Novedades & Claves en CÁNCER de PULMÓN 2023

INTRODUCCIÓN

DRA. REYES BERNABÉ

HOSPITAL VIRGEN DEL ROCIO

Con la colaboración de:

Bristol Myers Squibb™

Janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Organizado por:

GECP lung cancer research

CONFLICTOS DE INTERÉS

- Consultant or Advisory Role: Astra Zeneca, Roche, BMS, Lilly, MSD, Takeda, Sanofi, Janssen
- Research Funding: Roche
- Speaking: Astra Zeneca, Roche, BMS, Lilly, MSD, Takeda, Sanofi, Janssen

Organizado por:
GECP
lung cancer research

Las cifras del cáncer en España 2023

Estimación del número de nuevos casos de cáncer en hombres en España para el año 2023

TIPO TUMORAL	N
Cavidad oral y faringe	5.644
Esófago	1.899
Estómago	4.231
Colon	17.340
Recto	9.017
Hígado	5.164
Vesícula biliar	1.384
Páncreas	4.770
Laringe	2.983
Pulmón	22.266
Melanoma de piel	3.786
Próstata	29.002
Testículo	1.510
Riñón (sin pelvis)	5.924
Vejiga urinaria	17.731
Encéfalo y sistema nervioso	2.271
Tiroides	1.433
Linfoma de Hodgkin	844
Linfomas no hodgkinianos	5.491
Mieloma	1.757
Leucemias	3.430
Otros	10.669
Todos excepto piel no melanoma	158.544

Estimación del número de nuevos casos de cáncer en mujeres en España para el año 2023

TIPO TUMORAL	N
Cavidad oral y faringe	2.238
Esófago	403
Estómago	2.701
Colon	11.125
Recto	5.239
Hígado	1.531
Vesícula biliar	1.264
Páncreas	4.510
Laringe	395
Pulmón	9.016
Melanoma de piel	4.263
Mama	35.001
Cérvix uterino	2.326
Cuerpo uterino	7.171
Ovario	3.584
Riñón (sin pelvis)	2.702
Vejiga urinaria	3.963
Encéfalo y sistema nervioso	1.801
Tiroides	4.651
Linfoma de Hodgkin	696
Linfomas no hodgkinianos	4.452
Mieloma	1.325
Leucemias	2.981
Otros	7.377
Todos excepto piel no melanoma	120.715

Organizado por:
GECP lung cancer research

elcc European Lung Cancer Congress 2023

Radon gas & other lung cancer risk factors

Speaker: Laura Mezquita, MD, PhD

Clínic Barcelona

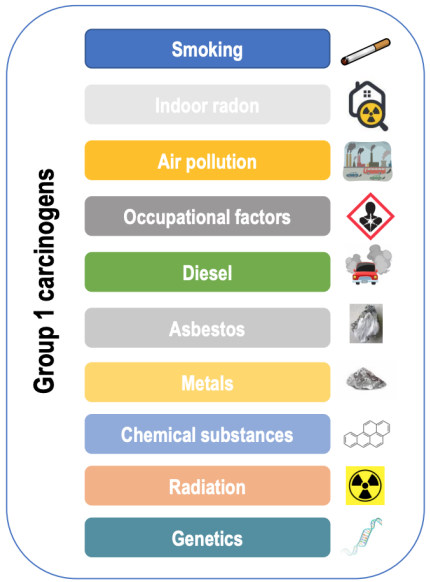
IDIBAPS

Universitat de Barcelona

Medical Oncology Department, Hospital Clinic of Barcelona
Laboratory of Translational Genomics, IDIBAPS, Barcelona
Department of Medicine, University of Barcelona

Organisers: ESMO, IASLC

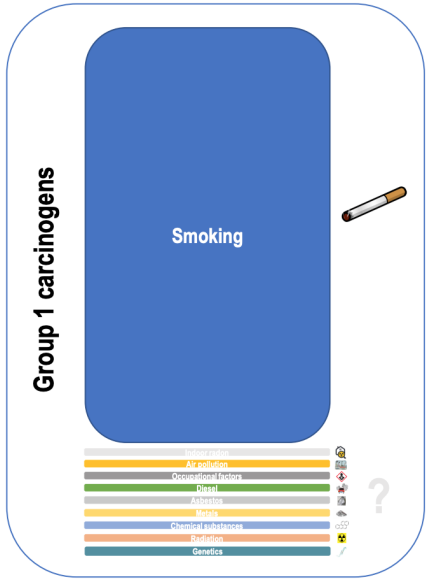
Partners: ESTRO, ESTS, ETOP-IBCSG PARTNERS



https://monographs.iarc.who.int/agents-classified-by-the-iarc/

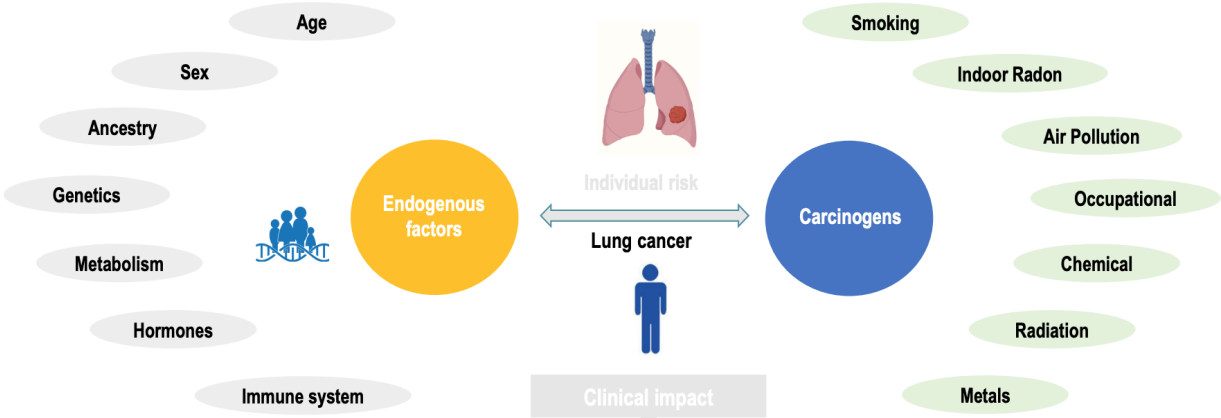
REALITY = misperception

TOBACCO Stigma minimizes the others



Lung Cancer Exposome

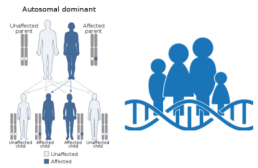
Generation of knowledge



elcc European Lung Cancer Congress 2023

Lung cancer development in one patient

PREDISPOSITION



Risk associated with genetics +/- others factors

SCAN study

CO-CARCINOGENS

SYNERGISM

Smoker + Radon
→ (Sub)multiplicative

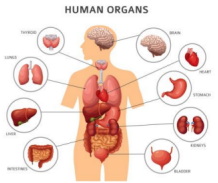
MIRROR study

EXPOSOME

Impact of the EXPOSOME in patients with lung cancer

EXPOSOME study

OTHER TUMORS



Association with other tumors (leukemia, brain, kidney, stomach, etc.)

RADON CLINIC study

elcc European Lung Cancer Congress 2023

Radon gas & other lung cancer risk factors

Speaker: Laura Mezquita, MD, PhD

Medical Oncology Department, Hospital Clinic of Barcelona
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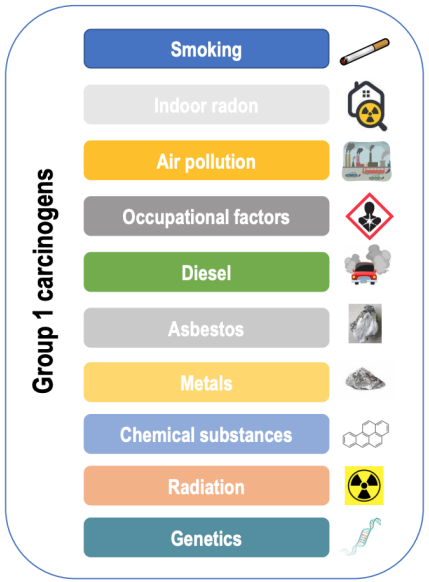

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REAL misper

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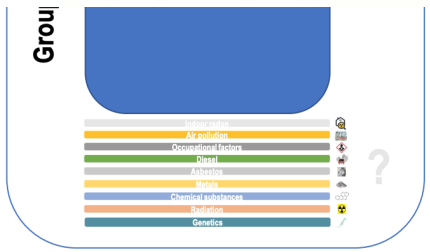

nature

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Article | Published: 05 April 2023

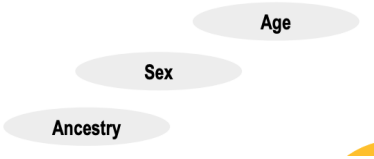
Lung adenocarcinoma promotion by air pollutants

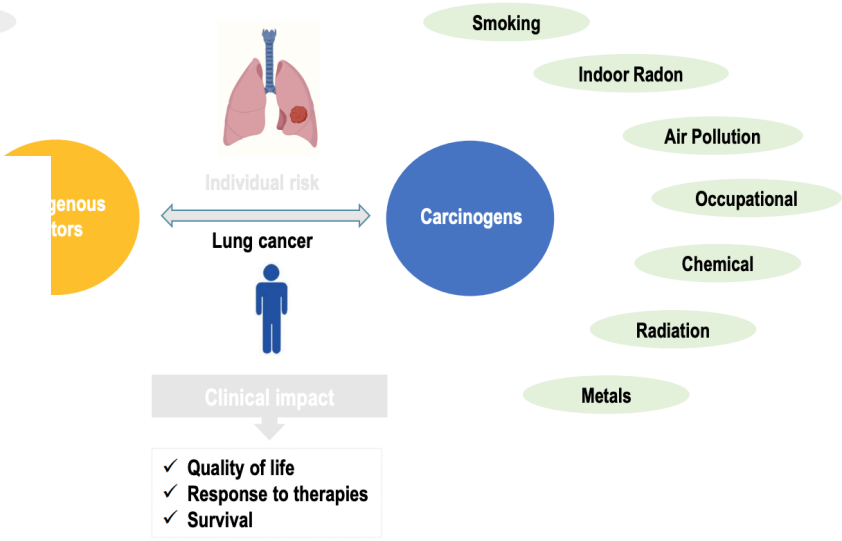
William Hill, Emilia L. Lim, Clare E. Weeden, Claudia Lee, Marcellus Augustine, Kezhong Chen, Feng-Che Kuan, Fabio Marongiu, Edward J. Evans Jr, David A. Moore, Felipe S. Rodrigues, Oriol Pich, Bjorn Bakker, Hongui Cha, Renelle Myers, Febe van Maldegem, Jesse Boumelha, Selvaraju Veeriah, Andrew Rowan, Cristina Naceur-Lombardelli, Takahiro Karasaki, Monica Sivakumar, Swapnanil De, Deborah R. Caswell, TRACERx Consortium, ... Charles Swanton + Show authors

Nature 616, 159–167 (2023) | Cite this article

Lung Cancer Exposome

Generation of knowledge





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Impact of the EXPOSOME in patients with lung cancer

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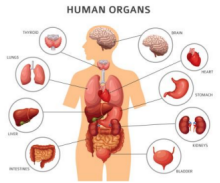
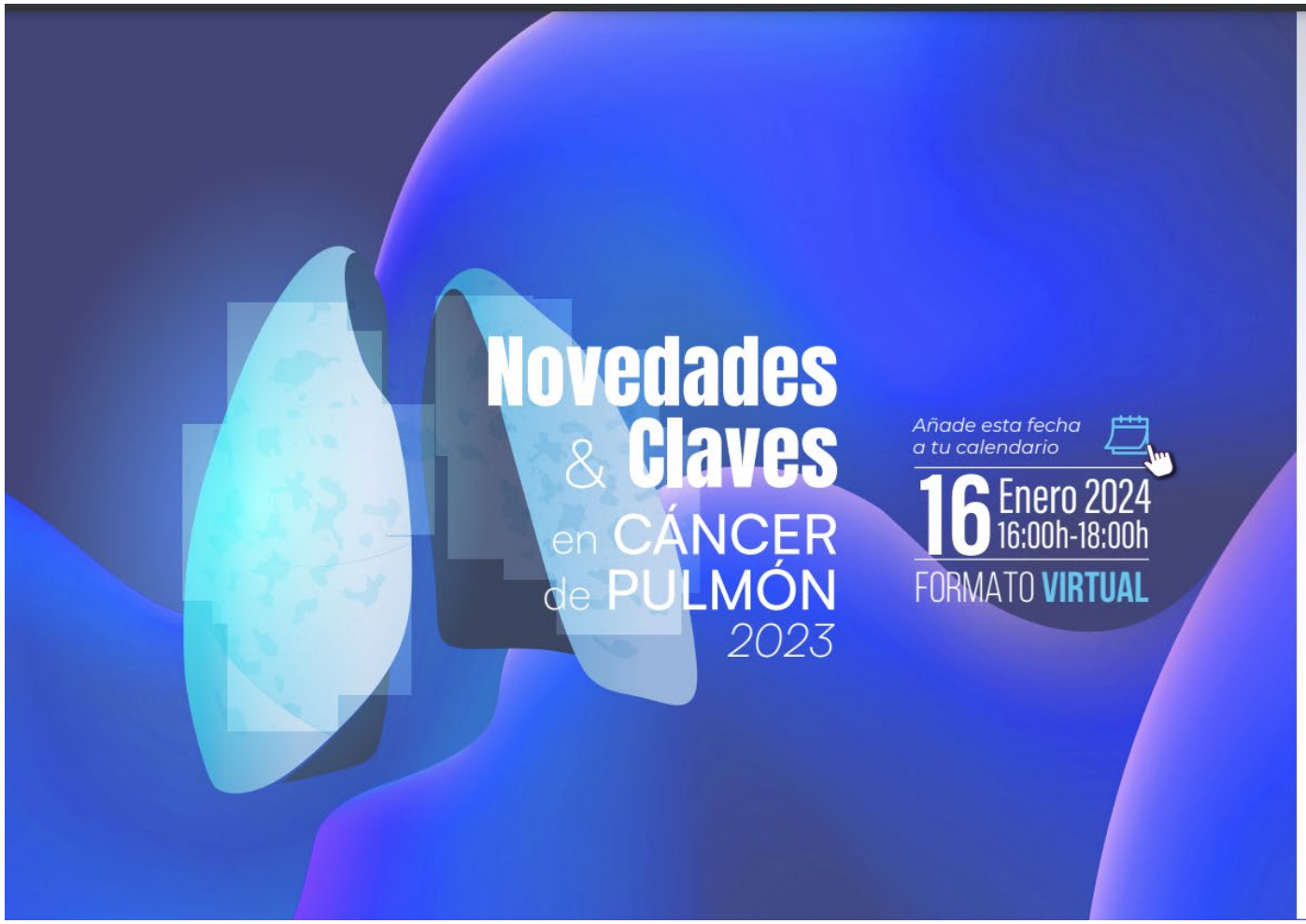
OTHER TUMORS



Association with other tumors (leukemia, brain, kidney, stomach, etc.)

RADON CLINIC study



Programa científico

16:00 - 16:20	Introducción	Dra. Reyes Bernabé Hospital Univ. Virgen del Rocío, Sevilla
16:20 - 16:40	Biomarcadores pronósticos	Dr. Airam Padilla Hospital Regional Univ. de Málaga
16:40 - 17:00	Estadios iniciales y enfermedad localmente avanzada	Dra. Ana Collazo Hospital Univ. Puerta de Hierro, Majadahonda, Madrid
17:00 - 17:20	Enfermedad metastática (incluyendo inmunoterapia)	Dr. Marc Cucurull ICO, Hospital Univ. Germans Trias i Pujol, Badalona, Barcelona
17:20 - 17:40	Cáncer de pulmón microcítico y otros tumores	Dr. Manuel Cobo Hospital Regional Univ. de Málaga
17:40 - 18:00	Conclusiones	Dr. Bartomeu Massutí Hospital General Univ. Dr. Balmis, Alicante

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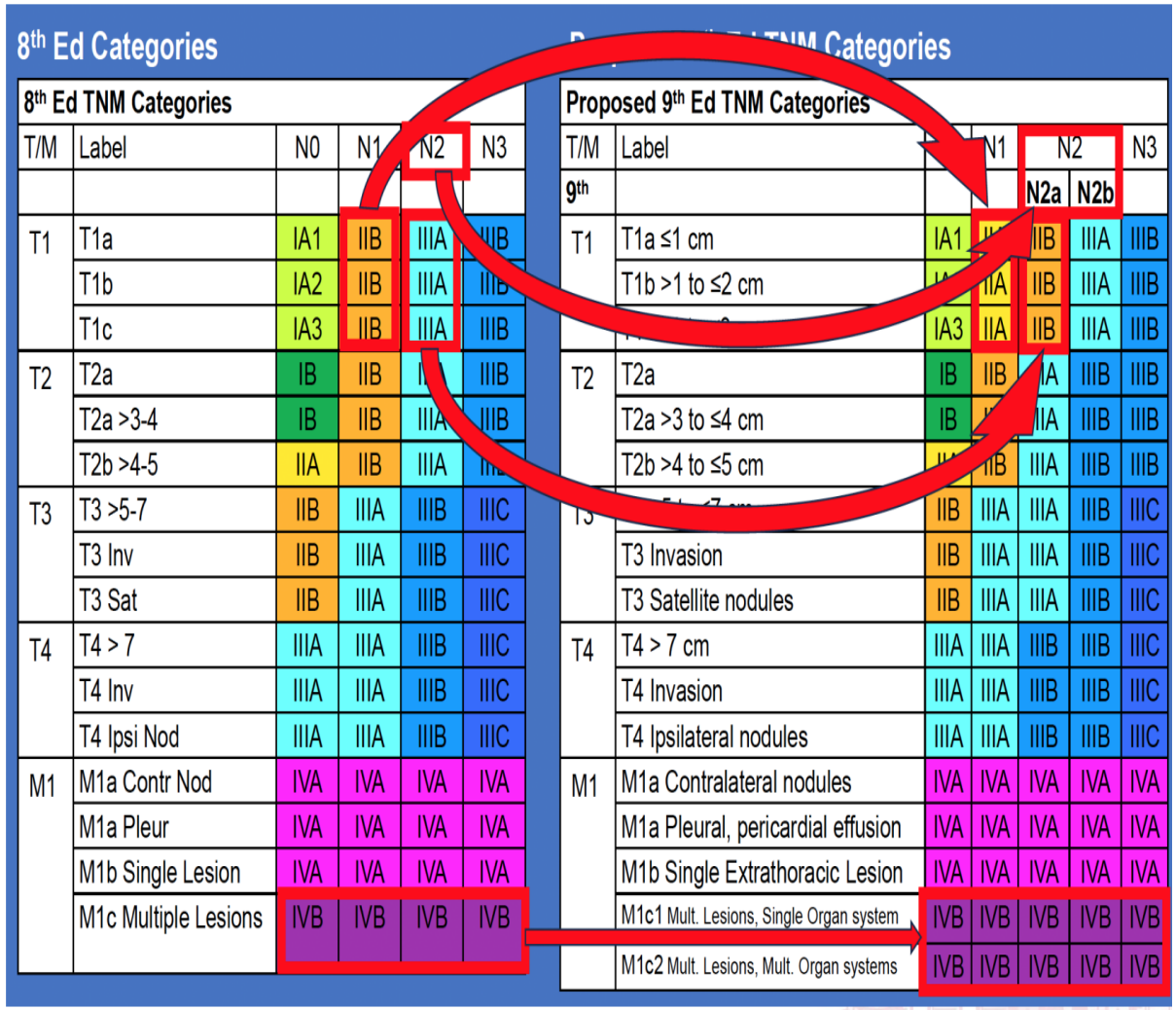
INTRODUCCIÓN: PROPUESTA CAMBIO TNM 9ºed

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



Hisao Asamura / WCLC23

GECP lung cancer research

INTRODUCCIÓN

SEAP-SEOM Guidelines On Testing Predictive Biomarkers In Non-small-cell Lung Cancer

Clinical and Translational Oncology
https://doi.org/10.1007/s12094-022-03046-9

SPECIAL ARTICLE

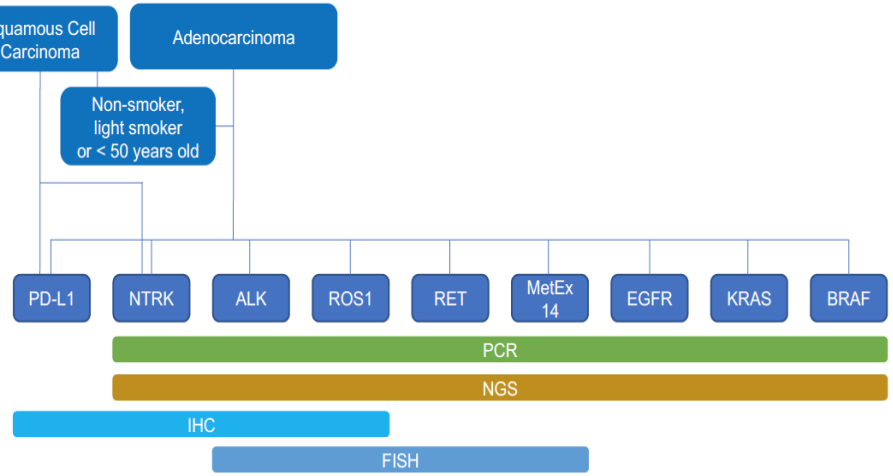
New update to the guidelines on testing predictive biomarkers in non-small-cell lung cancer: a National Consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology

Dolores Isla[1] · María D. Lozano[2] · Luis Paz-Ares[3] · Clara Salas[4] · Javier de Castro[5] · Esther Conde[6] · Enriqueta Felip[7] · Javier Gómez-Román[8] · Pilar Garrido[9] · Ana Belén Enguita[10]

Received: 2 November 2022 / Accepted: 7 December 2022

Abstract
Non-small cell lung cancer (NSCLC) presents the greatest number of identified therapeutic targets, some of which have therapeutic utility. Currently, detecting *EGFR*, *BRAF*, *KRAS* and *MET* mutations, *ALK*, *ROS1*, *NTRK* and *RET* translocations, and PD-L1 expression in these patients is considered essential. The use of next-generation sequencing facilitates precise molecular diagnosis and allows the detection of other emerging mutations, such as the *HER2* mutation and predictive biomarkers for immunotherapy responses. In this consensus, a group of experts in the diagnosis and treatment of NSCLC selected by the Spanish Society of Pathology and the Spanish Society of Medical Oncology have evaluated currently available information and propose a series of recommendations to optimize the detection and use of biomarkers in daily clinical practice.

Keywords *ALK* · Biomarkers · *BRAF* · *EGFR* · Non-small cell lung cancer · PD-L1 · *ROS1*



KRAS but should be included in NGS panels

ALK anaplastic lymphoma kinase, BRAF B-Raf proto-oncogene, EGFR epidermal growth factor receptor, FISH fluorescence in situ hybridisation, IHC immunohistochemistry, KRAS kirsten rat sarcoma virus, MetEx 14 mesenchymal epithelial transition factor exón 14, NGS next-generation sequencing, NSCLC non-small cell lung cancer, NTRK neurotrophic tyrosine receptor kinase, PCR polymerase chain reaction, PD-L1 programmed death ligand-1, ROS1 c-ros oncogene 1, RET rearranged during transfection

Isla D, et al. Clin Transl Oncol. 2023;10.1007/s12094-023-03103-x.

Nueva actualización de las recomendaciones para la determinación de biomarcadores predictivos en el carcinoma de pulmón no célula pequeña: Consenso Nacional de la Sociedad Española de Anatomía Patológica y de la Sociedad Española de Oncología Médica☆

Dolores Isla[a], María D. Lozano[b], Luis Paz-Ares[c], Clara Salas[d], Javier de Castro[e], Esther Conde[f], Enriqueta Felip[g], Javier Gómez-Román[h], Pilar Garrido[i] y Ana Belén Enguita[j,*]

Revista Española de Patología 56 (2023) 97-112

Tabla 1 Biomarcadores esenciales en pacientes con CPNCP

Gen/proteína	Alteración predictiva	Metodología
EGFR	Mutación	PCR: secuenciación de sanger, PCR en tiempo real y NGS
ALK	Reordenamiento	IHQ, FISH, PCR en tiempo real y NGS
ROS1	Reordenamiento	IHQ (cribado), FISH, PCR en tiempo real y NGS
BRAF V600	Mutación	PCR en tiempo real y NGS
PD-L1	Sobreexpresión	IHQ
NTRK	Reordenamiento	IHQ (cribado), PCR en tiempo real y NGS
RET	Reordenamiento	FISH, PCR en tiempo real y NGS
KRAS	Mutación	PCR: secuenciación de sanger, PCR en tiempo real y NGS
MET	Mutación	NGS
	Amplificación	FISH, PCR en tiempo real y NGS

ALK: *anaplastic lymphoma kinase*; BRAF: *B-Raf proto-oncogene*; CPNCP: carcinoma de pulmón de células no pequeñas; EGFR: *epidermal growth factor receptor*; FISH: hibridación fluorescente *in situ*; IHQ: inmunohistoquímica; KRAS: *kirsten rat sarcoma virus*; MET: *mesenchymal epithelial transition factor*; NGS: *next-generation sequencing*; NTRK: *neurotrophic tyrosine receptor kinase*; PCR: *polymerase chain reaction*; PD-L1: *programmed death ligand-1*; RET: *rearranged during transfection*; ROS1: *c-ros oncogene 1*.

Tabla 2 Otros biomarcadores de interés en pacientes con CPNCP

Gen/proteína	Alteración predictiva	Metodología
HER2	Mutación	NGS
	Amplificación	FISH, PCR en tiempo real, NGS
TMB	Mutaciones	NGS
STK11	Mutación	NGS
KEAP1	Mutación	NGS
MSI	Patrón de hipermutación	IHQ, PCR, NGS

FISH: hibridación fluorescente *in situ*; HER2: *human epidermal growth factor receptor 2*; IHQ: immunohistoquímica; KEAP1: *Kelch-like ECH-associated protein 1*; MSI: *microsatellite instability-high*; NGS: *next-generation sequencing*; PCR: *polymerase chain reaction*; STK11: *serine/threonine kinase 11*; TMB: *tumour mutation burden*.

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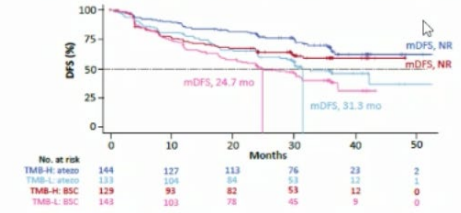
INTRODUCCIÓN

IMpower010

DFS by TMB status in the stage II-IIIA TMB-evaluable population

- Baseline characteristics of the stage II-IIIA TMB-evaluable population (n=549) were similar between treatment arms and consistent with those of the stage II-IIIA population[1] (not shown)



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)

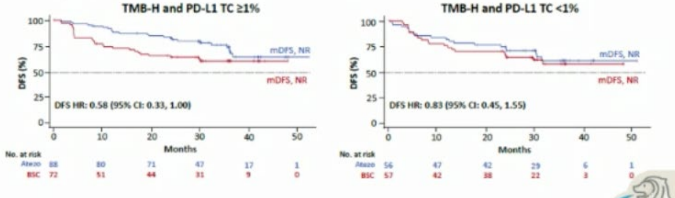
- In both treatment arms, impr
- DFS improvement with atezol

HR, hazard ratio; mDFS, median disease-free surviva (n=276) were defined as TMB levels above or below

Presented by: Dr Enriqueta Felip

DFS by PD-L1 status[a] in the stage II-IIIA TMB-H subgroup

- 53% of patients in the PD-L1–positive subgroup and 45% of patients in the PD-L1–negative subgroup were TMB-H
- DFS improvement with atezolizumab was greater in the PD-L1–positive than in the PD-L1–negative subgroup



[a] by the VENTANA SP263 PD-L1 assay

Presented by: Dr Enriqueta Felip

Felip et al. WCLC 2023

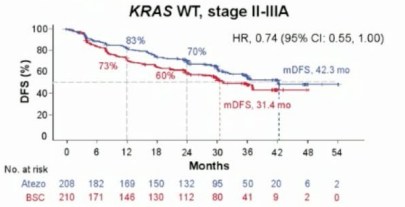
Mutation profile

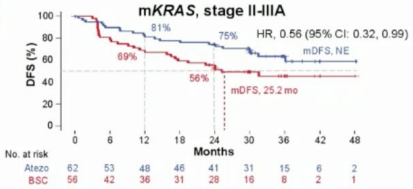
IMpower010

Baseline characteristics and DFS by *KRAS* status

Baseline Characteristics	ITT (n=1005)	WES-BEP (n=603)	*KRAS* WT (n=475)	m*KRAS* (n=128)
Median age, y (range)	62 (26-84)	62 (26-82)	62 (26-82)	63 (40-81)
Male, n (%)	672 (67)	414 (69)	328 (69)	86 (67)
Asian, n (%)	242 (24)	144 (24)	125 (26)	19 (15)
White, n (%)	738 (73)	446 (74)	339 (71)	107 (84)
ECOG PS 0, n (%)	601 (60)	382 (63)	299 (63)	83 (65)
Non-squamous, n (%)	659 (66)	399 (66)	278 (59)	121 (95)
Squamous, n (%)	346 (34)	204 (34)	197 (41)	7 (5)
Current/previous smoker, n (%)	783 (78)	480 (80)	364 (77)	116 (91)
Never smoked, n (%)	222 (22)	123 (20)	111 (23)	12 (9)
MRD (ctDNA) positivity, n (%)	118 (20)	117 (20)	91 (19)	26 (20)
Median CRP, mg/L (range)	2.69 (0.2-166)	2.32 (0.2-166)	2.51 (0.2-166)	1.75 (0.2-48.9)

- In the stage II-IIIA WES-BEP (n=536), improved DFS was seen with atezolizumab vs BSC for *KRAS* WT and m*KRAS* subgroups





2023 ASCO ANNUAL MEETING #ASCO23 PRESENTED BY: Martin Reck, MD, PhD IMpower010: DFS by *KRAS* status

ASCO KNOWLEDGE CONQUERS CANCER

Reck et al. ASCO 2023

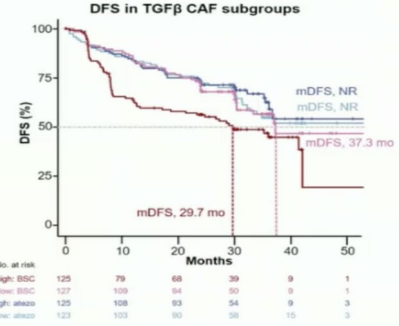
Inflammation signatures

IMpower-010

High TGFβ CAF was associated with poor DFS in the BSC arm, which was improved with atezolizumab

- Patients in the RNA-seq BEP were grouped into TGFβ CAF-low (<median; n=250) or -high (≥median; n=250) gene signature expression subgroups
- In the BSC arm, high TGFβ CAF was associated with reduced DFS compared with low TGFβ CAF
- In the atezolizumab arm, DFS was similar for the TGFβ CAF-high and -low subgroups
- In the TGFβ CAF-high subgroup, treatment with atezolizumab improved DFS to similar levels to those seen in the TGFβ CAF-low subgroups

	DFS HR (95% CI)
TGFβ CAF high: BSC vs TGFβ CAF low: BSC	1.61 (1.11, 2.35)
TGFβ CAF high: atezo vs TGFβ CAF low: atezo	0.90 (0.59, 1.37)
TGFβ CAF high: atezo vs TGFβ CAF high: BSC	0.54 (0.37, 0.80)
TGFβ CAF low: atezo vs TGFβ CAF low: BSC	0.94 (0.63, 1.41)



Altorki et al. IMpower010 RNA-seq. https://bit.ly/3tzc9f

Altorki et al. ESMO 2023

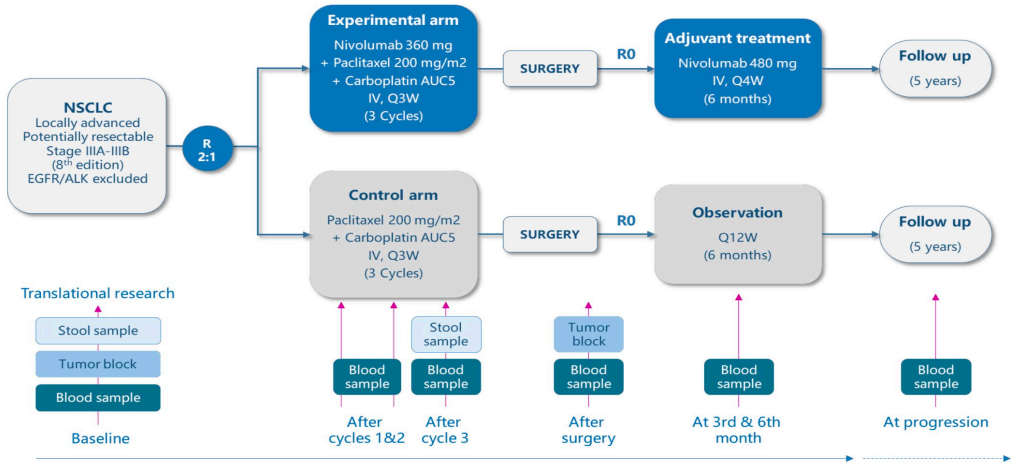
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

M. Provencio, E. Nadal, J.L. González-Larriba, A. Martínez-Martí, R. Bernabé, J. Bosch-Barrera, J. Casal-Rubio, V. Calvo, A. Insa, S. Ponce, N. Reguart, J. de Castro, J. Mosquera, M. Cobo, A. Aguilar, G. López Vivanco, C. Camps, R. López-Castro, T. Morán, I. Barneto, D. Rodríguez-Abreu, R. Serna-Blasco, R. Benítez, C. Aguado de la Rosa, R. Palmero, F. Hernando-Trancho, J. Martín-López, A. Cruz-Bermúdez, B. Massuti, and A. Romero

SUPPLEMENTARY FIGURES



IMPORTANCIA ctDNA en SLP y SG

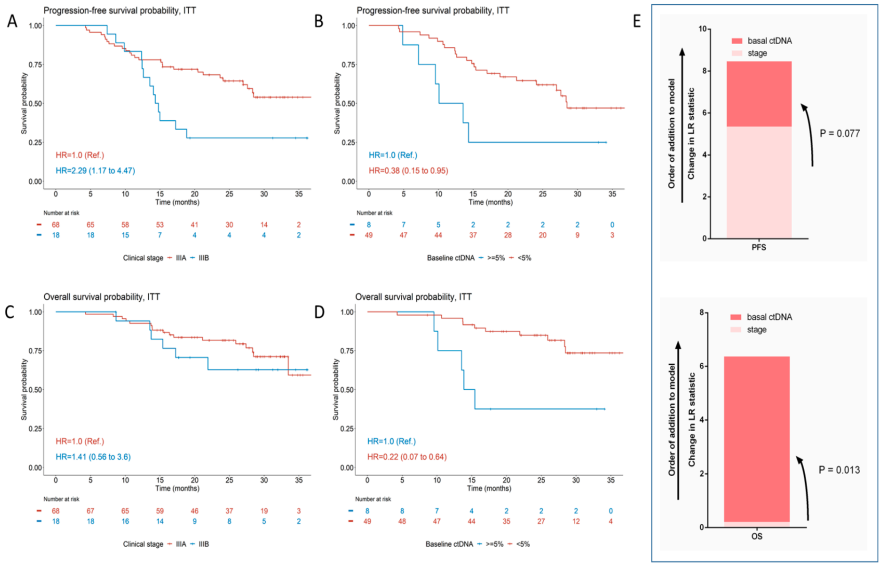


Figure S11. Kaplan-Meier curves for progression-free survival (PFS) according to clinical stage (A) and baseline ctDNA levels using a cutoff of 5% mutant allele fraction (MAF) (B). Kaplan-Meier curves for overall survival (OS) according to clinical stage (C) and baseline ctDNA levels using a cutoff of 5% MAF (D). Using a cutoff of <5% MAF, patients with low ctDNA levels at baseline had significantly improved PFS and OS than patients with high ctDNA levels (hazard ratio [HR]: 0.38; 95% CI 0.15–0.95 and HR: 0.22; 95% CI 0.07–0.64, for PFS and OS, respectively). (E) PFS (upper) and OS (lower) likelihood ratio statistic of tumor response assessed by clinical stage. The model was first conditioned for clinical stage, and then the significance of the ctDNA was added.

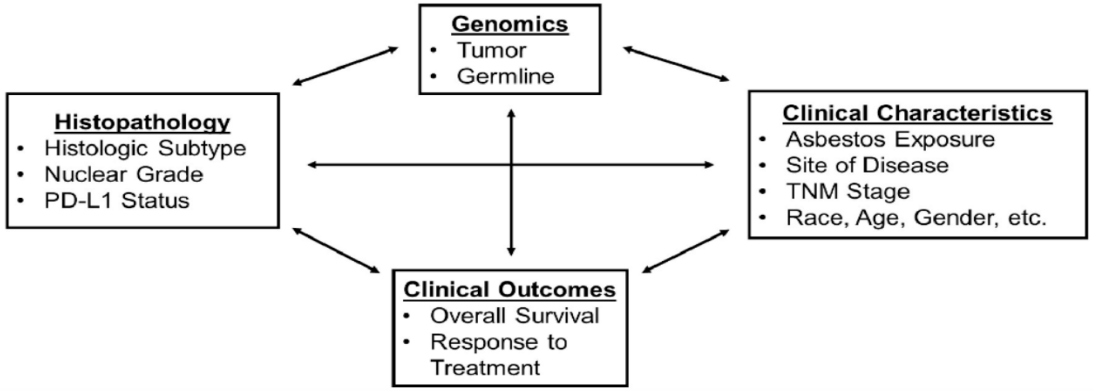
Organizado por:
GECP
lung cancer research

INTRODUCCIÓN: BIOMARCADORES PRONÓSTICOS

#8507: Association of somatic mutations and histologic subtype/grade on prognosis and PD-L1 expression in mesothelioma

Allen Zhu, Aliya N. Husain, Andrew Hermina, Owen Mitchell, Jeffrey S. Mueller, Michael William Drazer, Hedy L. Kindler, Jung Woo Kwon

Objectives: Identify how features in histopathology and genetics correlate with one another and with clinical outcomes



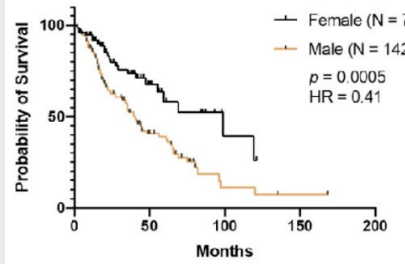
Characteristic		N (%)
Age at Diagnosis (years)	**Median (range)**	**66 (16-89)**
Gender	**Male**	**142 (65)**
	Female	75 (35)
Race	**White, non-Hispanic**	**205 (95)**
	White, Hispanic	5 (2)
	Black	4 (2)
	Asian	3 (1)
Self-reported asbestos exposure	**Definite**	**83 (39)**
	Probable	**56 (26)**
	Possible	64 (30)
	No known exposure	13 (6)
Personal cancer history	Present	54 (25)
Family cancer history	**Present**	**151 (70)**

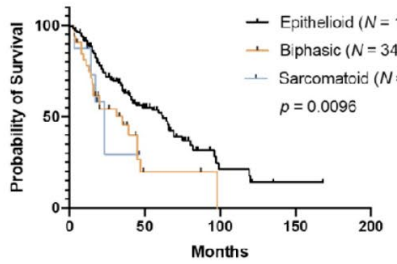
Characteristic	Categories	N = 217 (%)
Site of Disease	**Pleural**	**147 (68)**
	Peritoneal	63 (29)
	Bicavitary	4 (2)
	Tunica vaginalis testis	3 (1)
Germline Mutation	**Present**	**34 (16)**
Status at Follow-up	**Alive**	**111 (51)**
	Deceased	106 (49)

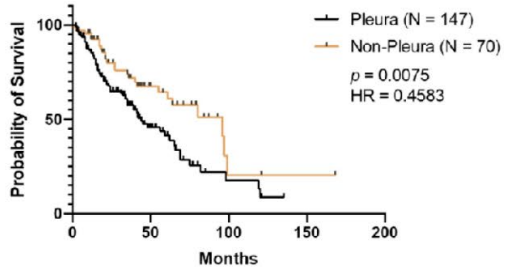
Characteristic	Categories	N (%)
Histologic Subtype N = 217	**Epithelioid**	**172 (79)**
	Sarcomatoid	8 (4)
	Biphasic	33 (15)
	Other	4 (2)
Nuclear Grade N = 166	I	55 (33)
	II	**96 (58)**
	III	15 (9)
Tumor Stage* N = 50	pT1	12 (24)
	pT2	12 (24)
	pT3	**18 (36)**
	pT4	8 (16)
Lymph Node Stage* N = 50	**pN0**	**32 (64)**
	pN1	18 (36)

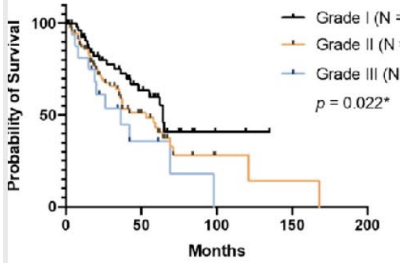
*staged only in resected tumors

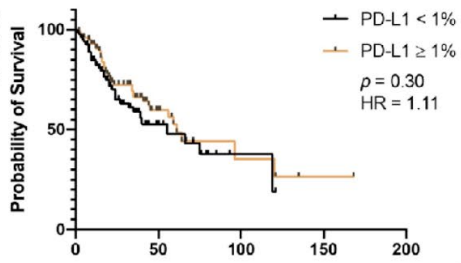
INTRODUCCIÓN: BIOMARCADORES PRONÓSTICOS

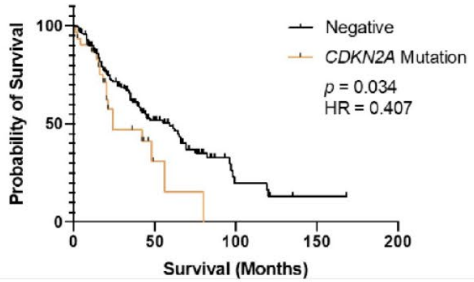


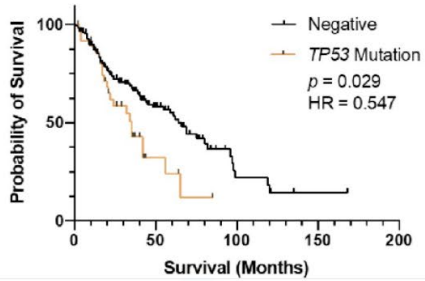




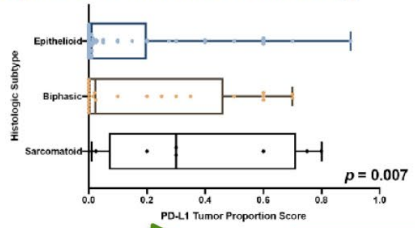








Epithelioid histology has lower PD-L1 expression than biphasic or sarcomatoid histology



In epithelioid mesothelioma, PD-L1 expression is not associated with nuclear grade

	Nuclear Grade – N (%)			p-value
	I	II	III	
PD-L1 < 1%	24 (47)	43 (50)	4 (36)	0.69
PD-L1 ≥ 1%	27 (53)	43 (50)	7 (64)	

PD-L1 expression is not associated with common somatic mutations

	N (%)		
	PD-L1 (+)	PD-L1 (-)	p-value
BAP1	40 (48.8)	38 (37.3)	0.13
TP53	15 (18.3)	15 (14.7)	0.51
NF2	14 (17.1)	26 (25.5)	0.17
CDKN2A	14 (17.1)	12 (11.8)	0.31
TERT	6 (7.3)	11 (10.8)	0.42

- **Epithelioid histology, TP53 somatic mutation and gender are the strongest predictors of survival**
- **Nuclear grade is useful for prognosis but somatic mutations should be taken into consideration**

#8507: Association of somatic mutations and histologic subtype/grade on prognosis and PD-L1 expression in mesothelioma

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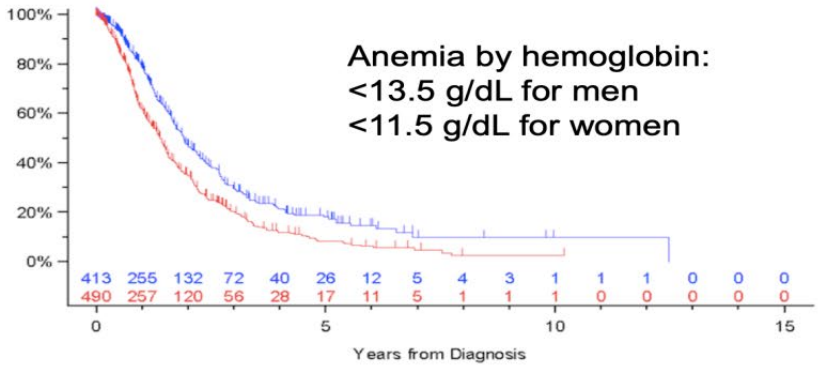
IASLC 2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE

The IASLC Pleural Mesothelioma Staging Project: Updated Modeling of Prognostic Factors in Pleural Mesothelioma

Andrea S. Wolf, MD, MPH
New York Mesothelioma Program
The Icahn School of Medicine at Mount Sinai
United States of America

Results: Univariate analysis overall survival

Overall Survival by Anemia

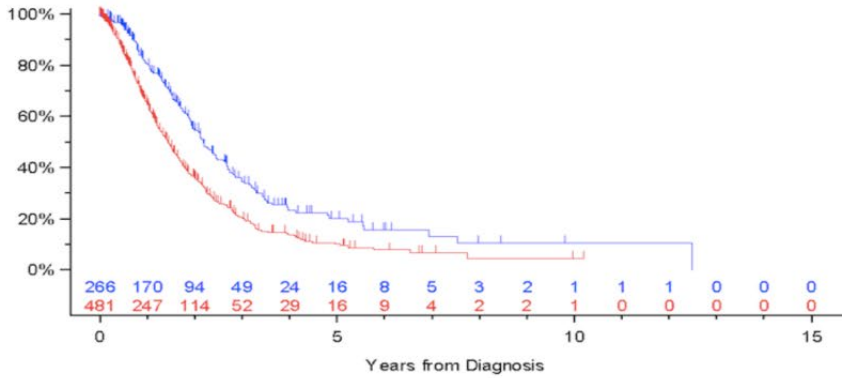


Anemia by hemoglobin:
<13.5 g/dL for men
<11.5 g/dL for women

	Deaths / N	Median in Years	3-Year Estimate
No Anemia	247 / 413	1.9 (1.7, 2.2)	30% (24, 35)
Anemia	358 / 490	1.4 (1.2, 1.5)	20% (16, 24)

Log-rank p-value < .0001

Overall Survival by Serum Mesothelin



	Deaths / N	Median in Years	3-Year Estimate
Serum Mesothelin < 6.7 nmol/L	149 / 266	2.2 (1.9, 2.6)	34% (27, 42)
Serum Mesothelin >= 6.7 nmol/L	319 / 481	1.4 (1.3, 1.6)	20% (16, 25)

Log-rank p-value < .0001

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INTRODUCCIÓN: ESTADIOS INICIALES Y LOCALMENTE AVANZADOS

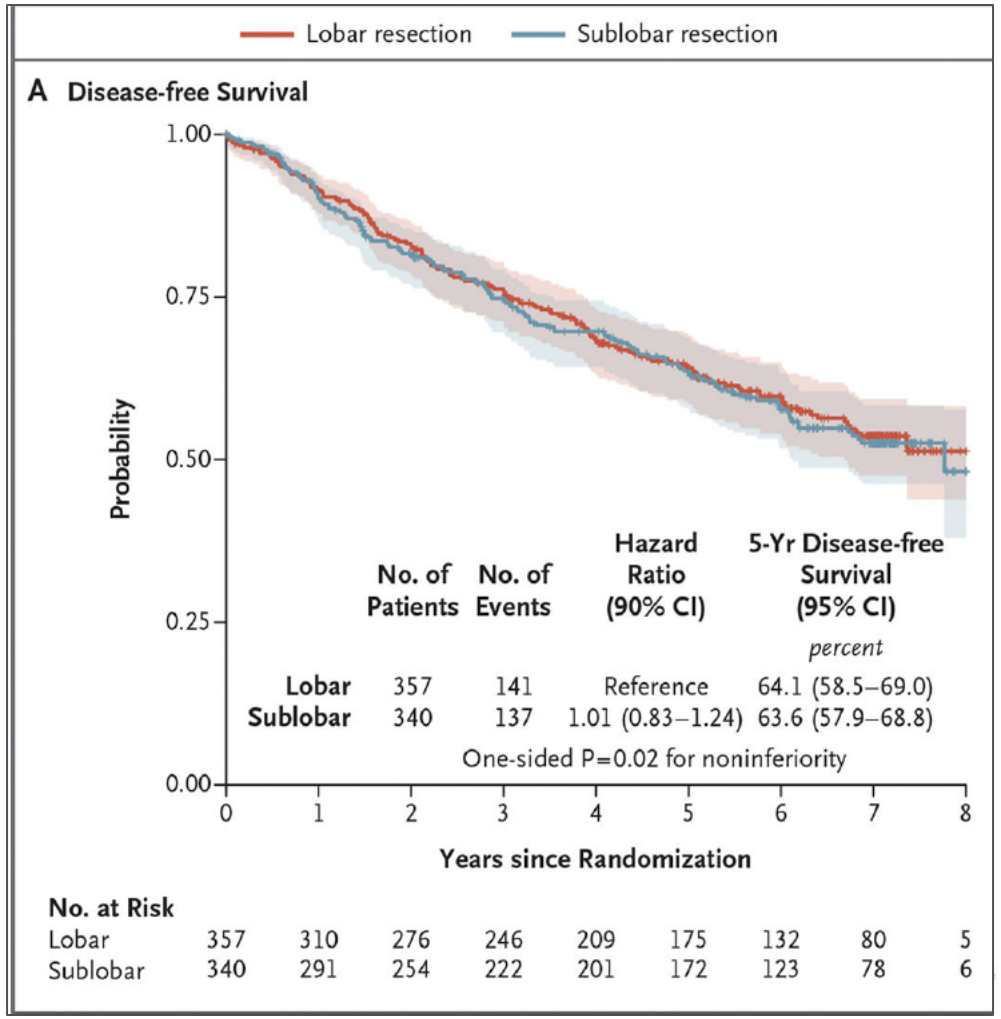
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 9, 2023 VOL. 388 NO. 6

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. Ashrafi, M.D., Moishe Liberman, M.D., Ph.D., Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, M.D., John D. Mitchell, M.D., Harvey Pass, M.D., Robert Keenan, M.D., Thomas Bauer, M.D., Daniel Miller, M.D., Leslie J. Kohman, M.D., Thomas E. Stinchcombe, M.D., and Everett Vokes, M.D.

AltorKi N. N Engl J Med.2023



In patients with peripheral NSCLC with a tumor size of 2 cm or less and pathologically confirmed node-negative disease in the hilar and mediastinal lymph nodes, sublobar resection was not inferior to lobectomy with respect to disease-free survival. Overall survival was similar with the two procedures

GECP lung cancer research

INTRODUCCIÓN: ESTADIOS INICIALES Y LOCALMENTE AVANZADOS

ORIGINAL ARTICLE

IASLC

Prospective Cohort Study to Compare Long-Term Lung Cancer-Specific and All-Cause Survival of Clinical Early Stage (T1a-b; ≤20 mm) NSCLC Treated by Stereotactic Body Radiation Therapy and Surgery

Claudia I. Henschke, PhD, MD,[a,b,*] Rowena Yip, PhD, MPH,[a] Qi Sun, MD,[a,c] Pengfei Li, MD,[a,c] Andrew Kaufman, MD,[d] Robert Samstein, MD,[e] Cliff Connery, MD,[f] Leslie Kohman, MD,[g] Paul Lee, MD,[h] Henry Tannous, MD,[i] David F. Yankelevitz, MD,[a] Emanuela Taioli, MD, PhD,[j] Kenneth Rosenzweig, MD,[e] Raja M. Flores, MD, MPH[d]; for the I-ELCAP and IELCART Investigators[**]

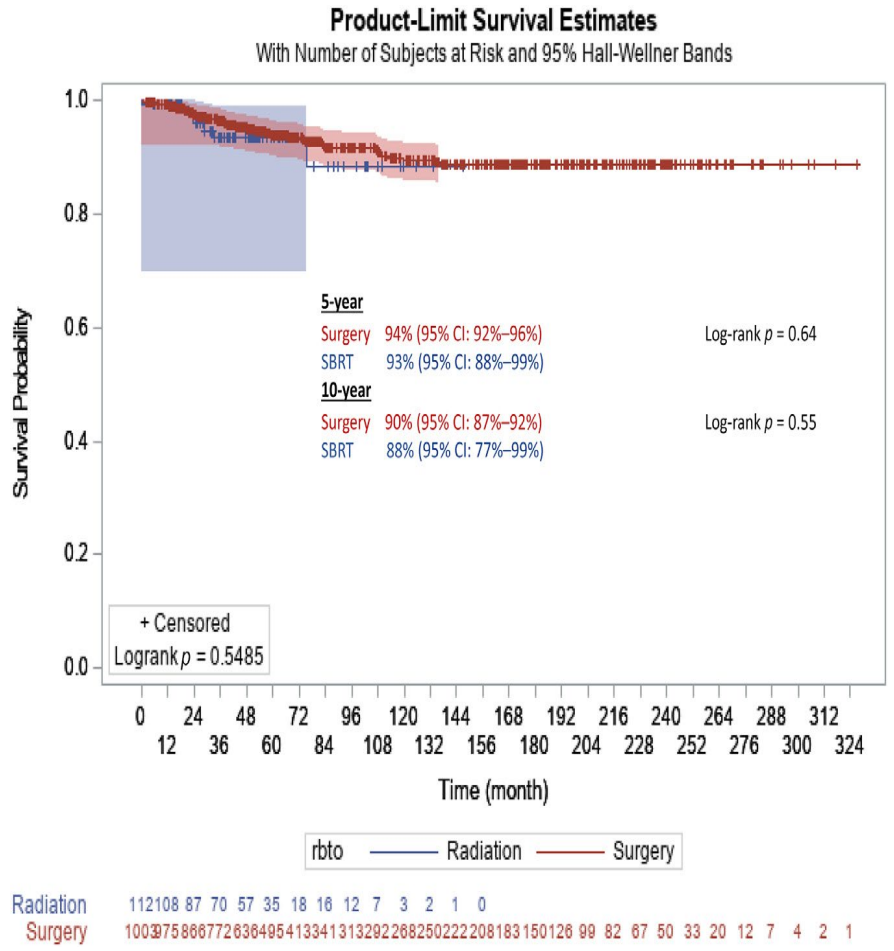
Henschke CI. J Thorac Oncol. 2023

First Primary NSCLC ≤20 mm (cT1a-1cN0M0) with surgery or SBRT

N = 1115

Surgery n = 1003 *(716 solid, 287 subsolid)*

SBRT n = 112 *(88 solid, 24 subsolid)*



Organizado por:

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ADYUVANCIA: CAMBIOS EN EL ESTANDAR DE TRATAMIENTO

EGFR +

ADAURA Phase III study design

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
- ≥18 years (Japan / Taiwan: ≥20)
- WHO performance status 0 / 1
- Confirmed primary non-squamous NSCLC Ex19del / L858R‡
- Brain imaging, if not completed pre-operatively
- Complete resection with negative margins§
- Maximum interval between surgery and randomization:
  - 10 weeks without adjuvant chemotherapy
  - 26 weeks with adjuvant chemotherapy

Stratification by:
Stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
Race (Asian vs non-Asian)

Osimertinib 80 mg, once daily

Randomization 1:1 (N=682)

Placebo, once daily

Planned treatment duration: 3 years

Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

Endpoints
- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

*At the time of recruitment, staging was determined by the AJCC / UICC Staging Manual 7th edition. Patients with stage IB disease were not eligible in Japan. †Pre-operative, post-operative, or planned radiotherapy was not allowed. ‡Centrally confirmed in tissue. §Patients received a CT scan after resection and within 28 days prior to treatment.

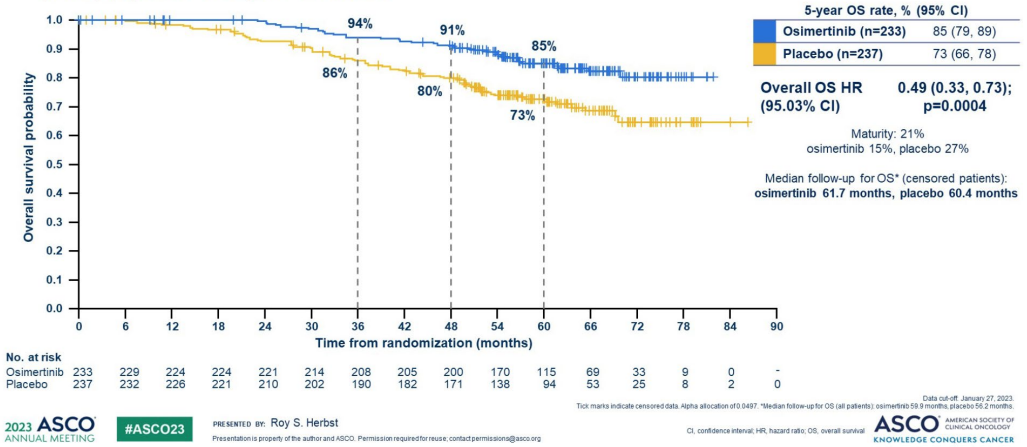
AJCC, American Joint Committee on Cancer; CT, computerized tomography; DFS, disease-free survival; EGFRm, epidermal growth factor receptor-mutated; Ex19del, exon 19 deletion; NSCLC, non-small cell lung cancer; OS, overall survival; UICC, Union for International Cancer Control; WHO, World Health Organization

2023 ASCO ANNUAL MEETING #ASCO23 PRESENTED BY: Roy S. Herbst

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Overall survival: patients with stage II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the primary population of stage II–IIIA disease

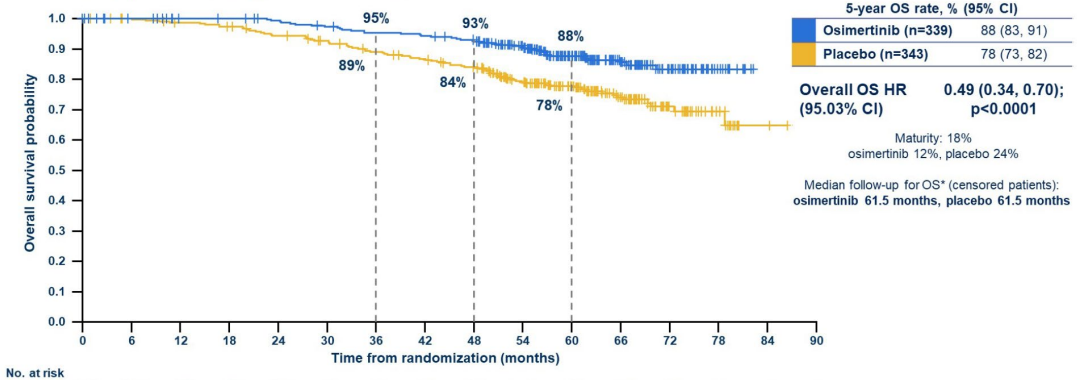


2023 ASCO ANNUAL MEETING #ASCO23 PRESENTED BY: Roy S. Herbst

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Overall survival: patients with stage IB / II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the overall population of stage IB–IIIA disease



2023 ASCO ANNUAL MEETING #ASCO23 PRESENTED BY: Roy S. Herbst

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

ADYUVANCIA: CAMBIOS EN EL ESTANDAR DE TRATAMIENTO

ALINA

ALINA study design*

Resected Stage IB (≥4cm)–IIIA *ALK*+ NSCLC
per UICC/AJCC 7th edition

Other key eligibility criteria:
- ECOG PS 0–1
- Eligible to receive platinum-based chemotherapy
- Adequate end-organ function
- No prior systemic cancer therapy

Stratification factors:
- Stage: IB (≥ 4cm) vs II vs IIIA
- Race: Asian vs non-Asian

R 1:1

N=257

- Alectinib 600 mg BID 2 years → Recurrence
- Platinum-based chemotherapy† Q3W; 4 cycles → Recurrence

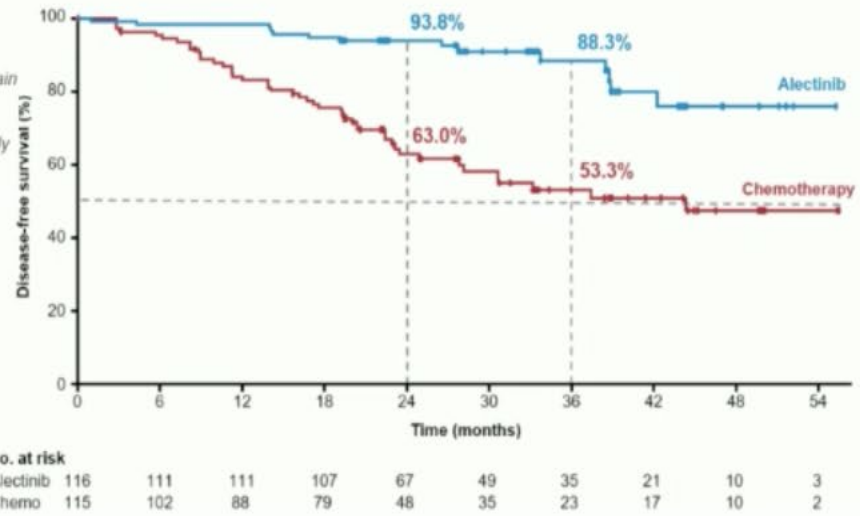
→ Further treatments at investigator's choice and survival follow-up

Primary endpoint
- DFS per investigator,‡ tested hierarchically:
  - Stage II–IIIA → ITT (Stage IB–IIIA)

Other endpoints
- CNS disease-free survival
- OS
- Safety

Disease assessments (including brain MRI)§ were conducted: at baseline, every 12 weeks for year 1–2, every 24 weeks for year 3–5, then annually

Disease-free survival: stage II–IIIA*



	Alectinib (N=116)	Chemotherapy (N=115)
Patients with event Death Recurrence	14 (12%) 0 14	45 (39%) 1 44
Median DFS, months (95% CI)	Not reached	44.4 (27.8, NE)
DFS HR (95% CI)	**0.24** (0.13, 0.45) p†<0.0001	

Solomon et al. ESMO 2023

Neoadjuvant nivolumab plus platinum-doublet chemotherapy for resectable NSCLC: 3-year update from CheckMate 816

Patrick M. Forde,[1] Jonathan Spicer,[2] Nicolas Girard,[3] Mariano Provencio,[4] Shun Lu,[5]

CheckMate 816: 3-y efficacy/safety update and biomarker analyses

CheckMate 816 study design[a]

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

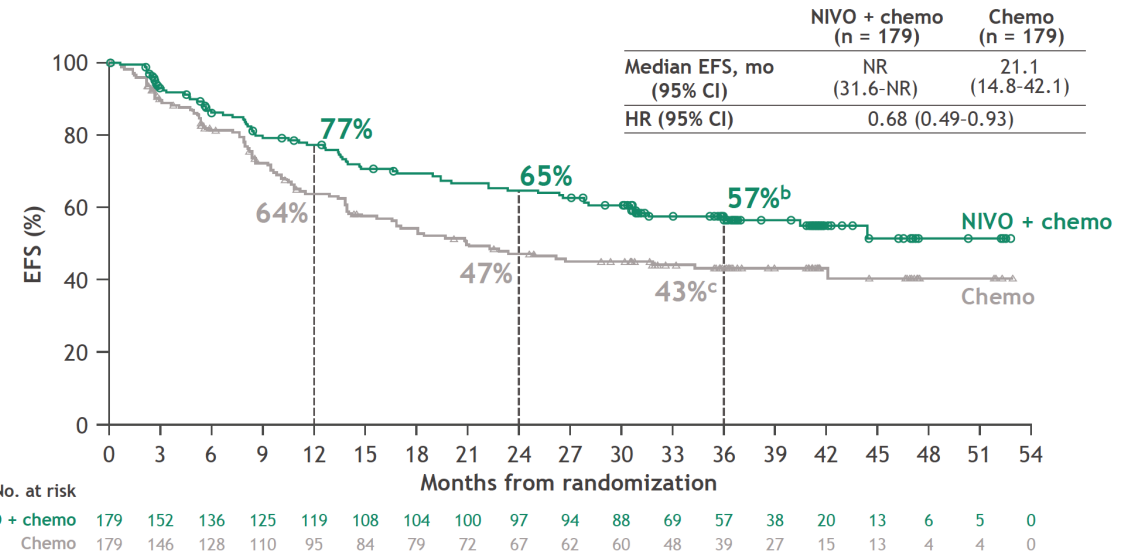
Stratified by stage (IB-II vs IIIA), PD-L1[b] (≥ 1% vs < 1%[c]), and sex

N = 358 → R 1:1 → NIVO 360 mg Q3W + chemo[d] Q3W (3 cycles) / Chemo[e] Q3W (3 cycles) → Radiologic restaging → Surgery (within 6 weeks post-treatment) → Optional adjuvant chemo and/or RT → Follow-up

Primary endpoints
- pCR by BIPR
- EFS by BICR

Secondary endpoints
- MPR by BIPR
- OS
- TTDM

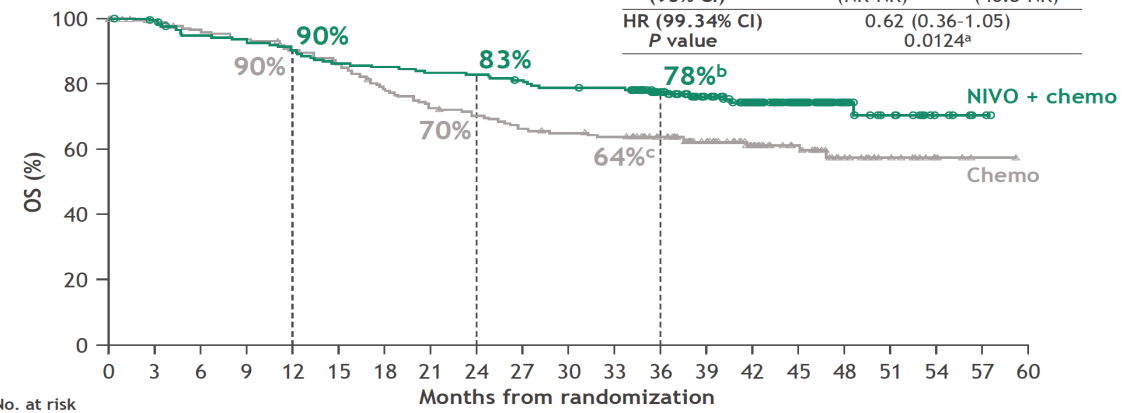
Exploratory analyses
- EFS by surgical outcomes
- pCR and EFS by 4-gene inflammatory signature score



	NIVO + chemo (n = 179)	Chemo (n = 179)
Median EFS, mo (95% CI)	NR (31.6-NR)	21.1 (14.8-42.1)
HR (95% CI)	0.68 (0.49-0.93)	

No. at risk

NIVO + chemo	179	152	136	125	119	108	104	100	97	94	88	69	57	38	20	13	6	5	0
Chemo	179	146	128	110	95	84	79	72	67	62	60	48	39	27	15	13	4	4	0



	NIVO + chemo (n = 179)	Chemo (n = 179)
Median OS, mo (95% CI)	NR (NR-NR)	NR (46.8-NR)
HR (99.34% CI)	0.62 (0.36-1.05)	
P value	0.0124[a]	

No. at risk

NIVO + chemo	179	176	166	163	158	151	149	146	145	141	137	136	117	95	67	44	23	14	6	2	0
Chemo	179	173	166	162	155	149	134	124	119	112	109	106	95	75	52	38	22	14	4	1	0

Minimum/median follow-up: 32.9/41.4 months.
[a]Significance boundary for OS was not crossed at this interim analysis. [b,c]95% CIs for 3-year OS rates: [b]71-83; [c]56-70.

MADRID 2023 ESMO congress

CheckMate 77T: Phase 3 study comparing neoadjuvant nivolumab plus chemotherapy with neoadjuvant placebo plus chemotherapy followed by surgery and adjuvant nivolumab or placebo for previously untreated, resectable stage II–IIIB NSCLC

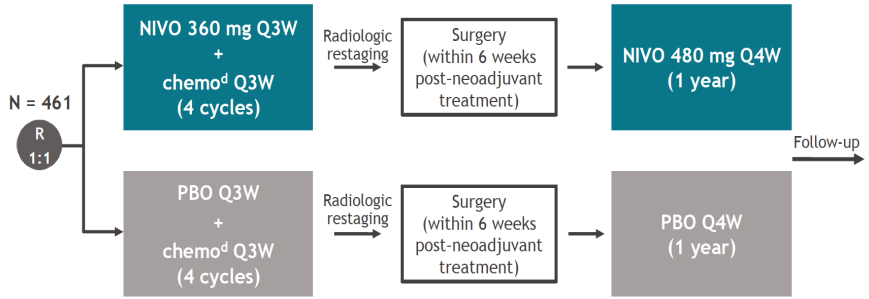
Tina Cascone,[1] Mark M. Awad,[2] Jonathan Spicer,[3] Jie He,[4] Shun Lu,[5] Boris Sepesi,[1] Fumihiro Tanaka,[6]

CheckMate 77T[a] study design

Key eligibility criteria

- Resectable, stage IIA (> 4 cm)-IIIB (N2) NSCLC (per AJCC 8th edition)
- No prior systemic anti-cancer treatment
- ECOG PS 0-1
- No *EGFR* mutation/known *ALK* alterations[b]

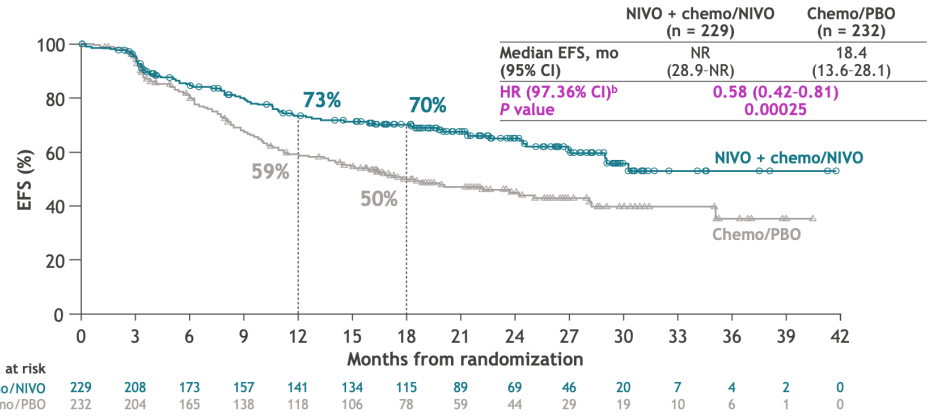
Stratified by histology (NSQ vs SQ) disease stage (II vs III), and tumor PD-L1[c] (≥ 1% vs < 1% vs not evaluable/indeterminate)



Follow-up, median (range): 25.4 (15.7-44.2) months

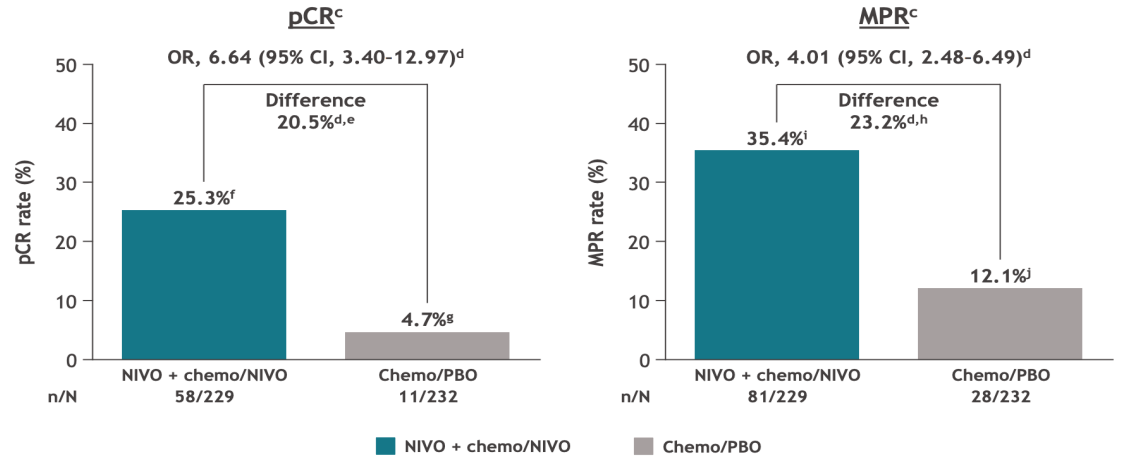
Primary endpoint	Secondary endpoints	Exploratory analyses
• EFS by BICR	• pCR[e] by BIPR • MPR[e] by BIPR • OS • Safety	• EFS by pCR/MPR • EFS by adjuvant treatment

Primary endpoint: EFS[a] per BICR with neoadjuvant NIVO + chemo/adjuvant NIVO vs chemo/PBO



- EFS per investigator assessment, NIVO + chemo/NIVO vs chemo/PBO: HR, 0.56; 95% CI, 0.41-0.76

pCR[a] and MPR[b] per BIPR



Overall Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC

Jonathan D Spicer,[1] Shugeng Gao,[2] Moishe Liberman,[3] Terufumi Kato,[4] Masahiro Tsuboi,[5] Se-Hoon Lee,[6]

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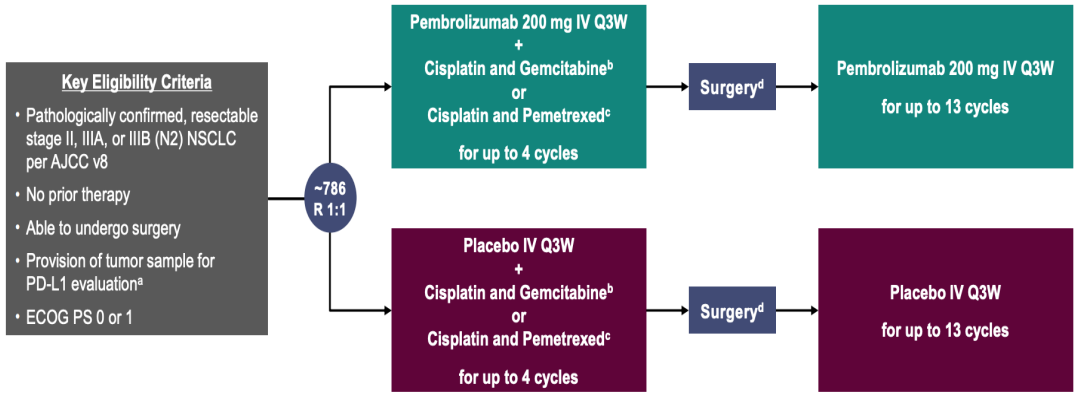
KEYNOTE-671 Study Design

Randomized, Double-Blind, Phase 3 Trial



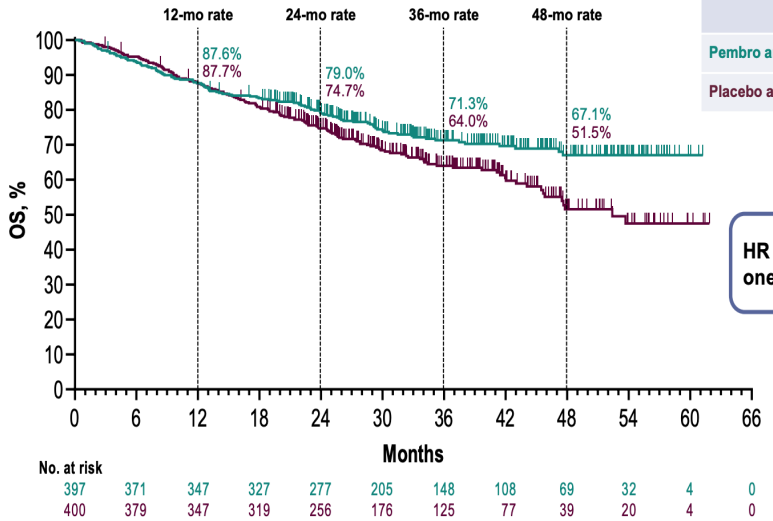
Stratification Factors
- Disease stage (II vs III)
- PD-L1 TPS[a] (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (east Asia vs not east Asia)

Dual primary end points: EFS per investigator review and OS

Key secondary end points: mPR and pCR per blinded, independent pathology review and safety

Overall Survival, IA2

Median Follow-Up: 36.6 months (range, 18.8-62.0)



	Pts w/ Event	Median (95% CI), mo
Pembro arm	27.7%	NR (NR-NR)
Placebo arm	36.0%	52.4 (45.7-NR)

HR 0.72 (95% CI, 0.56-0.93)
one-sided *P* = 0.00517[a]

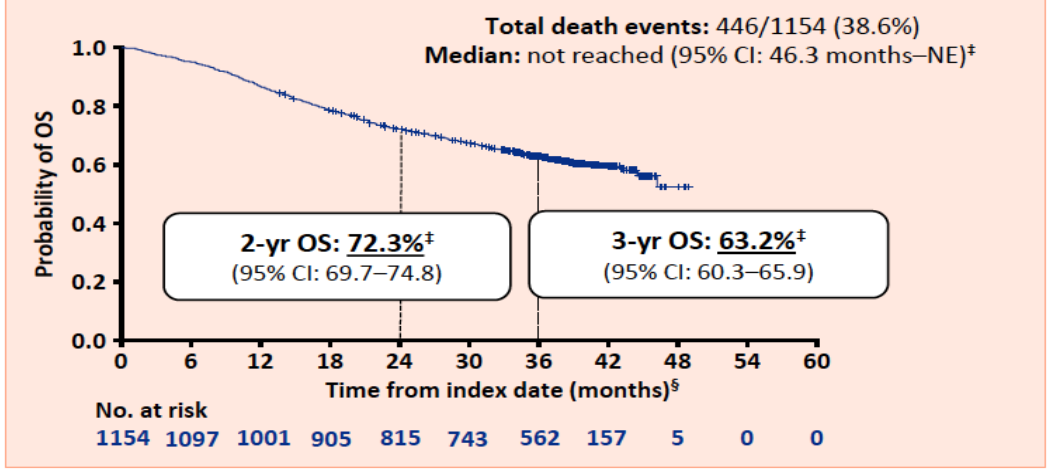
OS defined as time from randomization to death from any cause. [a] Significance boundary at IA2, one-sided *P* = 0.00543.
Data cutoff date for IA2: July 10, 2023.

Organizado por: GECP lung cancer research

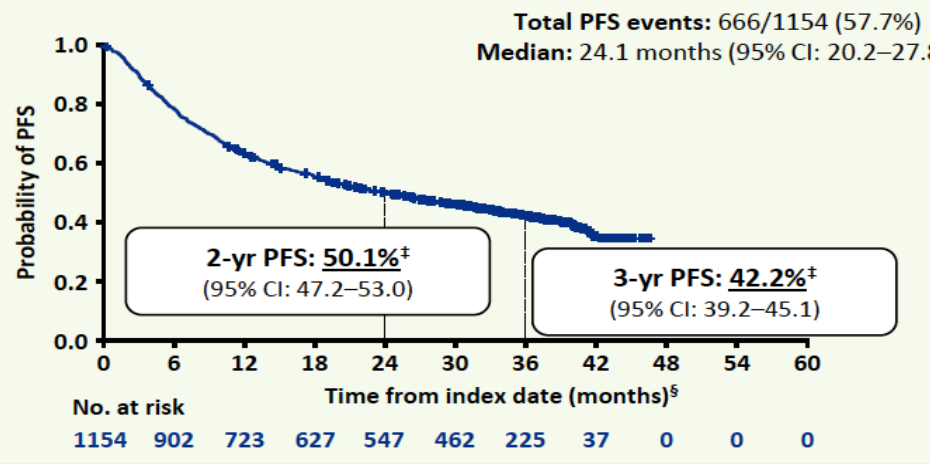
ESTADIO LOCALMENTE AVANZADO: PACIFIC-R

Outcomes in the full analysis set (N=1154)

Overall survival*



Investigator-assessed PFS*†



- As reported previously,[1] PACIFIC-R data continue to provide evidence for the effectiveness of consolidation durvalumab after CRT in a large, diverse, real-world population, consistent with findings from the pivotal, phase 3 PACIFIC trial[2-4]
  - These outcomes support the continued use of consolidation durvalumab after CRT (the 'PACIFIC regimen') as a global SoC for patients with unresectable stage III NSCLC

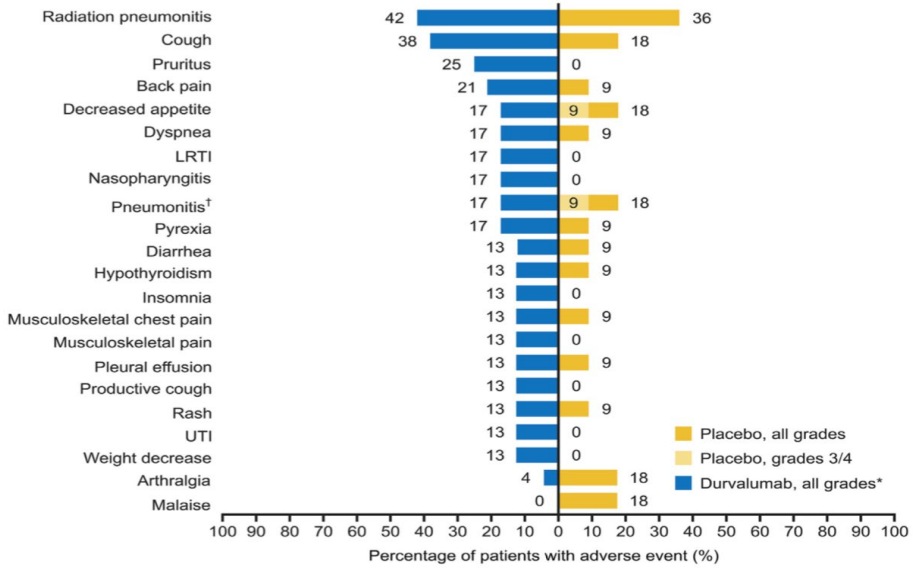
CI, confidence interval; CRT, chemoradiotherapy; EAP, early access programme; NE, not estimable; NSCLC, non-small-cell lung cancer; OS, overall survival; PFS, progression-free survival; SoC, standard of care; yr, year

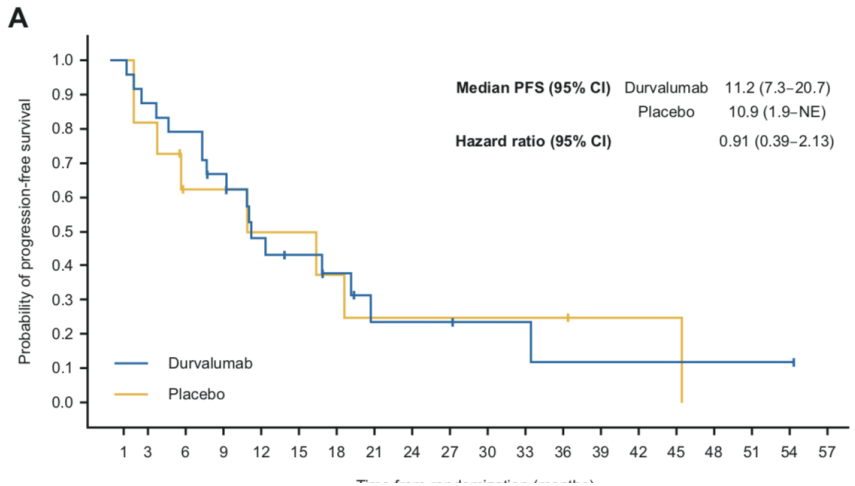
*Analyses are based on the 3rd chart extraction from PACIFIC-R (end date: Nov 30, 2021; reported previously[1]); the median follow-up duration in patients censored at the end of data extraction was 38.7 months (range: 13.6–49.0). †Because of the real-world nature of PACIFIC-R, progression could be documented by either radiological evaluation (per Response Evaluation Criteria in Solid Tumors [RECIST] v1.1) or the investigator's clinical judgment (depending on local practice). ‡Calculated using the Kaplan–Meier method. §The PACIFIC-R index date is the date that durvalumab was initiated within the EAP.[1]Girard N et al., Oral Presentation 580. Presented at ESMO IO 2022; [2]Antonia SJ et al., N Engl J Med 2018;379:2342–50; [3]Antonia SJ et al., N Engl J Med 2017;377:1919–29; [4]Spigel DR et al., J Clin Oncol 2022;40:1301–11

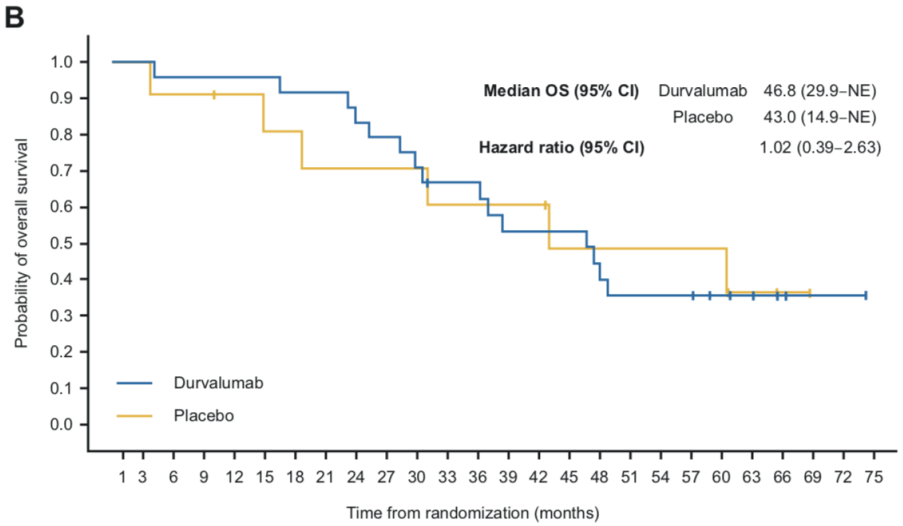
Brief Report: Durvalumab After Chemoradiotherapy in Unresectable Stage III EGFR-Mutant NSCLC: A Post Hoc Subgroup Analysis From PACIFIC

Table 1. Baseline Demographics and Characteristics for the PACIFIC *EGFR*m Subgroup

Demographic or Characteristic	Durvalumab (n = 24)	Placebo (n = 11)	Total (N = 35)
Age (y): median (range)	65 (42-83)	69 (57-90)	67 (42-90)
Sex: male/female, n (%)	13 (54)/11 (46)	8 (73)/3 (27)	21 (60)/14 (40)
Race: Asian/non-Asian, n (%)	15 (63)/9 (38)[c]	6 (55)/5 (45)	21 (60)/14 (40)
Disease stage[a] IIIA/IIIB, n (%)	11 (46)/13 (54)	7 (64)/4 (36)	18 (51)/17 (49)
WHO PS: 0/1, n (%)	13 (54)/11 (46)	7 (64)/4 (36)	20 (57)/15 (43)
Tumor history: Squamous/nonsquamous	3 (13)/21 (88)[c]	1 (9)/10 (91)	4 (11)/31 (89)
Smoking history Yes/no, n (%)	13 (54)/11 (46)	5 (45)/6 (55)	18 (51)/17 (49)
Best response to previous CRT: CR/PR/stable disease, n (%)	0/11 (46)/13 (54)	0/4 (36)/7 (64)	0/15 (43)/20 (57)
Positive *EGFR* mutation status: exon 19 del/L858R/other,[b] n (%)	10 (42)/6 (25)/8 (33)	3 (27)/5 (45)/3 (27)[c]	13 (37)/11 (31)/11 (31)[c]
PD-L1 status ≥25%/<25%/unknown, n (%)	4 (17)/16 (67)/4 (17)[c]	3 (27)/4 (36)/4 (36)[c]	7 (20)/20 (57)/8 (23)
Primary tumor stage T1a-b/T2a-b/T3/T4, n (%)	6 (25)/9 (38)/4 (17)/5 (21)[c]	2 (18)/6 (55)/1 (9)/2 (18)	8 (23)/15 (43)/5 (14)/7 (20)
Regional lymph nodes N0/N2/N3, n (%)	2 (8)/10 (42)/12 (50)	1 (9)/7 (64)/3 (27)	3 (9)/17 (49)/15 (43)[c]
Previous induction chemotherapy, n (%)	2 (8)	4 (36)	6 (17)







Organizado por:
GECP lung cancer research

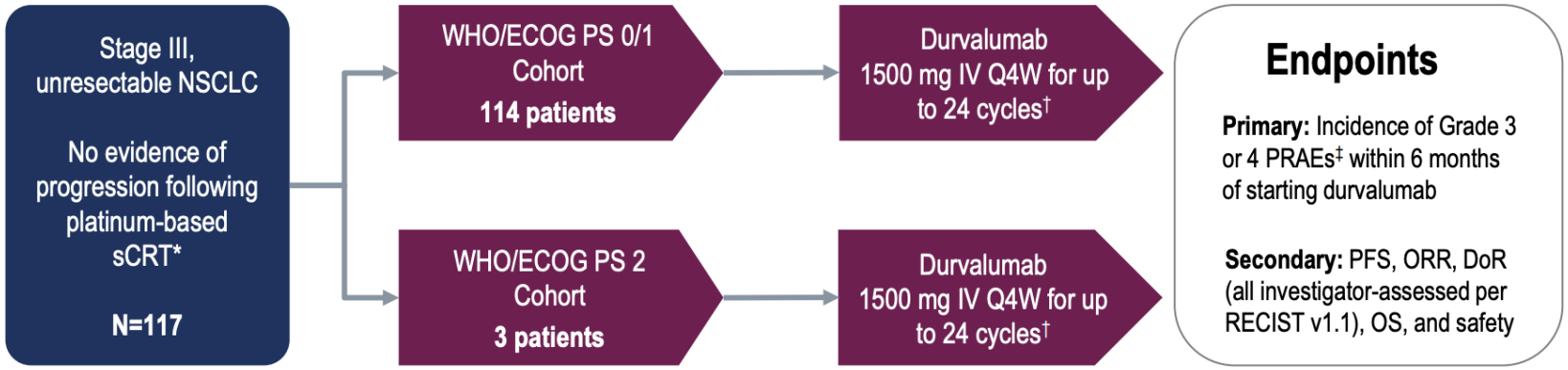
Naidoo, JTO 2023: 18, 5: 657–663

Durvalumab after sequential chemoradiotherapy in patients with unresectable Stage III NSCLC

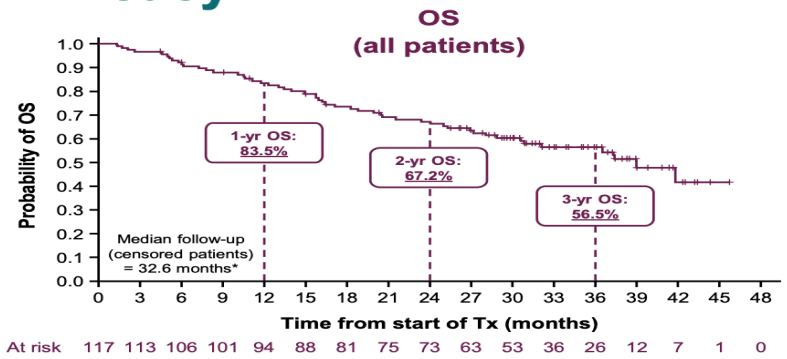
Final analysis from PACIFIC-6

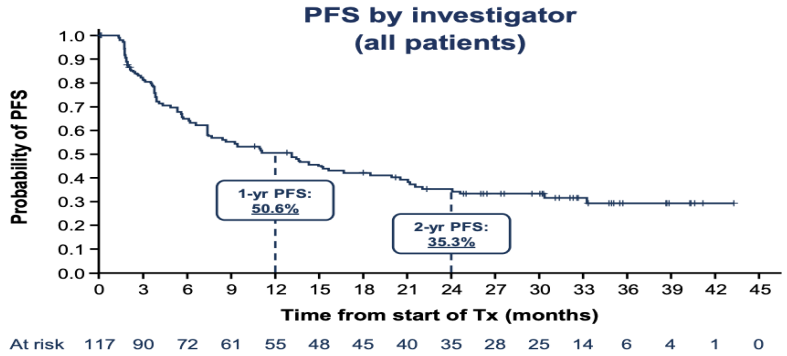
Marina Chiara Garassino,[1,2] Julien Mazieres,[3] Martin Reck,[4] Christos Chouaid,[5]

PACIFIC-6: phase II, open-label, international trial



Efficacy





Endpoint		All patients (N=117)	PS 0/1 cohort (n=114)†
OS	Median, months (95% CI)	39.0 (30.6–NC)	39.0 (30.6–NC)
	3-yr rate, % (95% CI)	56.5 (46.4–65.5)	57.2 (46.9–66.2)
PFS by investigator	Median, months (95% CI)	13.1 (7.4–19.9)	13.1 (7.4–19.9)
	2-yr rate, % (95% CI)	35.3 (26.5–44.3)	35.4 (26.4–44.5)
Confirmed ORR by investigator	n (%)	24 (20.5)‡	24 (21.1)‡
	[95% CI]§	[13.6–29.0]	[14.0–29.7]

INTRODUCCIÓN: ENFERMEDAD METÁSTASICA

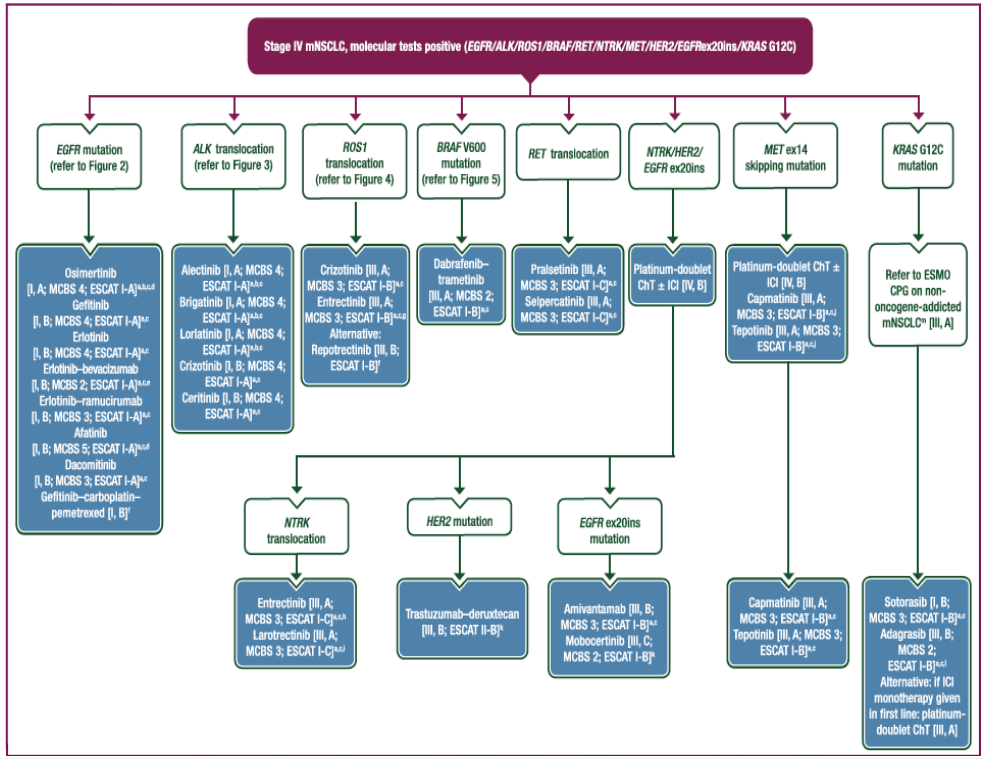
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

L. E. Hendriks[1], K. M. Kerr[2], J. Menis[3], T. S. Mok[4], U. Nestle[5,6], A. Passaro[7], S. Peters[8], D. Planchard[9], E. F. Smit[10,11], B. J. Solomon[12], G. Veronesi[13,14] & M. Reck[15], on behalf of the ESMO Guidelines Committee*



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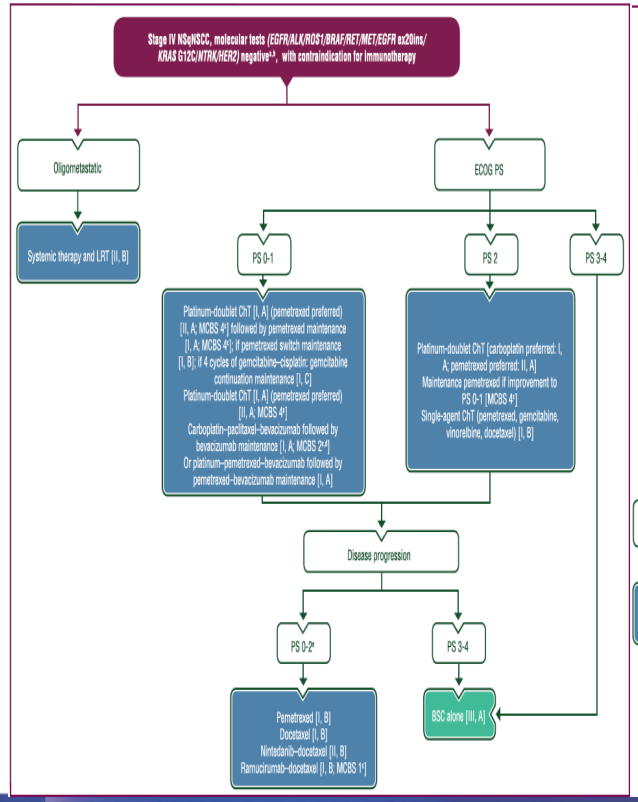
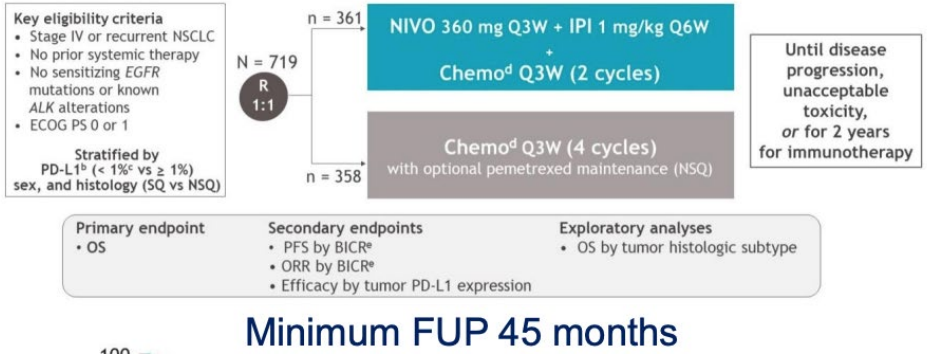


2023 ASCO ANNUAL MEETING
#ASCO23

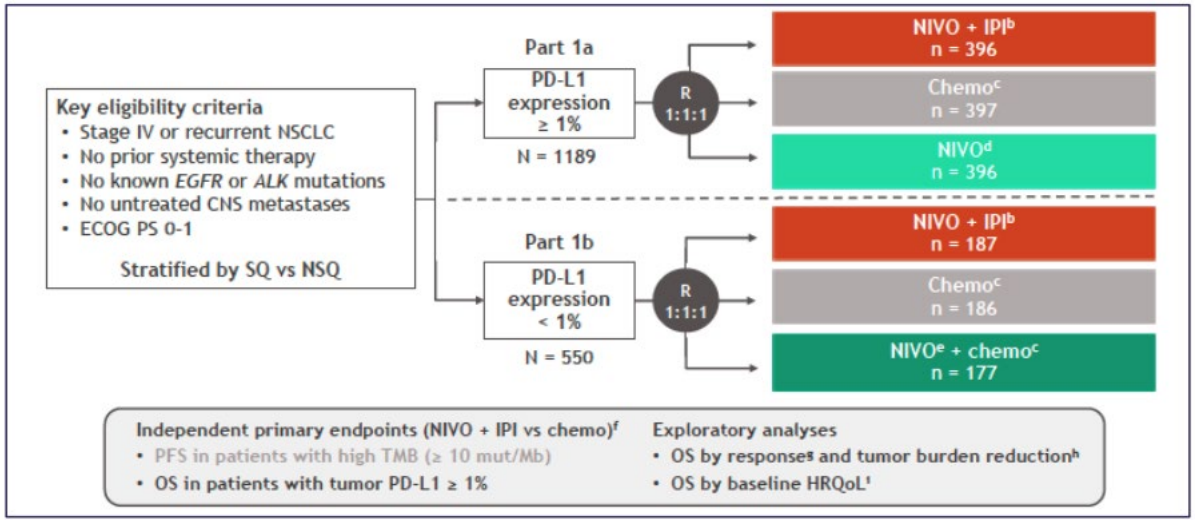
CheckMate 9LA 4-year clinical update



Minimum FUP 45 months

0A14.03: Six-year survival and HRQoL outcomes with 1L Nivolumab + Ipilimumab in patients with metastatic NSCLC from CheckMate227

IASLC 2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE



OA14.04: Three-year outcomes with first-line pembrolizumab, in patients with nonsmall cell lung cancer and a PD-L1 tumor proportion score > 90%

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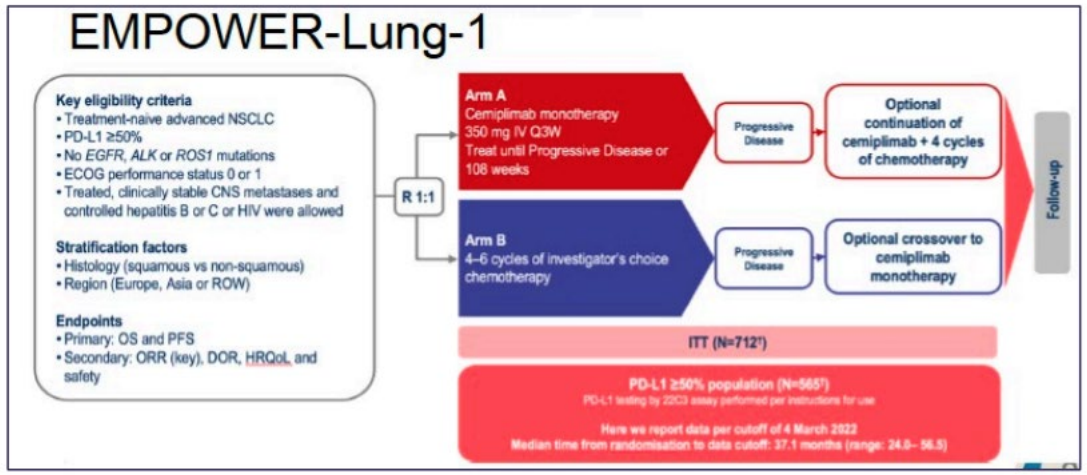
SEPTEMBER 9-12, 2023 | SINGAPORE



OA14.05: 5-year survival of pembrolizumab plus chemotherapy for metastatic NSCLC with PD-L1 tumor proportion score < 1%

IASLC 2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE

Clinical Study	Study Design
KEYNOTE-189 global[1] (NCT02578680) and **Japan Extension**[7] (NCT03950674)	• Previously untreated stage IV nonsquamous NSCLC; no *EGFR/ALK* alteration • Pembrolizumab 200 mg Q3W plus pemetrexed-platinum vs placebo plus pemetrexed-platinum • 2:1 randomization
KEYNOTE-407 global[2] (NCT02775435) and **China Extension**[8] (NCT03875092)	• Previously untreated stage IV squamous NSCLC • Pembrolizumab 200 mg Q3W plus carboplatin-paclitaxel/nab-paclitaxel vs placebo plus carboplatin-paclitaxel/nab-paclitaxel • 1:1 randomization

We present 5-year outcomes from a post-hoc exploratory pooled analysis of phase 3 trials of pembrolizumab plus chemotherapy vs placebo plus chemotherapy in patients with previously untreated metastatic NSCLC with PD-L1 TPS <1%

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GECP lung cancer research

Datopotamab deruxtecan (Dato-DXd) vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): Results of the randomized phase 3 study TROPION-Lung01

Myung-Ju Ahn,[1,a] Aaron Lisberg,[2,a,b] Luis Paz-Ares,[3] Robin Cornelissen,[4] Nicolas Girard,[5]

MADRID 2023 ESMO congress

Dato-DXd: Humanized anti-TROP2 IgG1 mAb[2-5]

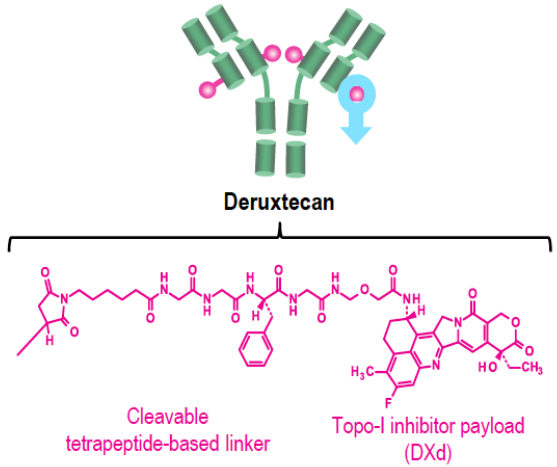


Image is for illustrative purposes only; actual drug positions may vary.

- **Dato-DXd** is a **TROP2-directed ADC** that selectively delivers a potent topoisomerase I inhibitor payload directly into tumor cells[1]
- **Promising antitumor activity** was seen with Dato-DXd in patients with adv/met NSCLC in the phase 1 TROPION-PanTumor01 trial (26% ORR)[1]

TROPION-Lung01 Study Design

Randomized, Phase 3, Open-Label, Global Study (NCT04656652)

Key Eligibility Criteria

- NSCLC (stage IIIB, IIIC, or IV)
- ECOG PS of 0 or 1
- No prior docetaxel

Without actionable genomic alterations[a]
- 1 or 2 prior lines, including platinum CT and anti–PD-(L)1 mAb therapy

With actionable genomic alterations
- Positive for *EGFR*, *ALK*, *NTRK*, *BRAF*, *ROS1*, *MET* exon 14 skipping, or *RET*
- 1 or 2 prior approved targeted therapies + platinum-based CT, and ≤1 anti–PD-(L)1 mAb

R 1:1

- **Dato-DXd** 6 mg/kg Q3W (N=299)
- **Docetaxel** 75 mg/m² Q3W (N=305)

Dual Primary Endpoints
- PFS by BICR
- OS

Secondary Endpoints
- ORR by BICR
- DOR by BICR
- Safety

Stratified by: histology,[b] actionable genomic alteration,[c] anti–PD-(L)1 mAb included in most recent prior therapy, geography[d]

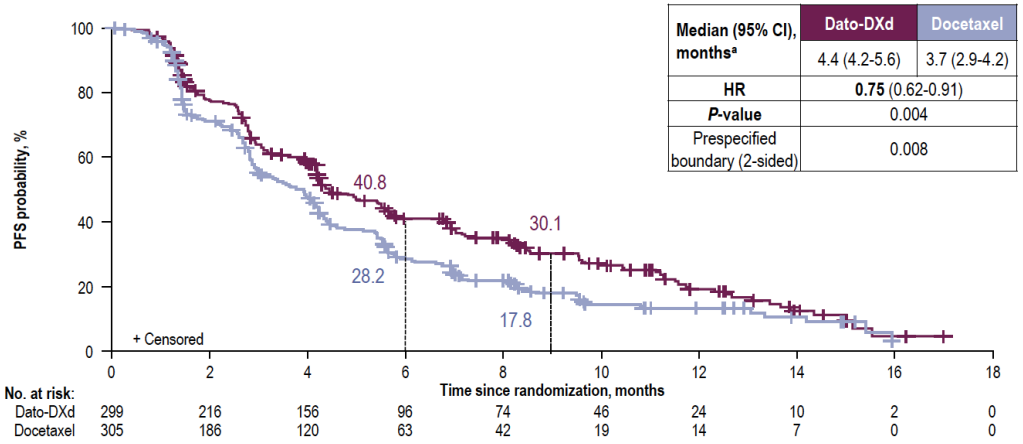
Organizado por: GECP lung cancer research

MADRID 2023 ESMO congress

PHASE III: TROPION Lung-01

Aaron Linberg

Progression-Free Survival: ITT



Median (95% CI), months[a]	Dato-DXd	Docetaxel
	4.4 (4.2-5.6)	3.7 (2.9-4.2)
HR	**0.75** (0.62-0.91)	
P-value	0.004	
Prespecified boundary (2-sided)	0.008	

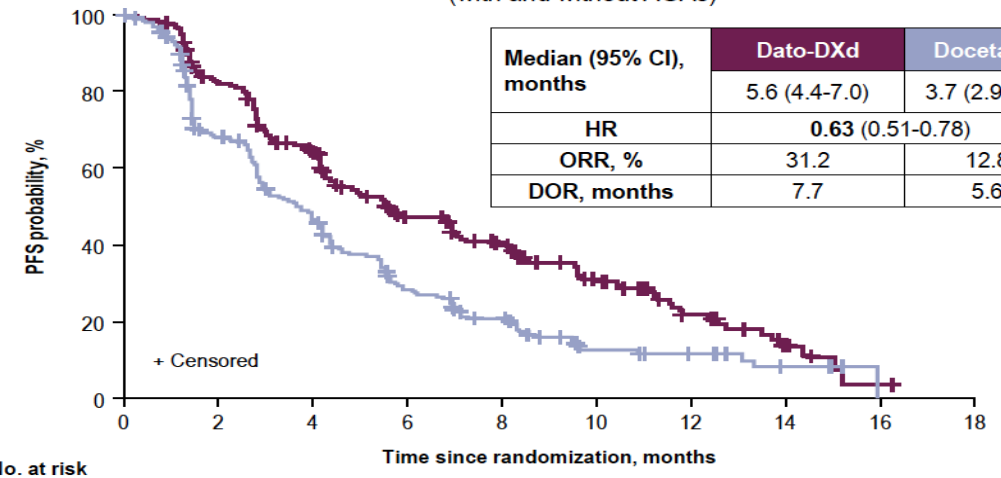
	Dato-DXd	Docetaxel
ORR (95% CI), %[b]	**26.4** (21.5-31.8)	**12.8** (9.3-17.1)
DOR (95% CI), mo	**7.1** (5.6-10.9)	**5.6** (5.4-8.1)

CR, complete response; DOR, duration of response; HR, hazard ratio; ITT, intention to treat; ORR, objective response rate; PFS, progression-free survival; PR, partial response.
[a]Median PFS follow-up was 10.9 (95% CI, 9.8-12.5) and 9.6 (95% CI, 8.2-11.9) months for Dato-DXd and docetaxel, respectively. [b]Included 4 CRs and 75 PRs for Dato-DXd and 39 PRs for docetaxel.

PFS by Histology

Non-squamous

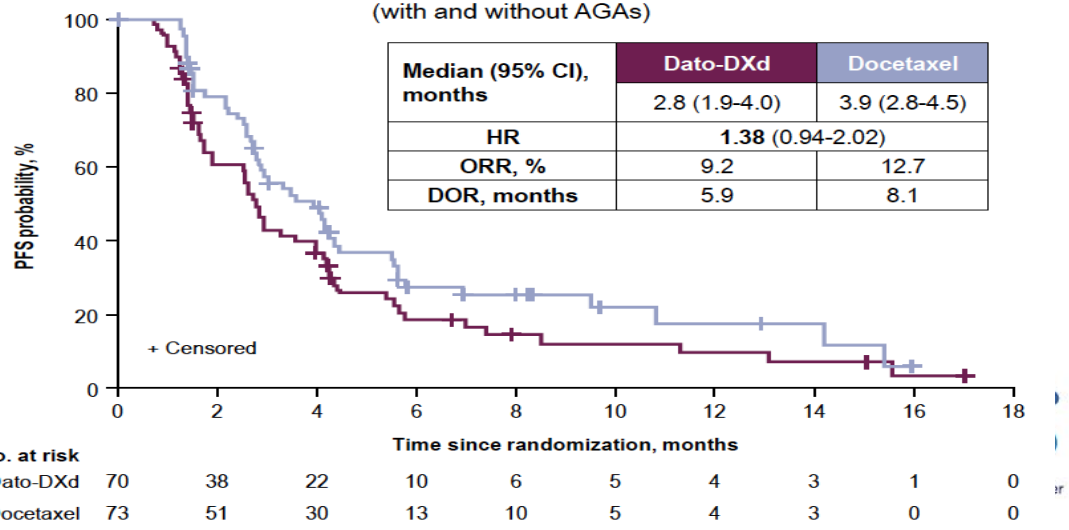
(with and without AGAs)



Median (95% CI), months	Dato-DXd	Docetaxel
	5.6 (4.4-7.0)	3.7 (2.9-4.2)
HR	**0.63** (0.51-0.78)	
ORR, %	31.2	12.8
DOR, months	7.7	5.6

Squamous

(with and without AGAs)



Median (95% CI), months	Dato-DXd	Docetaxel
	2.8 (1.9-4.0)	3.9 (2.8-4.5)
HR	**1.38** (0.94-2.02)	
ORR, %	9.2	12.7
DOR, months	5.9	8.1

ENFERMEDAD METASTASICA CON MUTACIONES DRIVER:1ºL

Osimertinib With / Without Platinum-Based Chemotherapy as First-Line Treatment in Patients with EGFRm Advanced NSCLC (FLAURA2)

ESTUDIO FLAURA-2

Safety run-in period (N = 30)
Published in ESMO Open, 2021[1]

Patients with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:
- Aged ≥18 years (Japan: ≥20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- No prior systemic therapy for advanced NSCLC
- Stable CNS metastases were allowed*
- CT/MRI scan at baseline

Stratification by:
- **Race** (Chinese Asian / non-Chinese Asian / non-Asian)
- **EGFRm** (local / central test)
- **WHO PS** (0 / 1)

Randomization 1:1 (N = 557)

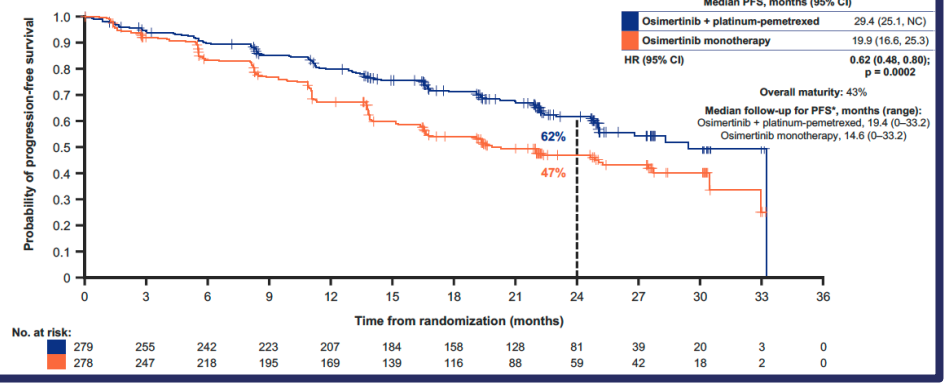
- Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75mg/m² (Q3W for 4 cycles for platinum-based treatments) → Maintenance osimertinib 80 mg (QD) + pemetrexed (Q3W)†
- Osimertinib 80 mg (QD)

Follow-up:
- RECIST 1.1 assessment at 6 and 12 weeks, then every 12 weeks until RECIST 1.1 defined radiological disease progression or other withdrawal criteria were met

- **Primary endpoint:** PFS (by investigator and BICR assessment per RECIST 1.1)‡§
- **Secondary endpoints:** OS, ORR, DoR, DCR, HRQoL, safety (AEs by CTCAE v5) and PFS2‡

Progression-free survival per BICR

- Median PFS was improved by 9.5 months with osimertinib plus platinum-pemetrexed vs osimertinib monotherapy



Amivantamab Plus Lazertinib Versus Osimertinib as First-line Treatment in *EGFR*-mutated Advanced NSCLC

Primary Results from MARIPOSA, a Phase 3, Global, Randomized, Controlled Trial

Byoung Chul Cho,[1] Enriqueta Felip,[2] Alexander I. Spira,[3] Nicolas Girard,[4]

MARIPOSA: Phase 3 Study Design

Key Eligibility Criteria
- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS 0 or 1

Stratification Factors
- *EGFR* mutation type (Ex19del or L858R)
- Asian race (yes or no)
- History of brain metastases[a] (yes or no)

Serial brain MRIs were required for all patients[a]

2:2:1 Randomization (N=1074)

- **Amivantamab + Lazertinib** (n=429; open-label)
- **Osimertinib** (n=429; blinded)
- **Lazertinib** (n=216; blinded)

Dosing (in 28-day cycles)
Amivantamab: 1050 mg (1400 mg if ≥80 kg) weekly for the first 4 weeks, then every 2 weeks
Lazertinib: 240 mg daily
Osimertinib: 80 mg daily

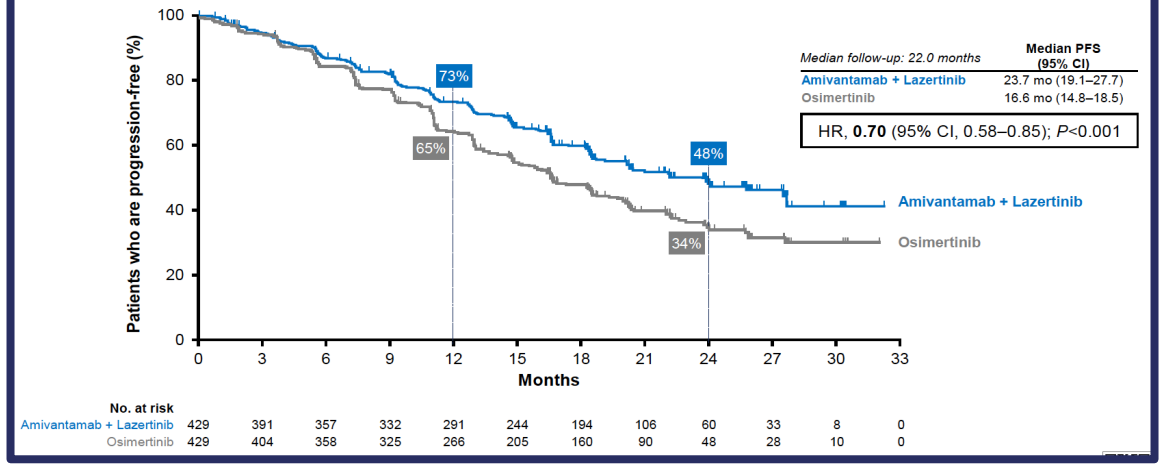
Primary endpoint of progression-free survival (PFS)[b] by BICR per RECIST v1.1:
- Amivantamab + lazertinib vs osimertinib

Secondary endpoints of amivantamab + lazertinib vs osimertinib:
- Overall survival (OS)[b]
- Objective response rate (ORR)
- Duration of response (DoR)
- PFS after first subsequent therapy (PFS2)
- Symptomatic PFS[c]
- Intracranial PFS[c]
- Safety

Lazertinib monotherapy arm was included to assess the contribution of components

Primary Endpoint: Progression-free Survival by BICR[a]

Amivantamab + lazertinib reduced the risk of progression or death by 30% and improved median PFS by 7.1 months



NUEVA POLÉMICA: ¿TENDRÍAMOS QUE CAMBIAR EL ESTANDAR DE 1L EN TODOS LOS EGFR+?

ENFERMEDAD EGFR 2ºL METASTASICA

ESTUDIO MARIPOSA-2

Amivantamab Plus Chemotherapy (With or Without Lazertinib) vs Chemotherapy in *EGFR*-mutated, Advanced NSCLC After Progression on Osimertinib

MARIPOSA-2, a Phase 3, Global, Randomized, Controlled Trial

Antonio Passaro,[1] Byoung Chul Cho,[2] Yongsheng Wang,[3] Barbara Melosky,[4] Raffaele Califano,[5] Se-Hoon Lee,[6] Nicolas Girard,[7] Karen Reckamp,[8] Toshiaki Takahashi,[9] Enriqueta Felip,[10] Ryan D. Gentzler,[11] Sanjay Popat,[12] William Nassib William Jr,[13] Tao Sun,[14] Sujay Shah,[15] Brooke Diorio,[16] Roland E. Knoblauch,[15] Joshua M. Bauml,[15] Rosario Garcia Campelo,[17] Jie Wang[18]

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R
- *Progressed on or after osimertinib monotherapy (as most recent line)*
- ECOG PS 0 or 1
- Stable brain metastases were allowed; radiation/definitive therapy was not required (untreated)

Stratification Factors

- Osimertinib line of therapy (1st vs 2nd)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=657)

Serial brain MRIs were required for all patients[a]

- Amivantamab-Lazertinib-Chemotherapy (n=263)
- Chemotherapy (n=263)
- Amivantamab-Chemotherapy (n=131)

Dosing (in 21-day cycles)

Amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) every 3 weeks starting at Cycle 3 (week 7)

Lazertinib: 240 mg daily starting after completion of carboplatin[b]

Chemotherapy administered at the beginning of every cycle:

- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m² until disease progression

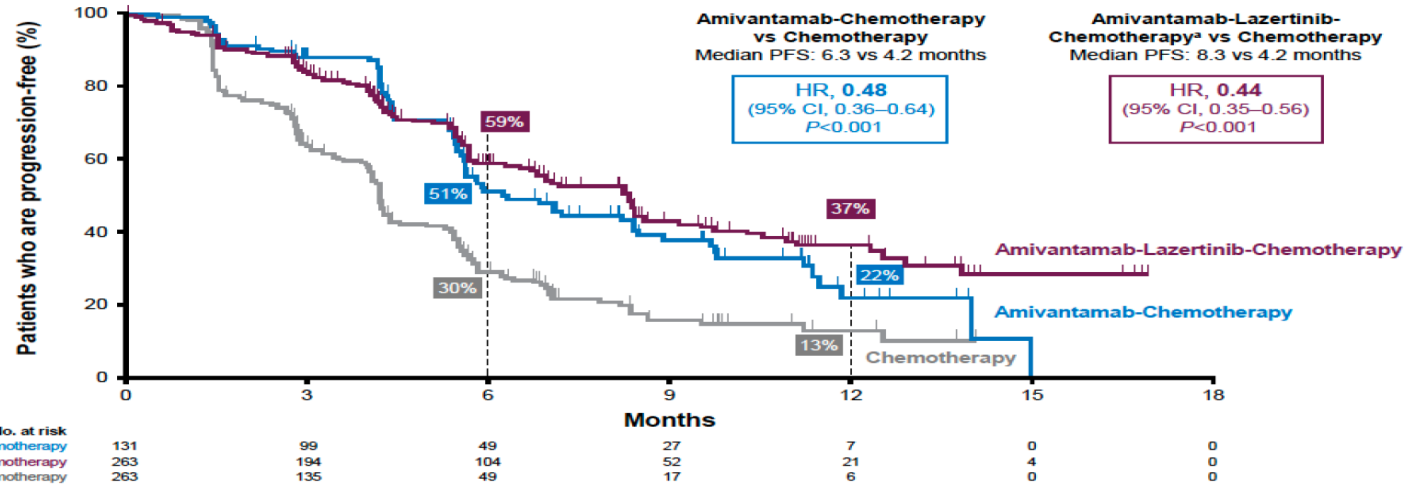
Dual primary endpoint of PFS[c] by BICR per RECIST v1.1:

- Amivantamab-Lazertinib-Chemotherapy vs Chemotherapy
- Amivantamab-Chemotherapy vs Chemotherapy

Secondary endpoints:

- Objective response rate (ORR)[c]
- Duration of response (DoR)
- Overall survival (OS)[c]
- Intracranial PFS
- Time to subsequent therapy[d]
- PFS after first subsequent therapy (PFS2)[d]
- Symptomatic PFS[d]
- Safety

Primary Endpoint: PFS by BICR



Consistent PFS benefit by investigator: HR, 0.41 (8.2 vs 4.2 mo; *P*<0.001[b]) & HR, 0.38 (8.3 vs 4.2 mo; *P*<0.001[b])

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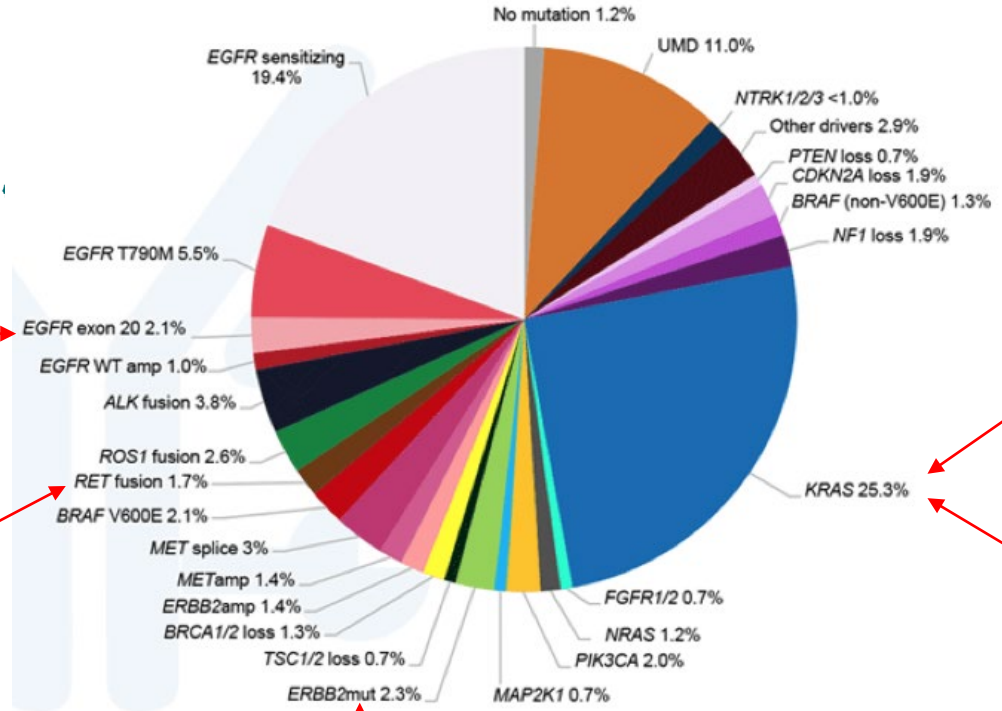
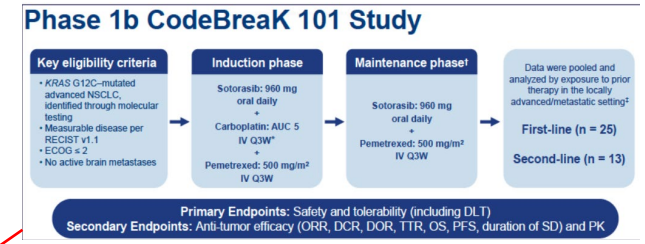
ENFERMEDAD METASTASICA CON MUTACIONES DRIVER

Amivantamab Plus Chemotherapy vs Chemotherapy as First-line Treatment in *EGFR* Exon 20 Insertion–mutated Advanced Non-small Cell Lung Cancer (NSCLC)

Primary Results From PAPILLON, a Randomized Phase 3 Global Study



Phase 1b CodeBreaK 101 Study



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KRYSTAL-7: Efficacy and Safety of Adagrasib With Pembrolizumab in Patients With Treatment-Naïve, Advanced Non-Small Cell Lung Cancer (NSCLC) Harboring a KRAS^{G12C} Mutation

Marina C. Garassino[1], Willemijn S.M.E. Theelen[2], Robert Jotte[3],

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Randomized Phase 3 Study of First-line Selpercatinib versus Chemotherapy and Pembrolizumab in *RET* Fusion-positive NSCLC

LIBRETTO-431 (NCT04194944)

Herbert H. Loong, Koichi Goto, Benjamin J. Solomon, Keunchil Park, Maurice Pérol, Edurne Arriola, Silvia Novello, Ying Cheng, Andrea Ardizzoni, Milena P. Mak, Fernando C. Santini, Yasir Y. Elamin, Alexander Drilon, Jürgen Wolf, Baohui Han, Hongmei Han, Minji K. Uh, Tarun Puri, Viktoriya Soldatenkova, Caicun Zhou

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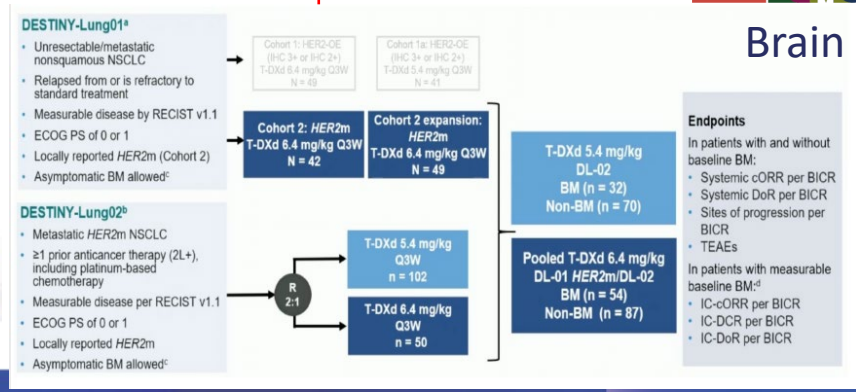
Brain mets



IASLC 2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE

Organizado por: GECP lung cancer research

INTRODUCCIÓN: CÁNCER MICROCITICO

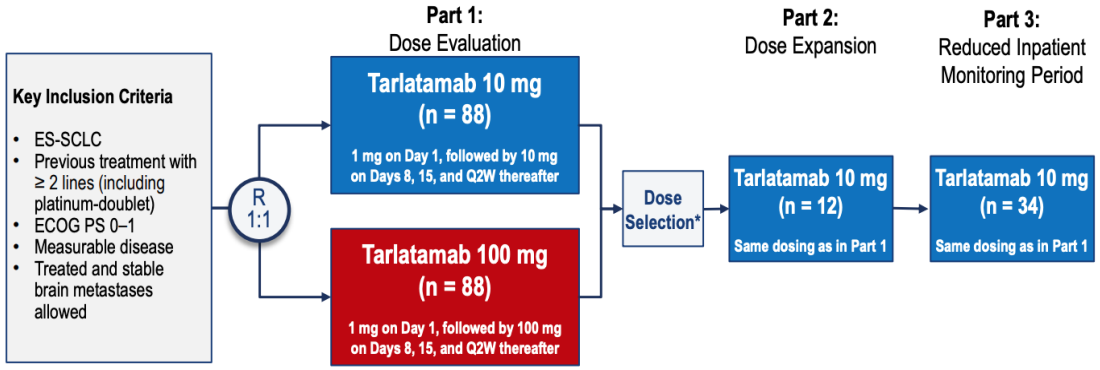
MADRID 2023 ESMO congress

Tarlatamab for patients with previously treated small cell lung cancer (SCLC): Primary analysis of the phase 2 DeLLphi-301 study

Luis Paz-Ares[1], Myung-Ju Ahn[2], Enriqueta Felip[3], Sabin Handzhiev[4],

DeLLphi-301 Study Design

Phase 2, open-label study (NCT05060016)



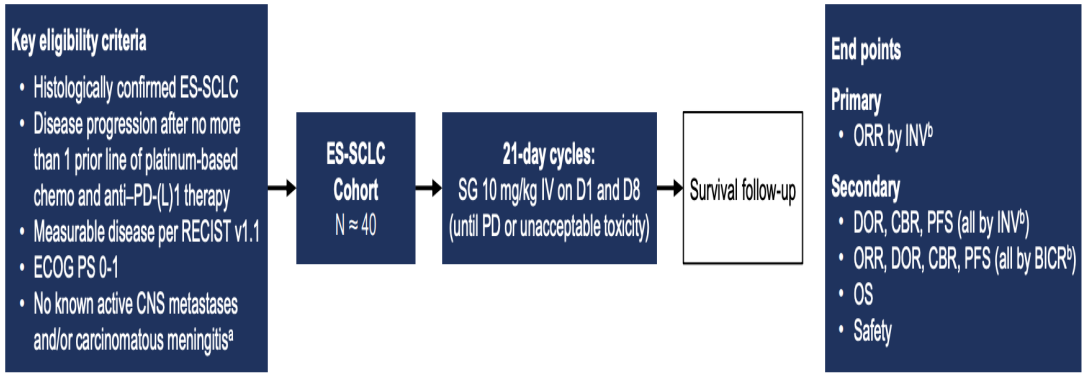
Primary Endpoint: ORR per RECIST v1.1 by BICR, TEAEs, tarlatamab serum concentrations
Secondary Endpoints Included: DOR, DCR, PFS per RECIST v1.1 by BICR, OS

MADRID 2023 ESMO congress

Sacituzumab govitecan as second-line treatment for extensive stage small cell lung cancer

Preliminary results from the phase 2 TROPiCS-03 basket trial

Afshin Dowlati,[1] Andres Cervantes,[2] Sunil Babu,[3] Erika Hamilton,[4] Shu Fen Wong,[5]



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MARS 2 trial schema

- Tissue confirmed mesothelioma
- Disease in one hemi-thorax
- Deemed surgically resectable
- PS (0-1)
- No end-organ failure

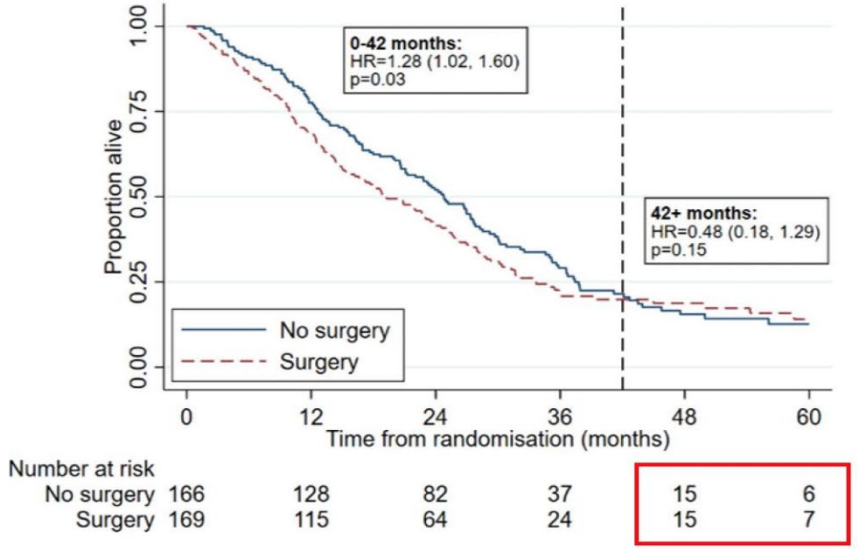
2 cycles platinum + pemetrexed → CT (still resectable) → R

R → (extended) pleurectomy decortication → Up to 4 cycles platinum + pemetrexed

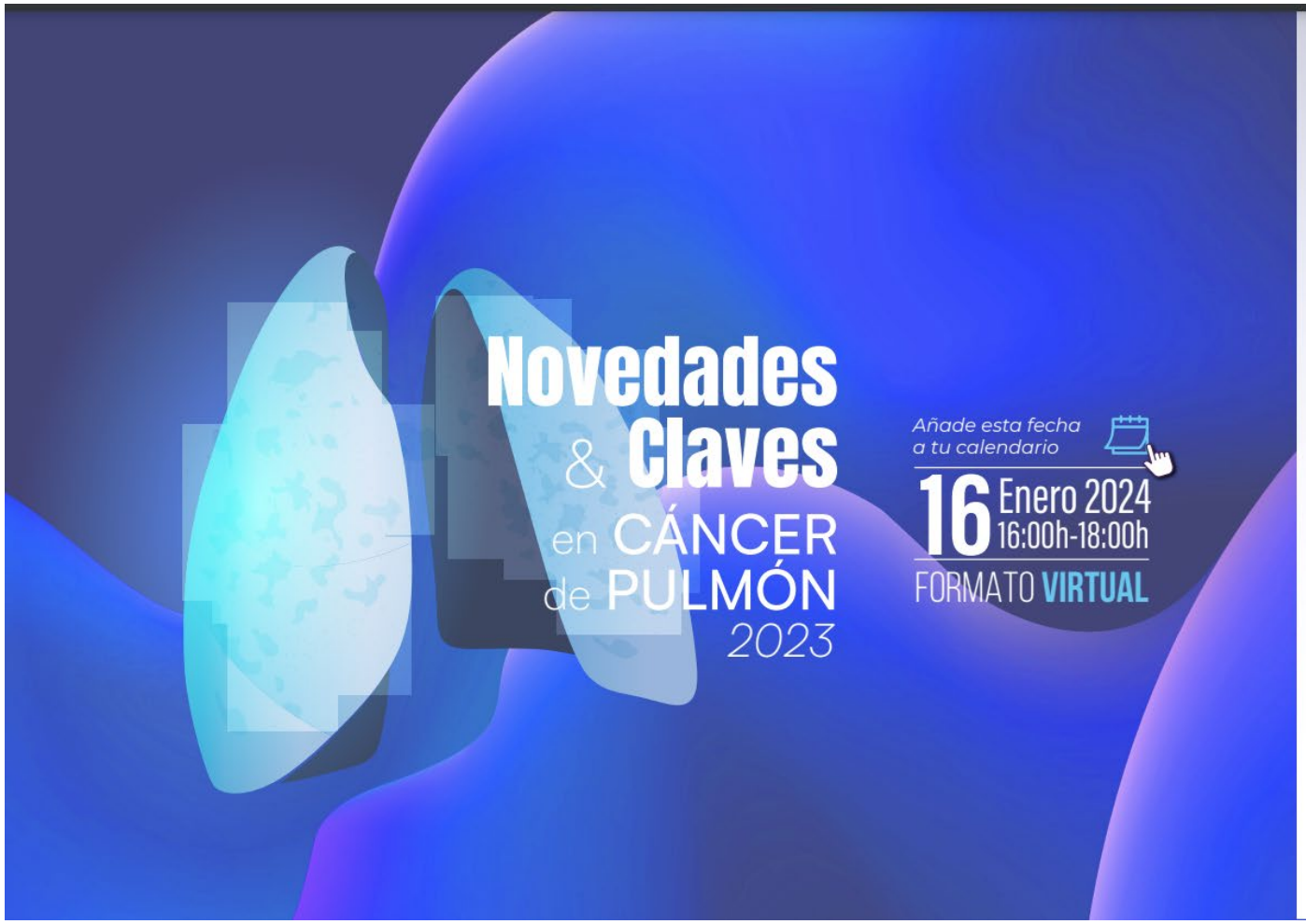
R → Up to 4 cycles platinum + pemetrexed

MARS 2 trial: Which is the role of pleurectomy/decortication?

Surgery was associated with worse OS compared with chemotherapy



Lim et al. WCLC 2023



Programa científico

16:00 - 16:20	Introducción	Dra. Reyes Bernabé Hospital Univ. Virgen del Rocío, Sevilla
16:20 - 16:40	Biomarcadores pronósticos	Dr. Airam Padilla Hospital Regional Univ. de Málaga
16:40 - 17:00	Estadios iniciales y enfermedad localmente avanzada	Dra. Ana Collazo Hospital Univ. Puerta de Hierro, Majadahonda, Madrid
17:00 - 17:20	Enfermedad metastática (incluyendo inmunoterapia)	Dr. Marc Cucurull ICO, Hospital Univ. Germans Trias i Pujol, Badalona, Barcelona
17:20 - 17:40	Cáncer de pulmón microcítico y otros tumores	Dr. Manuel Cobo Hospital Regional Univ. de Málaga
17:40 - 18:00	Conclusiones	Dr. Bartomeu Massutí Hospital General Univ. Dr. Balmis, Alicante

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