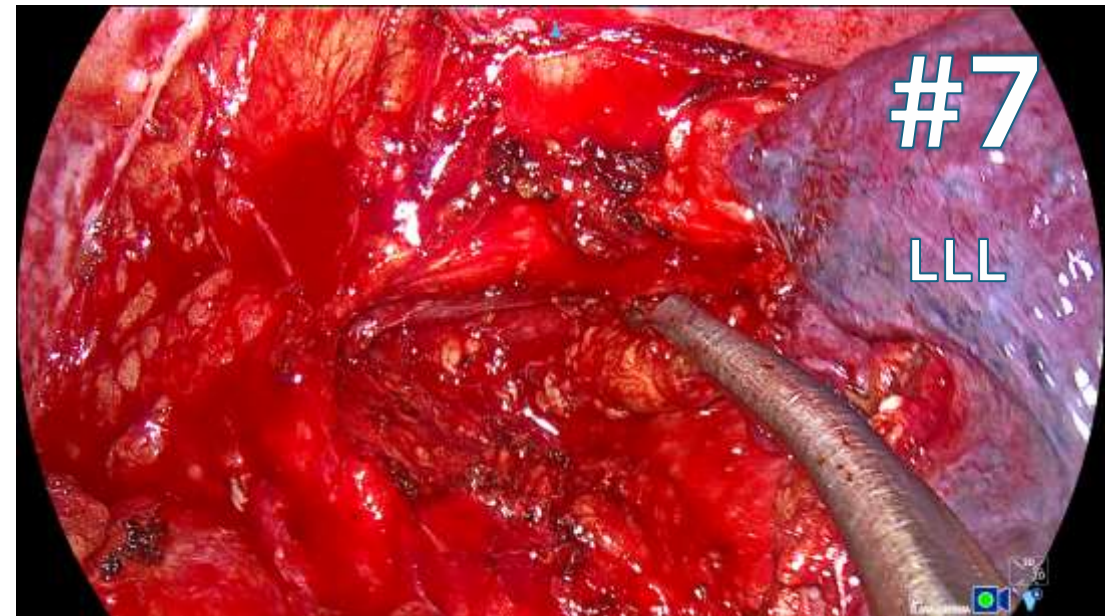
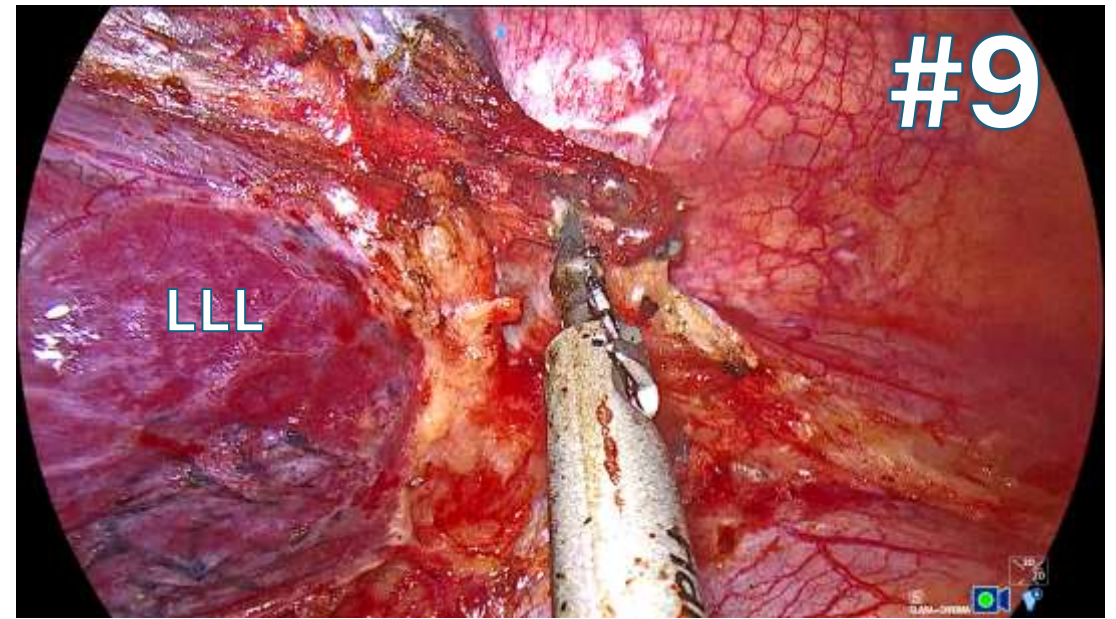
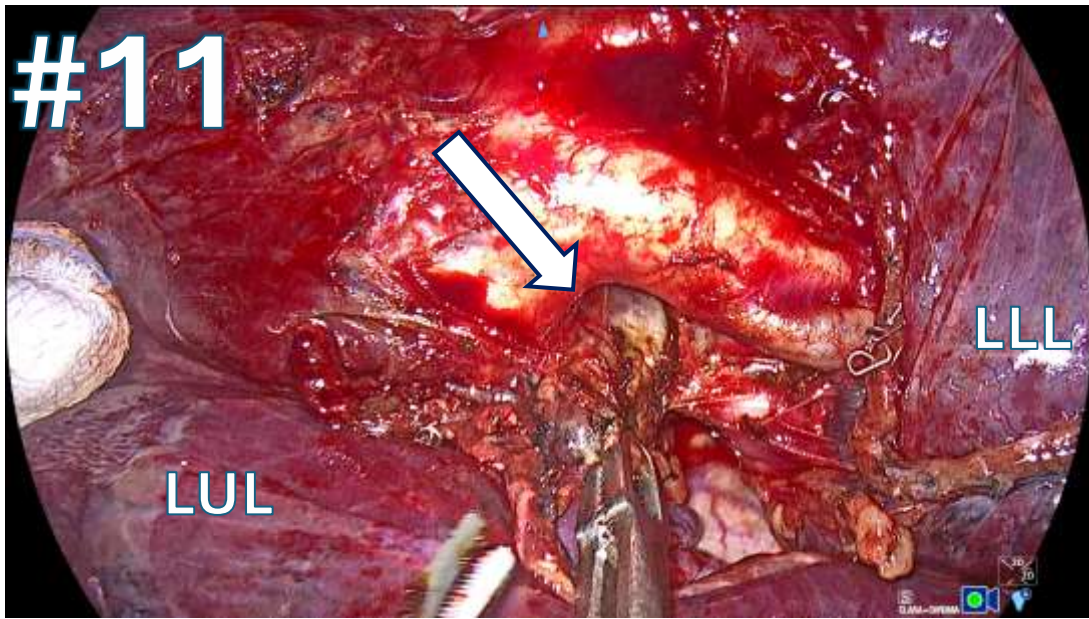
Initial



Postinduction

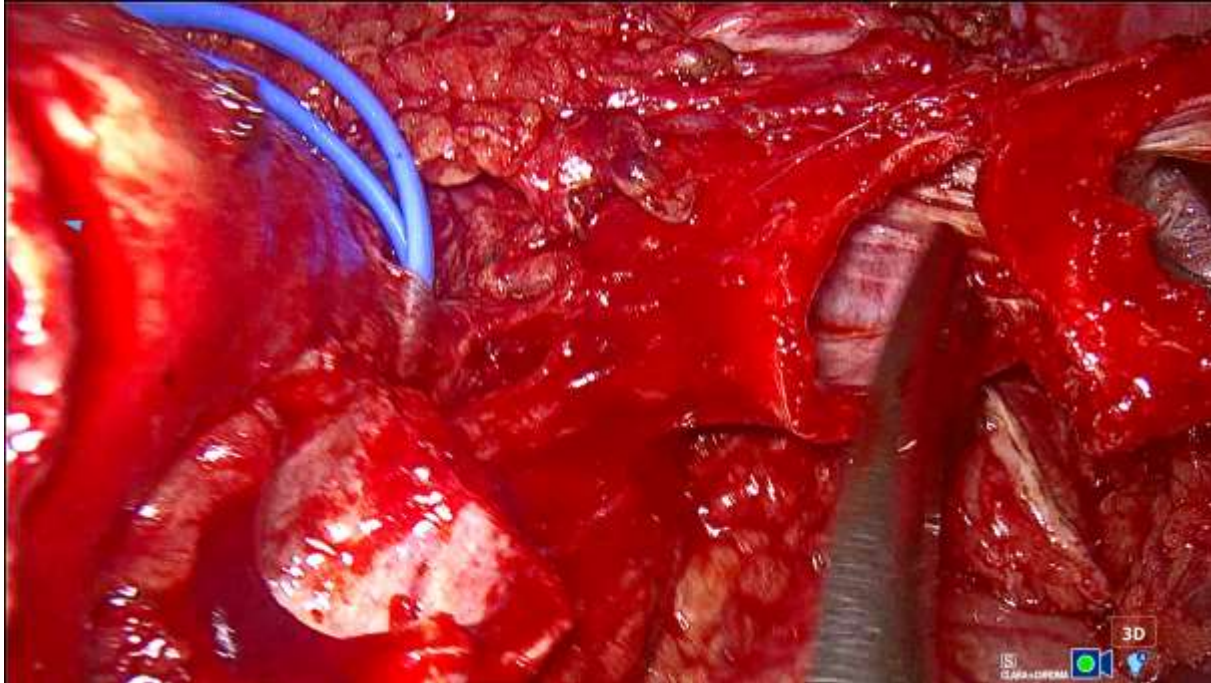


- Should have been more exhaustively staged?
- Is CT scan accurate enough for LN involvement?



- Intraoperative: #11, #5, #7, #9 positive (**N1+N2 multistation**)

- **LLL Sleeve lobectomy U-VATS**



¿Inaccurate LN staging vs progression?

But, what has been done during the surgery...?

But, what has been done during the surgery...?					Published results		
Study (year)	n	Drug	cTNM	Protocol	Sampled lymph nodes	Stations (#)	Downstaging
CheckMate816 (2022)	358	NIVO (ind)	IB-IIIA	Systematic <i>sampling</i> OR MLND (right: 4R, 7, 9, 10R, 11R Left: 5, 6, 7, 9, 10L, 11L)	18.5-19	-	-
<i>CheckMate 77T (2024)</i>	461	NIVO (peri)	IIA-IIIB	Systematic <i>sampling</i> OR MLND (right: 4R, 7, 9, 10R, 11R Left: 5, 6, 7, 9, 10L, 11L)	-	-	-
NADIM 2 (2023)	86	NIVO (ind)	IIIA-B	3 N2 stations (#7) + 3 N1 stations (IASLC standards)	-	-	37 YES – 4 NO
Keynote 671 (2023)	797	PEMBRO (Peri)	II-IIIB	Preferred: all N2 stations accessible/ 3 N1 stations <i>Acceptable: 2 N2 stations (#7) and 1 N1 station</i>	-	-	-
AEGEAN (2023)	802	DURVA (Peri)	II-IIIB	3 lobe-specific N2(#7) and <i>1 N1</i> Formal ipsi N2 dissection if N2 disease	-	-	-
NEOCOAST (2023)	83	DURVA + other (ind)	IA3-IIIA	<i>Surgeon's discretion and institutional standards</i>	-	-	-
NEOSTAR (2023)	42	IPILIMUMA B (ind)	IB-IIIA	<i>Surgeon's discretion and specialty standards</i>	-	-	-
Neotorch (2024)	404	TORIPALIM AB (peri)	IIA-IIIB	<i>Surgeon's standard for mediastinal</i> (#7 always) (right: 4R, 7, 9, 10R, 11R Left: 5, 6, 7, 9, 10L, 11L)	-	-	-

Systematic lymphadenectomy versus sampling of ipsilateral mediastinal lymph-nodes during lobectomy for non-small-cell lung cancer: a systematic review of randomized trials and a meta-analysis

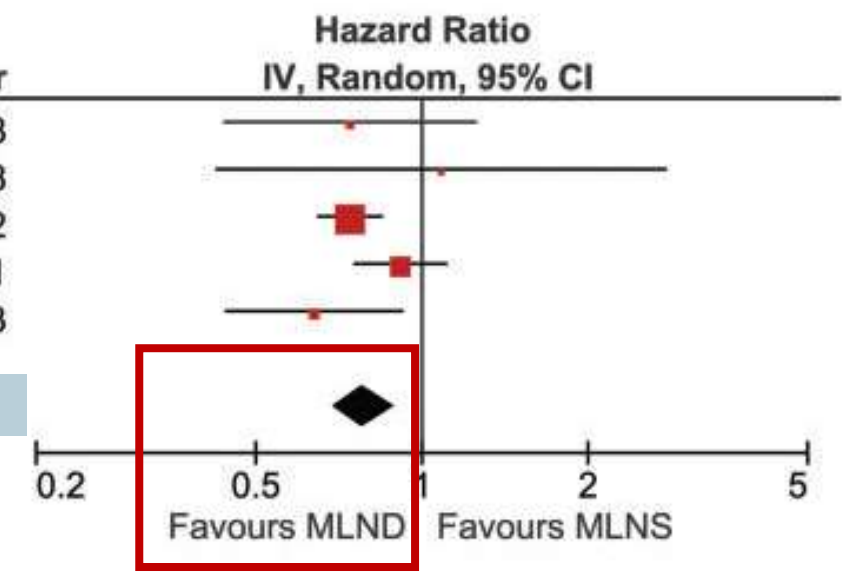
2017

Sahar Mokhles^a, Fergus Macbeth^b, Tom Treasure^{c*}, Riad N. Younes^d, Robert C. Rintoul^e, Francesca Fiorentino^f, Ad J.J.C. Bogers^a and Johanna J. M. Takkenberg^a

B





Study or Subgroup	log[Hazard Ratio]	SE	MLND MLNS		Weight	Hazard Ratio	
			Total	Total		IV, Random, 95% CI	Year
Izbicki et al	-0.3	0.27	76	93	5.5%	0.74 [0.44, 1.26]	1998
Sugi et al	0.08	0.48	59	56	1.8%	1.08 [0.42, 2.78]	1998
Wu et al	-0.3	0.07	240	231	50.6%	0.74 [0.65, 0.85]	2002
ACOSOG Z0031 trial	-0.09	0.1	525	498	31.4%	0.91 [0.75, 1.11]	2011
Zhang et al	-0.45	0.19	95	107	10.7%	0.64 [0.44, 0.93]	2013
Total (95% CI)			995	985	100.0%	0.78 [0.69, 0.89]	

Heterogeneity: Tau² = 0.00; Chi² = 4.68, df = 4 (P = 0.32); I² = 15%
 Test for overall effect: Z = 3.75 (P = 0.0002)



Long-term survival is better after MLND compared to sampling

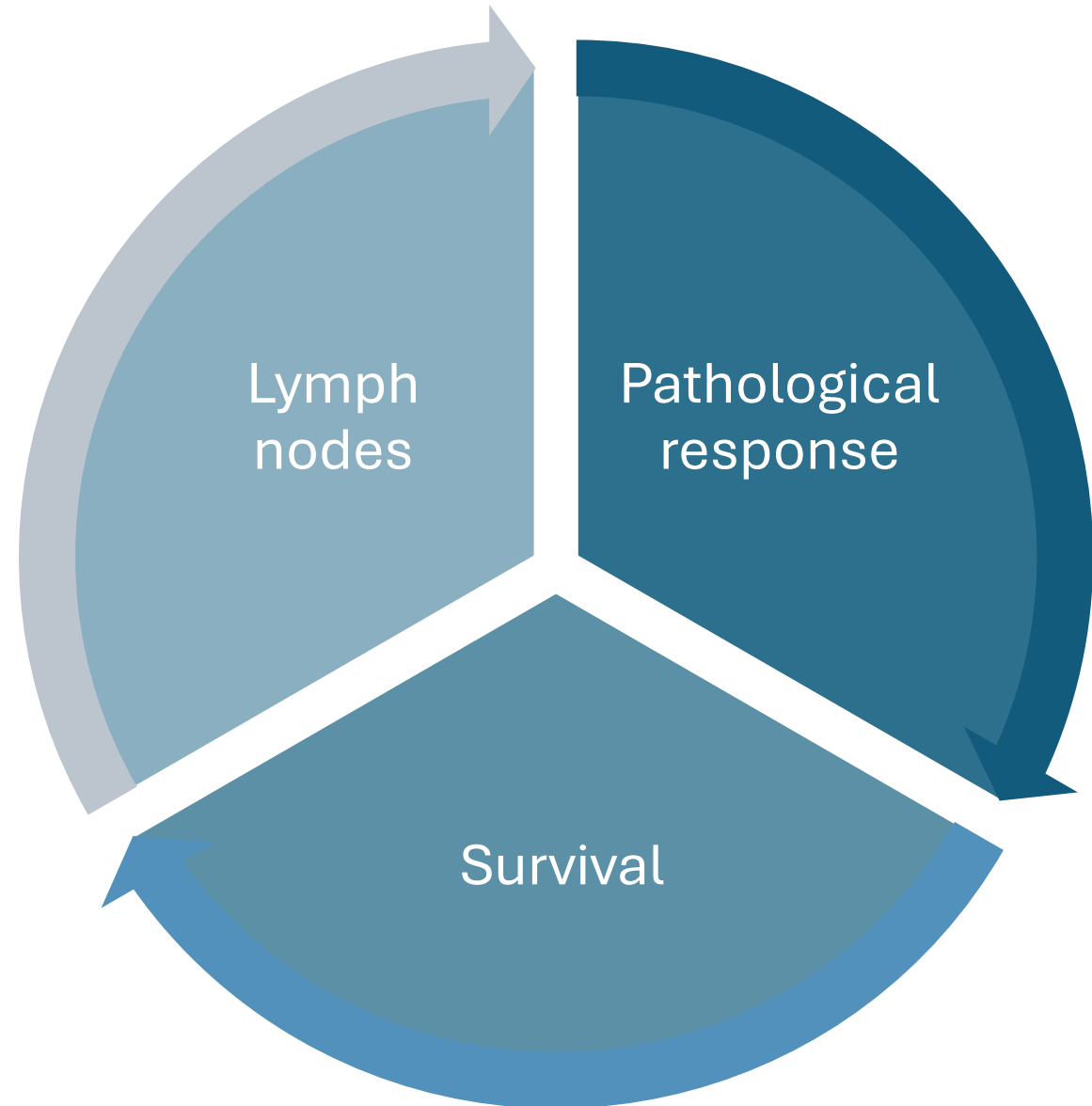
There is no published data from RCT's regarding:

- Number of LN's examined 
- Stations examined 
- Accomplishment of IASLC Complete Resection/R0 descriptor criteria 
- Downstaging (N descriptor) 

- What has been done on RCT's?
- Why is LN evaluation important?
- Extent of LN evaluation

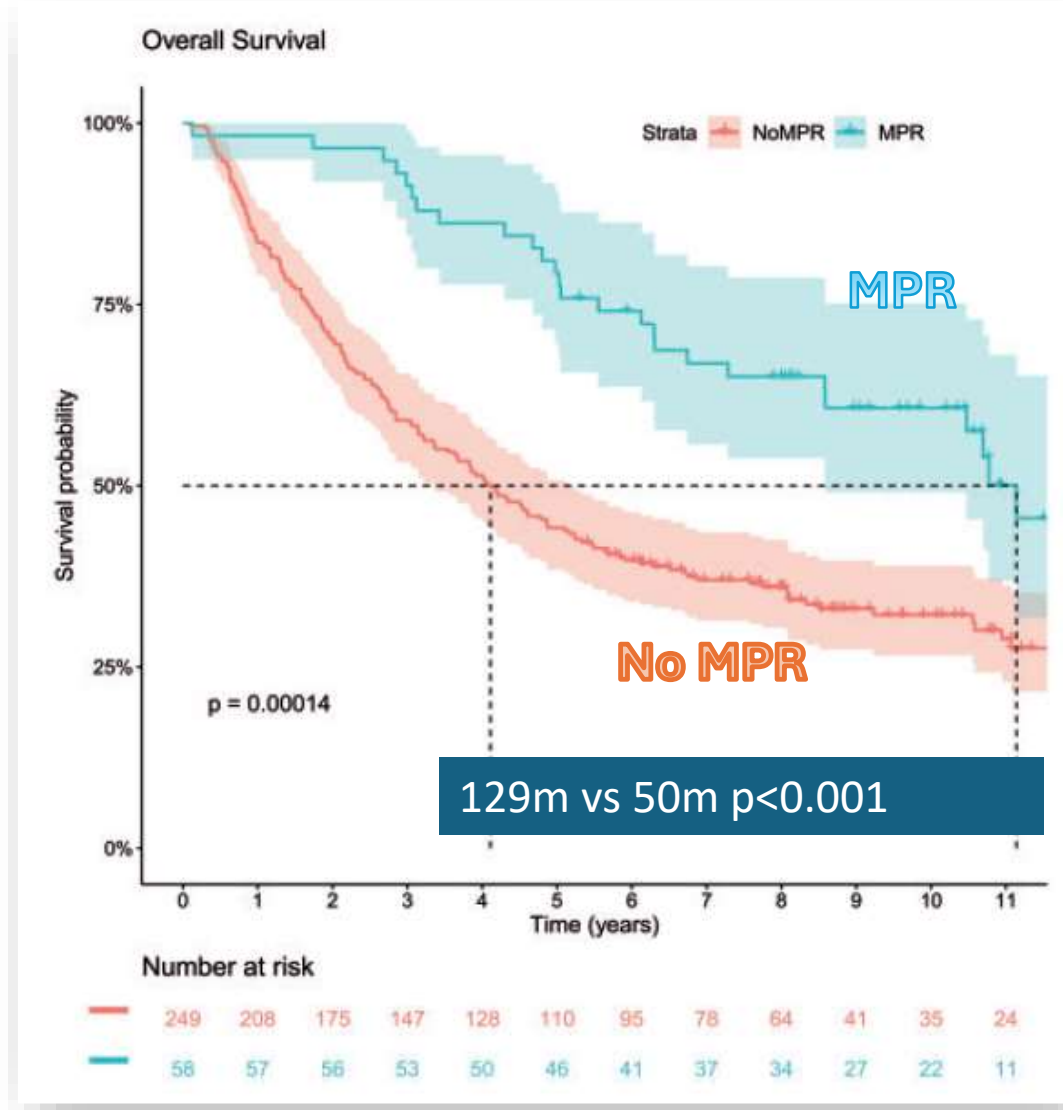
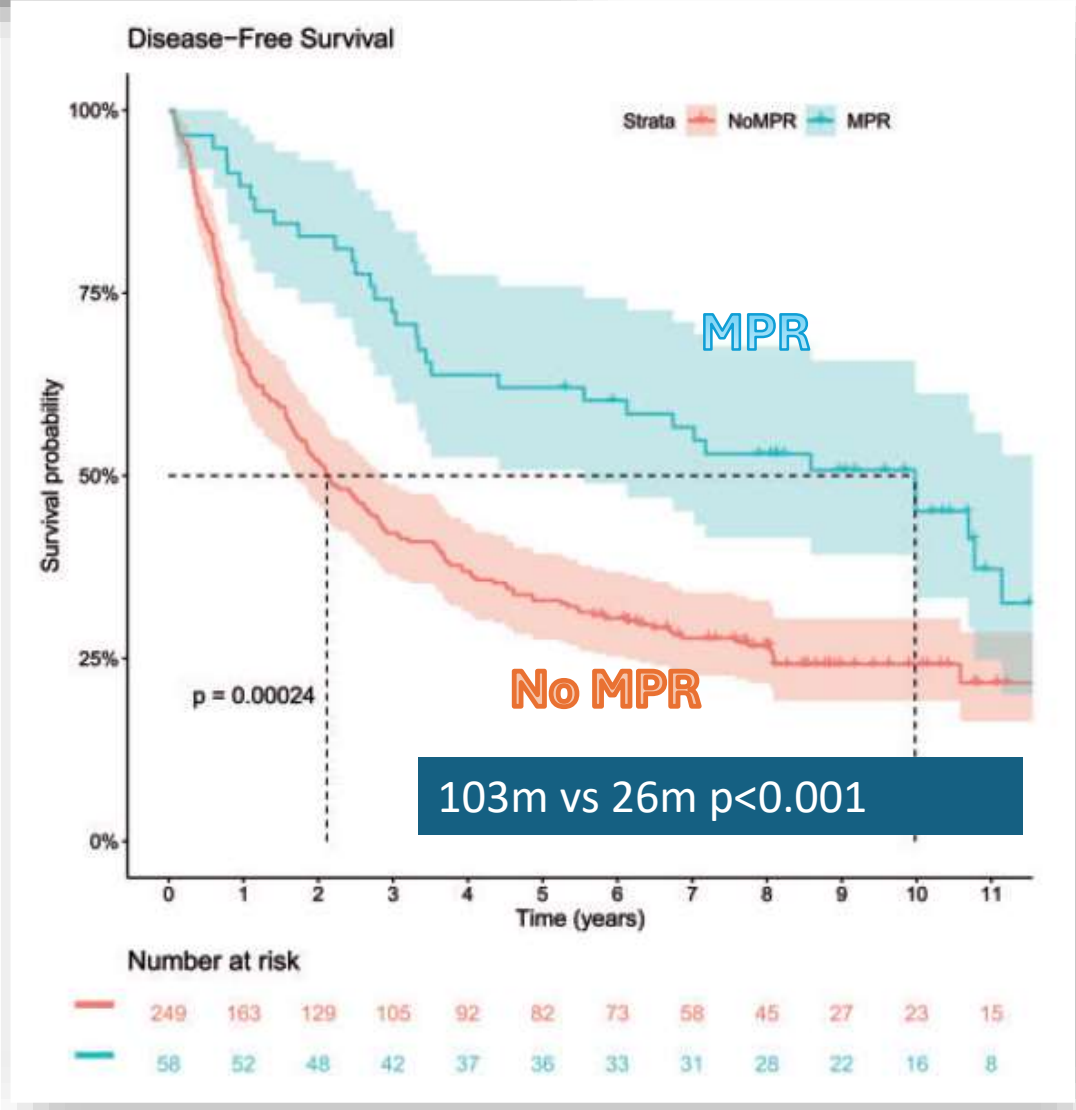


Patients with NSCLC and N2 disease deemed resectable by the MDT board who undergo multimodality therapy must undergo repeat staging after receiving neoadjuvant therapy. Restaging must include at least a chest CT scan and/or positron emission tomography/CT scan. These imaging studies intend to rule out disease progression. If there is no radiographic progression (ie, any response or stable disease), then proceeding with surgical resection is indicated. Certainly, response to neoadjuvant therapy has been associated with favorable long-term cancer-specific outcomes in patients with NSCLC and N2 disease who undergo multimodality therapy. In particular, pathologic downstaging or mediastinal clearance (ie, ypN0-1) has been associated with improved OS and PFS.^{36,42} Invasive mediastinal restaging is not routinely indicated without suspected disease progression on imaging. Phase III randomized clinical trials studying multimodality therapy, including surgery, in patients with NSCLC and N2 disease have not mandated invasive mediastinal restaging in their protocols and only excluded patients in the event of disease progression after neoadjuvant therapy.^{5,6,35,36}



Pathological nodal disease defines survival outcomes in patients with lung cancer with tumour major pathological response following neoadjuvant chemotherapy

Erin M. Corini¹, Anikka Weisferdt², Apar Patra³, Nicolas Zhou⁴, Maria B. Antonoff⁵, Wayne L. Hobbster⁶, Raza J. Mehran⁷, Ravi Rajaram⁸, David C. Rice⁹, Jack A. Roth¹⁰, Ara A. Vaporciyan¹¹, Garrett L. Walsh¹², Tina Caccese¹³, John V. Heymach¹⁴, Stephen G. Swisher¹⁵ and Boris Sepeshkar¹⁶

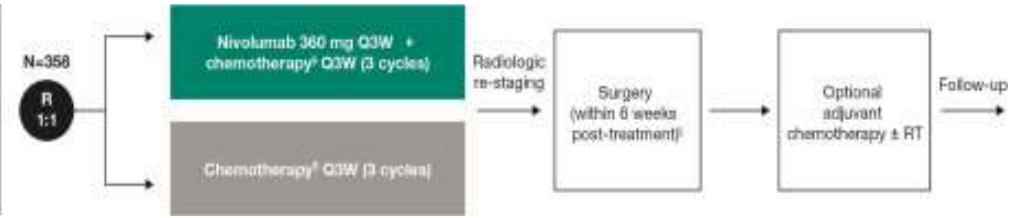


Pathological response predicted DFS and OS with Chemotherapy

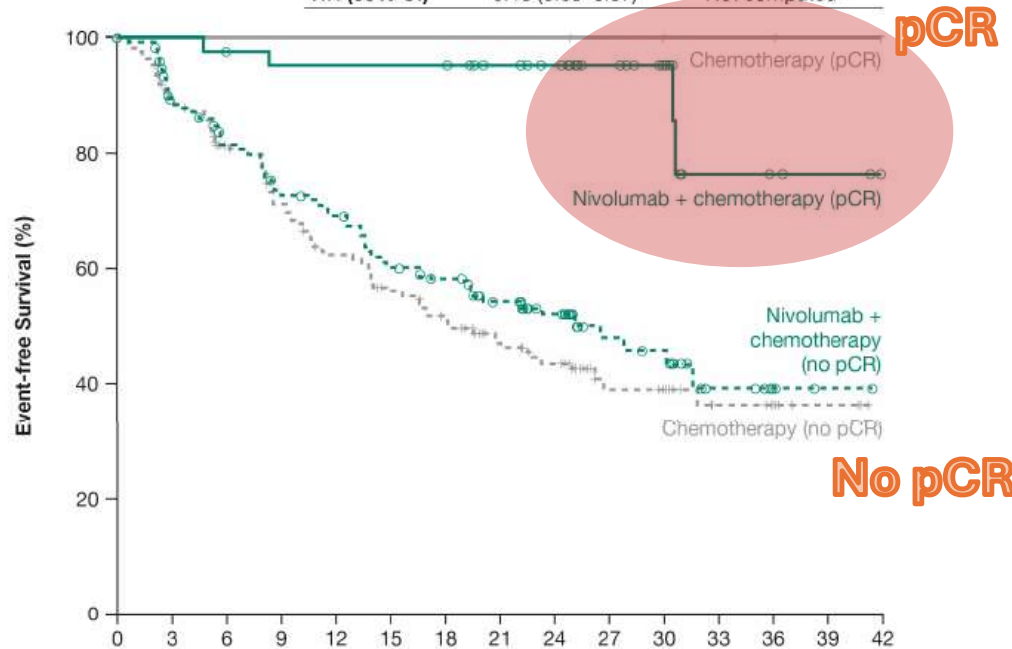
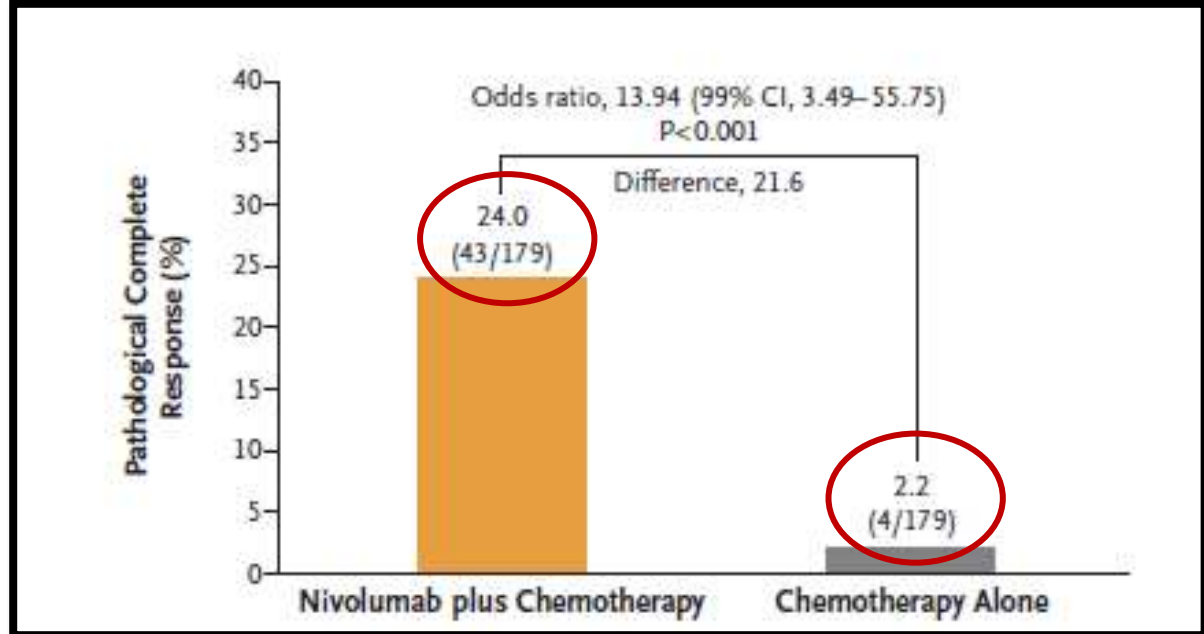
Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

P.M. Forde, J. Spicer, S. Lu, M. Provencio, T. Mitsudomi, M.M. Awad, E. Felip, S.R. Broderick, J.R. Brahmer, S.J. Swanson, K. Kerr, C. Wang, T.-E. Ciuleanu, G.B. Saylor, F. Tanaka, H. Ito, K.-N. Chen, M. Liberman, E.E. Vokes, J.M. Taube, C. Dorange, J. Cai, J. Fiore, A. Jarkowski, D. Balli, M. Sausen, D. Pandya, C.Y. Calvet, and N. Girard, for the CheckMate 816 Investigators[®]

- Key Eligibility Criteria**
- Newly diagnosed, resectable, stage IB (≥ 4 cm)-IIIA NSCLC (per TNM 7th edition)
 - ECOG PS 0-1
 - No known sensitizing EGFR mutations or ALK alterations
- Stratified by stage (IB/II vs. IIIA), PD-L1[†] (≥1% vs. <1%), and sex**



	Nivolumab + chemotherapy		Chemotherapy	
	pCR (n=43)	No pCR (n=136)	pCR (n=4)	No pCR (n=175)
Median EFS, mo (95% CI)	NR (30.6–NR)	26.6 (16.6–NR)	NR (NR–NR)	18.4 (13.9–26.2)
HR (95% CI)*	0.13 (0.05–0.37)		Not computed [†]	



pCR is more frequent after Ch-IO, and these patients live longer

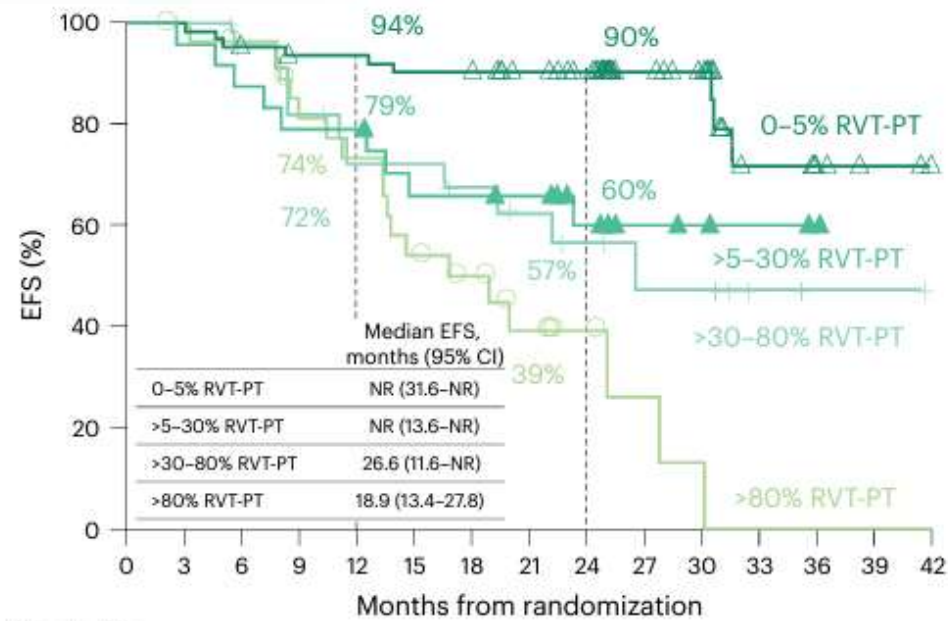
	No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42
Nivolumab + chemotherapy (pCR)	43	43	41	40	40	40	40	35	32	19	14	6	3	2	0	0
Chemotherapy (pCR)	4	4	4	4	4	4	4	4	4	3	2	2	2	1	0	0
Nivolumab + chemotherapy (no pCR)	136	108	95	84	78	67	62	52	42	22	20	7	3	1	0	0
Chemotherapy (no pCR)	175	140	122	105	90	79	71	57	48	23	22	11	9	3	0	0

Pathological response as SV predictor

CheckMate816



f

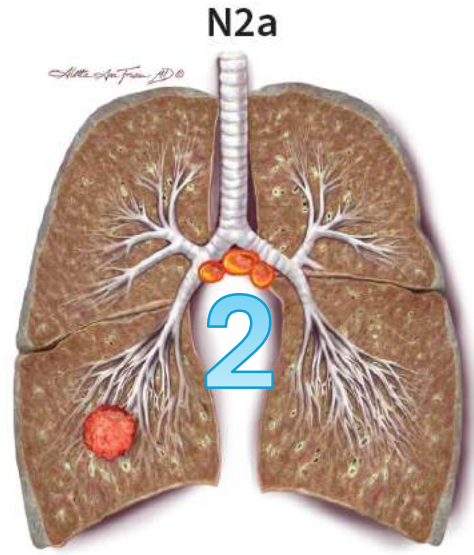


No. at risk

63	63	59	57	57	55	55	50	46	26	21	9	4	2	0
24	23	21	19	19	15	15	14	10	5	4	2	1	0	0
25	24	21	18	15	15	13	11	9	5	5	2	1	1	0
29	28	26	22	19	14	11	7	4	2	1	0	0	0	0

Direct correlation between RVT-PT and 2y-EFS

1



**Double complete responders
(primary + LN's)**

**Single complete responders
(primary or LN's)**

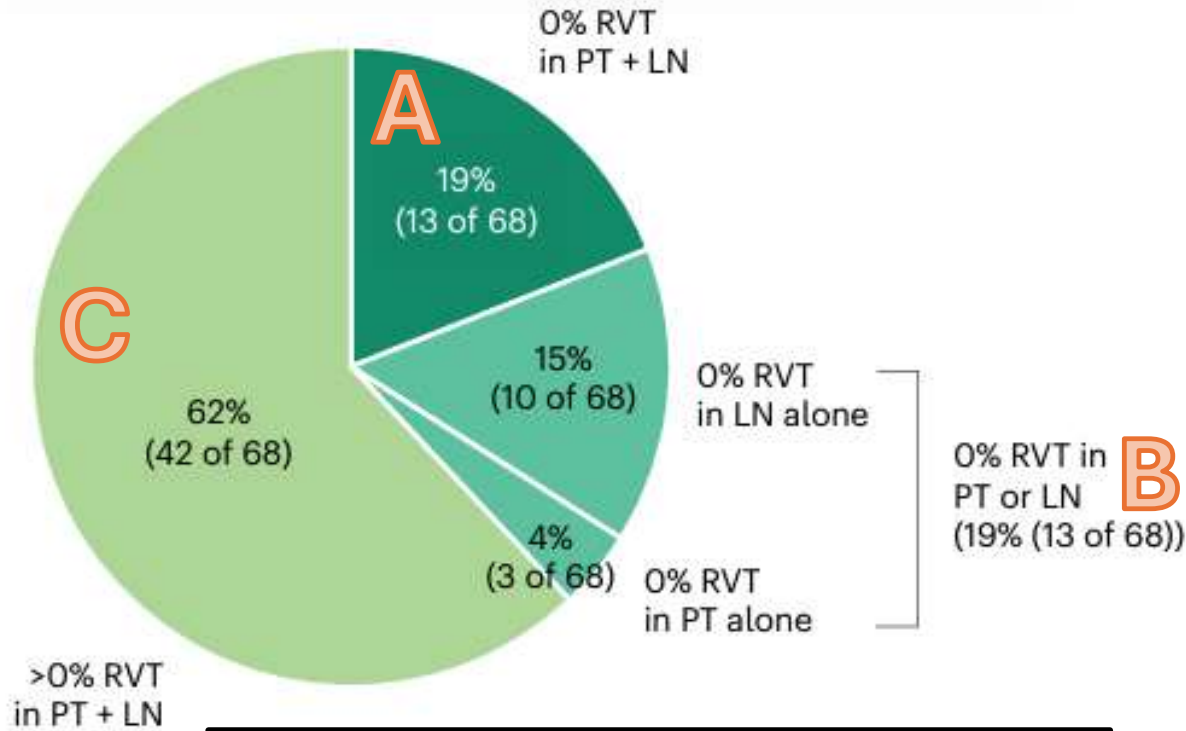
Partial responders

**Non-responders
(stable disease)**

Progression

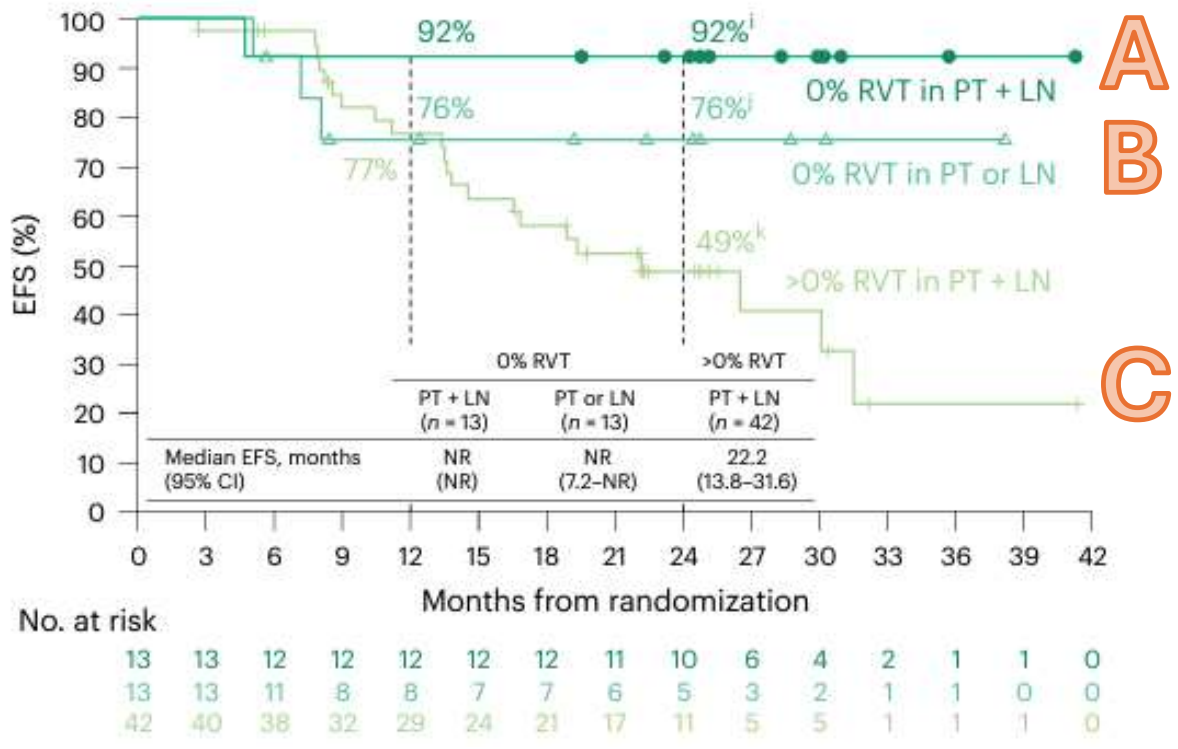


Association between pathologic response and survival after neoadjuvant therapy in lung cancer



- 19% Double complete responders (A)
- 19% Single complete responders (B)
- 62% Partial responders (C)

CheckMate816

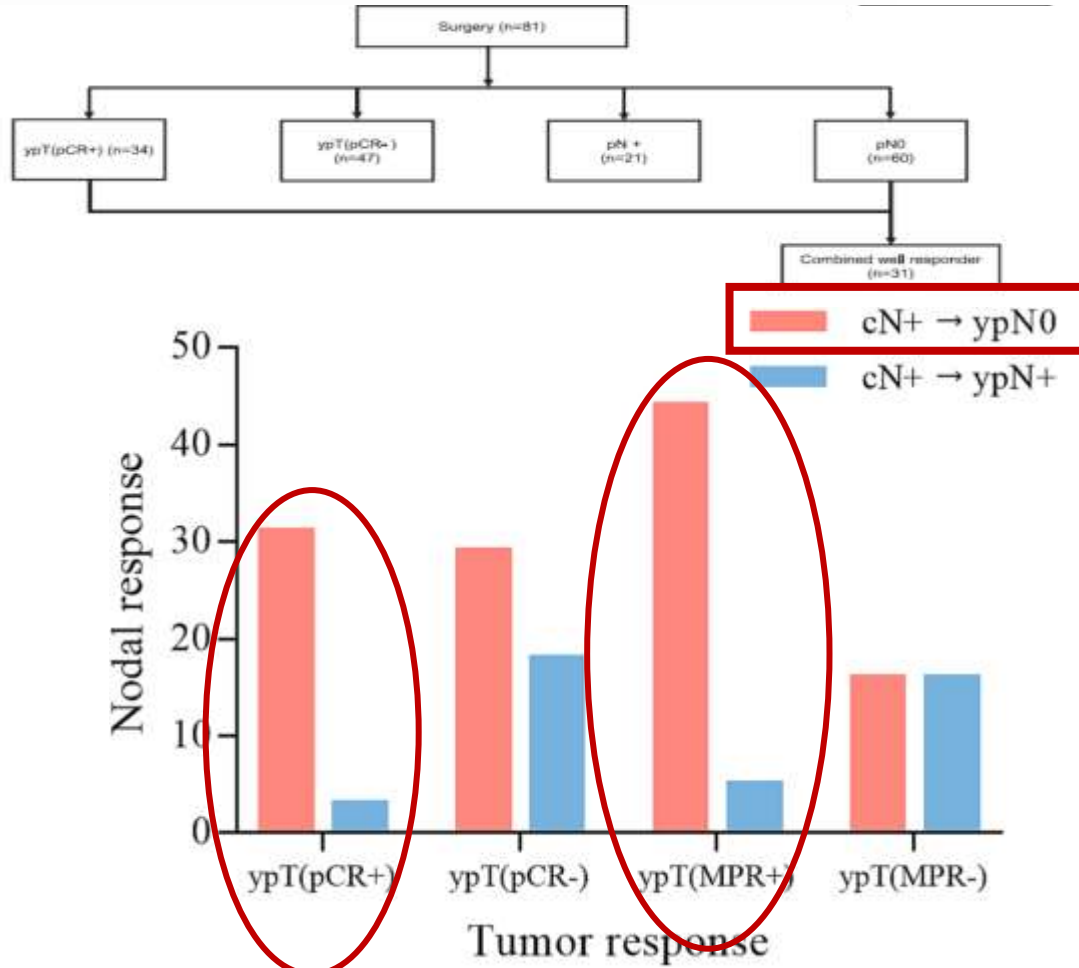


pCR in BOTH primary tumor and LN's predicted the best EFS

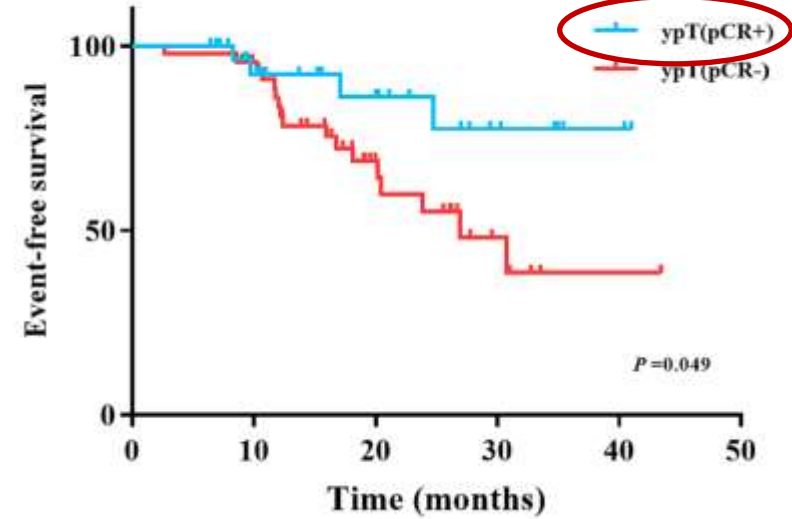
Evaluation of combined pathological responses in primary tumor and lymph nodes following neoadjuvant chemimmunotherapy in non-small cell lung cancer

Shujie Huang^{1,2,3,4}, Junhan Wu^{1,2,3,4}, Shaopeng Li^{1,2,3,4,5}, Xianglin Li^{1,2,3,4}, Ruijie Zeng^{1,2}, Yong Tang¹, Jiming Tang¹, Xiaosong Ben¹, Dongkun Zhang¹, Liang Xie¹, Haiyu Zhou¹, Gang Chen¹, Sichao Wang¹, Zhen Gao¹, Hansheng Wu¹, Rixin Chen^{1,2}, Fangping Xu^{1,2}, Guibin Qiao^{1,2}

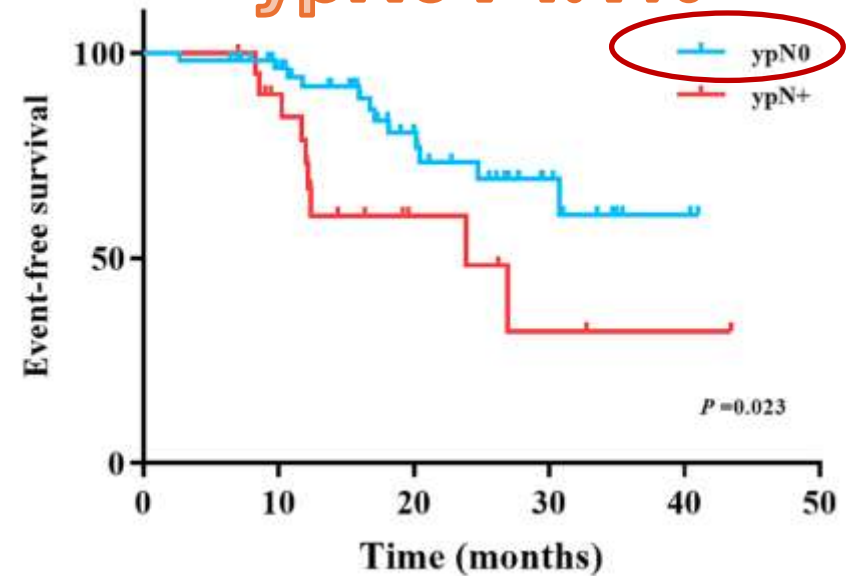
n=81 cN+ with induction
 cIIIA-C 87.7%
 cN1 29.6%
 cN2 60.5%
 cN3 9.9%



ypT(pCR) 42%



ypN0 74.1%

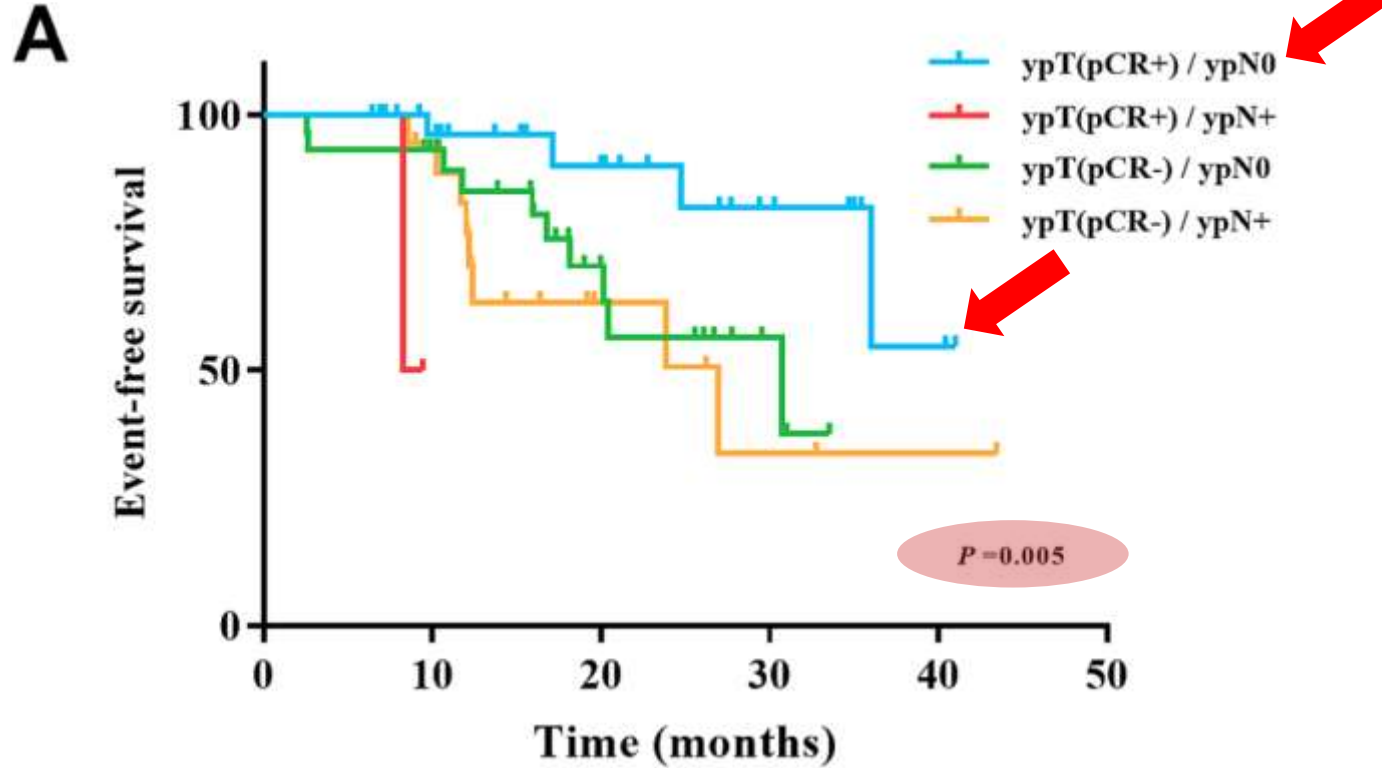


Correlation between ypT (pCR) and ypN0
Complete response at any site, better SV than not complete response

Evaluation of combined pathological responses in primary tumor and lymph nodes following neoadjuvant chemimmunotherapy in non-small cell lung cancer

Shujie Huang^{1,2,3,4}, Junhan Wu^{1,2,3,4}, Shaopeng Li^{1,2,3,4,5}, Xianglin Li^{1,2,3,4}, Ruijie Zeng^{1,2}, Yong Tang¹, Jiming Tang¹, Xiaosong Ben¹, Dongkun Zhang¹, Liang Xie¹, Haiyu Zhou¹, Gang Chen¹, Sichao Wang¹, Zhen Gao¹, Hansheng Wu¹, Rixin Chen^{1,2}, Fangping Xu^{1,2}, Guibin Qiao^{1,2}

n=81 cN+ with induction
 cIIIA-C 87.7%
 cN1 29.6%
 cN2 60.5%
 cN3 9.9%



**ypT(pCR) + ypN0 show better survival
(DOUBLE COMPLETE RESPONDERS)**

How to be sure a patient is a double complete responder?

- What has been done on RCT's?
- Why is LN evaluation important?
- Extent of LN evaluation



Table 1. Residual tumor classification.

Categories	Descriptors
RX	The presence of residual tumor cannot be assessed
R0	There is no residual tumor
R1	There is microscopic residual tumor
R2	There is macroscopic residual tumor

Did not consider the intensity of nodal assessment

Table 2. Elements used to define complete resection.

Naruke et al. 1978 [9]	Mountain 1983 [19]	Martini and Ginsberg 1995 [20]	Bronchogenic Carcinoma Cooperative Group 1998 [21]
Visceral pleura	Surgeon's assessment	Lobectomy or pneumonectomy	Resection margins
Suture line	Most distant lymph node	Tumor integrity and en bloc resection	Most distant lymph node
Mediastinal lymph nodes	Resection margins	Resection margins	Lymph node capsule
Complete lymphadenectomy	Lymph node capsule	Mediastinal lymphadenectomy	Mediastinal lymphadenectomy

Collaborative effort for better describing complete resection

Complete Resection

Free resection margins proved microscopically (bronchial, venous and arterial stumps, peribronchial soft issue, any peripheral margin near the tumor or of additionally resected tissue)

Systematic nodal dissection in its wider form or, if it is not performed, **lobe-specific** systematic nodal dissection: The latter implies dissection and histological examination of intrapulmonary (lobar, interlobar and segmental) and hilar nodes and, at least, three of the following mediastinal nodal stations depending on the lobar location of the primary tumor.

- For right upper and middle lobes, these should include the subcarinal nodes and two of the following three stations: superior paratracheal, inferior paratracheal and pretracheal.
- For the right lower lobe, the subcarinal and right inferior paratracheal nodes, and either
- the paraesophageal or pulmonary ligament nodes.
- For the left upper lobe, subcarinal, subaortic and anterior mediastinal nodes.
- For the left lower lobe, subcarinal, paraesophageal and pulmonary ligament nodes.

The lymph node specimen should include, **at least , six nodes, three removed from intrapulmonary and/or hilar stations and three removed from mediastinal stations, one of which must be the subcarinal station.**

There should be **no extracapsular extension** of tumor in nodes removed separately or those at the margin of the main lung specimen.

The **highest mediastinal node that has been removed must be negative.**

Uncertain Resection (no R1-2 but...)

~~Resection margins are proved to be free of disease microscopically~~

The intraoperative **lymph node evaluation has been less rigorous than systematic nodal dissection or lobe-specific** systematic nodal dissection as described above.

~~The **highest mediastinal node removed is positive**~~

The bronchial margin shows carcinoma in situ.

Pleural lavage cytology is positive (R1 cy+).

**Complete resection in lung cancer surgery:
proposed definition**

Ramón Rami-Porta^{a,*}, Christian Wittekind^b, Peter Goldstraw^c





The International Association for the Study of Lung Cancer Lung Cancer Staging Project: Proposals for Revision of the Classification of Residual Tumor After Resection for the Forthcoming (Ninth) Edition of the TNM Classification of Lung Cancer



Table 7. Residual Tumor After Surgical Resection

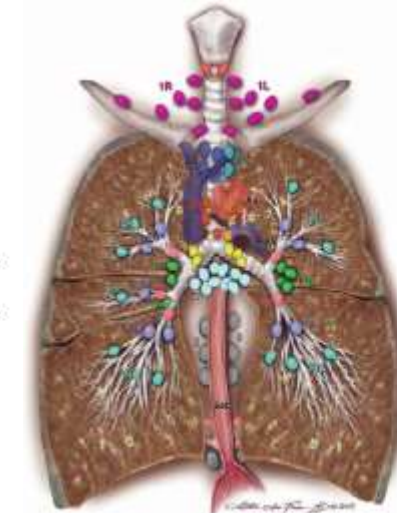
Symbol	Name	Descriptor	Evidence Basis ^a
R0	No residual	No identifiable tumor remaining, negative surgical margins, adequate node assessment, ^b and highest node station assessed is negative	Reference
R0(un)	Uncertain residual	Limited node assessment ^b Highest station assessed is positive	Moderate ^c Conflicting
R1(un)		R1(is) carcinoma in situ at the bronchial margin R1(cy+) pleural lavage performed with malignant cytology	Conflicting Strong
R1	Microscopic residual	Microscopically positive surgical margin but no visible tumor remaining ^d Extranodal extension of an involved hilar or mediastinal node ^e Malignant pleural or pericardial nodules or effusion ^f	Good Conflicting Moderate
R2	Gross residual	Gross (visible or palpable) tumor remaining ^d Involved nodes not resected	Intuitive Intuitive
RX	Unknown	Margin cannot be assessed	Intuitive

Residual tumor descriptor (R) includes adequate LN assessment

Table 3. Required intraoperative nodal assessment for complete resection.

Type of Lymphadenectomy	Requirement *
Systematic nodal dissection	<p>Step (1) Complete excision of the mediastinal fat and enclosed lymph nodes, which are dissected and identified in accordance with an internationally accepted nodal chart.</p> <p>Step (2) Excision of hilar and intrapulmonary lymph nodes and their identification in accordance with an internationally accepted nodal chart. Dissection should proceed in a centrifugal manner until the extent of resection has been determined.</p>
Lobe-specific systematic nodal dissection	<p>For right upper and middle lobes: subcarinal, superior and inferior paratracheal lymph nodes.</p> <p>For right lower lobe: subcarinal, right inferior paratracheal and either the paraesophageal or pulmonary ligament lymph nodes.</p> <p>For left upper lobe: subcarinal, subaortic and para-aortic lymph nodes.</p> <p>For left lower lobe: subcarinal, paraesophageal and pulmonary ligament lymph nodes.</p> <p>For all lobes: dissection and histological examination of hilar and intrapulmonary (lobar, interlobar, segmental) lymph nodes.</p>

* The recommended nodal chart is the one proposed by the IASLC. The nodal stations mentioned in this table are in accordance with this nodal chart [12].



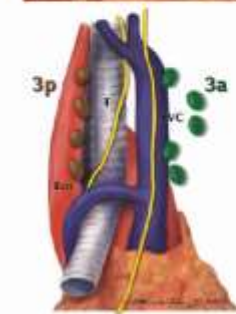
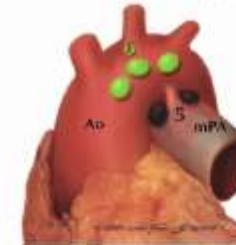
Supraclavicular zone
 1 Low cervical, supraclavicular, and sternal notch nodes

Superior mediastinal nodes
Upper zone
 2R Upper paratracheal (right)
 2L Upper paratracheal (left)
 3a Prevascular
 3p Retrotracheal
 4R Lower paratracheal (right)
 4L Lower paratracheal (left)

Aortic nodes
AP zone
 5 Subaortic
 6 Para-aortic (ascending aorta or phrenic)

Inferior mediastinal nodes
Subcarinal zone
 7 Subcarinal
Lower zone
 8 Paraesophageal (below carina)
 9 Pulmonary ligament

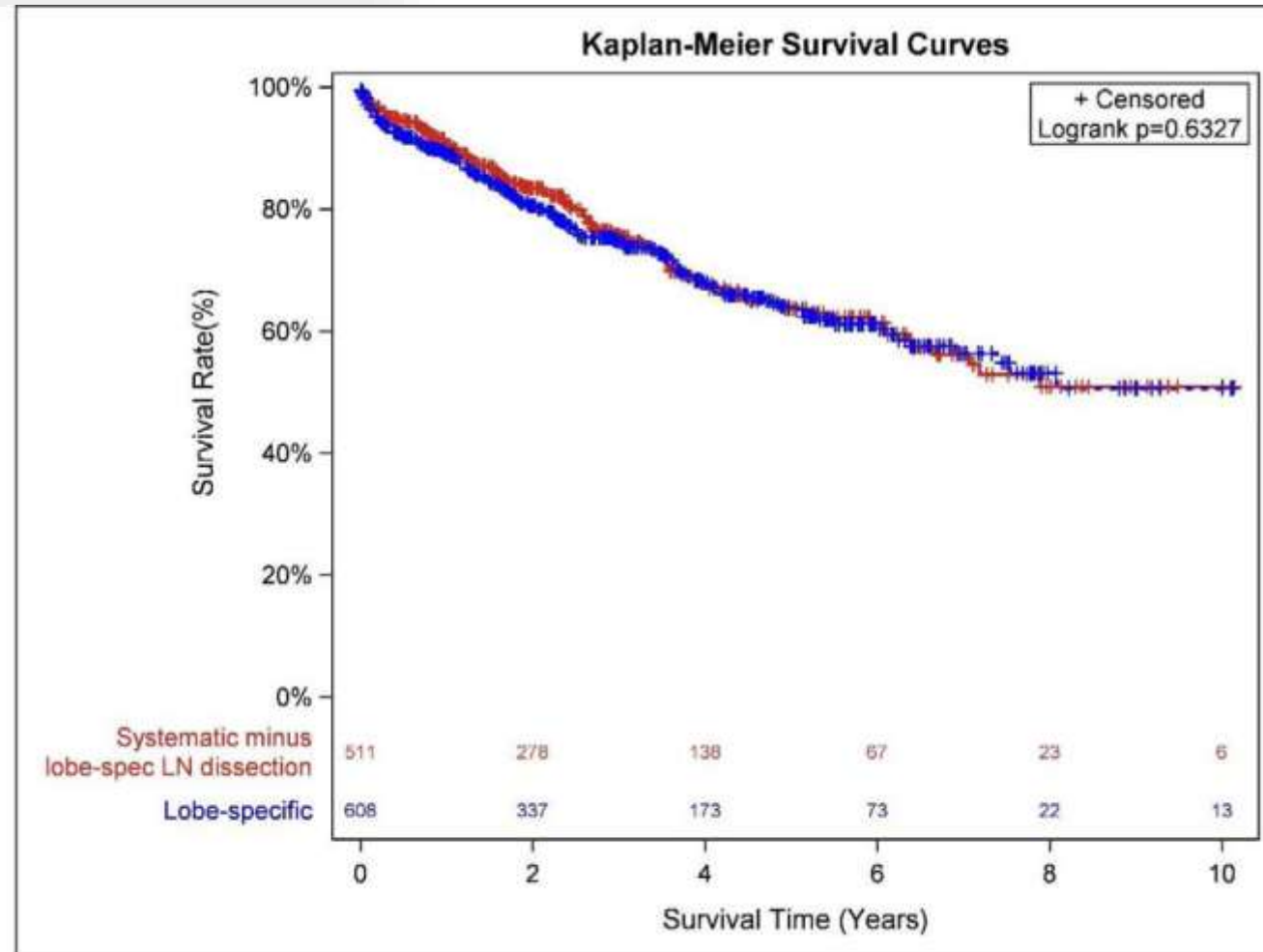
N1 nodes
Hilar/interlobar zone
 10 Hilar
 11 Interlobar
Peripheral zone
 12 Lobar
 13 Segmental
 14 Subsegmental



≥6 lymph nodes: 3 from the intrapulmonary and/or hilar nodal stations and 3 from the mediastinal nodal stations, always including the subcarinal (#7)

Beyond Margin Status: Population-Based Validation of the Proposed IASLC Residual Tumor Classification Re-categorization

Raymond U. Osarogiagbon, MBBS¹, Nicholas R. Faris, M Div¹, Walter Stevens, MPH¹, Carrie Fehnel, BBA¹, Cheryl Houston-Harris, BS¹, Philip Ojeabulu, MBBS¹, Olawale Akinbobola, BS¹, Yu-Shen Lee, MS², Meredith A. Ray, PhD², Matthew P. Smeltzer, PhD²



There is no evidence of SV differences between Systematic and lobe-specific

Table 4. Characteristics and survival rates of the published validations of the IASLC definitions of completeness of resection.

Characteristics	Gagliasso et al. [37]	Edwards et al. [17]		Osarogiagbon et al. [38]	Yun et al. [39]
Year	2017	2019		2019	2021
Type of study	Single institution	International database		Population-based	Single institution
Study period	1998–2007	1999–2010		2009–2019	2004–2018
Country	Italy	World (mainly Japan)		USA	South Korea
No. of patients	1277	14,712		3361	1039
No. (%) of R0	1003 (78.5%)	6070 (41%)		1119 (33%)	432 (41.6%)
No. (%) of R0(un)	185 (14.5%)	8185 (56%)		2044 (61%)	212 (20.4%)
No. (%) of R1 + 2	89 (7%)	457 (3%) (301 + 156)		196 (6%)	395 (38%)
5-year survival rates					
	All pN	pN0	pN+	All pN	pN2
R0	58.8%	82%	55%	64%	54.7%
R0(un)	37.3%	79%	45%	54%	45.8%
R1 + 2	15.7%			33%	36.2%
R1		46%	34%		
R2		38%	22%		
<i>p</i> value	0.0001	0.04	<0.001	<0.0001	0.043 (R0 vs. R0(un)) 0.010 (R0(un) vs. R1 + 2)

R(un) presents lower SV than R0, but higher SV than R1-2

The International Association for the Study of Lung Cancer Lung Cancer Staging Project: Proposals for Revision of the Classification of Residual Tumor After Resection for the Forthcoming (Ninth) Edition of the TNM Classification of Lung Cancer



Frank C. Detterbeck, MD,^{a*} Marcin Ostrowski, MD,^b Hans Hoffmann, MD,^c

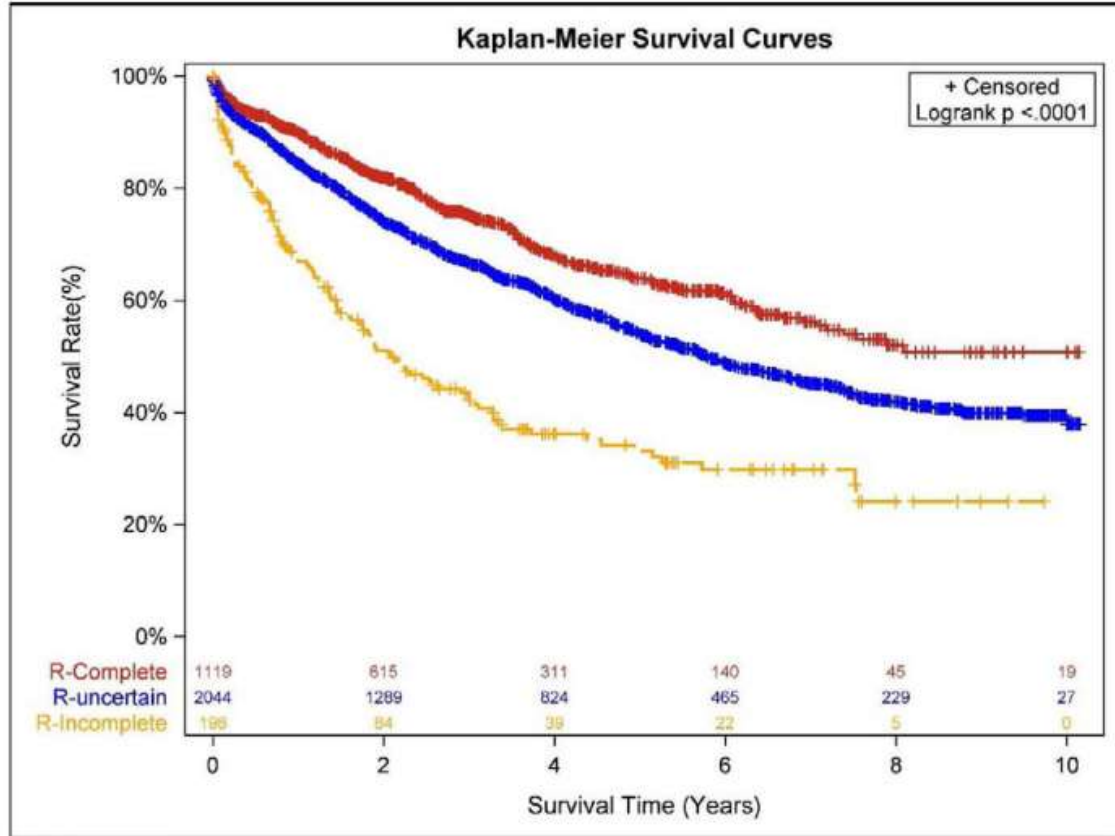
Table 1. Studies Evaluating the R(un) Category

First Author	n	Cohort	% Limited N Among R(un)	Adjusted HR for OS		Multivariate Adjustment	Data Source, Years
				R0 vs. R(un)	R(un) vs. R1,2		
Ren ⁹	5293	All	85%	1.41	1.23	10 factors	China 2009-2013
Osarogiagbon ¹⁰	3361	All	98%	1.36	2.18	8 factors	MSQSR 2009-2019
Gagliasso ¹¹	1277	All	58%	1.69	1.70	9 factors	Torino 1998-2007
Edwards ¹²	8839	pl	96%	1.22	-	4 factors	IASLC 1999-2010
Ren ⁹	3733	N0	85%	1.76	2.38	10 factors	China 2009-2013
Osarogiagbon ¹⁰	2453	N0	98%	1.31	1.81	8 factors	MSQSR 2009-2019
Edwards ¹²	3494	N+	96%	1.27	1.36 ^a	4 factors	IASLC 1999-2010
Ren ⁹	1556	N+	85%	1.14	1.61	10 factors	China 2009-2013
Osarogiagbon ¹⁰	682	N+	98%	1.24	2.15	8 factors	MSQSR 2009-2019
Kadomatsu ¹³	119	N+	34%	2.66	-	6 factors	Japan 2014-2015
Yun ¹⁴	1039	N2	10%	1.06	1.40	10 factors	Korea 2004-2018

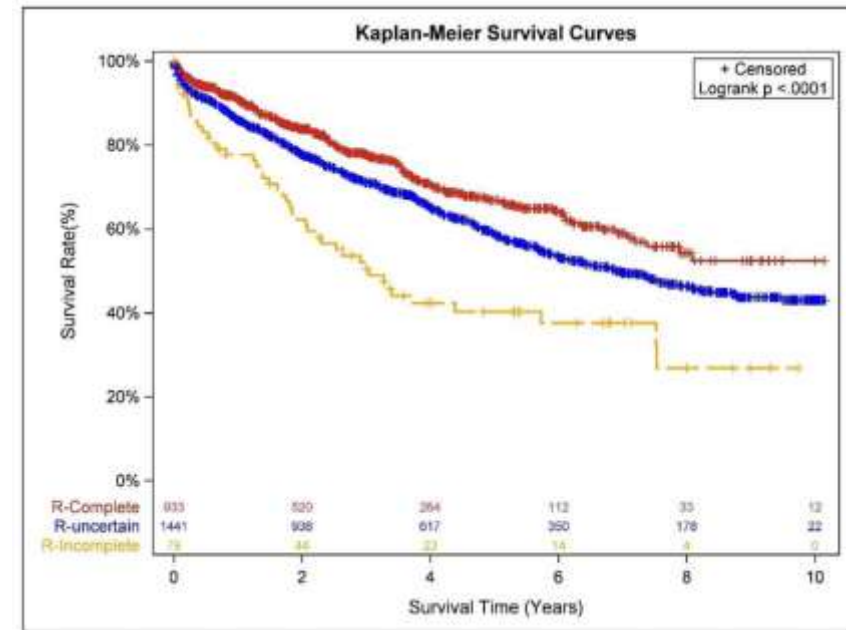
R(un) presents lower SV than R0, but higher SV than R1-2

Beyond Margin Status: Population-Based Validation of the Proposed IASLC Residual Tumor Classification Re-categorization

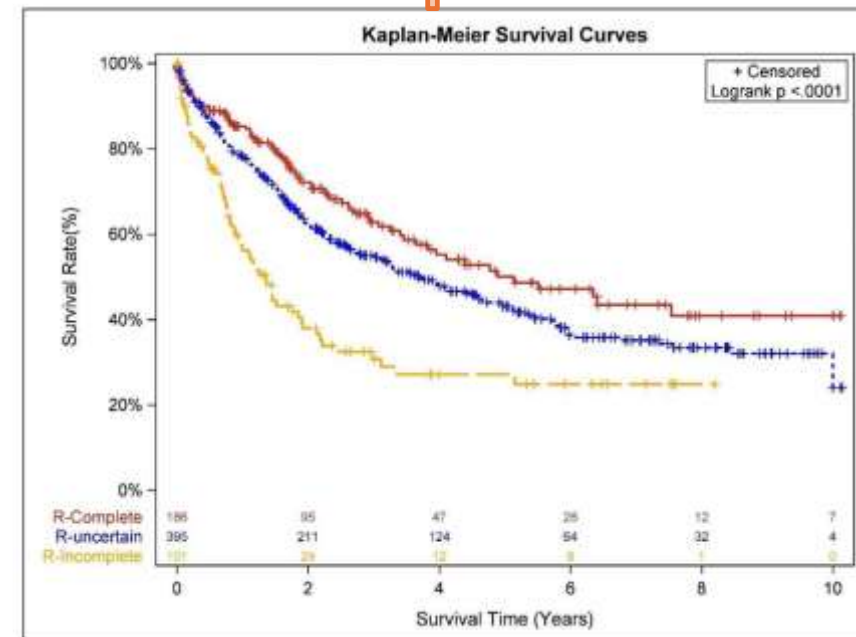
Raymond U. Osarogiagbon, MBBS¹, Nicholas R. Faris, M Div¹, Walter Stevens, MPH¹, Carrie Fehnel, BBA¹, Cheryl Houston-Harris, BS¹, Philip Ojeabulu, MBBS¹, Olawale Akinbobola, BS¹, Yu-Shen Lee, MS², Meredith A. Ray, PhD², Matthew P. Smeltzer, PhD²



All cases



pN-



pN+

The IASLC Lung Cancer Staging Project: Analysis of Resection Margin Status and Proposals for Residual Tumor Descriptors for Non-Small Cell Lung Cancer



Table 2. Data Completeness and Distribution of Each R Factor

Factor	Yes, n	No, n	Data Available, n	Not Done or No Data, n
≥3 N2 stations explored	9290 (63.1%)	5422 (36.9%)	14,712 (100%)	0
Lobe-specific nodal dissection	6641 (45.1%)	7918 (53.9%)	14,559 (99.0%)	153 (1.0%)
≥3 N1 nodes explored	970 (52.9%)	865 (47.1%)	1835 (12.5%)	12,877 (87.5%)
≥3 N2 nodes explored	1146 (62.7%)	681 (37.3%)	1827 (12.4%)	12,885 (87.6%)
N1 extracapsular extension	42 (70.0%)	18 (30.0%)	365 (2.5%)	14,347 (97.5%)
N2 extracapsular extension	24 (40.0%)	36 (60.0%)	365 (2.5%)	14,347 (97.5%)
Positive status of highest lymph node station	942 (6.4%)	13,717 (93.6%)	14,659 (99.6%)	53 (0.4%)
Presence of BRM CIS	13 (0.8%)	1533 (99.2%)	1546 (10.5%)	13,166 (89.5%)
Presence of BRM CIS (among 263 R1 cases)	13 (39.4%)	20 (60.6%)	33 (12.6%)	230 (87.4%)
Positive pleural lavage cytologic examination results	59 (3.5%)	1646 (96.5%)	1705 (12%)	13,007 (88%)

R0 → R(un)

Table 5. Reasons for Reassignment to the R(un) Category from the R0 Category

Reason	n	%
Highest station positive only	312	3.8%
Pleural lavage positive only	34	0.5%
Pleural lavage positive and highest station positive	4	0.05%
Any of the following: <3 N1 nodes, <3 N2 nodes, no station 7 nodes, no systematic nodal dissection, no lobe-specific nodal dissection	7824	95.7%

R(un), uncertain resection; R, resection.

Main reason for R0 to R(un) reassignment is poor quality of LN evaluation

...what happens if we consider R(un)?

Table 1. Distribution of Conventional R Status according to pT and pN Stage

Stage	R0, n	R1, n	R2, n	Total with R Status Data, n
pT1	6700 (99.1%)	32 (0.5%)	30 (0.4%)	6762
pT2	5039 (97.5%)	86 (1.7%)	44 (0.9%)	5169
pT3	1841 (93.9%)	85 (4.3%)	35 (1.8%)	1961
pT4	713 (87.0%)	60 (7.3%)	47 (5.7%)	820
pN0	11,058 (98.6%)	106 (0.9%)	54 (0.5%)	11,218
pN1	1395 (95.5%)	44 (3.0%)	21 (1.4%)	1460
pN2	1800 (90.9%)	105 (5.3%)	75 (3.8%)	1980
pN3	40 (74.1%)	8 (14.8%)	6 (11.1%)	54
Total	14,293 (97.2%)	263 (1.8%)	156 (1.1%)	14,712

 R(un) reassignment

Table 6. pN Status of the Proposed R Categories Once Cases Had Been Reassigned to R(un) Status

pN Status	R0, n	R(un), n	R1, n	R2, n	Total
pN0	5672 (50.6%)	6391 (57.0%)	101 (0.9%)	54 (0.5%)	11,218
pN1	665 (45.5%)	706 (48.4%)	68 (4.7%)	21 (1.4%)	1460
pN2	725 (36.6%)	1057 (53.4%)	123 (6.2%)	75 (3.8%)	1980
pN3	8 (14.8%)	31 (57.4%)	9 (16.7%)	6 (11.%)	54
Total	6070 (41.3%)	8185 (55.6%)	301 (2.0%)	156 (1.1%)	14,712

Only 50% of pN0 patients can be defined as R0

Only in 40% of pN2 we can state the resection is complete (R0)

Perioperative Nivolumab and Chemotherapy in Stage III Non-Small-Cell Lung Cancer

M. Provencio, E. Nadal, J.L. González-Larriba, A. Martínez-Martí, E. Bernald, J. Bosch-Barrera, J. Casal-Rubio, V. Calvo, A. Insa, S. Pons, N. Reguart, J. de Castro, J. Miquel, M. Cobos, A. Aguiló, C. López-Vivanco, C. Camps, R. López-Castro, T. Morán, J. Barrios, D. Rodríguez-Alonso, E. Serra-Blasco, R. Santar, C. Aguado de la Rosa, R. Palmero, F. Hernández-Triunfo, J. Martín-López, A. Cruz-Bermudez, S. Mansueti, and A. Romero

NADIM 2

Resection degree (n (%))	Nivolumab + Chemo (n = 53)	Chemo (n = 20)
R0	50 (94.3%)	17 (85.0%)
R1	1 (1.9%)	2 (10.0%)
R2	0 (0%)	1 (5.0%)
R(un)	2 (3.8%)	0 (0%)

Table S8. Resection degree according to treatment arm. R0, no residual tumor; R1, microscopic residual tumor; R2, macroscopic residual tumor; R (un), uncertain resection.

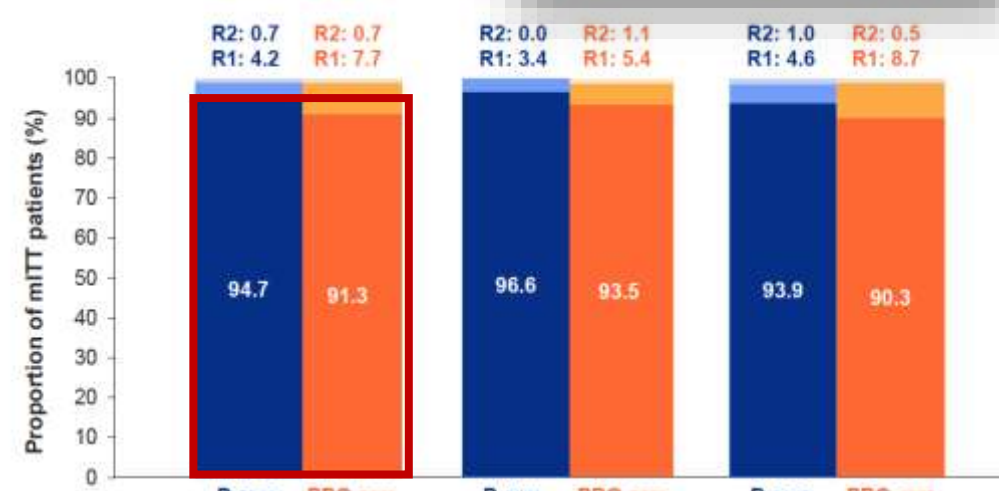
Nivo+Chemo 94.3% vs 85% Chemo

¿IS R(un) BEING CONSIDERED IN Ch-IO TRIALS?

Perioperative Durvalumab for Resectable Non-Small-Cell Lung Cancer

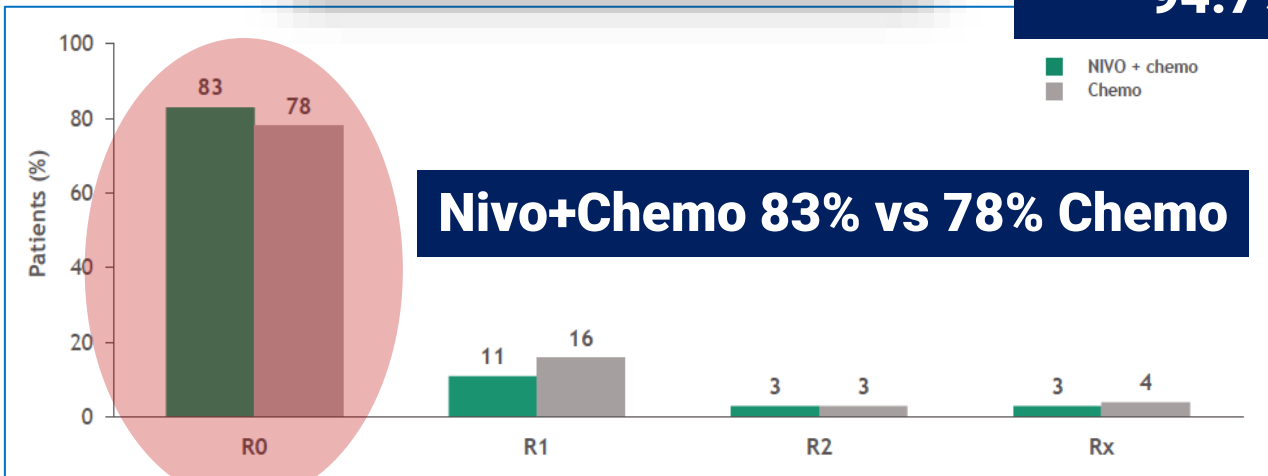
J.Y. Heymach, D. Haggitt, T. Mitsudomi, J.M. Taube, C. Gaffy, M. Hochman, T. Winder, R. Zukin, C. Garbano, S. Gan, H. Suroda, C. Oshiro, T.V. Tran, J. Yoo, K.-Y. Lee, L. Antonuzzi, Z. Pappai Givels, H. Akamatsu, S. Biessels, A. Spis, J. Crawford, H.F. Lu, M. Agregho, G.J. Doherty, H. Mann, T.M. Fouad, and M. Reck, for the AEGEAN Investigators*

AEGEAN



CheckMate816

P.M. Forde, J. Spicer, S. Lu, M. Provencio, T. Mitsudomi, M.M. Awad, E. Felip, S.R. Broderick, J.R. Brahmer, S.J. Swanson, K. Kerr, C. Wang, T.-E. Ciuleanu, G.B. Saylor, F. Tanaka, H. Ito, K.-N. Chen, M. Liberman, E.E. Vokes, J.M. Taube, C. Dorange, J. Cai, J. Fiore, A. Jankowski, D. Balli, M. Sausen, D. Pandya, C.Y. Calvet, and N. Girard, for the CheckMate 816 Investigators*



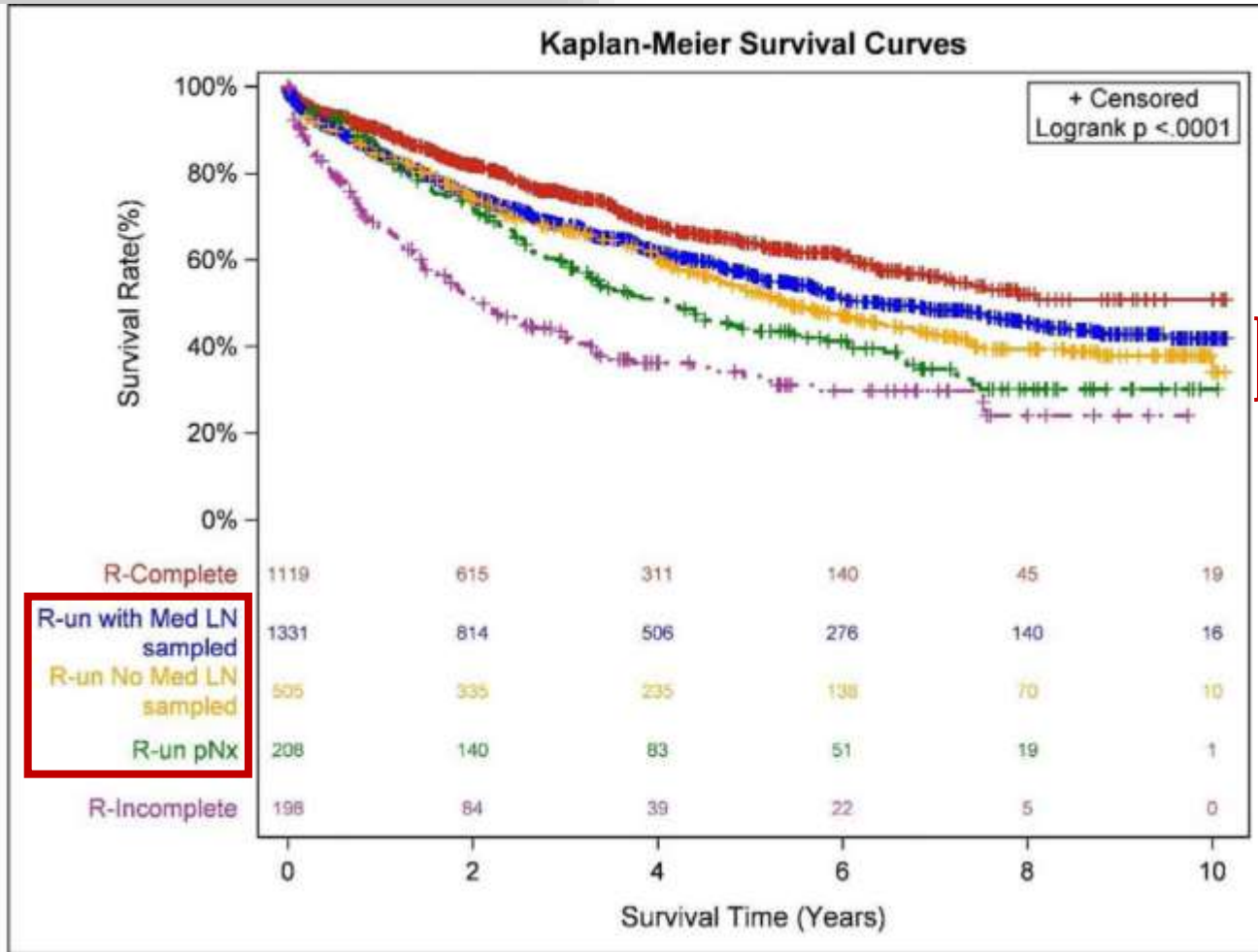
Nivo+Chemo 83% vs 78% Chemo

94.7% vs 91.3% Chemo

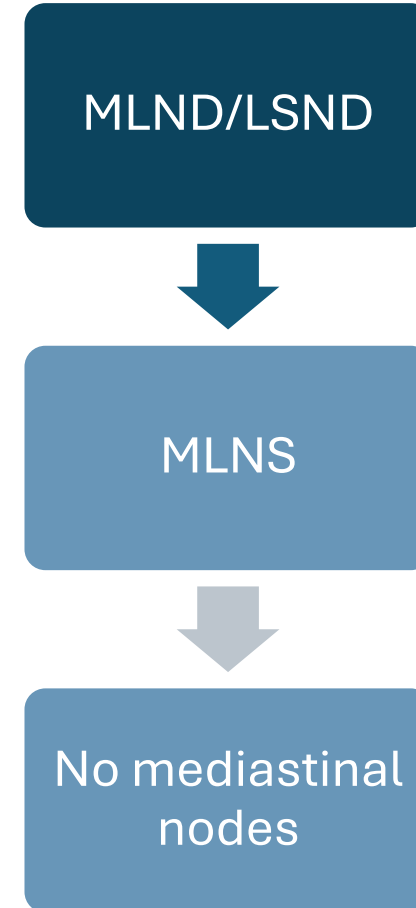
Legend: R0 (dark blue), R1 (medium blue), R2 (light blue), Missing (grey)

Beyond Margin Status: Population-Based Validation of the Proposed IASLC Residual Tumor Classification Re-categorization

Raymond U. Osarogiagbon, MBBS¹, Nicholas R. Faris, M Div¹, Walter Stevens, MPH¹, Carrie Fehnel, BBA¹, Cheryl Houston-Harris, BS¹, Philip Ojeabulu, MBBS¹, Olawale Akinbobola, BS¹, Yu-Shen Lee, MS², Meredith A. Ray, PhD², Matthew P. Smeltzer, PhD²



R(un)



R(un) resections present dose-response relationship regarding LN examination

- In this age of new treatment modalities, should our standards regarding lymph node evaluation remain?

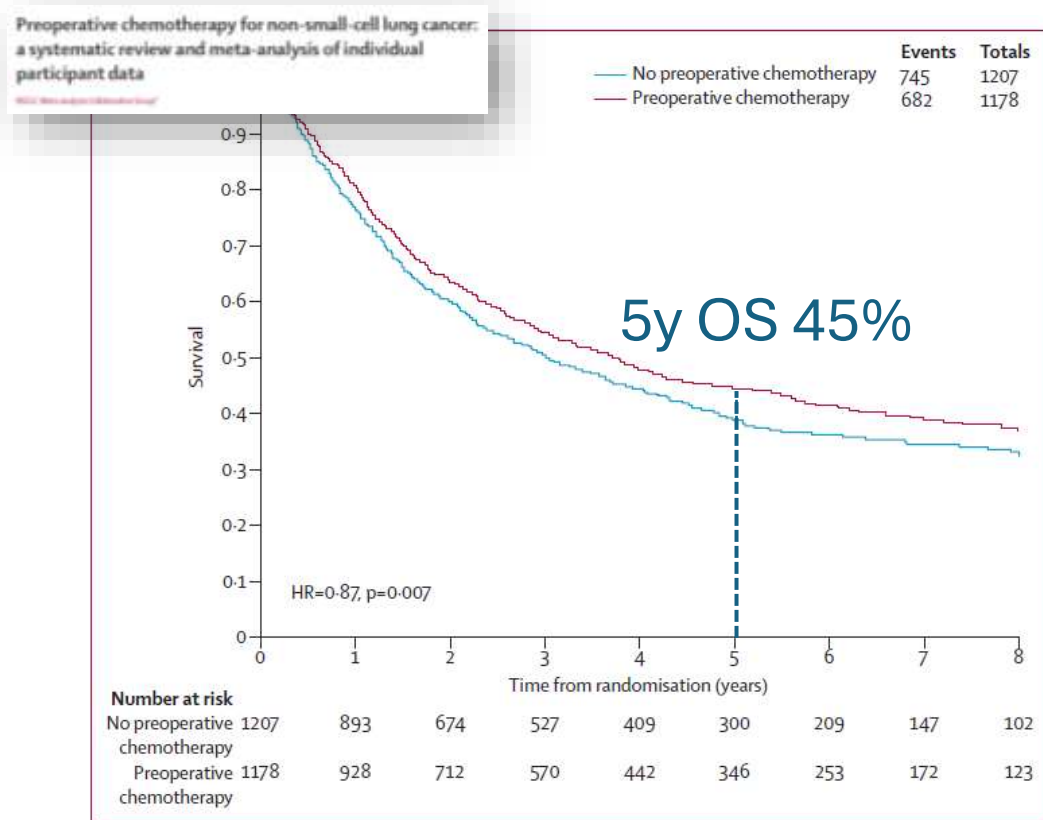
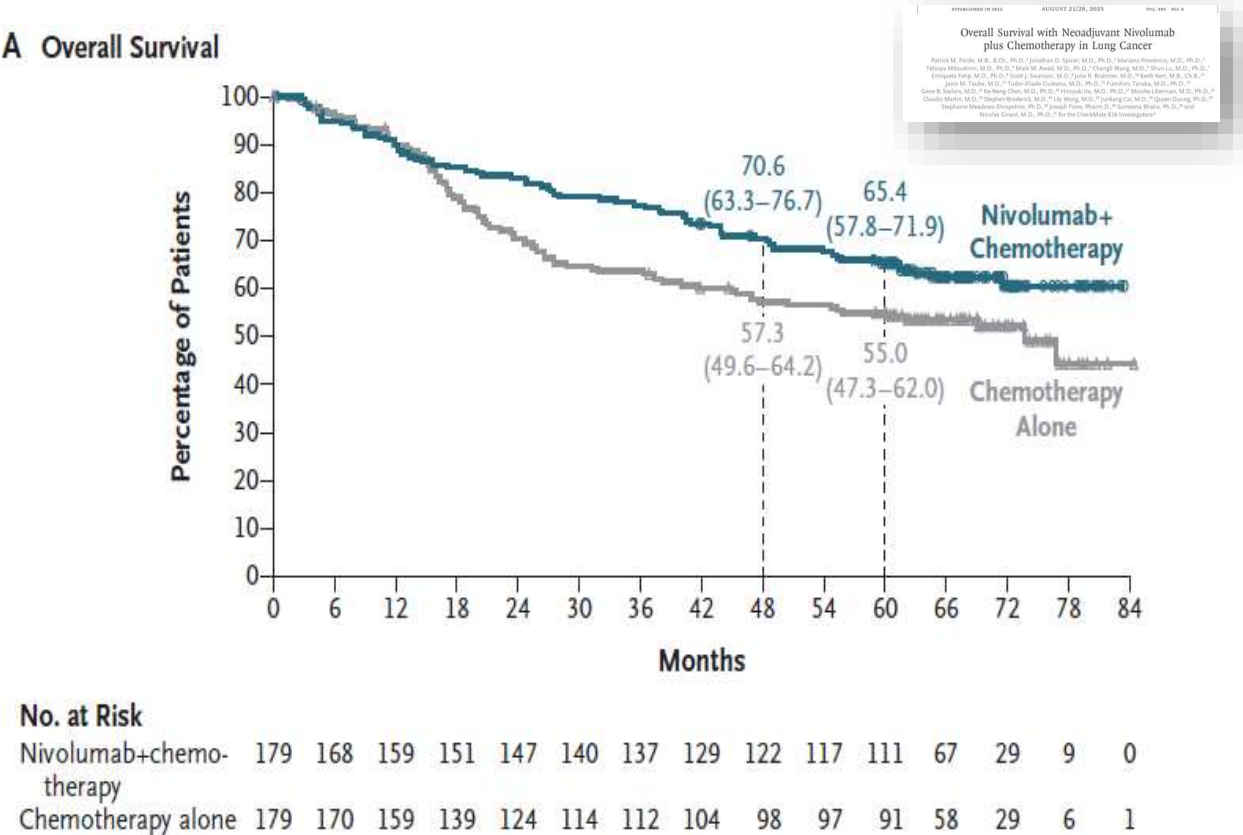


Figure 2: Kaplan-Meier curves (non-stratified) of the effect of preoperative chemotherapy on time to survival

Induction ChT

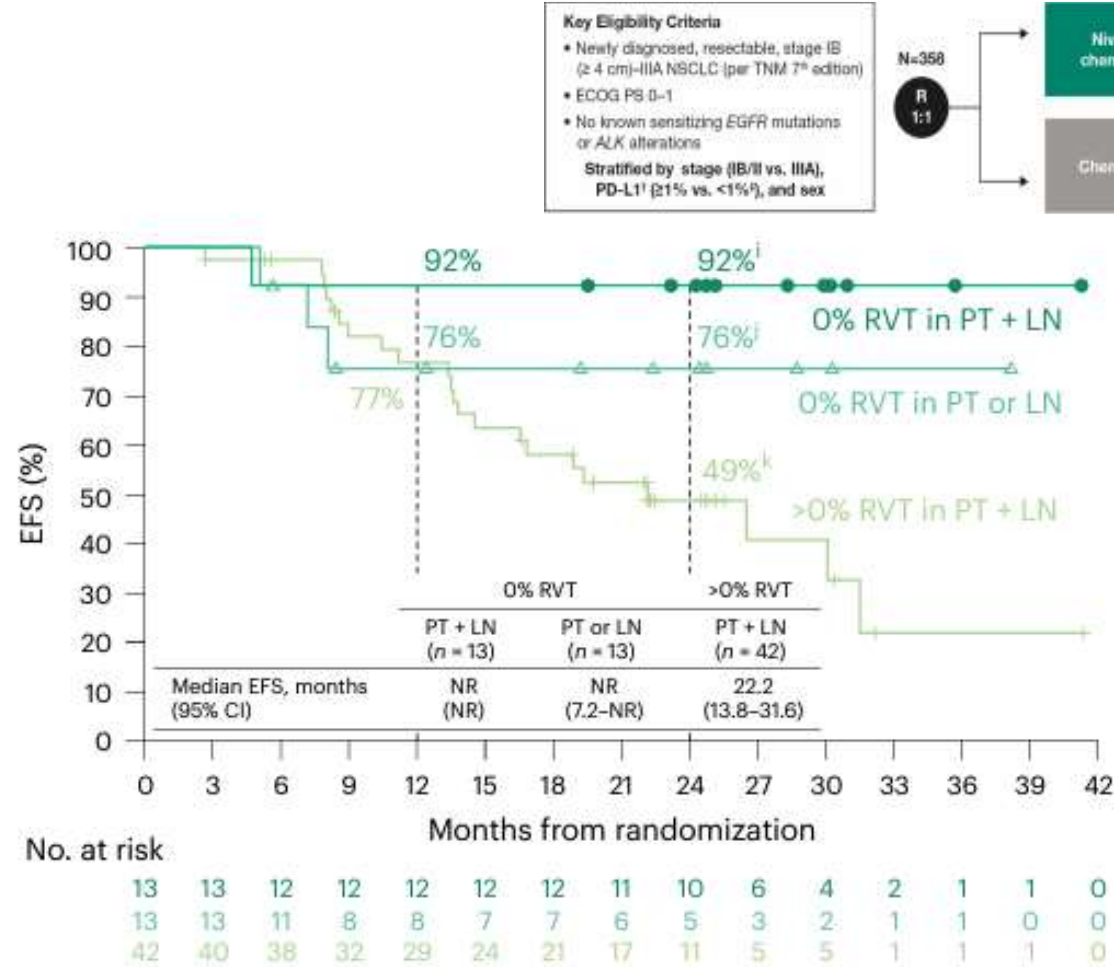
A Overall Survival



Induction ChT+IO

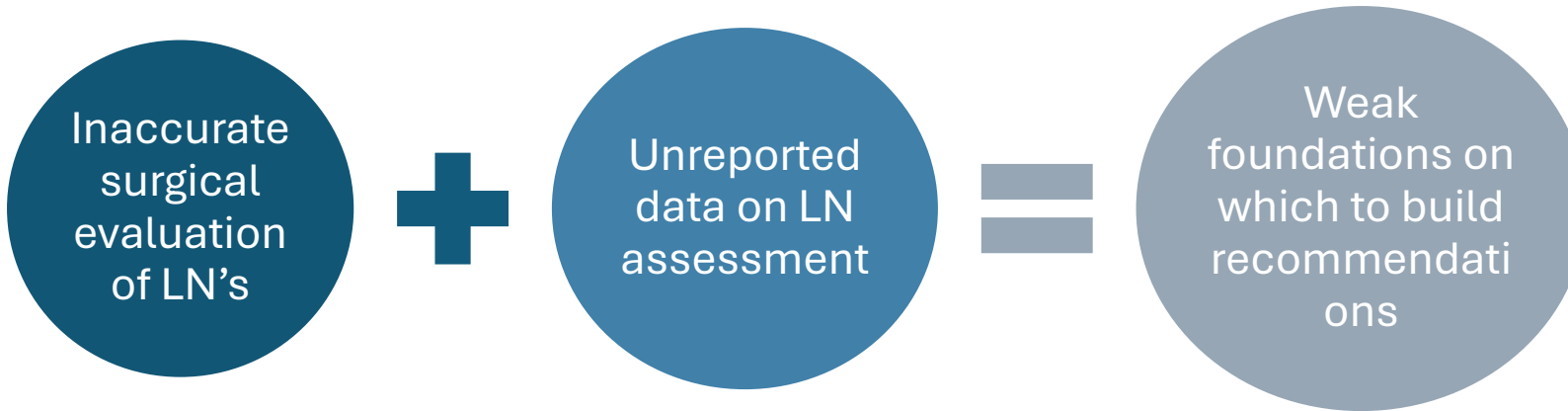
- Are survival benefits with Ch-IO the same regardless of lymph node assessment?

CheckMate816



- Until we develop or discover reliable predictive factors of survival, lymph node evaluation is crucial to determine:
 - pathological response
 - persistent nodal disease
 - incomplete resections

- Insufficient nodal evaluation poses the patient into risk:
 - Omit adjuvant therapy in patients with residual disease
 - Omit relevant prognostic information
 - Leave behind oligometastatic nodal disease



- After induction Ch-IO, are there differences between Surgery and cCRT?

Chemoradiotherapy versus surgery after neoadjuvant chemoimmunotherapy in patients with stage III NSCLC: a real-world multicenter retrospective study

Song Guan¹ · Jifeng Sun² · Yuan Wang³ · Sibel Han^{1,4} · Chen Chen⁵ · Dongsheng Yue⁵ · Yubei Huang⁶ · Kai Ren¹ · Jun Wang² · Jun Wang³ · Lujun Zhao¹

TRAE's

Table 3 Baseline characteristics between the rSurgery and dCCRT groups

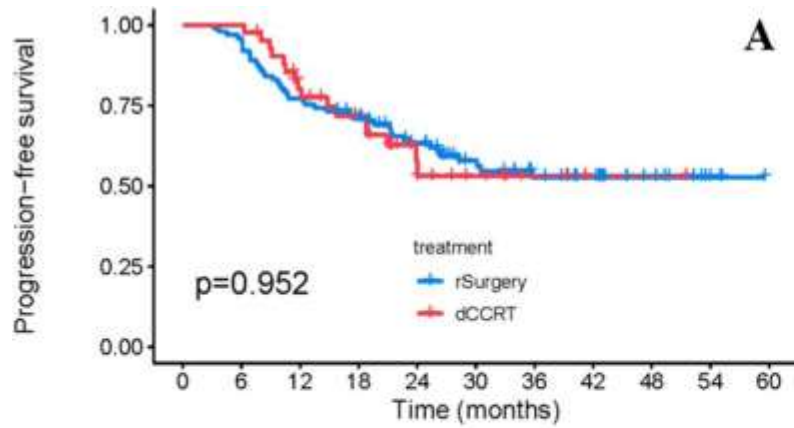
Characteristics	Before PSM		<i>P</i>	After PSM		<i>P</i>
	rSurgery (n= 101)	dCCRT (n= 42)		rSurgery (n= 40)	dCCRT (n= 40)	
	No (%)	No (%)		No (%)	No (%)	
Age						
< 65	66(65.3)	29(69.0)	0.669	27(67.5)	27(67.5)	1.000
≥ 65	35(34.7)	13(31.0)		13(32.5)	13(32.5)	
Sex						
Male	84(83.2)	39(92.9)	0.128	38(95.0)	37(92.5)	1.000
Female	17(16.8)	3(7.1)		2(5.0)	3(7.5)	
WHO histology						
Squamous	71(70.3)	29(69.0)	0.013	26(65.0)	28(70.0)	0.066
Non-squamous	29(28.7)	8(19.0)		14(35.0)	8(20.0)	
NOS	1(1.0)	5(11.9)		0(0.0)	4(10.0)	
Stage						
IIIA	51(50.5)	20(47.6)	0.076	18(45.0)	20(50.0)	0.133
IIIB	45(44.6)	15(35.7)		20(50.0)	13(32.5)	
IIIC	5(5.0)	7(16.7)		2(5.0)	7(17.5)	
Adjuvant ICI						
No	54(53.5)	26(61.9)	0.355	24(60.0)	24(60.0)	1.000
Yes	47(46.5)	16(38.1)		16(40.0)	16(40.0)	
ECOG						
0	23(22.8)	1(2.4)	0.001	1(2.5)	1(2.5)	1.000
1	78(77.2)	40(95.2)		39(97.5)	39(97.5)	
2	0(0.0)	1(2.4)		0(0.0)	0(0.0)	
aCCI						
≤ 2	60(59.4)	23(54.8)	0.608	21(52.5)	22(55.0)	0.823
> 2	41(40.6)	19(45.2)		19(47.5)	18(45.0)	

Table 2 TRAEs between the surgery and CRT groups

TRAE	Surgery		CRT		<i>P</i>
	No	%	No	%	
Pneumonitis	67	64.4	89	65.9	0.809
G3/4 pneumonitis	6	5.8	16	11.9	0.107
Postoperative pneumonia	40	38.5	0	0.0	
Esophagitis	3	2.9	30	22.2	
G3/4 esophagitis	0	0.0	0	0.0	
Hematologic toxicity	63	60.6	89	65.9	0.394
G3/4 hematologic toxicity	8	7.7	24	17.8	0.023
Dermatitis	4	3.8	5	3.7	1.000
G3/4 dermatitis	1	1.0	1	0.7	1.000

Table 5 TRAEs between the rSurgery and dCCRT groups after PSM

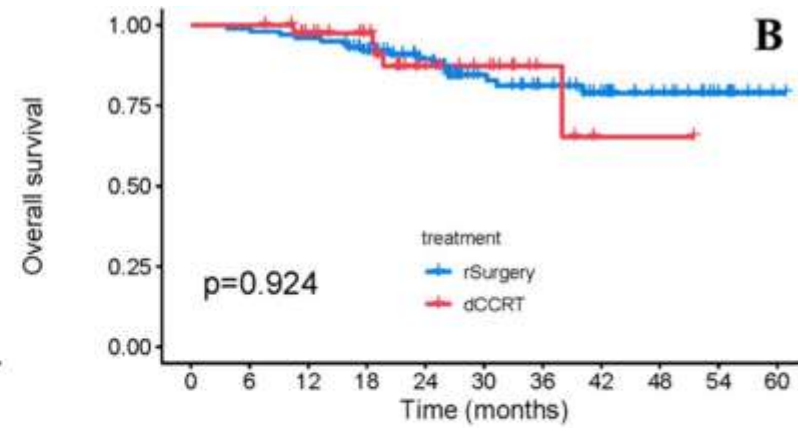
TRAE	rSurgery		dCCRT		<i>P</i>
	No	%	No	%	
Pneumonitis	25	62.5	25	62.5	1.000
G3/4 pneumonitis	2	5.0	2	5.0	1.000
Postoperative pneumonia	16	40.0	0	0.0	
Esophagitis	0	0.0	7	17.5	
G3/4 esophagitis	0	0.0	0	0.0	
Hematologic toxicity	21	52.5	29	72.5	0.065
G3/4 hematologic toxicity	4	10.0	12	30.0	0.025
Dermatitis	1	2.5	1	2.5	1.000
G3/4 dermatitis	0	0.0	0	0.0	NA



Number at risk

treatment	0	6	12	18	24	30	36	42	48	54	60
rSurgery	101	97	78	68	53	36	27	22	12	5	0
dCCRT	42	42	30	24	12	7	3	1	1	0	0

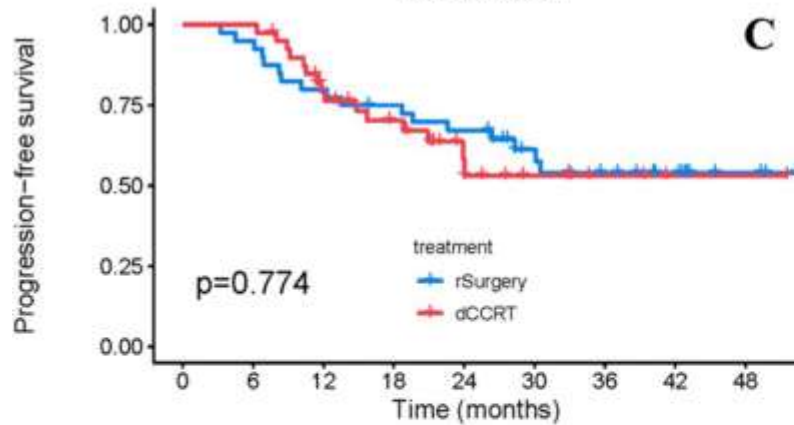
Time (months)



Number at risk

treatment	0	6	12	18	24	30	36	42	48	54	60
rSurgery	101	100	97	86	73	50	40	32	19	10	1
dCCRT	42	42	36	30	16	11	4	1	1	0	0

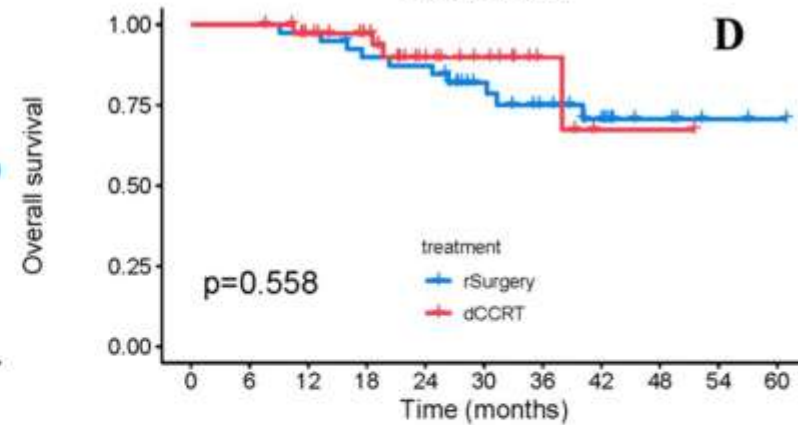
Time (months)



Number at risk

treatment	0	6	12	18	24	30	36	42	48
rSurgery	40	38	32	29	26	17	13	9	3
dCCRT	40	40	28	22	11	6	3	1	1

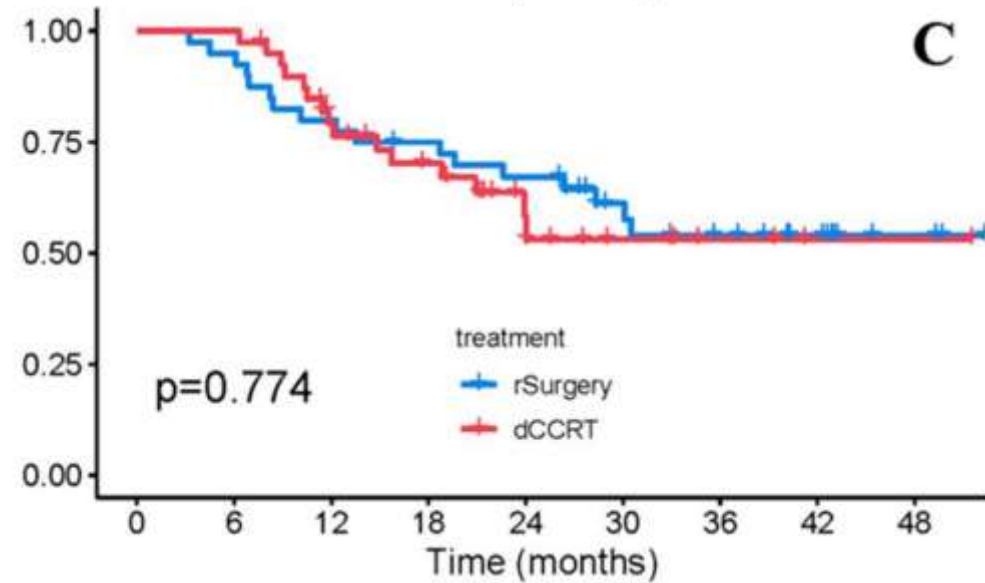
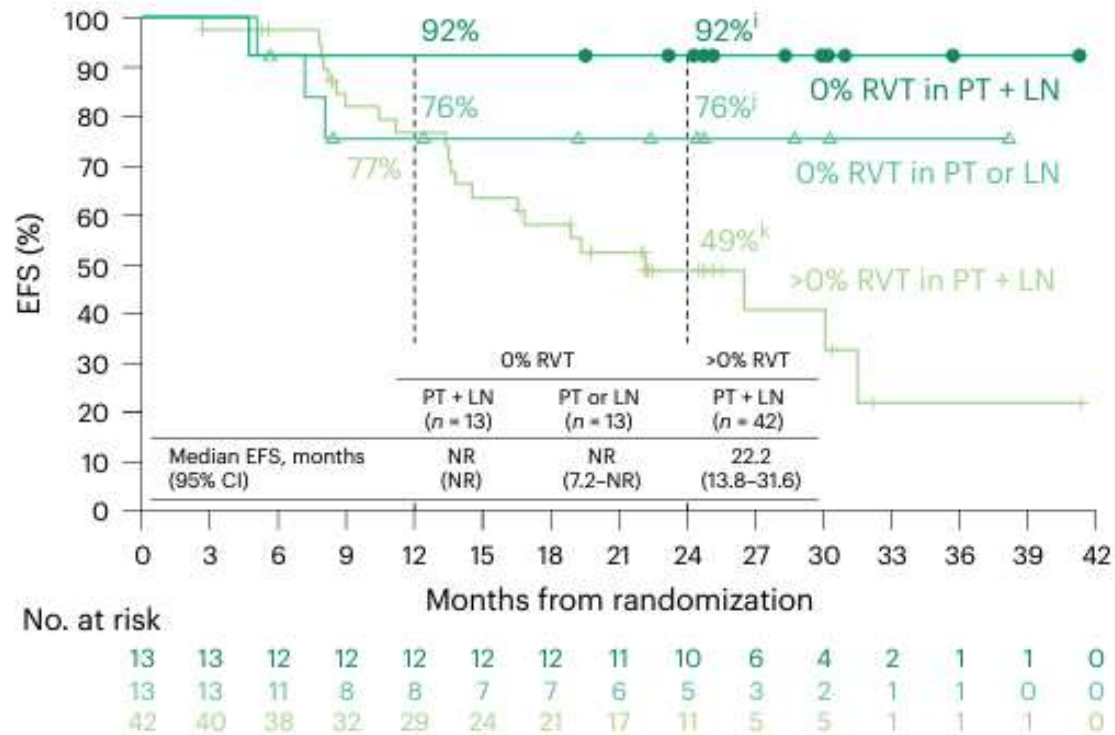
Time (months)



Number at risk

treatment	0	6	12	18	24	30	36	42	48	54	60
rSurgery	40	40	39	35	34	24	19	14	5	2	1
dCCRT	40	40	34	28	15	10	4	1	1	0	0

Time (months)

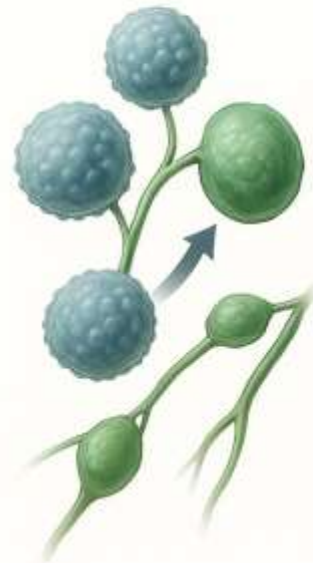


¿Can cCRT be considered an alternative local treatment in some cases after induction Ch-10?

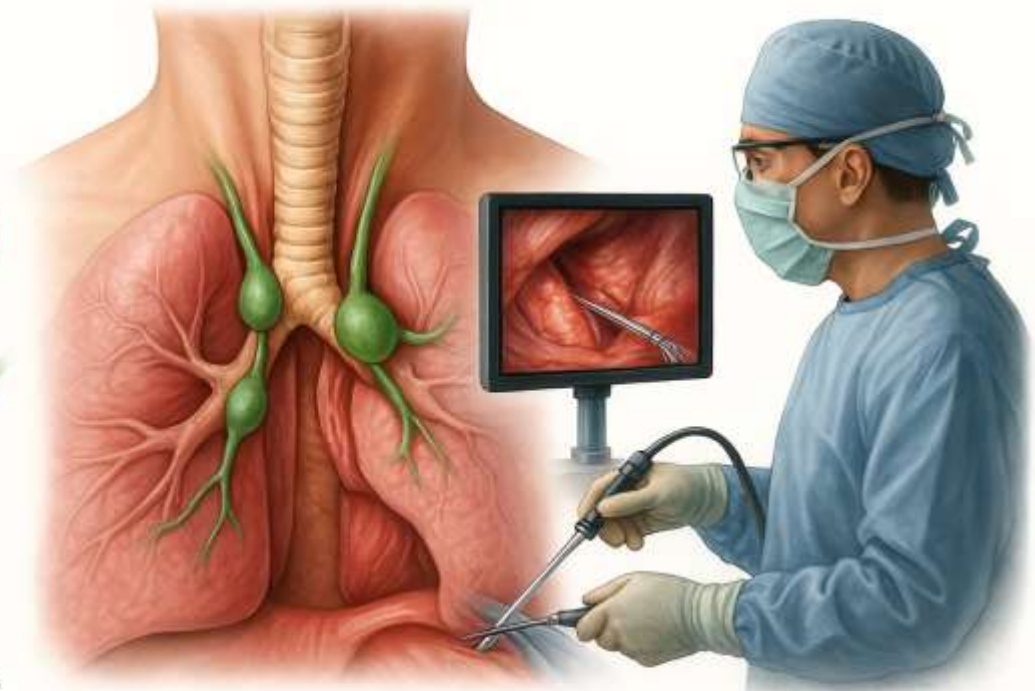
dLN's (draining lymph nodes)

Table 4 Failure patterns between the rSurgery and dCCRT groups

Failure pattern	rSurgery		dCCRT		<i>P</i>
	No	%	No	%	
Before PSM					
Locoregional	32	82.1	11	78.6	1.000
Distant	20	51.3	6	42.9	0.589
1-year locoregional	18	18.6	6	15.8	0.705
1-year distant	9	9.3	4	10.5	1.000
After PSM					
Locoregional	13	76.5	11	78.6	1.000
Distant	12	70.6	6	42.9	0.119
1-year locoregional	7	17.9	6	16.7	0.883
1-year distant	5	12.8	4	11.1	1.000



**T Lymphocytes
Migrating to a
Lymph Node**



**Intrathoracic
Lymph Nodes**

**Surgeon Excising
a Lymph Node**

TAKE HOME MESSAGES

- Pathological response is a predictor of survival after induction Ch-IO
- Residual disease poses the patient at higher risk of death
- Pathological complete response and residual disease descriptor can not be attributed if LN's are not accurately examined during surgery
- Systematic or lobe-specific lymph node dissection should be the standard
- Combined effort between surgeons and pathologists is crucial to perform and describe sufficient nodal assessment
- Induction trials should accomplish these standards and report these data
- cCRT after induction Ch-IO should be studied as an alternative for some subsets of patients as local treatment modality

16th
CONGRESS
Lung ON
CANCER

BARCELONA
27 / 28
NOVEMBER 2025

THANK YOU