Lung Cancer UPDATES
IASLC HIGHLIGHTS
09-12 SEPTIEMBRE 2023
Singapore

Iniciativa científica de:
GECP
lung cancer research

Estadios iniciales, adyuvancia y localmente avanzado

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Estadificacion TNM / 9ª Ed

Iniciativa científica de: GECP lung cancer research

Proposed 9th Edition N-categories			9th Edition
NX		Regional lymph nodes cannot be assessed	No changes
N0		No regional lymph node metastasis	No changes
N1		Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension	No changes
N2		Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)	
	N2a	Single N2 station involvement	Subdivided
	N2b	Multiple N2 station involvement	Subdivided
N3		Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)	No changes

Proposed 9th Edition M-categories			9th Edition
M0		No distant metastasis	No changes
M1		Distant metastasis	No changes
	M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural or pericardial effusion. Most pleural (pericardial) effusions with lung cancer are due to tumor. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is non-bloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging descriptor.	No changes
	M1b	**Single** extrathoracic metastasis in a **single** organ and involvement of a single distant (non-regional) node	No changes
	M1c1	**Multiple** extrathoracic metastases in a **single** organ system	Subdivided
	M1c2	**Multiple** extrathoracic metastases in **multiple** organ systems	Subdivided

Estadificacion TNM 9ª Ed

Iniciativa científica de: GECP lung cancer research

8th Ed Categories

8th Ed TNM Categories

T/M	Label	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
	T2a >3-4	IB	IIB	IIIA	IIIB
	T2b >4-5	IIA	IIB	IIIA	IIIB
T3	T3 >5-7	IIB	IIIA	IIIB	IIIC
	T3 Inv	IIB	IIIA	IIIB	IIIC
	T3 Sat	IIB	IIIA	IIIB	IIIC
T4	T4 > 7	IIIA	IIIA	IIIB	IIIC
	T4 Inv	IIIA	IIIA	IIIB	IIIC
	T4 Ipsi Nod	IIIA	IIIA	IIIB	IIIC
M1	M1a Contr Nod	IVA	IVA	IVA	IVA
	M1a Pleur	IVA	IVA	IVA	IVA
	M1b Single Lesion	IVA	IVA	IVA	IVA
	M1c Multiple Lesions	IVB	IVB	IVB	IVB

Proposed 9th Ed TNM Categories

Proposed 9th Ed TNM Categories

T/M	Label	N0	N1	N2		N3
9th				N2a	N2b	
T1	T1a ≤1 cm	IA1	IIA	IIB	IIIA	IIIB
	T1b >1 to ≤2 cm	IA2	IIA	IIB	IIIA	IIIB
		IA3	IIA	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB	IIIB
	T2a >3 to ≤4 cm	IB	IIB	IIIA	IIIB	IIIB
	T2b >4 to ≤5 cm	IIA	IIB	IIIA	IIIB	IIIB
T3		IIB	IIIA	IIIA	IIIB	IIIC
	T3 Invasion	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Satellite nodules	IIB	IIIA	IIIA	IIIB	IIIC
T4	T4 > 7 cm	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Invasion	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Ipsilateral nodules	IIIA	IIIA	IIIB	IIIB	IIIC
M1	M1a Contralateral nodules	IVA	IVA	IVA	IVA	IVA
	M1a Pleural, pericardial effusion	IVA	IVA	IVA	IVA	IVA
	M1b Single Extrathoracic Lesion	IVA	IVA	IVA	IVA	IVA
	M1c1 Mult. Lesions, Single Organ system	IVB	IVB	IVB	IVB	IVB
	M1c2 Mult. Lesions, Mult. Organ systems	IVB	IVB	IVB	IVB	IVB

Importancia Comités Multidisciplinares

Iniciativa científica de:
GECP lung cancer research

Tsuguo Naruke Lectureship Award for Surgery

What Thoracic Surgeons need to bring to the Multi-Modality Conversation

Alan D. L. Sihoe 司徒達麟 醫生

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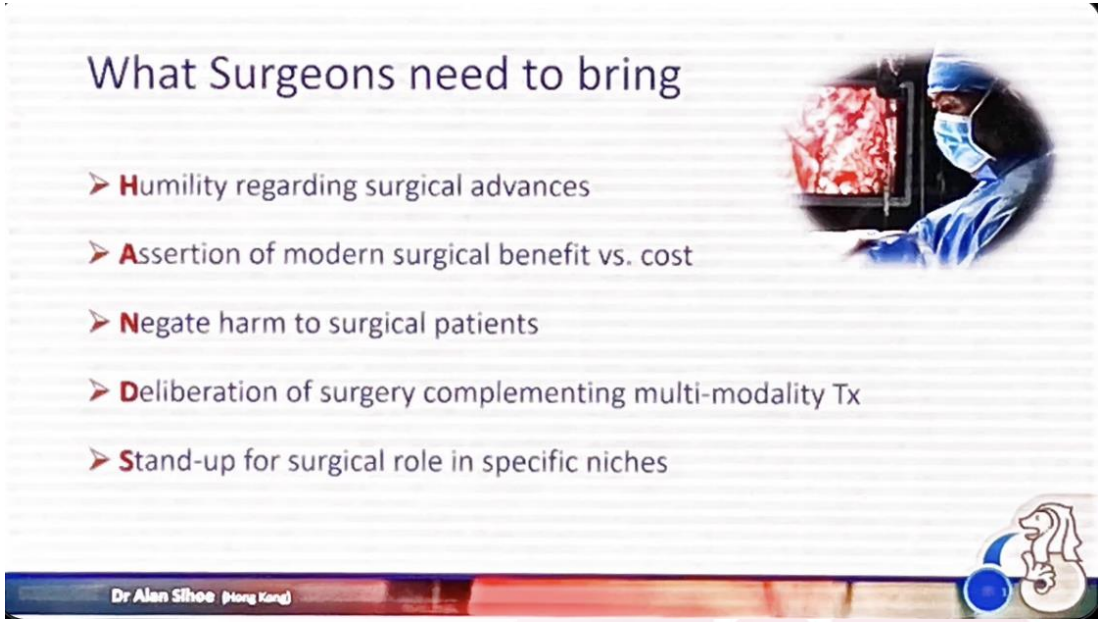
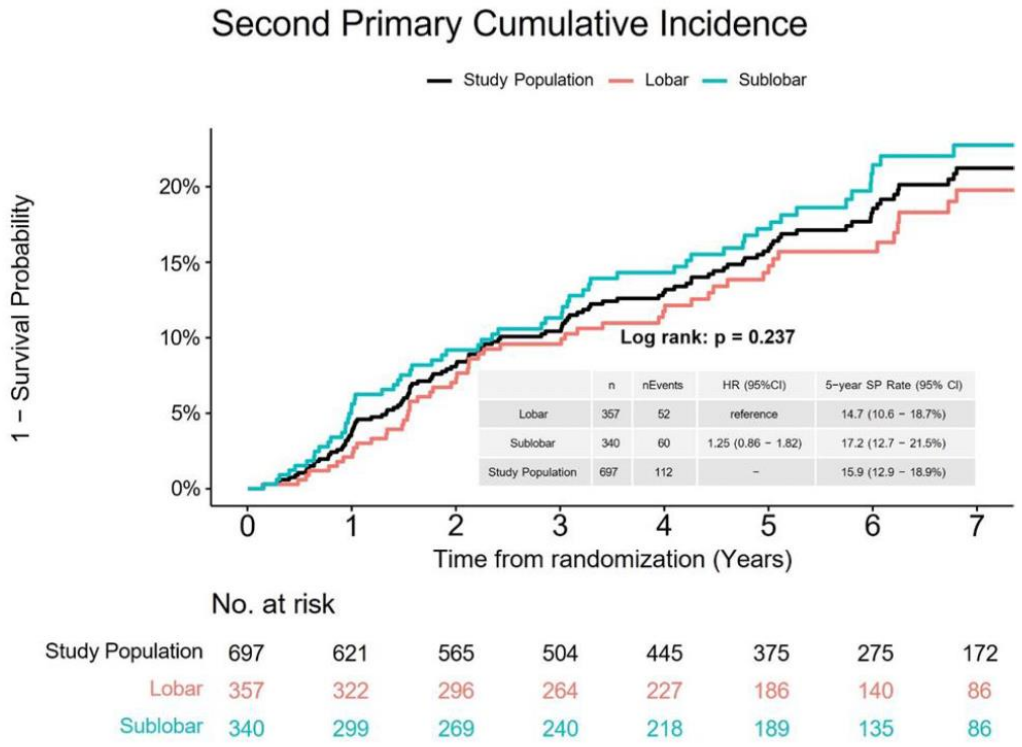
Councillor, Asian Society for Cardio-Vascular and Thoracic Surgery (ASCVTS)
Secretary General, Asia Thoracoscopic Surgery Education Platform (ATEP)
International Director, Society of Thoracic Surgeons (STS)



Recaidas / 2º primarios en cirugía sublobar CALGB 140503

Cumulative incidence of second primary lung cancer



5-year second primary rate

Lobectomy: 14.7% (95%CI: 10.6-18.7%)

Sub-lobar resection: 17.2% (95%CI: 12.7-21.5%)

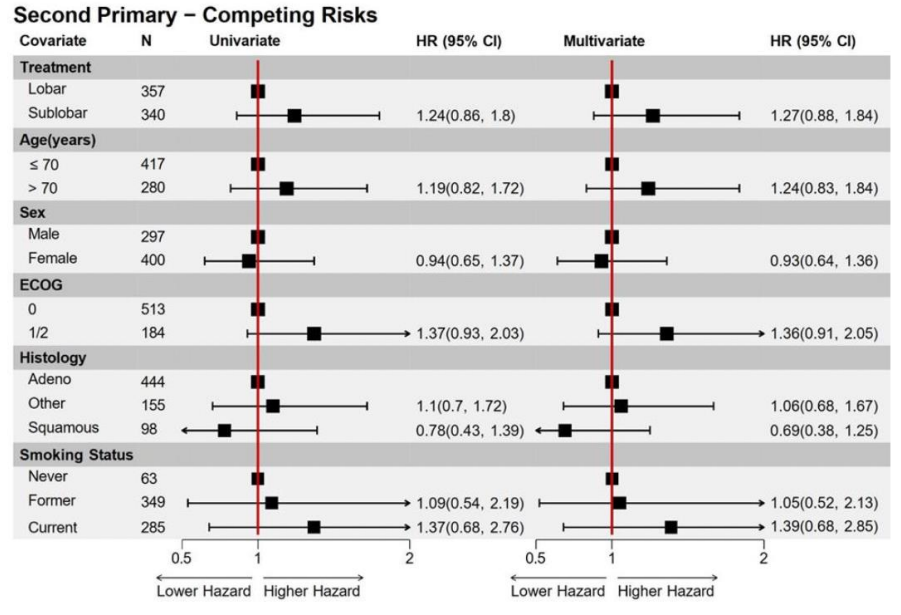
Study population: 15.9% (95% CI: 12.9-18.9%)

Rate per patient per year

Lobectomy: 3.1% (95% CI: 2.4-4.1%)

Sub-lobar resection: 3.8% (95% CI: 2.9-4.9%)

Study population: 3.4% (95% CI: 2.9-4.1%)



Thomas Stinchcombe/ WCLC23

Resección sublobar en factores de riesgos (VPI, LVI, High grade)

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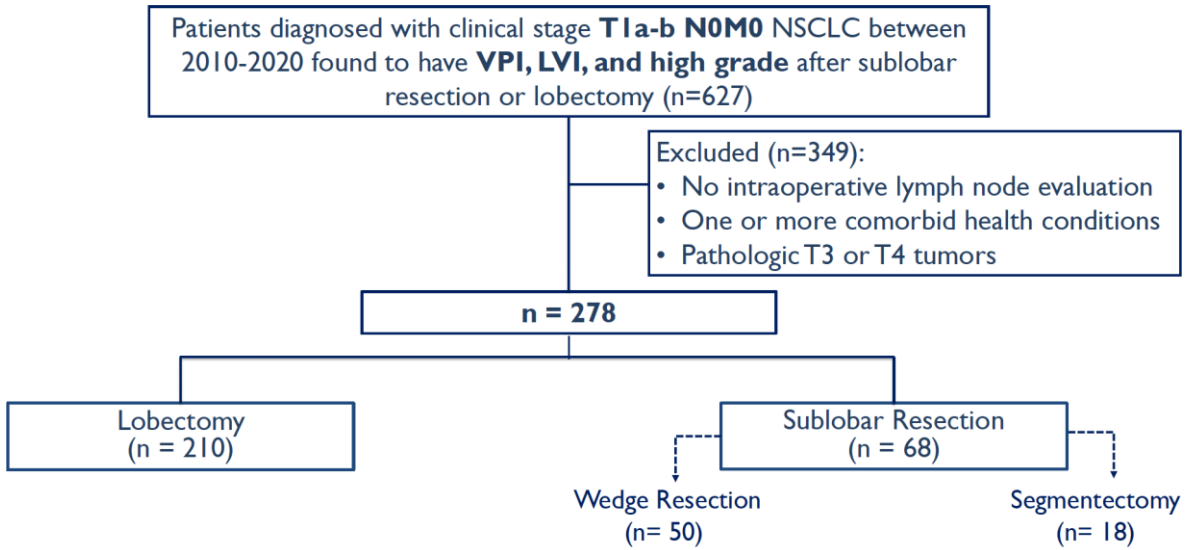
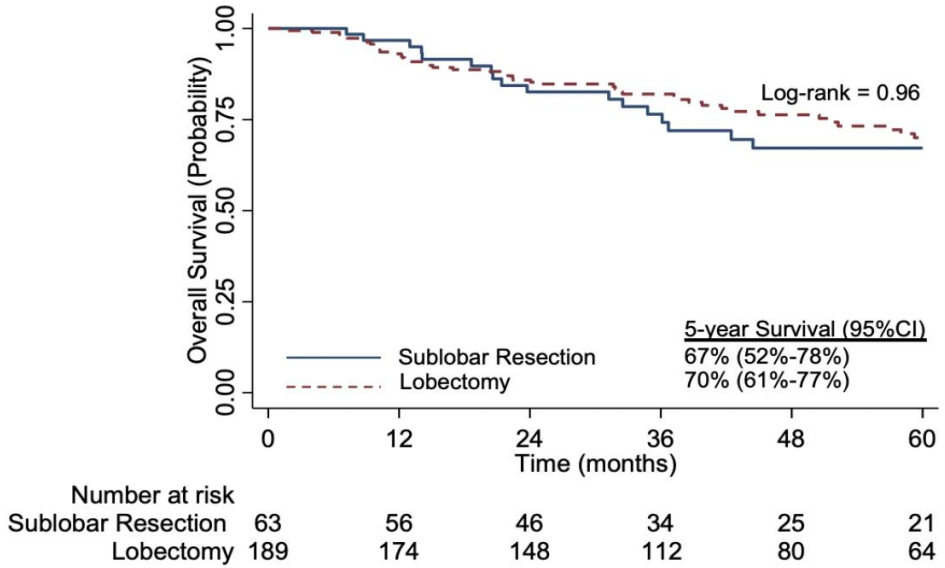
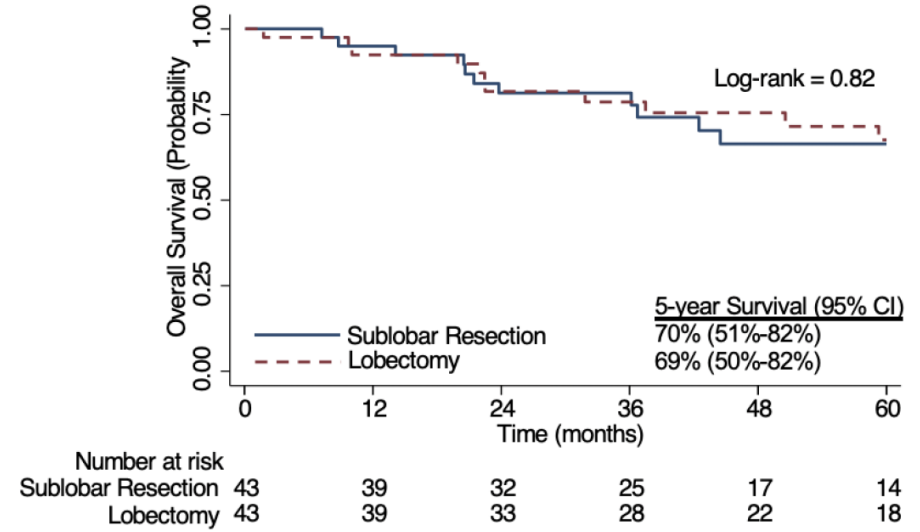
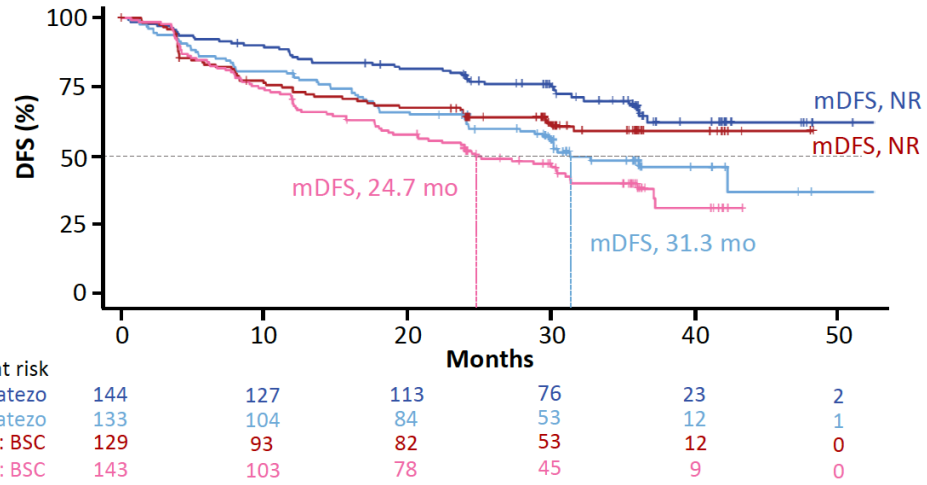






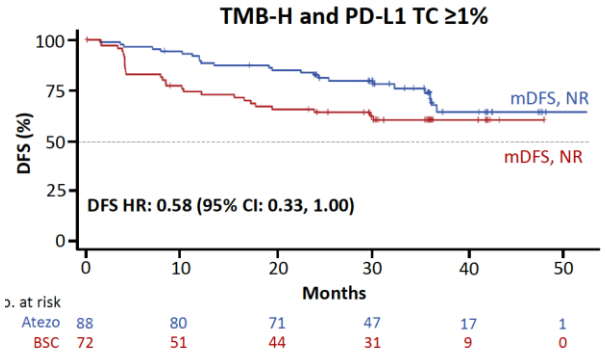
Camille Mathey-Andrews/ WCLC23

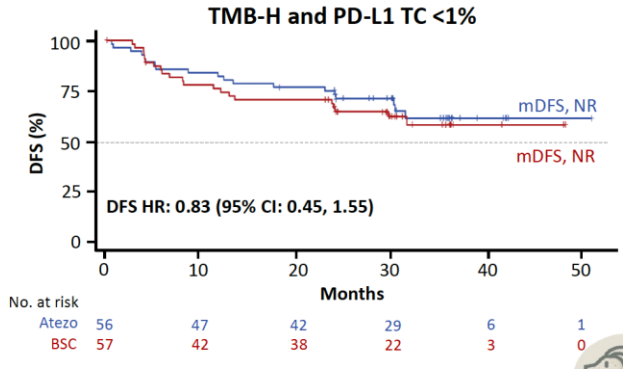
Tratamiento adyuvante: TMB en IMPower 010

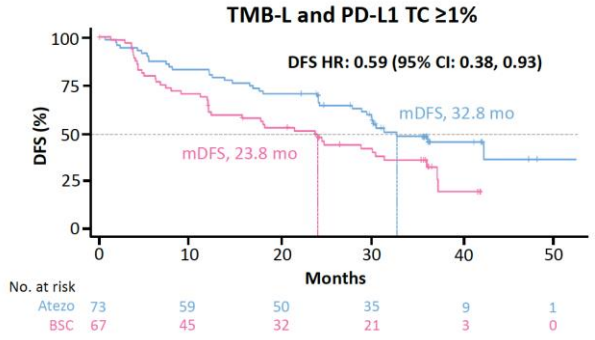


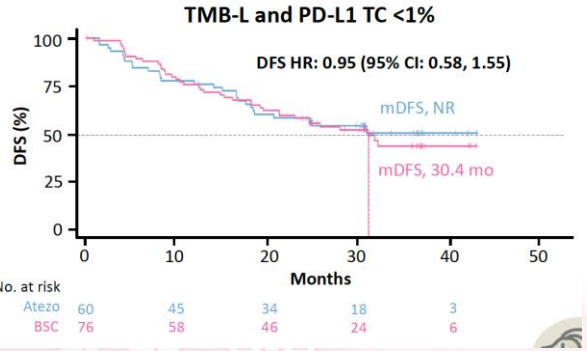
TMB-H vs TMB-L	DFS HR (95% CI)
TMB-H: atezo vs TMB-L: atezo	0.52 (0.36, 0.78)
TMB-H: BSC vs TMB-L: BSC	0.62 (0.44, 0.89)

Atezolizumab vs BSC	DFS HR (95% CI)
TMB-H: atezo vs TMB-H: BSC	0.67 (0.44, 1.01)
TMB-L: atezo vs TMB-L: BSC	0.76 (0.54, 1.05)

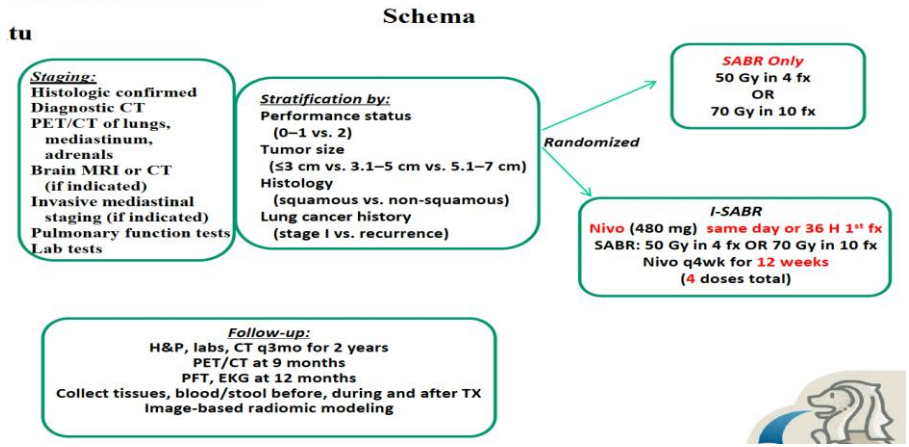








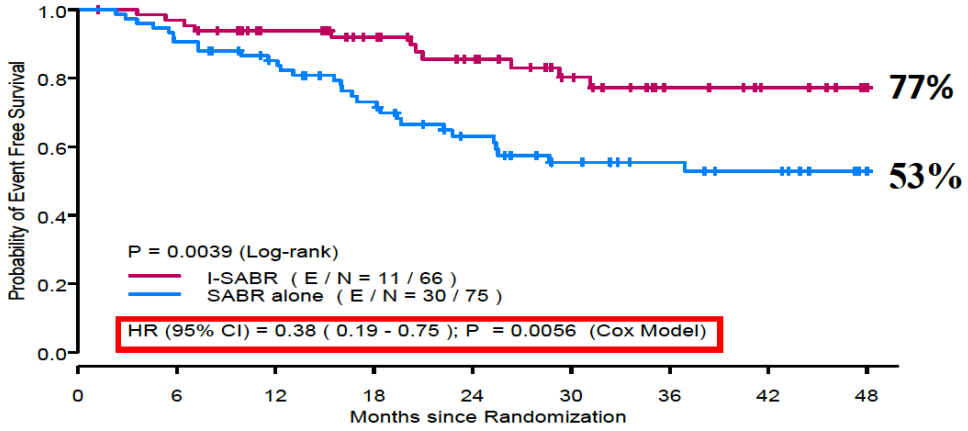
Nivolumab adyuvante SABRT



Pattern of failure

Event	I-SABR (n=66)	SABR (n=75)
Local Failure Only	0 (0%)	7 (9.3%)
Regional Failure Only	4 (6.1%)	2 (2.7%)
Distant Metastasis Only	2 (3.0%)	3 (4.0%)
Local + Regional Failure	0 (0%)	0 (0%)
Local + Distant Failure	0 (0%)	2 (2.7%)
Local + Regional + Distant Failure	0 (0%)	1 (1.3%)
Regional + Distant Failure	0 (0%)	5 (6.7%)
Second Primary Lung Cancer	2 (3.0%)	6 (8.0%)
Any Local Failure	0 (0%)	10 (13.3%)
Any Regional Failure	4 (6.1%)	8 (10.7%)
Any Distant Failure	2 (3.0%)	12 (16.0%)
Any Death	4 (6.1%)	9 (12.0%)
Any Recurrence and/or Death Event	8 (12.1%)	27 (36.0%)
No Relapse or Death	58 (87.9%)	48 (64.0%)

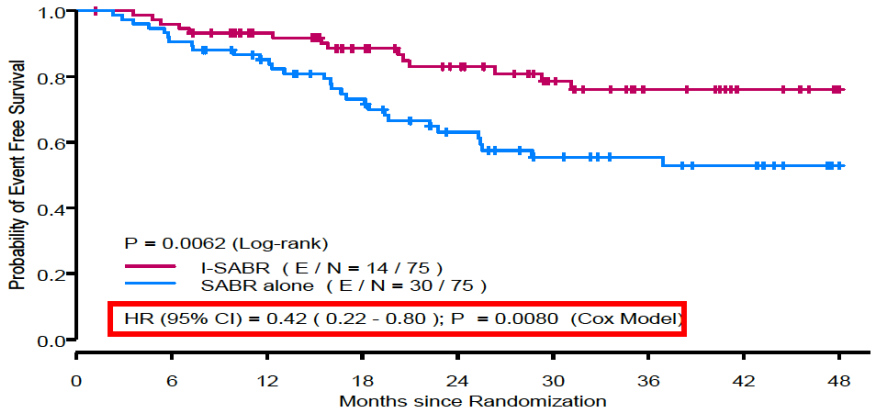
Per protocol



No. at Risk (No. of Event)

I-SABR	66 (0)	54 (4)	38 (4)	18 (3)	7 (0)
SABR	75 (0)	59 (11)	34 (14)	22 (4)	11 (1)

Per ITT



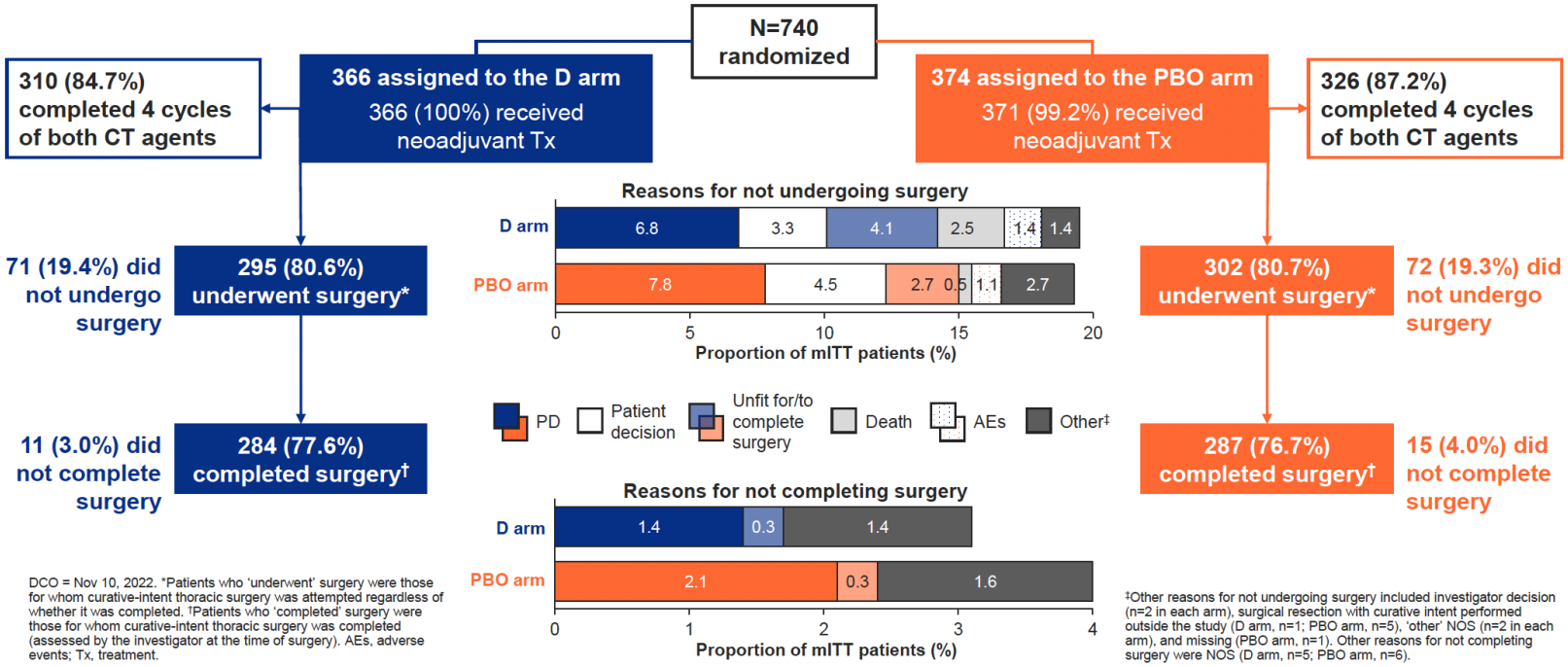
No. at Risk (No. of Event)

I-SABR	75 (0)	62 (5)	43 (6)	22 (3)	9 (0
SABR	75 (0)	59 (11)	34 (14)	22 (4)	11 (

Joey Y Chang / WCLC23

Cirugia en Fase III AEGEAN (Durvalumab perioperatorio)

Iniciativa científica de: GECP lung cancer research



DCO = Nov 10, 2022. *Patients who 'underwent' surgery were those for whom curative-intent thoracic surgery was attempted regardless of whether it was completed. †Patients who 'completed' surgery were those for whom curative-intent thoracic surgery was completed (assessed by the investigator at the time of surgery). AEs, adverse events; Tx, treatment.

‡Other reasons for not undergoing surgery included investigator decision (n=2 in each arm), surgical resection with curative intent performed outside the study (D arm, n=1; PBO arm, n=5), 'other' NOS (n=2 in each arm), and missing (PBO arm, n=1). Other reasons for not completing surgery were NOS (D arm, n=5; PBO arm, n=6).

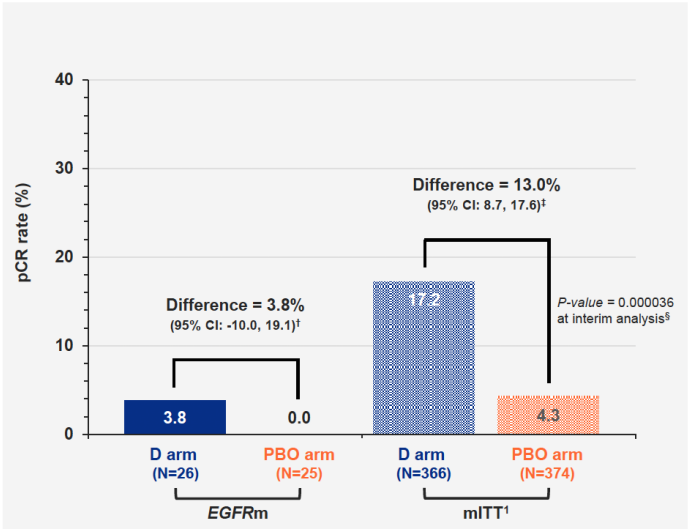
Tetsuya Mitsudomi / WCLC23

EC Fase III AEGEAN. Subanálisis EGFR mut+

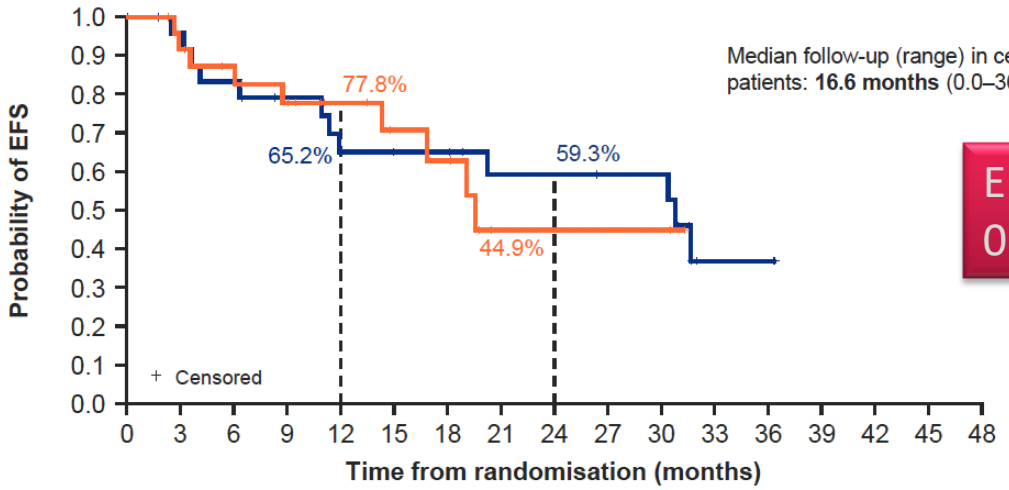
Iniciativa científica de: GECP lung cancer research

Disease and planned treatment characteristics		Durvalumab arm (n=26)	Placebo arm (n=25)
Disease stage (AJCC 8th ed.), %	II	42.3	36.0
	IIIA	34.6	44.0
	IIIB	23.1	20.0
Histology, %	Squamous	11.5	4.0
	Non-squamous	88.5	96.0
EGFR mutation type§, %	Exon 19 deletions¶	53.8	36.0
	L858R mutations¶	11.5	16.0
	Other¶	3.8	24.0
	Not specified#	30.8	28.0
PD-L1 expression, %	TC <1%	38.5	32.0
	TC 1–49%	50.0	60.0
	TC ≥50%	11.5	8.0
Planned neoadj. platinum agent, %	Cisplatin	23.1	36.0
	Carboplatin	76.9	64.0

pCR (central lab)



*EGFR*m subgroup	Durvalumab arm	Placebo arm
No. events / no. patients (%)	12/26 (46.2)	9/25 (36.0)
mEFS, months (95% CI)	30.8 (11.4, NR)	19.6 (14.3, NR)
Unstratified HR† (95% CI)	**0.86 (0.35, 2.19)**	



Median follow-up (range) in censored patients: **16.6 months** (0.0–36.4)

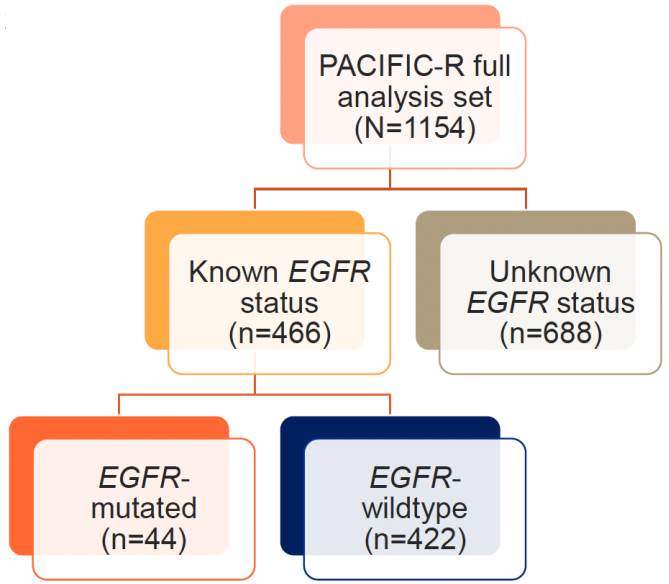
No. at risk:																	
D arm	26	23	20	17	14	13	13	10	10	9	9	2	2	0	0	0	0
PBO arm	25	22	19	16	12	9	8	2	2	2	2	0	0	0	0	0	0

EFS HR Global: 0.68 (0.53-0.88)

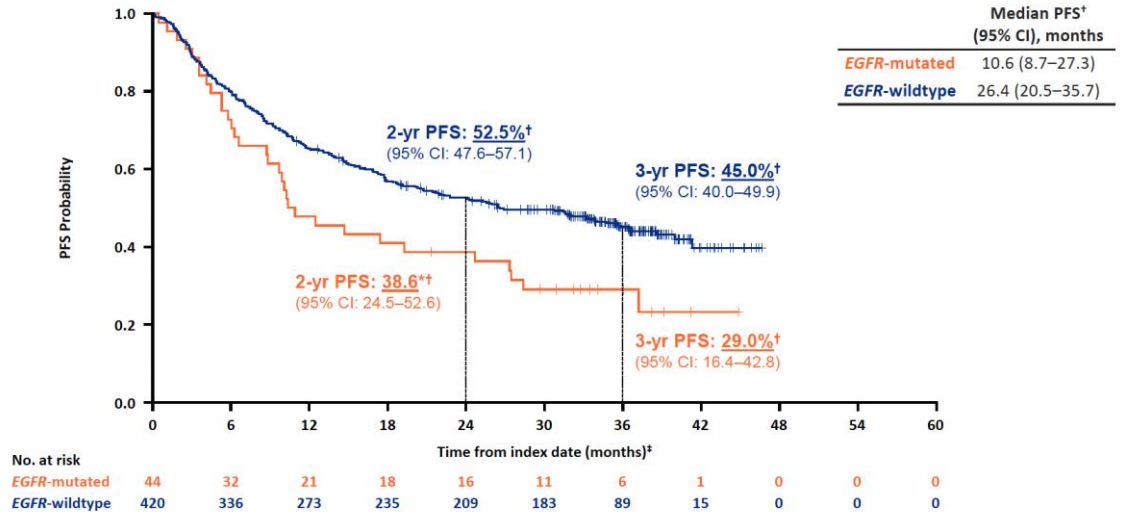
David Harpole / WCLC23

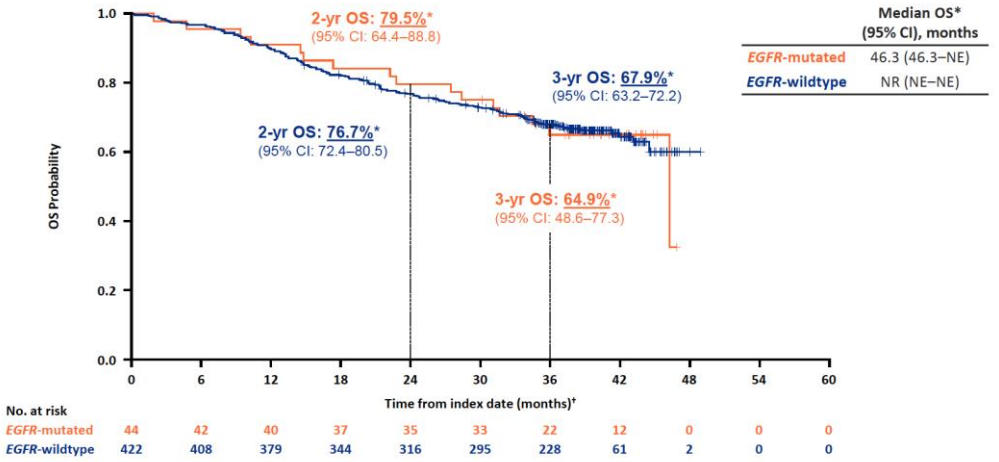
Estudio PACIFIC-R. Subanálisis EGFR mut+

Iniciativa científica de: GECP lung cancer research



	EGFR-mutated (n=44)	*EGFR*-wildtype (n=422)
Patients with distant metastases, n (%)	20 (**45.5**)	124 (**29.4**)
First subsequent Tx (post durvalumab)†	n=20	n=124
EGFR-TKIs, n (%)	15 (**75.0**)	1 (**0.8**)
Afatinib	2 (**10.0**)	1 (**0.8**)
Erlotinib	5 (**25.0**)	0
Gefitinib	2 (**10.0**)	0
Osimertinib	9 (**45.0**)	0
Any immunotherapy, n (%)	0	29 (**23.4**)
Any chemotherapy, n (%)	3 (**15.0**)	57 (**46.0**)
Any radiotherapy, n (%)	8 (**40.0**)	43 (**34.7**)
Any surgery, n (%)	3 (**15.0**)	14 (**11.3**)

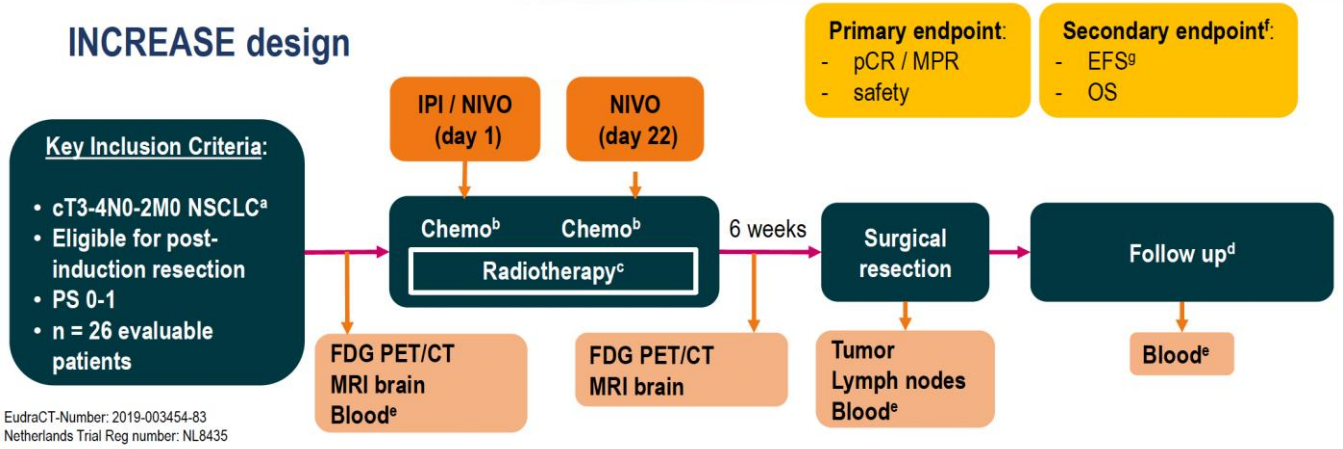


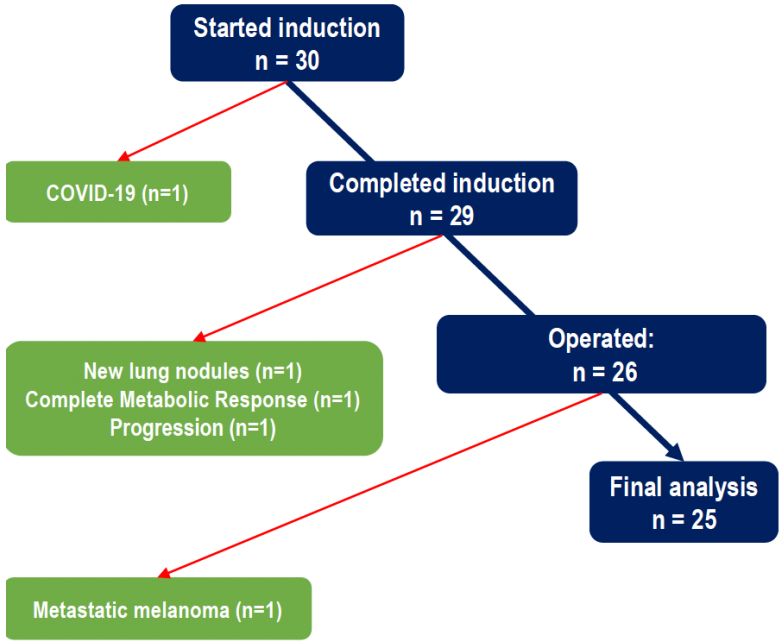


Solange Peters / WCLC23

QT-IT-RT neoadyuvante. INCREASE

Iniciativa científica de: GECP lung cancer research





73% EAs G3-4

	n (%)
Time from last radiotherapy to surgery (days, median (IQR))	43 (41-44)
Pulmonary resection	
Lobectomy	13 (52%)
Lobectomy + chest wall	10 (40%)
Lobectomy + chest wall + partial vertebrectomy	1 (4%)
Pneumonectomy	1 (4%)
Resection margin	
R0	25 (100%)
Pathological response	
pCR	15 (60%)
MPR	19 (76%)
No MPR	6 (24%)
Hospital stay (days, median (IQR))	6 (5-9)

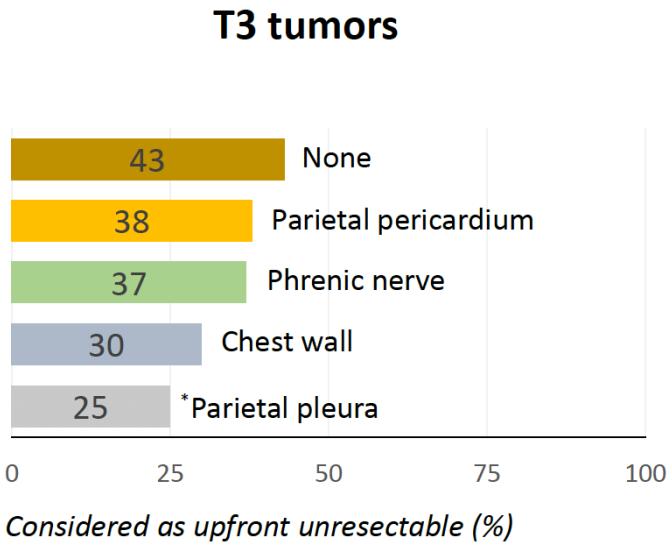
C. Dickhoff/ WCLC23

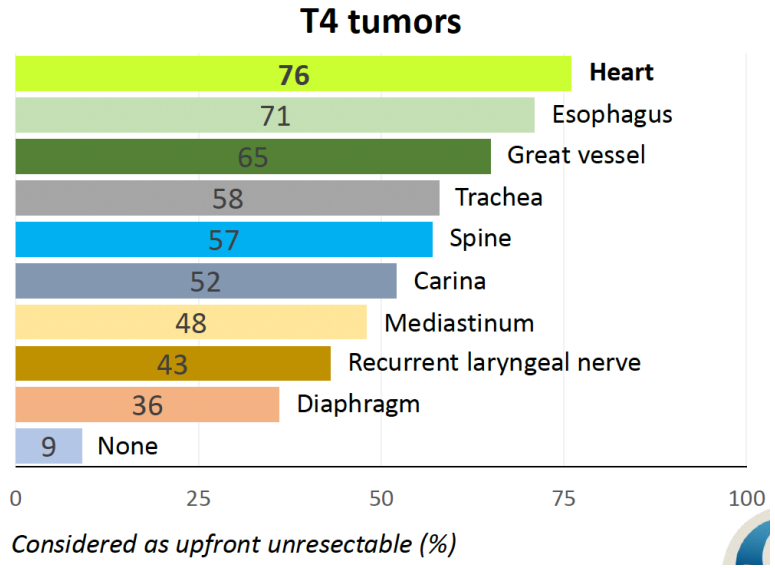
Consenso metodología Delphi resecabilidad Est III

Iniciativa científica de: GECP lung cancer

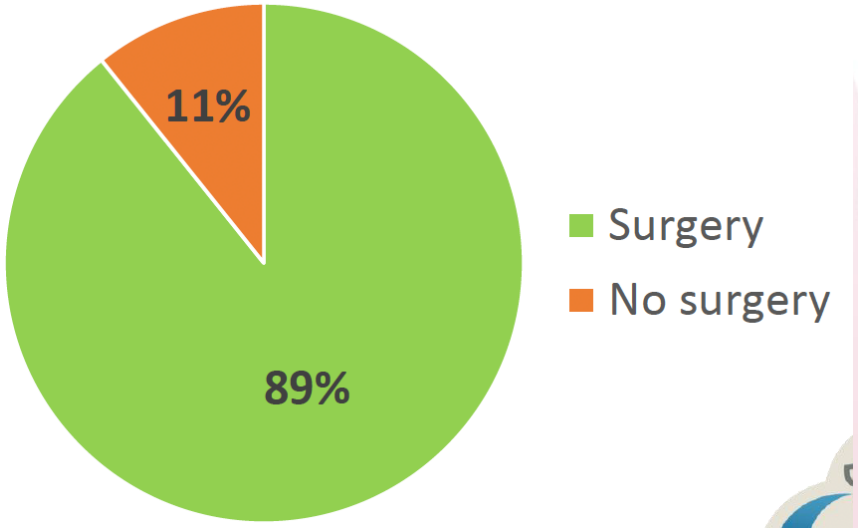
	N0	N1	N2 SINGLE	N2 MULTI	N2 BULKY	N2 INVASIVE	N3
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	?	UNRESECTABLE[2]	UNRESECTABLE	UNRESECTABLE
T3 size	NOT STAGE III DISEASE	RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE	UNRESECTABLE	
T3 satellite	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE	UNRESECTABLE	
T3 invasion	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	?[1]	?	UNRESECTABLE	UNRESECTABLE	
T4 size	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE[2]	UNRESECTABLE	UNRESECTABLE	
T4 satellite	POTENTIALLY RESECTABLE	?[1]	?	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE	
T4 invasion	?[1]	?[1]	?	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE	

Consenso metodología Delphi resecabilidad Est III





- The **majority (89%) would recommend surgery** after downstaging with neoadjuvant chemo-IO, assumed to be available.



Propuesta límites resecabilidad Estadio III

Iniciativa científica de: GECP lung cancer

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

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

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

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

Propuesta límites resecabilidad Estadio III

Iniciativa científica de: GECP lung cancer research

Bulky N2

- No consensual definition of "bulky" N2
- Most cases are considered as **unresectable** in the survey and literature review
- During the clinical case review, 14% of N2 bulky tumors considered as ***resectable***

Table 1	Unre-sectable	Potentially resectable
Pulmonary artery in the pericardium		✓
Superior vena cava		✓
Diaphragm		✓
Heart	✓*	
Carina		✓
Trachea	✓*	
Oesophagus	✓*	
Spinal cord	✓	
Vertebral body		✓
Recurrent laryngeal nerve		✓
Mediastinal fat		✓
Great vessels: aorta, inferior vena cava, pulmonary vein		✓

Stage IIIB – cT3-4 N2 tumors

- cT3N2 and cT4 (size or satellite) N2 are considered **resectable** if **single-station N2**
- **Case-by-case discussion:** highly and carefully selected patients with ***"limited" discrete N2 multi-station*** *involvement* (non bulky, non invasive), while the exact number of nodes/stations defining "limited" cannot be defined

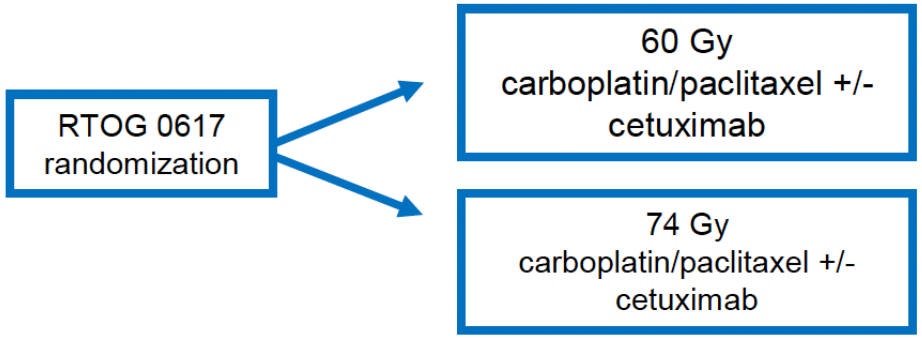
Stage IIIB – cT1-2 N3 tumors

- cT1-2N3 tumors are considered **unresectable**

Stage IIIC – cT3-4 N3 tumors

- Tumors with major structures infiltration and N3 disease are considered **unresectable**

Seguimiento a 5 años. Seguridad NRG-RTOG 0617



Stratified: 3D-CRT 53%, IMRT 47% in both 60/74Gy dose arms (N = 482)

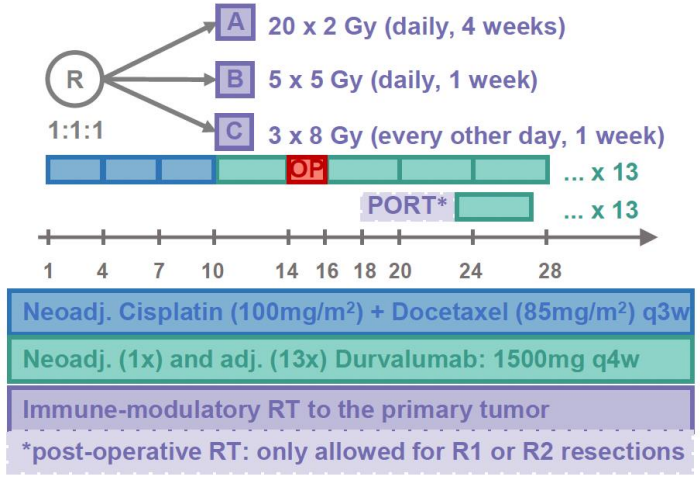
IMRT PTVs 59 mL larger than 3D-CRT

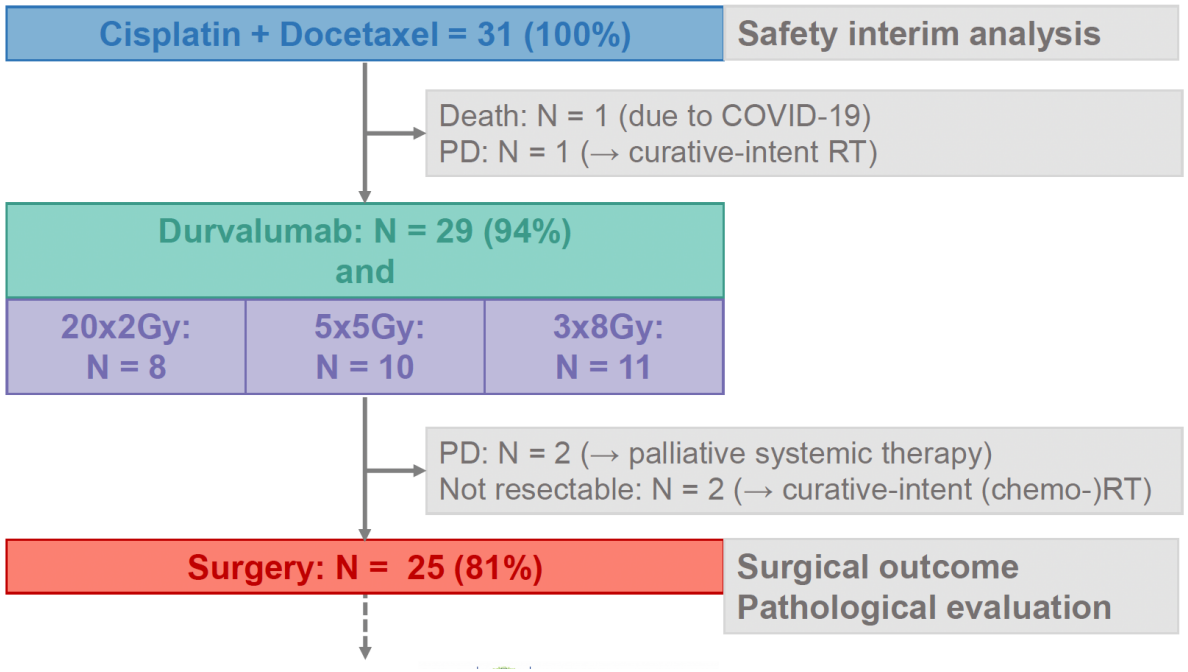
Grade ≥ 3 Adverse Event	Radiation Technique Comparison		Univariate logistic regression
	IMRT	3D-CRT	Lung V5Gy
Pneumonitis	**3.5%**	**8.2%**	OR = 1.02 (95% CI: 0.99-1.05) p = 0.13
	p = 0.03		
Esophagitis	13.2%	15.3%	OR = 1.01 (95% CI: 0.996-1.03) p = 0.15
	p = 0.50		
Weight loss	3.9%	3.1%	OR = 1.01 (95% CI: 0.98-1.04) p = 0.52
	p = 0.63		
Cardiovascular	5.3%	8.2%	OR = 1.00 (95% CI: 0.98-1.02) p = 0.99
	p = 0.20		
Neurologic	5.7%	5.9%	OR = 1.00 (95% CI: 0.98-1.03) p = 1.00
	p = 0.93		
Hematologic	58.8%	50.2%	OR = 1.00 (95% CI: 0.99-1.01) p = 0.66
	p = 0.06		

Outcome	IMRT	3D-CRT	P-value
Overall survival	2.2 years (median)	2.0 years (median)	0.59
PFS	0.8 years (median)	1.0 years (median)	0.67
DMFS	1.1 years (median)	1.2 years (median)	0.86
Second Malignancy	6.6%	5.5%	N/A

Stephen Chun / WCLC23

Tratamiento neoady con QT→IT+RT en Est IIIA N2 SAKK 16/18

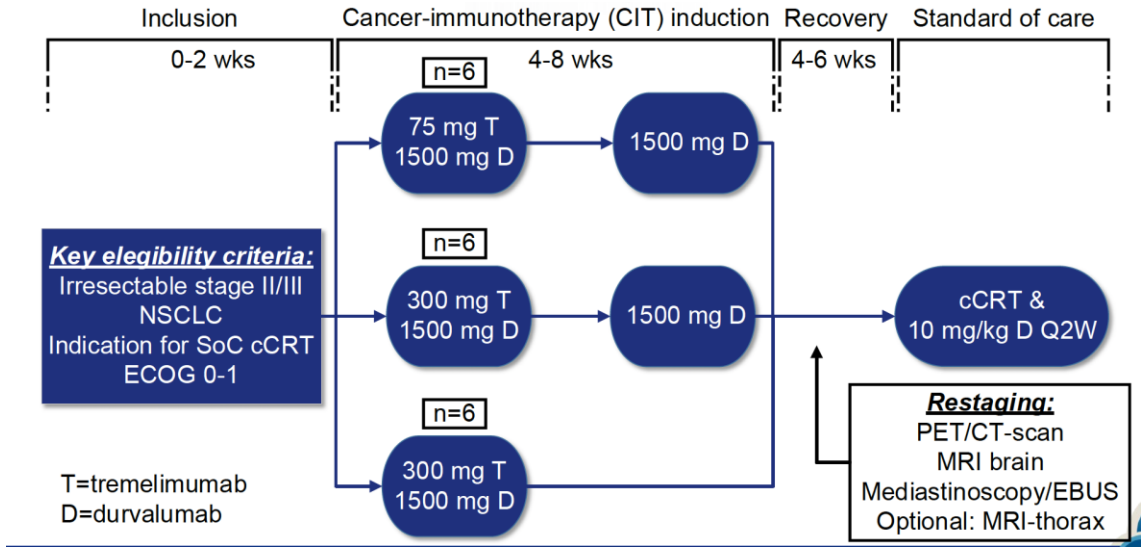




Variable	Arm A N = 7	Arm B N = 9	Arm C N = 9	Total N = 25
MPR	4	8	7	19
pCR	0	3	2	5
<ypN2	3	6	6	15

Patrick Dorn/ WCLC23

Tremelimumab-Durvalumab previos a QT-RT concomitante



	75T+1500D & 1500D†	300T+1500D & 1500D	300T+1500D†
Feasibility			
cCRT impossible due to PD	0/5	1/6	0/4
Start cCRT impossible <12 weeks	0/5	0/6	0/4
Failure to complete RTx	0/5	0/6	1/4‡
Safety			
Grade III ICI-related AE	1/5	2/6	3/4
Hepatitis	1	0	0
Colitis	0	2	2
Pulmonary abscess	0	0	1
Significant grade II ICI-related AE	0/5	2/6	0/4

†One withdrawal of consent during CIT-induction

‡Due to pulmonary abscess

18 SAEs in 10 patients

4 patients received infliximab due to AE

MM Smeenk / WCLC23