

Novedades & Claves en CÁNCER de PULMÓN 2024

Conclusiones

J.L. González Larriba

*Hospital Clínico San Carlos. Madrid
Universidad Complutense*

Organizado por:



Patrocinado por:



Johnson&Johnson

Novedades & Claves en CÁNCER de PULMÓN 2024

Añade esta fecha
a tu calendario 

21 Enero 2025
16:00h-18:00h

FORMATO **VIRTUAL**

ACCEDER

Programa científico

- 16:00 - 16:10 **Introducción**
Dr. Jose Luís González Larriba
Hospital Clínico San Carlos, Madrid
- 16:10 - 16:30 **Biomarcadores pronósticos**
Dra. Ana Cardeña
Hospital Univ. Nuestra Señora de Candelaria, Santa Cruz de Tenerife
- 16:30 - 16:50 **Estadios iniciales y enfermedad localmente avanzada**
Dr. Eider Akcona
Hospital Univ. de Cruces, Baracaldo, Vizcaya
- 16:50 - 17:10 **Enfermedad metastática (incluyendo inmunoterapia)**
Dra. Noelia Vilaríño
ICO, Hospital Duran i Reynals, L'Hospitalet de Llobregat, Barcelona
- 17:10 - 17:30 **Cáncer de pulmón microcítico y otros tumores**
Dr. Juan Luis Martí
Hospital General Univ. Dr. Balmis, Alicante
- 17:30 - 17:45 **Debate**
- 17:45 - 18:00 **Conclusiones**
Dr. Jose Luís González Larriba
Hospital Clínico San Carlos, Madrid

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Biomarcadores (Dra. Cardeña)

¿Qué sabemos?

	Índice	Definición	Mal pronóstico
2010	NLR: Neutrophil-to-Lymphocyte Ratio	Recuento de neutrófilos Recuento de linfocitos =	NLR ≥ 3
	ALI: Advanced Lung Cancer Inflammation Index.	$\frac{IMC \times Albúmina (g/L)}{NLR}$ =	ALI <18
	A/G: Albumin-to-Globulin Ratio.	$\frac{Albúmina(g/L)}{Globulina sérica (g/L)}$ =	A/G <1
	LIPI : Lung Immune Prognostic Index	= dNLR LDH (U/L) dNLR = $\frac{Neutrófilos}{Leucocitos - Neutrófilos}$	Buen pco. dNLR <3 y LDH N Pco. Intermedio: dNLR ≥ 3 ó LDH >250 U/L Mal pco: dNLR ≥ 3 y LDH >250 U/L
2018			

PD-L1 y TMB

Biomarcadores predictivos

¿Qué sabemos?

- PD-L1: La heterogeneidad intratumoral y la variabilidad en las técnicas de medición pueden afectar su precisión como biomarcador.
- TMB: Aplicación rutinaria limitada debido a la falta de estandarización y consenso sobre los puntos de corte óptimos (aunque ≥ 10 es el más usado).

¿Novedades?

- Combinación con otros biomarcadores emergentes: radiómica, inteligencia artificial y marcadores séricos y genómicos con valor PRONÓSTICO.

#1320P **I3LUNG: Digital pathology predicts PD-L1 expression in metastatic NSCLC patients treated with immunotherapy**

Arnela Prinjha¹, Matteo Sacco², Yanga Mskovic³, Daniele Lorenzin⁴, Francesco Trovò⁵, Aleksandra Zec⁶, Lalla Rossmann⁷, Leonardo Provenzano⁸, Claudia Prota⁹, Andrea Spagnolelli¹⁰, Cecilia Silverio¹¹, Alba Moya¹², Alessandro Pedrotchi¹³, Evangelos Sarras¹⁴, Filippos G.M. Di Braese¹⁵, Martin Reich¹⁶, Giuseppe La Russa¹⁷, Alexander T. Pearson¹⁸, Marina Chiara Garrone¹⁹

1. Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy; 2. University of Chicago Department of Medicine, Section of Hematology/Oncology, Chicago, United States of America; 3. Policlinico di Milano, Milan, Italy; 4. Sharda Zedek Medical Center, Jerusalem, Israel; 5. UNIM: Università degli Studi di Milano-Saravali, Milan, Italy; 6. IREC3F: IMBIA Scientia Innovation Research, Barcelona, Spain; 7. Metropolitan Hospital, Athens, Greece; 8. Vall d'Hebron University Hospital, Barcelona, Spain; 9. Anker Research Center North, German Center for Lung Research, LungClinic, Grieshaberfeld, Germany

13-17 SEPTEMBER 2024

INTRODUCTION

- Immunotherapy (IO) is the new standard of care for patients with advanced NSCLC, yet only 30-50% of patients benefit from it long-term.
- A better understanding of tumor features could help guide treatment decisions.
- To date, Programmed Death-Ligand 1 (PD-L1) remains the only biomarker used to predict IO efficacy, demonstrating its unique predictive ability, even if not perfect.
- A specific morphology has been found to be associated with PD-L1 expression, introducing new scenarios for the biological interpretation of the immune response.
- Utilizing AI and machine learning processes to analyze DPS could help create decision making tools for more individualized prediction of response.

METHODS

Digital Pathology whole slide images are very large images, and to feed them into Artificial Neural Network-based models we extracted square tiles (299x299px) at six magnification from the whole slide images.

Rebatch normalization was employed to reduce batch effect.

Positive bags: $\sum_{i=1}^n \mu_i \cdot \mu_i$
Negative bags: $\sum_{i=1}^n \mu_i \cdot \mu_i$

Large-scale AI models, known as foundation models, are developed using vast datasets and a training approach called self-supervised learning. This method does not rely on manually labeled data. Instead, it presents the model with a complex task inherent to the data itself. By solving this task, the model learns to identify and extract important features from the input information on its own. For this task, we used RetCCCL, a model trained on TCGA and PAIP datasets. Once processed through RetCCCL, tiles are converted into vectors of biologically relevant features.

Slides are now converted into bags of vectors. Assuming that not all tiles are equally relevant for our task, we need a model able to learn not only the patterns associated with a certain outcome, but also which tiles to focus on to find those patterns. For this goal, we used an Attention-Based Multiple Instance Learning model, which employs the attention mechanism to infer the importance of each tile vector.

RESULTS

- Among the 1388 pt enrolled in the I3LUNG retrospective cohort, 424 patients had available DPS and PD-L1 status to be considered for the present analysis.
- PD-L1 expression was high (>50%), low (<10%) and negative in 145 (34%), 128 (30%) and 122 (33%) patients within the training cohort, respectively, and 24 (33%), 23 (32%) and 26 (35%) among the validation cohort, respectively.
- PD-L1 high vs low/negative status through DPS were able to be predicted with an area under the curve (AUC) of 0.86, while for PD-L1 positive vs negative an AUC of 0.71 was achieved.

CONCLUSIONS

- To our knowledge, this is the largest series to date demonstrating a correlation between morphological features and PD-L1 expression in lung cancer.
- Data suggests that PD-L1 high and negative have different morphological phenotype.
- This report and generalizable model underscores the potential for morphological features to serve as valuable biomarkers in elucidating the mechanisms of immune responses.
- Within I3LUNG integration of genomic and radiomic data will probably allow to improve the ability to assess patient prognosis at diagnosis.

ACKNOWLEDGEMENTS

We sincerely thank the patients and their families for their invaluable participation in this study. This project has received funding from the European Union's Horizon Europe research and innovation programme. We are grateful for the collaborative efforts of our consortium partners. Their expertise has been crucial to the success of the I3LUNG project.

Corresponding author email: arnela.prinjha@istitutotumori.it

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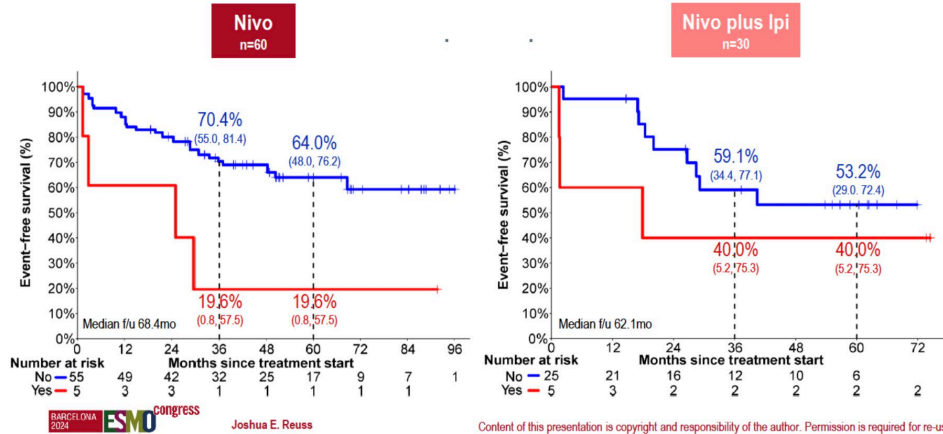


Biomarcadores (Dra. Cardeña)

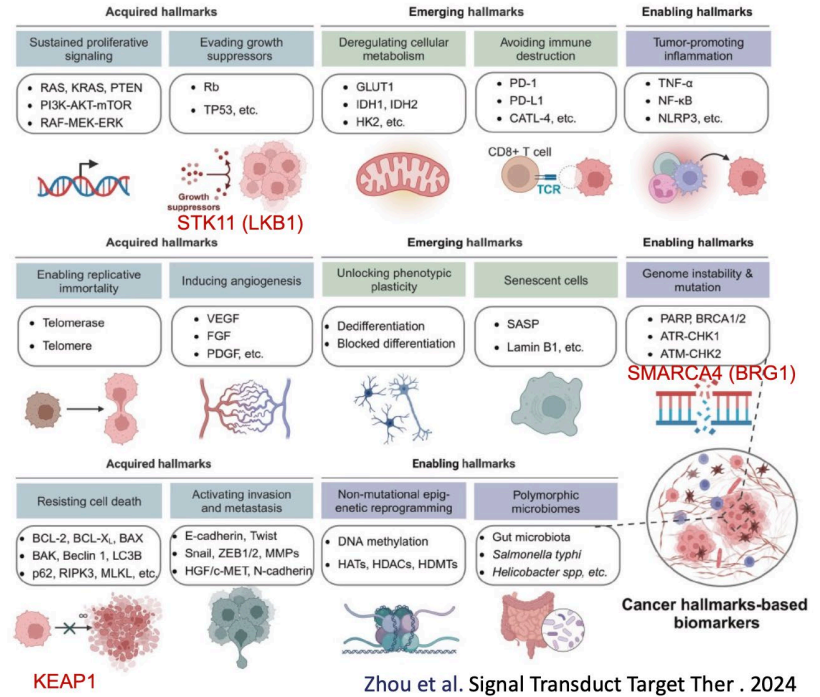
¿Futuro?

EFS analysis by key molecular subgroups

EFS by KRAS co-mutation w/ STK11, KEAP1, and/or SMARCA4 status (No/Yes)

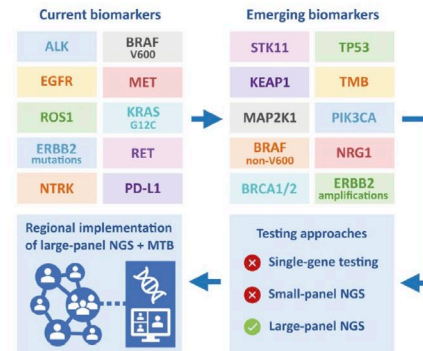


Reuss J. ESMO 2024



NGS

Next-generation sequencing



De Jager VD et al. Lancet Reg Health Eur. 2024

• Ventajas de ampliar paneles

- Detección de múltiples alteraciones de forma simultánea.
- Facilita la identificación de mutaciones accionables.
- Mejora la comprensión de la heterogeneidad tumoral.

• Limitaciones

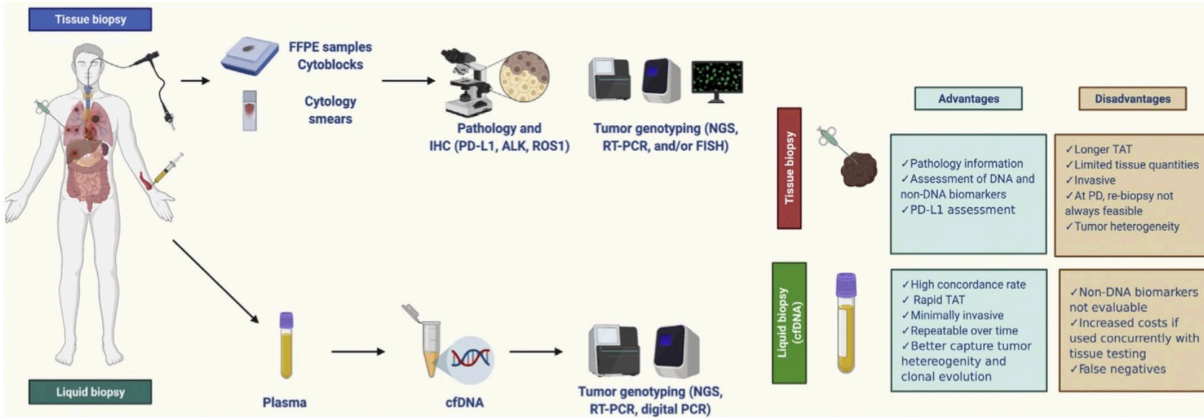
- No identifica alteraciones epigenéticas.
- Pueden pasar por alto genes no mutados del microambiente tumoral.



Organizado por:



Biomarcadores (Dra. Cardeña)



Biopsia líquida

MRD – ctDNA

Exosomas

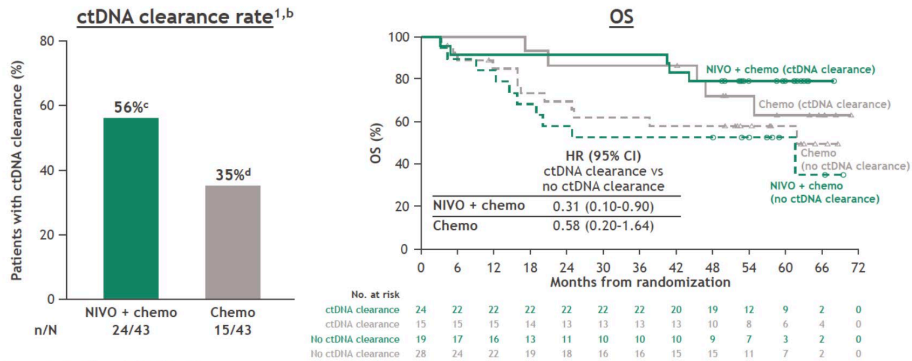
Perfiles de metilación DNA

Tasa de mutaciones somáticas (SMR)

CheckMate 816: 4-y survival update

ctDNA clearance rate and OS by ctDNA clearance

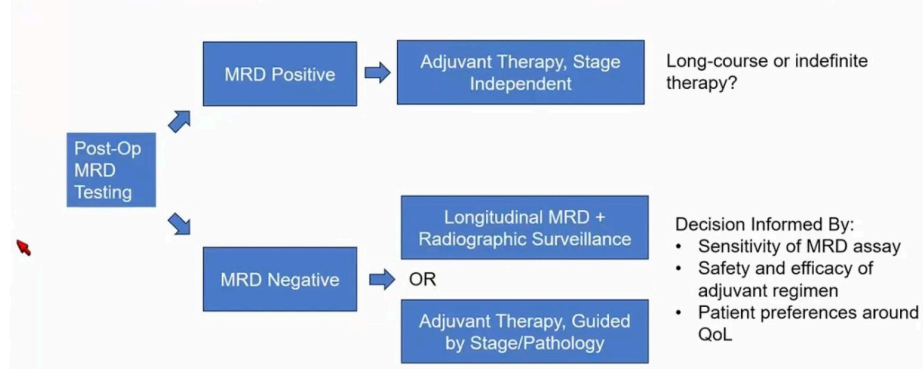
- Among concurrently randomized patients, 89 (25%) had evaluable ctDNA levels, and 86 (24%) had detectable ctDNA levels at baseline^{1,a}



Minimum/median follow-up, 49.1/57.6 months.
^aThe main reasons for sample attrition were lack of tissue for WES and lack of quality control pass for tissue and plasma. ^bctDNA clearance was defined as pre-surgical change from detectable ctDNA levels before cycle 1 to undetectable ctDNA levels before cycle 3. Analysis was performed using a WES tumor-guided personalized ctDNA panel (ArcherDX Personalized Cancer Monitoring). ^c95% CI: *90-71; *21-51. 1. Forde PM, et al. *N Engl J Med* 2022;386:1973-1985.

Spicer J. Abstract number LBA8010 (ASCO 2024).

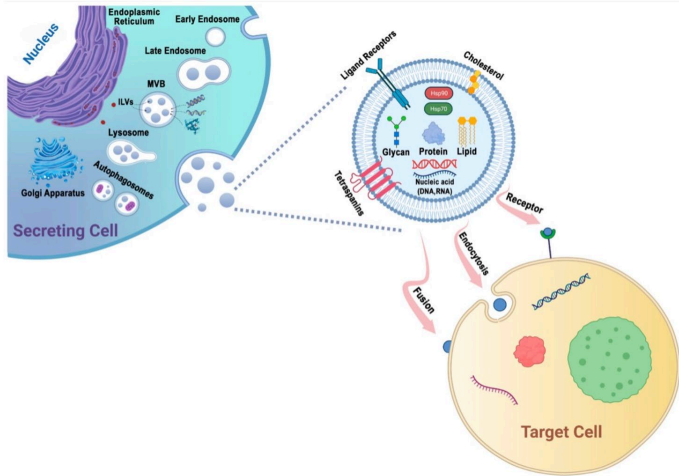
Prospective studies are needed to understand how best to modify therapy based on MRD findings



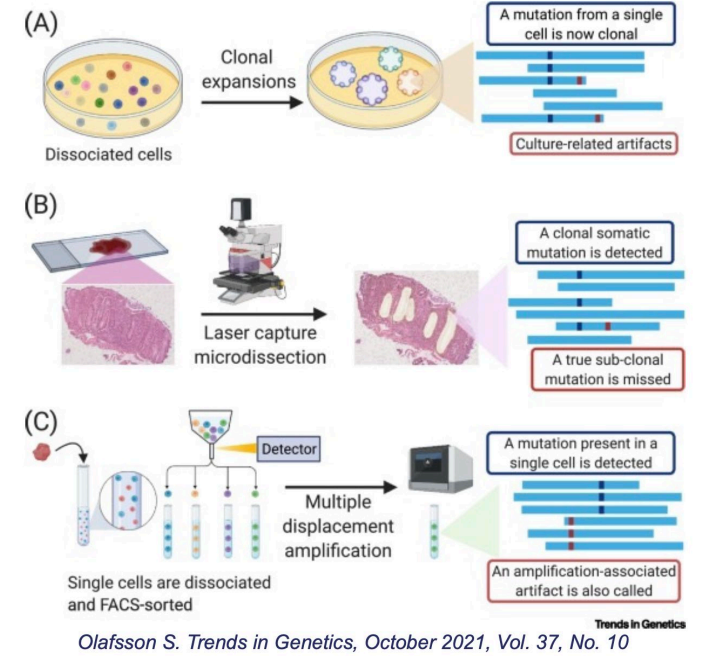
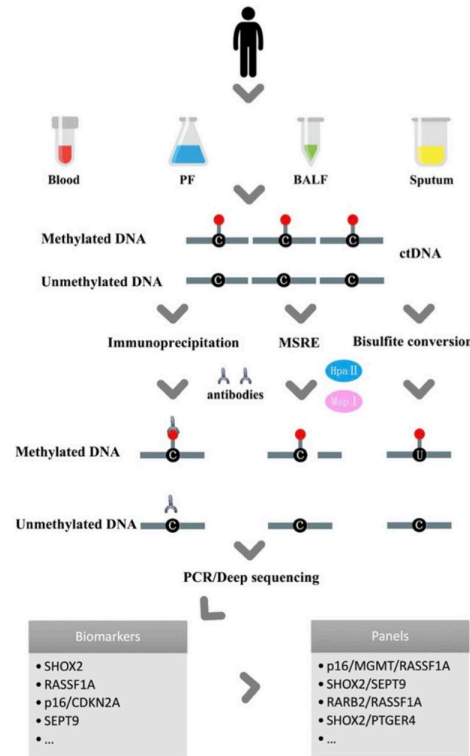
2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Julia Rotow, MD Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

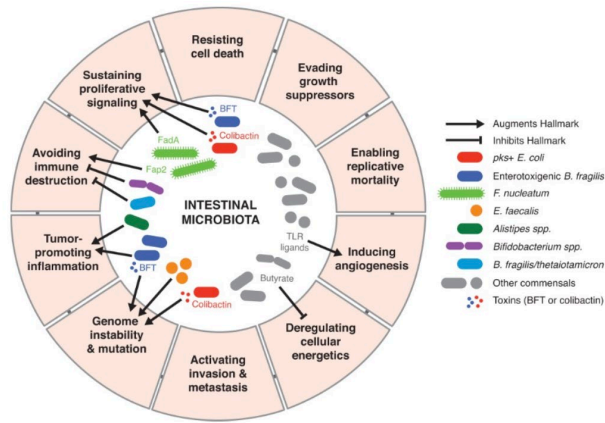
Biomarcadores (Dra. Cardeña)



Rahimian S. *Biomedicines* 2024, 12(1), 123



Olafsson S. *Trends in Genetics*, October 2021, Vol. 37, No. 10



Fulbright LE *PLoS Pathog* 13(9): e1006480

Exosomas Epigenética SMR Microbiota



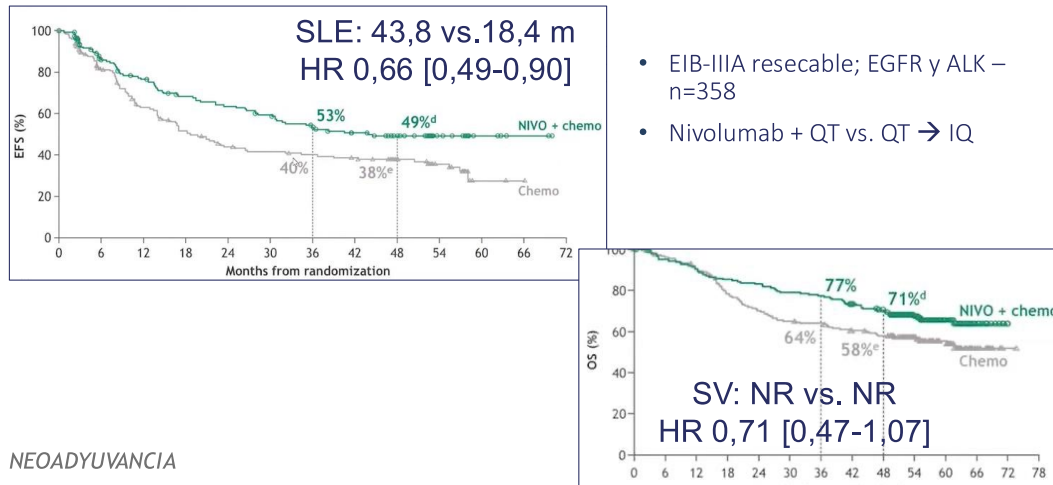
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Estudios Iniciales y Enfermedad Localmente Avanzada (Dr. Azkcona)

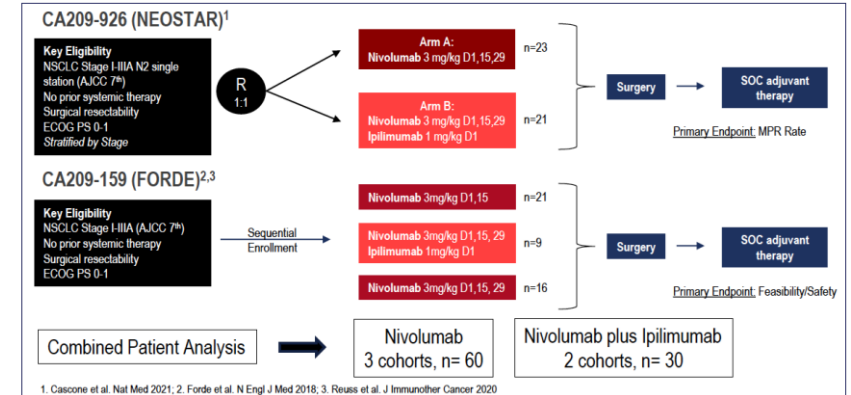
Neoadjuvant T.

Neoadjuvant nivolumab (NIVO) + chemotherapy (chemo) vs chemo in patients (pts) with resectable NSCLC: 4-year update from CheckMate 816. ASCO 2024. J.Spicer



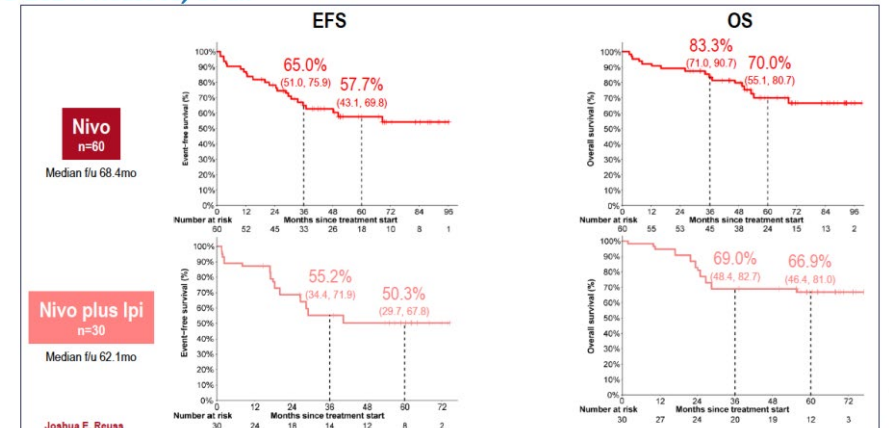
NEOADYUVANCIA

1209MO -Neoadjuvant nivolumab and nivolumab plus ipilimumab in resectable non-small cell lung cancer: Combined analysis of 5-year outcomes from NEOSTAR and CA209-159. ESMO 2024. Reuss JE, et al.



NEOADYUVANCIA

1209MO -Neoadjuvant nivolumab and nivolumab plus ipilimumab in resectable non-small cell lung cancer: Combined analysis of 5-year outcomes from NEOSTAR and CA209-159. ESMO 2024. Reuss JE, et al.



NEOADYUVANCIA



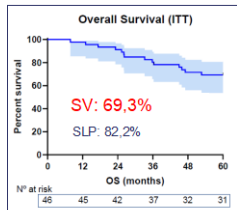
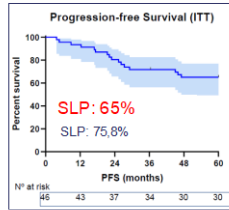
Estudios Iniciales y Enfermedad Localmente Avanzada (Dr. Azkcona)

Tratamiento Perioperatorio

5-Year Clinical Outcomes of Perioperative Nivolumab and Chemotherapy in Stage III NSCLC (NADIM trial). WCLC 2024, M. Provencio.

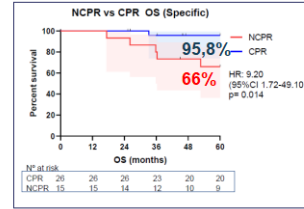
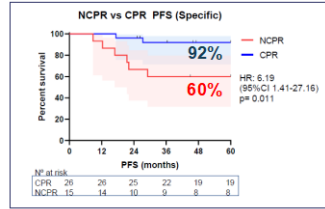
- CNMP EIIIA resecable (AJCC 7ª Ed), EGFR y ALK -
- CBDCA-Taxol + Nivolumab x 3c □ IQ □ Nivolumab x1 año

NADIM Patient baseline characteristics	N=46 (ITT)
Age (median, range)	63(41-77)
Co-morbidities, N (%)	43 (92.5)
N2	33 (89.2)
Multiple station	25 (75.8)



PERIOPERATORIO **gecp**

5-Year Clinical Outcomes of Perioperative Nivolumab and Chemotherapy in Stage III NSCLC (NADIM trial). WCLC 2024, M. Provencio.

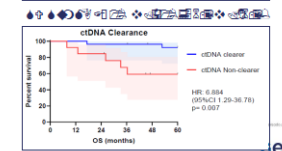
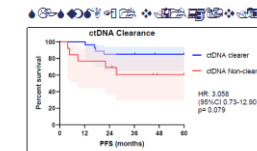
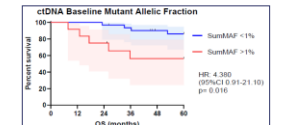
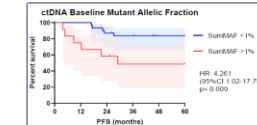


BIOMARCADORES:

- No diferencias: PD-L1, TMB
- Predictivos: ctDNA basal, aclaramiento ctDNA

PERIOPERATORIO **gecp**

5-Year Clinical Outcomes of Perioperative Nivolumab and Chemotherapy in Stage III NSCLC (NADIM trial). WCLC 2024, M. Provencio.

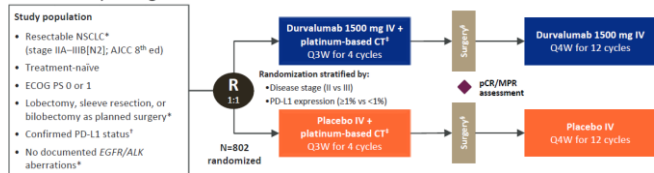


SLP No-ctDNA clearer vs. Si: 60.6 vs. 85.2%

SV No-ctDNA clearer vs. Si: 59.2 vs. 92.3%

PERIOPERATORIO **gecp**

Perioperative Durvalumab for Resectable NSCLC. Updated Outcomes from the Phase 3 AEGEAN Trial. WCLC 2024, J.V. Heymach.

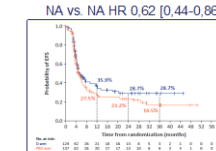
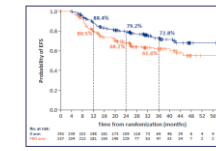
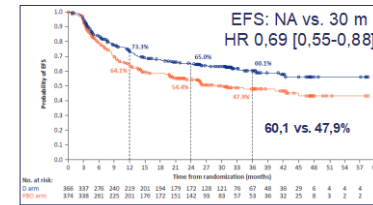


	DURVALUMAB	PLACEBO
Completan 4c neoad	86,9%	88,5%
IQ	77,6%	76,7%
RO	94,7%	91,3%
Completan adyuv	68,6%	63,7%

PERIOPERATORIO

gecp

Perioperative Durvalumab for Resectable NSCLC. Updated Outcomes from the Phase 3 AEGEAN Trial. WCLC 2024, J.V. Heymach.



5.1 vs. 5.2 HR 0.62 [0.60-1.14]

PERIOPERATORIO

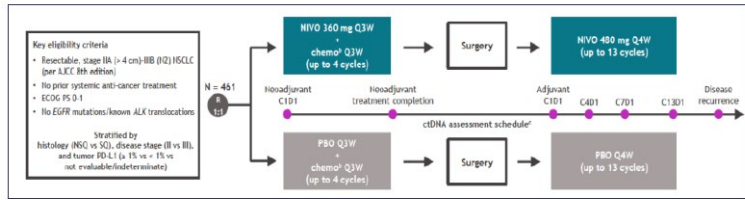
gecp

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Estudios Iniciales y Enfermedad Localmente Avanzada (Dr. Azkcona)

Tratamiento Perioperatorio

LBA50 - Perioperative nivolumab (NIVO) vs placebo (PBO) in patients (pts) with resectable NSCLC: clinical update from the phase 3 CheckMate 77T study. ESMO 2024. M. Provencio. (Spicer JD)

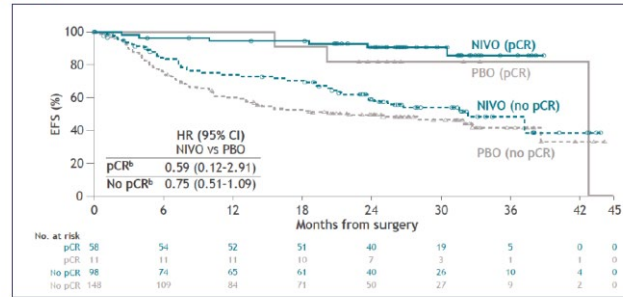


Obj 1º: EFS

PERIOPERATORIO



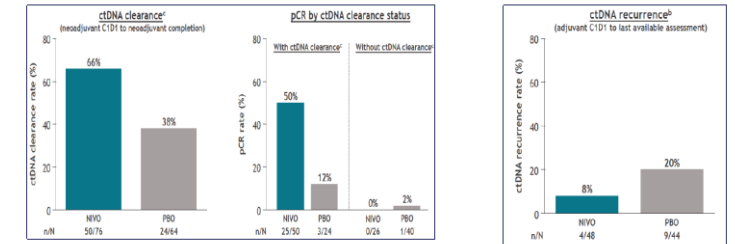
LBA50 - Perioperative nivolumab (NIVO) vs placebo (PBO) in patients (pts) with resectable NSCLC: clinical update from the phase 3 CheckMate 77T study. ESMO 2024. M. Provencio. (Spicer JD)



PERIOPERATORIO



LBA50 - Perioperative nivolumab (NIVO) vs placebo (PBO) in patients (pts) with resectable NSCLC: clinical update from the phase 3 CheckMate 77T study. ESMO 2024. M. Provencio. (Spicer JD)



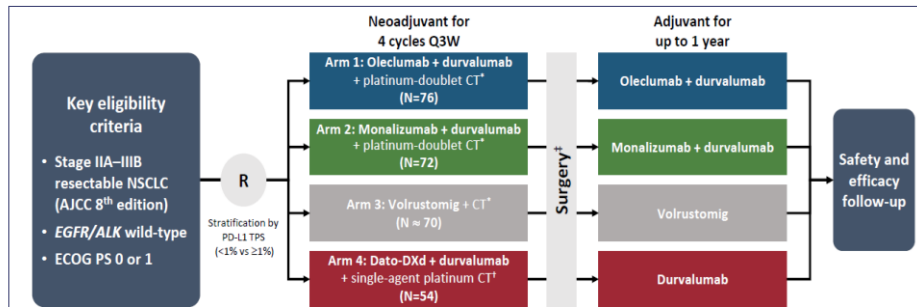
EFS:

- Aclaran ctDNA: 0,38 [0,16-0,88]
- No aclaran ctDNA: 0,74 [0,39-1,42]

PERIOPERATORIO



NeoCOAST-2: Efficacy and Safety of Neoadjuvant Durvalumab (D) + Novel Anticancer Agents + CT and Adjuvant D ± Novel Agents in Resectable NSCLC. WLCLC 2024. T. Cascone.



Obj 1º: pCR y seguridad

PERIOPERATORIO



Perioperatorio vs Neoadjuvant



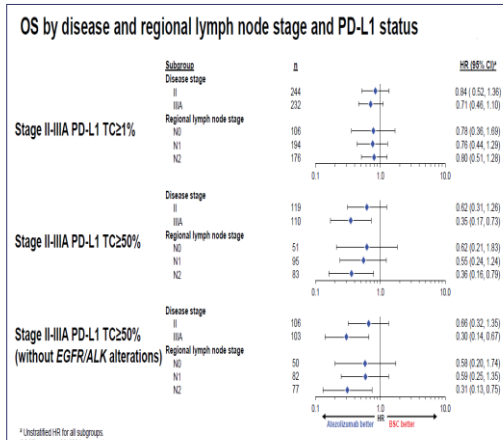
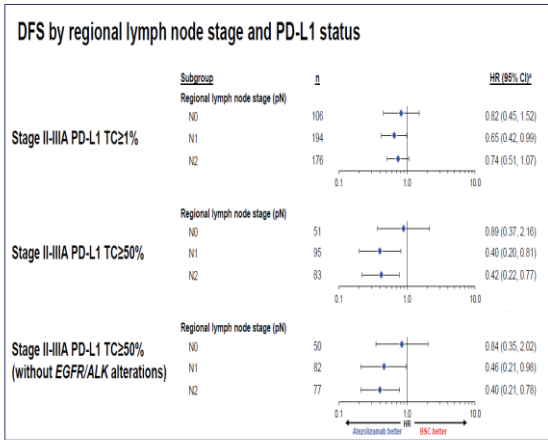
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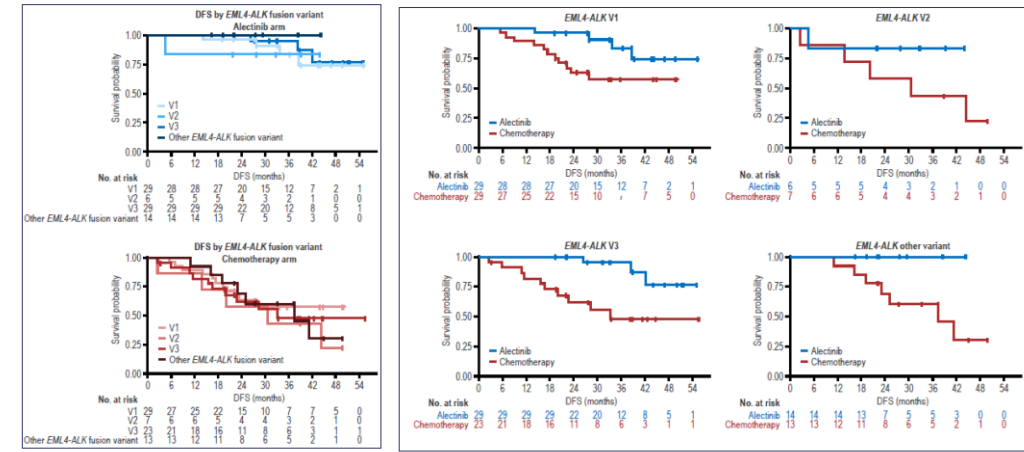
Adyuvancia

IMpower010 5-y subgroup analysis and relapse patterns: Phase 3 study of atezolizumab vs BSC in stage II-IIIa NSCLC. WCLC 2024. E. Felip.

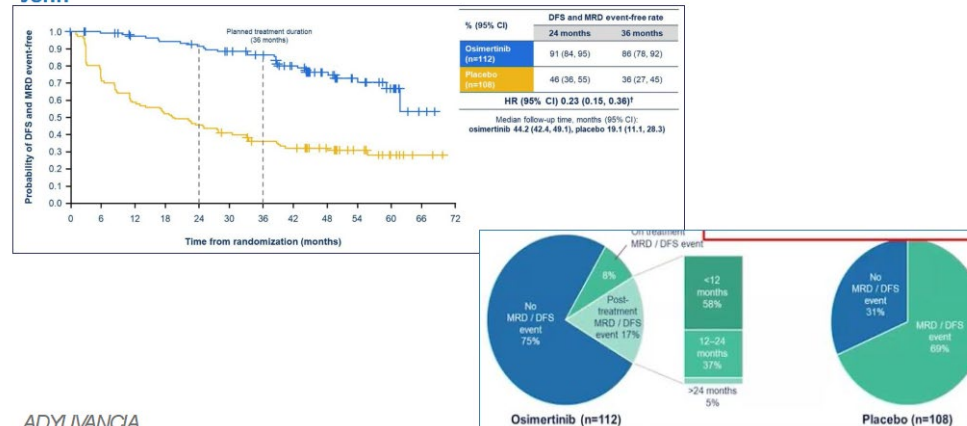


ADYUVANCIA

ALINA: exploratory biomarker analyses in patients with resected ALK+ non-small cell lung cancer (NSCLC) treated with adjuvant alectinib vs chemotherapy. ESMO24. BJ. Salomon



Molecular residual disease analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated stage IB-IIIa non-small cell lung cancer. ASCO 2024. T. John



ADYUVANCIA

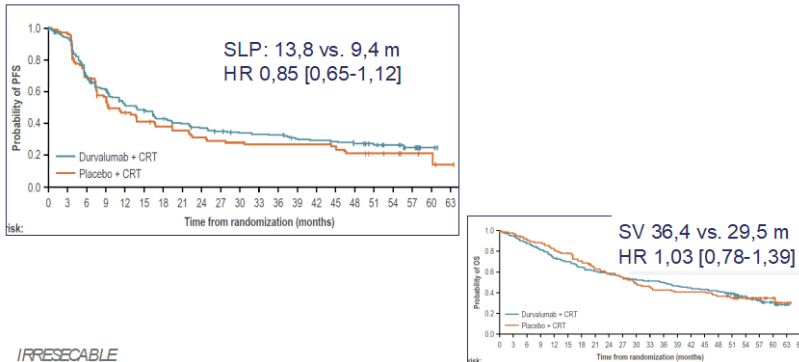
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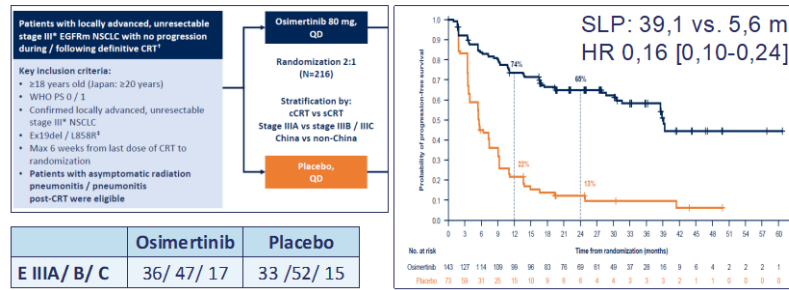
Estudios Iniciales y Enfermedad Localmente Avanzada (Dr. Azkcona)

Tumores Irresecables

LBA1 –Durvalumab in Combination with Chemoradiotherapy for Patients with Unresectable, Stage III NSCLC: Final Results from PACIFIC-2. ELCC 2024. JD.Bradley

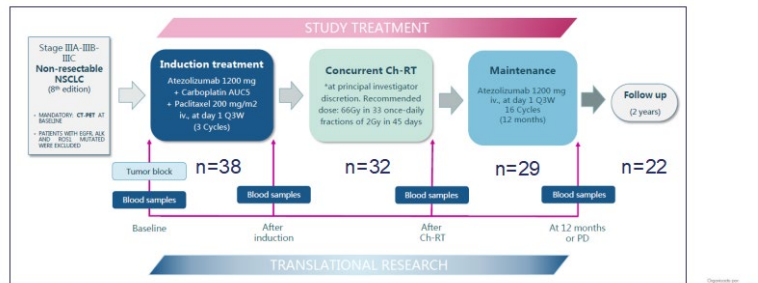


Osimertinib after definitive CRT in patients with unresectable stage III EGFRm NSCLC: Primary results of the phase 3 LAURA study. WCLC 2024. Ramalingam SS.



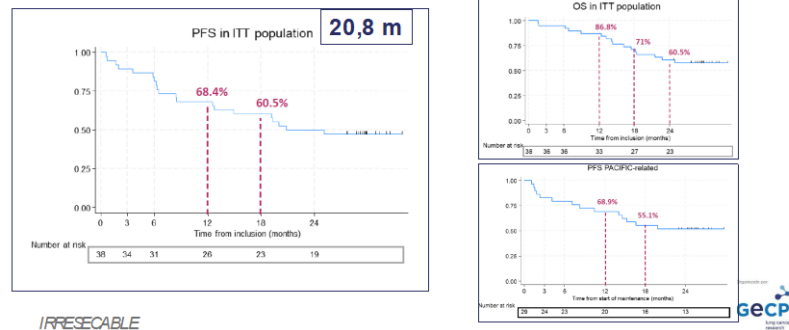
• Obj 1º: SLP

Atezolizumab + induction chemotherapy (Ch) + chemo-radiotherapy (Ch-RT) and atezolizumab maintenance in non-resectable stage IIIA-III B-III C non-small cell lung cancer (NSCLC): APOLO trial. WCLC 2024. M.Provencio



• Obj 1º: SLP 12m

Atezolizumab + induction chemotherapy (Ch) + chemo-radiotherapy (Ch-RT) and atezolizumab maintenance in non-resectable stage IIIA-III B-III C non-small cell lung cancer (NSCLC): APOLO trial. WCLC 2024. M.Provencio

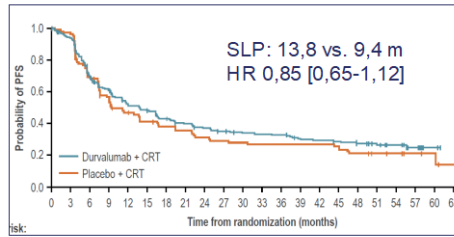


Organizado por:

Estudios Iniciales y Enfermedad Localmente Avanzada (Dr. Azkcona)

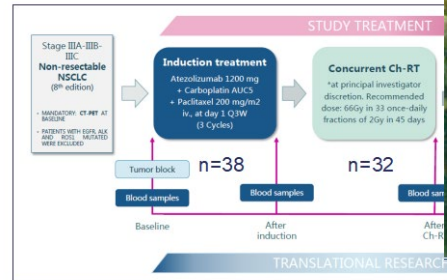
Tumores Irresecables

LBA1 –Durvalumab in Combination with Chemoradiotherapy in Unresectable, Stage III NSCLC: Final Results from PACIFIC



IRRESECABLE

Atezolizumab + induction chemotherapy (Ch) + chemoradiotherapy (Ch-RT) and atezolizumab maintenance in non-resectable stage III (NSCLC): APOLO trial. WCLC 2024. M.Provencio

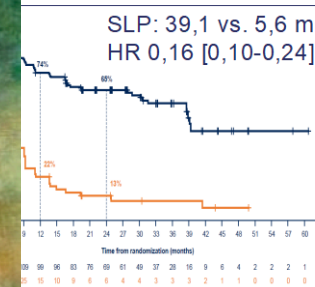


• Obj 1º: SLP 12m

IRRESECABLE Gecp



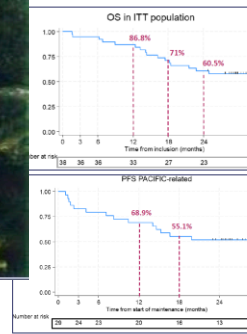
table stage III EGFRm NSCLC: Ramalingam SS.



IRRESECABLE

Gecp

chemoradiotherapy (Ch-RT) and atezolizumab maintenance in non-resectable stage III (NSCLC): APOLO trial. WCLC 2024. M.Provencio



IRRESECABLE

Gecp

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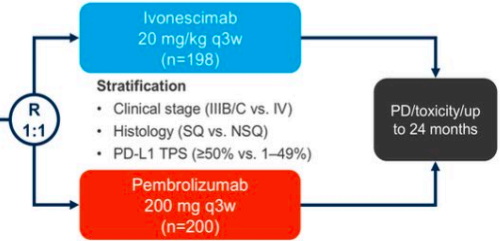
Gecp
lung cancer
research

Enfermedad Metastásica (Dra. N. Vilariño)

Sin genes drivers

HARMONi-2 Study Design

- Key patient inclusion criteria**
- Stage IIIB–IV NSCLC
 - No EGFRm or ALK rearrangements
 - No prior systemic therapy
 - PD-L1 TPS $\geq 1\%$
 - ECOG PS 0–1 (n=398)

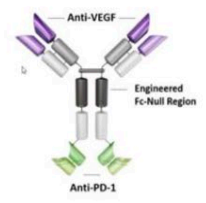


Primary endpoint

- PFS (BIRC, RECIST v1.1)

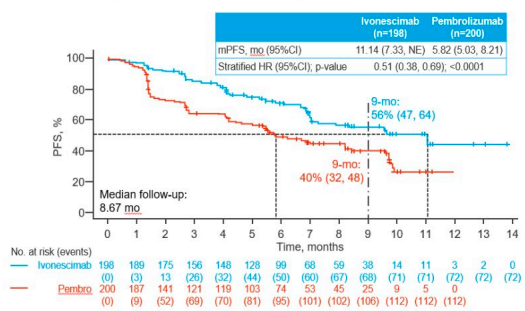
Secondary endpoints

- OS, ORR, DoR, TTR, QoL, safety



HARMONi-2

Progression-free survival (BIRC)

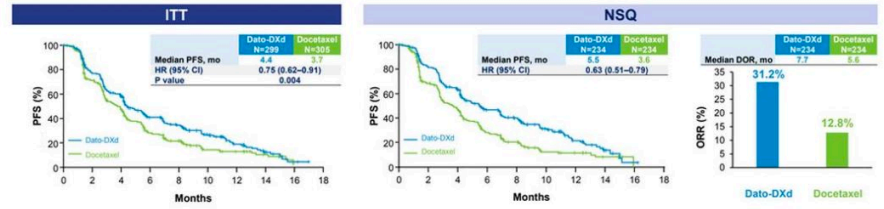
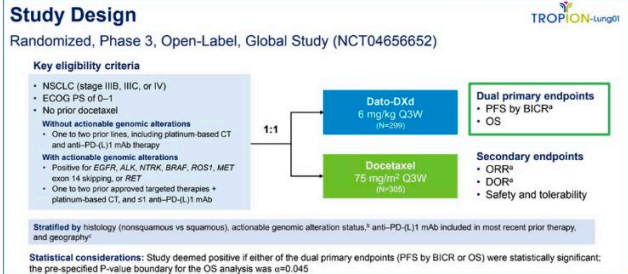


Characteristic	Ivonescimab (n=198)	Pembrolizumab (n=200)	Control Hazard Ratio (95% CI)
Overall			
Age	1587	1681	0.93 (0.74, 1.16)
Sex	1616	1671	0.92 (0.74, 1.15)
Race	1634	1689	0.93 (0.74, 1.16)
ECOG PS	421	408	0.93 (0.74, 1.16)
Smoking Status	4817	4918	0.93 (0.74, 1.16)
Time to event	1239	1202	0.93 (0.74, 1.16)
Time to death	4728	4823	0.93 (0.74, 1.16)
Time to death or relapse	4613	4672	0.93 (0.74, 1.16)
Time to death or relapse or death	4613	4672	0.93 (0.74, 1.16)
Time to death or relapse or death or death	4613	4672	0.93 (0.74, 1.16)
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Time to death or relapse or death or death or death or death or death	4613	4672	0.93 (0.74, 1.16)

Outcomes	Ivonescimab (n=198)	Pembrolizumab (n=200)
ORR, % (95% CI)	50.0 (42.8, 57.2)	38.5 (31.7, 45.6)
DCR, % (95% CI)	89.9 (84.8, 93.7)	70.5 (63.7, 76.7)
mDoR, mo (95% CI)	NR (NE, NE)	NR (8.3, NE)

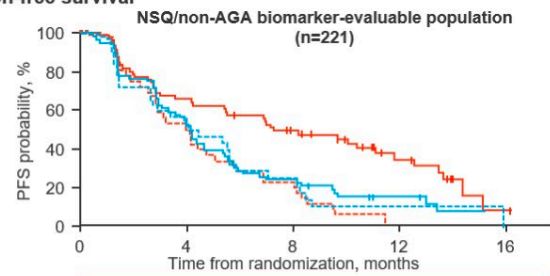
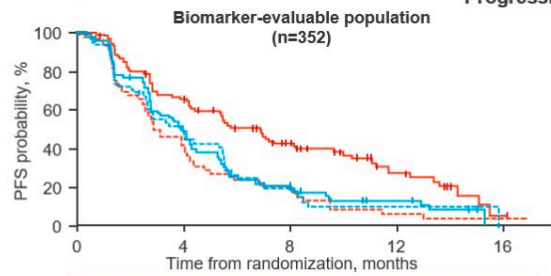
Ivonescimab demonstrated a statistically significant improvement in PFS vs. pembrolizumab with HR = 0.51, and a 5.3 months improvement in mPFS.

OA08.03: Datoprotamab Deruxtecán Vs Docetaxel in Patients with Non-Small Cell Lung Cancer: Final Overall Survival from TROPION-Lung01



Differential PFS outcomes by histology for Dato-DXd have been independently reported in two other NSCLC trials^{5,6}

Key results



	TROP2 QCS-NMR+ Dato-DXd (n=107)		TROP2 QCS-NMR- Dato-DXd (n=65)	
ORR, %	32.7	10.3	16.9	15.1
mPFS, mo	6.9	4.1	2.9	4.0
HR (95%CI)	0.57 (0.41, 0.79)		1.16 (0.79, 1.70)	

Treatment by biomarker status interaction: p=0.0063

— Dato-DXd, QCS-NMR+ - - - Dato-DXd, QCS-NMR-

	TROP2 QCS-NMR+ Dato-DXd (n=68)		TROP2 QCS-NMR- Dato-DXd (n=41)	
ORR, %	36.8	15.3	22.5	12.2
mPFS, mo	7.2	4.1	4.0	4.4
HR (95%CI)	0.52 (0.35, 0.78)		1.22 (0.74, 2.00)	

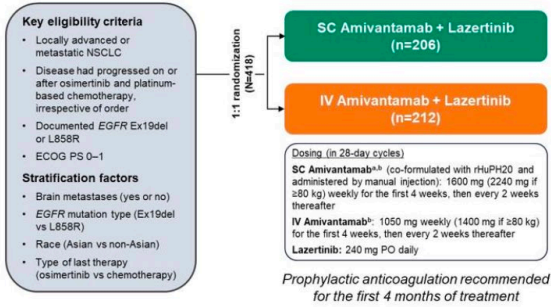
Treatment by biomarker status interaction: p=0.0098

— Docetaxel, QCS-NMR+ - - - Docetaxel, QCS-NMR-

Enfermedad Metastásica (Dra. N. Vilariño)

EGFR +

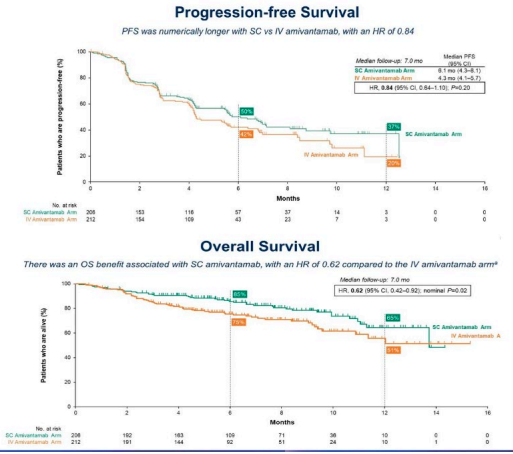
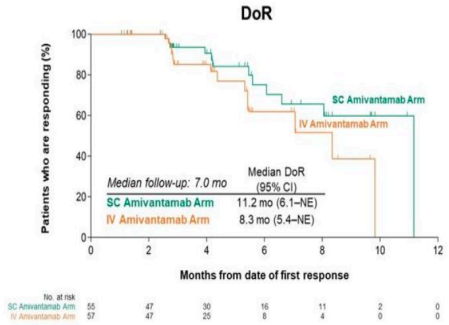
PALOMA-3: Phase 3 Study Design



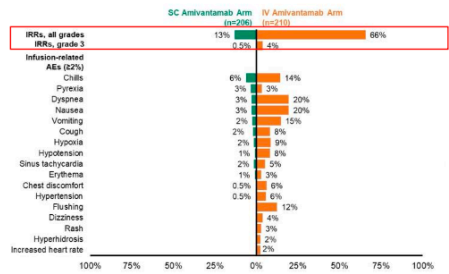
- Co-primary endpoints[†]:**
- C_{through} (noninferiority)^d
 - C2 AUC (noninferiority)^e
- Secondary endpoints:**
- ORR (noninferiority)
 - PFS (superiority)
 - DoR
 - Patient satisfaction^f
 - Safety
- Exploratory endpoints:**
- OS

ORR and DoR

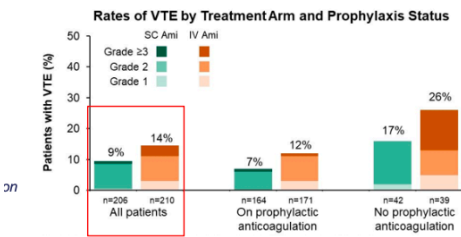
	SC Amivantamab Arm (n=206)	IV Amivantamab Arm (n=212)
ORR, % (95% CI)^a		
All responders	30 (24-37)	33 (26-39)
Confirmed responders	27 (21-33)	27 (21-33)
	Relative risk, 0.92 (95% CI, 0.70-1.23); P=0.001	
Best response, n (%)		
CR	1 (0.5)	1 (0.5)
PR	61 (30)	68 (32)
SD	93 (45)	81 (38)
PD	37 (18)	42 (20)
Not evaluable	14 (7)	20 (9)
DCR, % (95% CI)^b	75 (69-81)	71 (64-77)
Median time to response (range), mo	1.5 (1.2-6.9)	1.5 (1.2-9.9)



Incidence of IRR-related Symptoms



Adverse Event of Special Interest: VTE^a

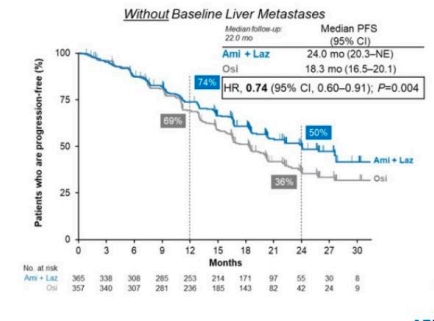
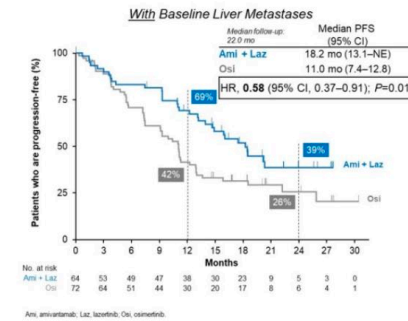
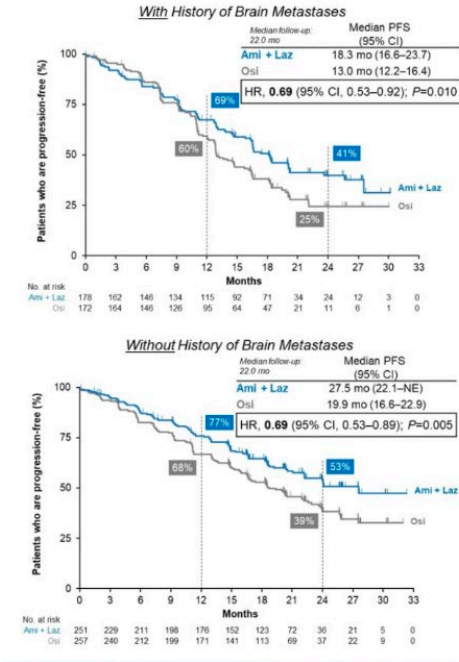
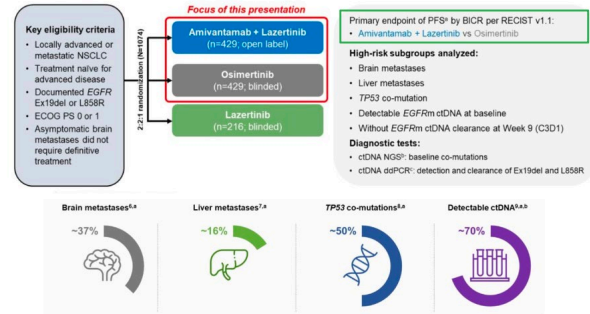


Enfermedad Metastásica (Dra. N. Vilariño)

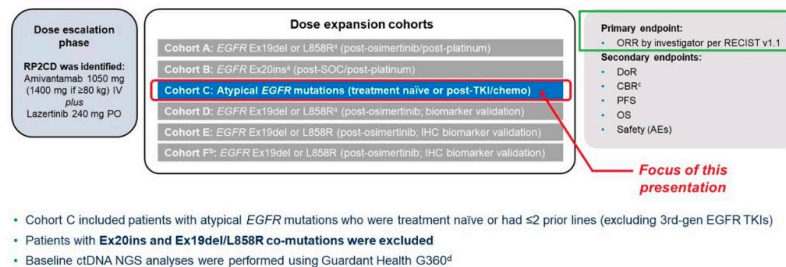
EGFR +

MARIPOSA Study Design and Methods

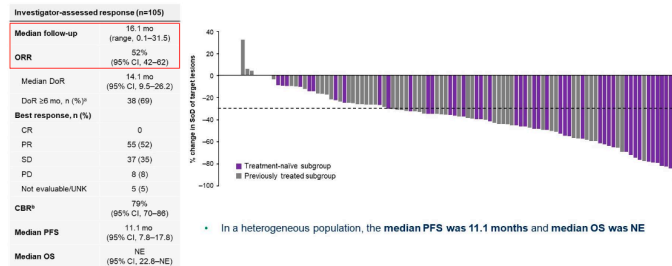
- Amivantamab is an EGFR-MET bispecific antibody with immune cell-directing activity^{1,3}
- Lazertinib is a CNS-penetrant, 3rd-generation EGFR TKI⁴



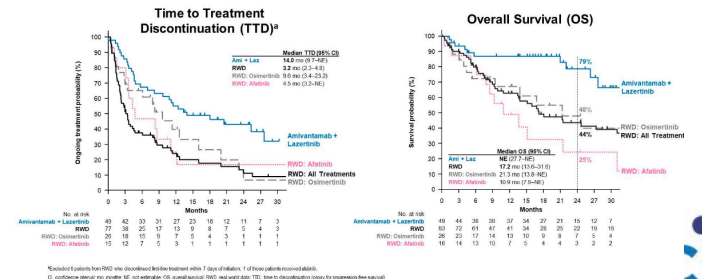
CHRYSALIS-2 Study Design



Efficacy Outcomes of Amivantamab + Lazertinib Among All Patients in Cohort C



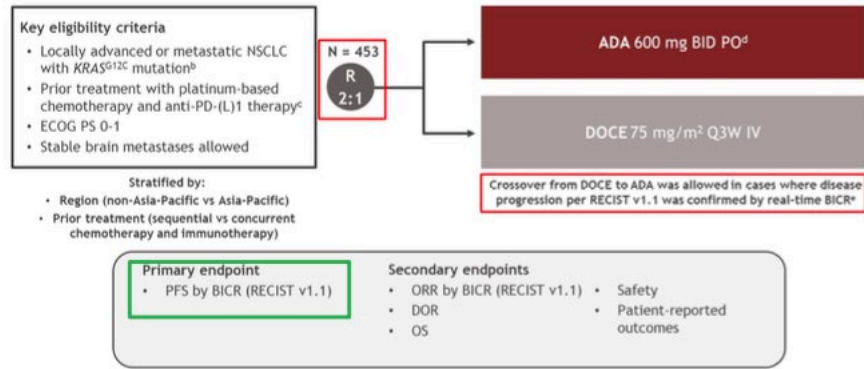
Longer TTD and OS Seen With Amivantamab + Lazertinib than Available Treatments



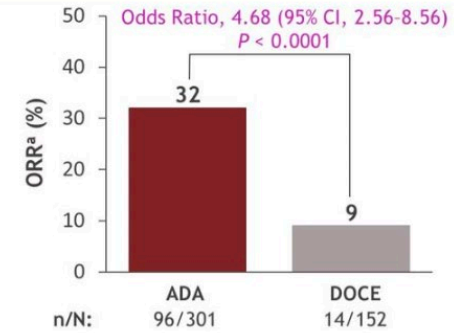
Enfermedad Metastásica (Dra. N. Vilariño)

KRAS +

KRYSTAL-12^a study design

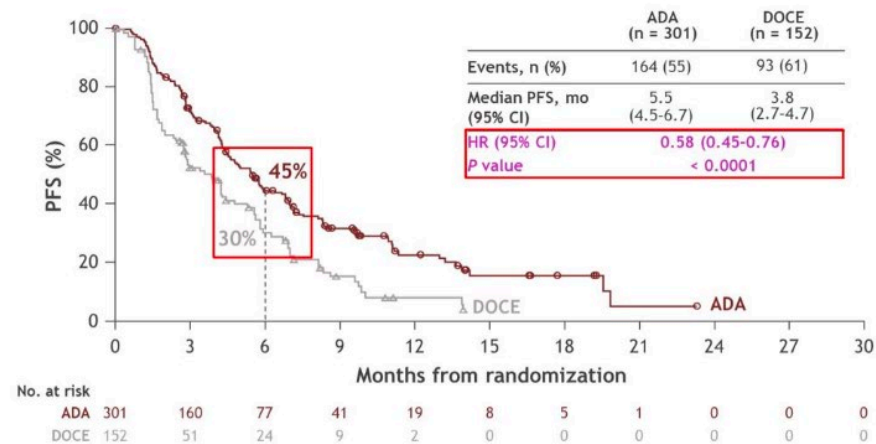


Tumor response per BICR



Tumor response	ADA (n = 301)	DOCE (n = 152)
DCR, ^b n (%)	236 (78)	89 (59)
Median DOR, ^c mo (95% CI)	8.3 (6.1-10.4)	5.4 (2.9-8.5)
Remaining in response at 6 mo, %	64	39

Primary endpoint: PFS^a per BICR



Organizado por:

Enfermedad Metastásica (Dra. N. Vilariño)

ALK +

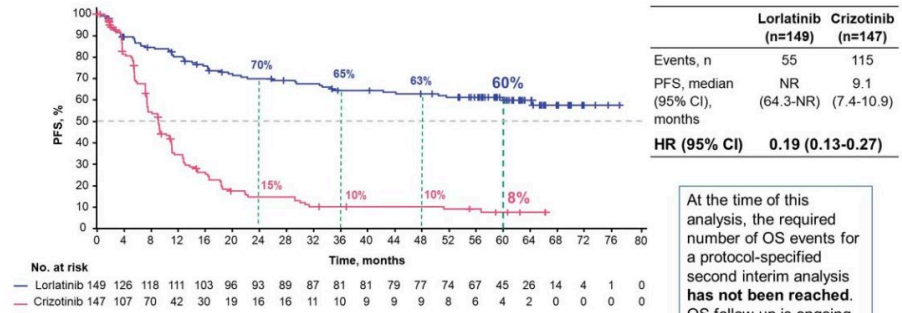
Current Post Hoc Analyses at 5 Years

Endpoint evaluation by BICR stopped after the 3-year analysis



- The median duration of follow-up for PFS was 60.2 months (95% CI, 57.4-61.6) in the lorlatinib arm and 55.1 months (95% CI, 36.8-62.5) in the crizotinib arm

At 60.2 Months of Median Follow-Up, Median PFS by Investigator Was Still Not Reached With Lorlatinib



HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival.

ALKove-1

PATIENT POPULATION

- Advanced solid tumors harboring an ALK fusion or activating mutation (by local testing)
- Patients with NSCLC: ≥ 1 prior 2G or 3G ALK TKI
- ≤ 2 prior chemotherapies/immunotherapies
- Excluded: concurrent oncogenic drivers (e.g., EGFR/ROS1/MET/RET/BRAF alterations)^a
- Evaluable but non-measurable disease allowed^b

PHASE 1 OBJECTIVES

- Primary: Selection of RP2D and, if applicable, MTD
- Overall safety and tolerability
- PK characterization
- Preliminary antitumor activity
- Intracranial activity

A Global First-in-Human Phase 1/2 Clinical Trial of NVL-655 in Advanced ALK-Positive NSCLC and Other Solid Tumors (NCT05384626)

PHASE 1 DOSE-ESCALATION COMPLETED, FOLLOW-UP CONTINUES

Enrollment June 2022 to February 2024 (Data cut-off: 15 June 2024)

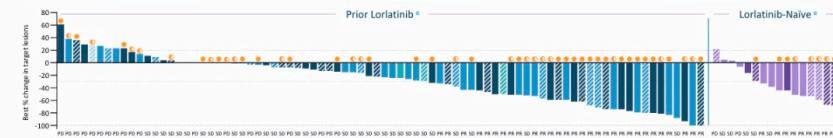
NVL-655 Phase 1	All Doses	RP2D					
		15 mg QD	25 mg QD	50 mg QD	100 mg QD	200 mg QD	
All-Treated Population	N = 133	3	12	12	32	52	22
NSCLC Response-Evaluable Population	N = 103	3	7	10	27	39	17

2G, 2nd generation ALK TKI (i.e., ceritinib, alectinib, or brigatinib); 3G, 3rd generation ALK TKI (i.e., lorlatinib); MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; PK, pharmacokinetics; QD, once daily; RP2D, recommended phase 2 dose; TKI, tyrosine kinase inhibitor

^aResponse-evaluable population prospectively defined as all NSCLC patients with measurable disease, without concurrent oncogenic driver, and who undergo ≥ 3 post-baseline response assessment for discontinued treatment due to clinical progression/death prior to the first response assessment. Patients unmeasurable for response at baseline (n = 38), tumor with alternate oncogenic driver (MET amplification [n = 4], BRAF G469A [n = 2], BRAF fusion [n = 1], NTRK fusion [n = 1]), post-baseline scan and discontinued treatment for reasons other than progressive disease (n = 2), other solid tumor (n = 2).

Preliminary Activity: Radiographic Tumor Responses Across Previously Treated Patients with ALK+ NSCLC

RECIST 1.1 ORR, % (n/N)	NSCLC Response-Evaluable (Any Prior ALK TKI, range 1 – 5)			Prior Lorlatinib (≥2 ALK TKIs)			Lorlatinib-naïve (≥1G ± 1G)		
	All patients ± chemotherapy	All	Any ALK mutation ^a	G1202R	All	Any ALK mutation	Compound ALK mutation	All	Any ALK mutation
All Doses	38% (39/103)	52% (30/58)	69% (22/32) ^a		35% (30/85)	47% (23/49)	54% (15/28)	53% (9/17)	88% (7/8)
RP2D	38% (15/39)	55% (12/22)	71% (10/14)		35% (11/31)	50% (8/16)	64% (7/11)	57% (4/7)	80% (4/5)



Data cut-off: 15 June 2024. Response-evaluable patients with NSCLC. All responses were confirmed.

NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; RP2D, Recommended Phase 2 dose (150 mg QD); SD, stable disease; TKI, tyrosine kinase inhibitor.

^aIncludes all patients with ≥ 1 identified ALK resistance mutation as per local or central testing of blood (ctDNA) or tissue. Responses observed in patients with ALK (G1202R, V1180L, L1196G, L1198F, G1209R, or G1210R) mutations, including where multiple mutations co-occur, in addition to those with G1202R.

^bIncludes patients with G1202R single and compound (≥2) mutations.

^cCo-administration has not been confirmed for all patients with compound (≥2) ALK resistance mutations.

^dORR = 67% (20/30) for G1202R patients with prior lorlatinib, and ORR = 100% (2/2) for lorlatinib-naïve G1202R patients.

^eFive response-evaluable patients (3 with no known ALK mutations and 2 with single ALK mutations) not shown due to re-evaluation or missing post-baseline tumor assessments in the setting of PD or symptomatic deterioration.

KEY: PATIENT DETAILS

- Lorlatinib Pre-treated:**
 - ≥ 2 prior ALK TKIs
 - 2 prior, 2G + lorlatinib
 - 1 prior (lorlatinib only)
- Lorlatinib-naïve:**
 - ≥ 2 prior ALK TKIs
 - 1 prior, alectinib
- ALK single resistance mutation** (orange)
- ALK compound (≥2) resistance mutation** (purple)
- Patient treated at RP2D

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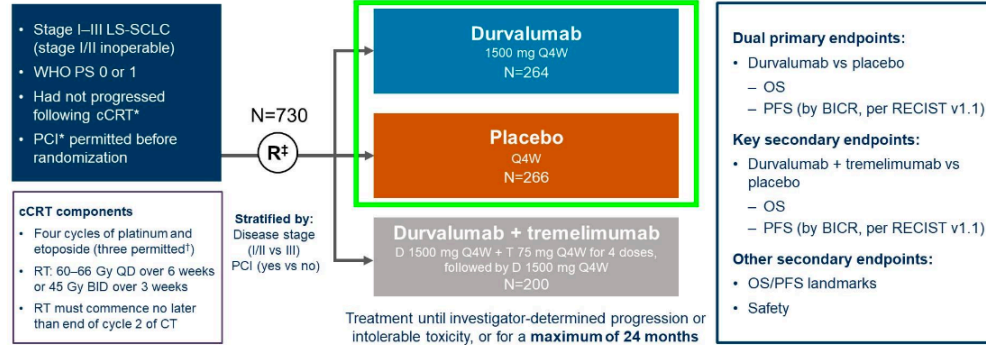


Cáncer de Pulmón Microcítico y otros tumores (Dr. Martí)

Enfermedad Limitada

ADRIATIC study design

Phase 3, randomized, double-blind, placebo-controlled, multicenter, international study (NCT03703297)



*cCRT and PCI treatment, if received per local standard of care, must have been completed within 1–42 days prior to randomization. †If disease control was achieved and no additional benefit was expected with an additional cycle of chemotherapy, in the opinion of the investigator. ‡The first 600 patients were randomized in a 1:1:1 ratio to the 3 treatment arms; subsequent patients were randomized 1:1 to either durvalumab or placebo.

2024 ASCO ANNUAL MEETING

#ASCO24

PRESENTED BY: Dr David R. Spigel

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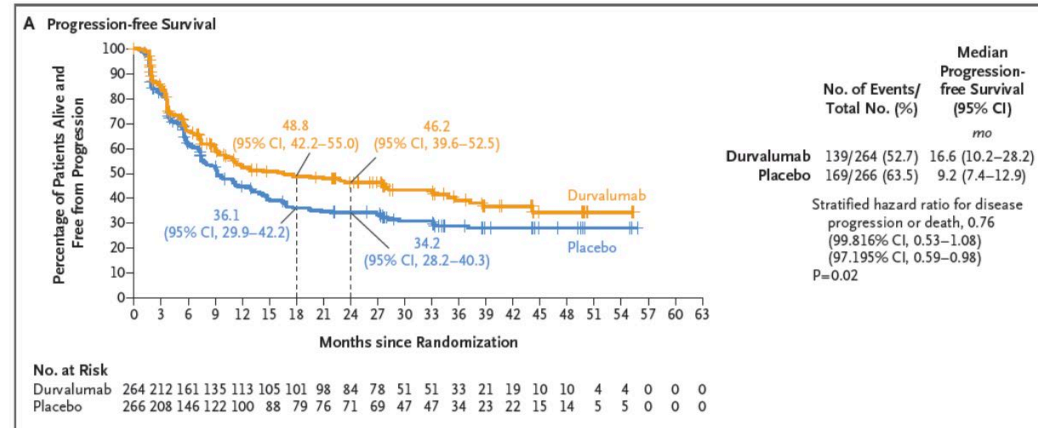
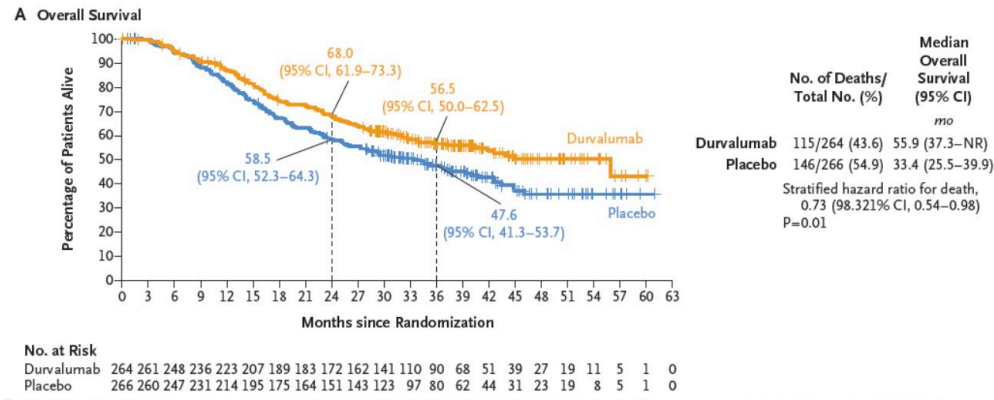
BICR, blinded independent central review; BID, twice daily; CT, chemotherapy; D, durvalumab; PCI, prophylactic cranial irradiation; PS, performance status; Q4W, every 4 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy; T, tremelimumab; WHO, World Health Organization

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

ORIGINAL ARTICLE

Durvalumab after Chemoradiotherapy in Limited-Stage Small-Cell Lung Cancer

Y. Cheng, D.R. Spigel, B.C. Cho, K.K. Laktionov, J. Fang, Y. Chen, Y. Zanki, K.H. Lee, Q. Wang, A. Navarro, R. Bernabe, E.L. Buchmeier, J.W.C. Chang, Y. Shiraishi, S.S. Goksu, A. Badzio, A. Shi, D.B. Daniel, N.T.T. Hoa, M. Zemanova, H. Mann, H. Gowda, H. Jiang, and S. Senan, for the ADRIATIC Investigators*



Organizado por:



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Cáncer de Pulmón Microcítico y otros tumores (Dr. Martí)

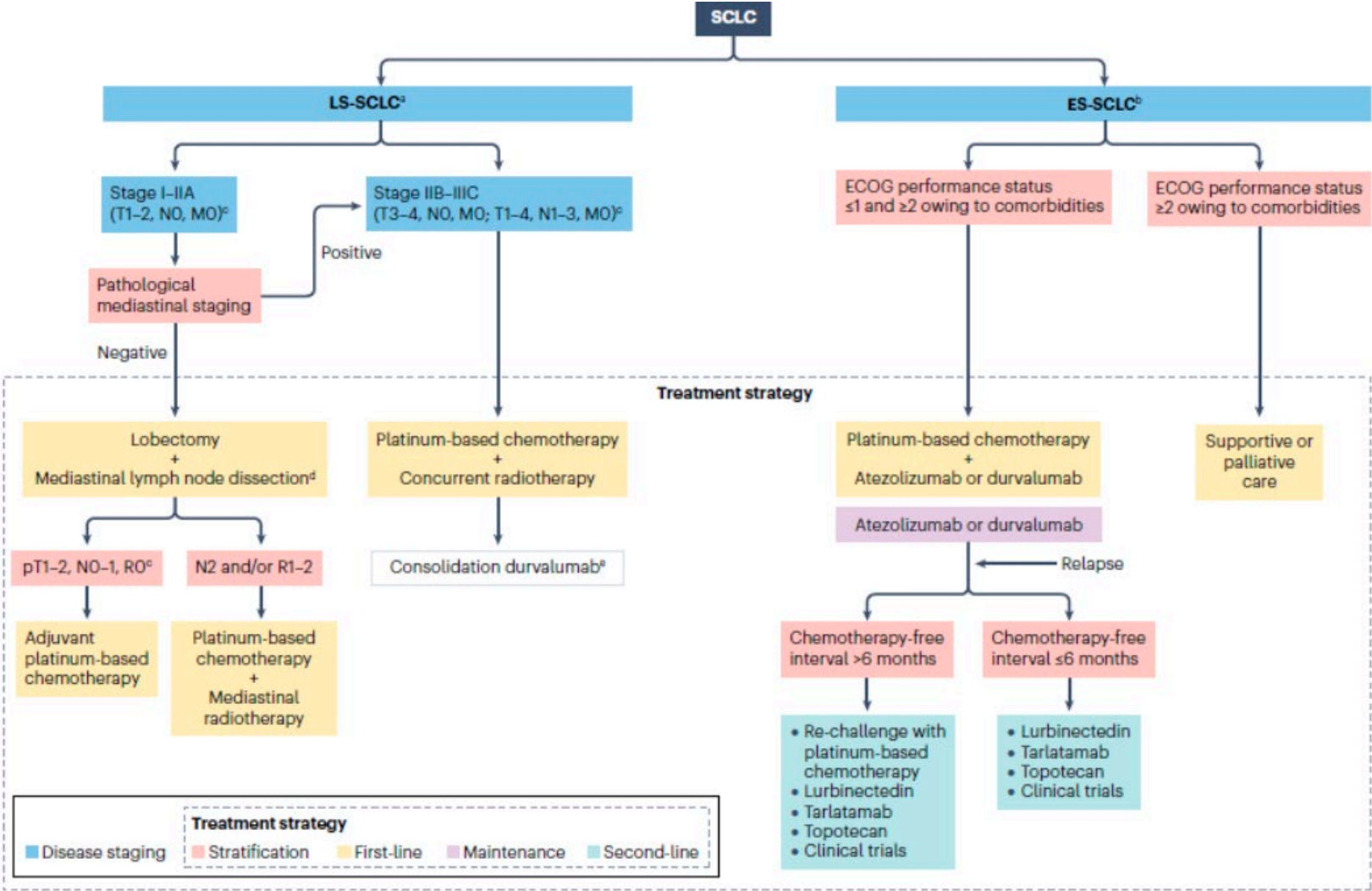


Fig. 4 | Current management strategy for SCLC. Proposed strategy for the management of patients with small-cell lung cancer (SCLC) as of 2024. ^aLimited-

plan. ^bExtensive-stage (ES-SCLC) includes stage IV (T any, N any, M 1a/b/c) and T3-4 disease. ^cDefined according to the Eighth Edition of TNM Staging of Lung

Cáncer de Pulmón Microcítico y otros tumores (Dr. Martí)

Nuevos fármacos



Ahn M.J. N Engl J Med 2023;389:2063-75

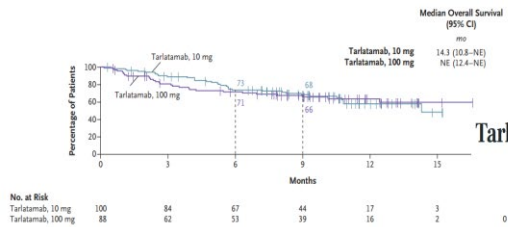
SPECIALTIES TOPICS MULTIMEDIA CURRENT ISSUE LEARNING/CME AUTHOR CENTER PUBLICATIONS

ORIGINAL ARTICLE

Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer

Authors: Myung-Ju Ahn, M.D., Ph.D., Byoung Chul Cho, M.D., Ph.D., Enriqueta Felip, M.D., Ph.D., Ippokratris Kor M.D., Kadoaki Ohashi, M.D., Ph.D., Margarita Majem, M.D., Ph.D., Oscar Juan-Vidal, M.D., Ph.D., for DeLLphi-301 Investigators* Author Info & Affiliations

Published October 20, 2023 | N Engl J Med 2023;389:2063-2075 | DOI: 10.1056/NEJMoa2307980



Tarlatamab greenlighted by MHRA for small cell lung cancer

On May 16, 2024, the U.S. Food and Drug Administration (FDA) granted an accelerated approval for IMDELLTRA™ (tarlatamab-dlle) for the treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy. The approval was based on surrogate endpoints, including response rate and duration of response observed in clinical studies, and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

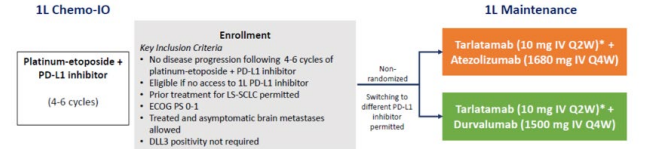
IMDELLTRA is bispecific T cell engager (BiTE)®. (scFv)-Fc antibody that targets DLL3 on tumor cells and CD3 on the patient's T cells and has mutations in the Fc (N297G, R292C, V302C) to extend the half-life of the molecules.

Biotechnology • 31 December 2024

2024 World Conference on Lung Cancer SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA #WCLC24 wclc2024.lasinc.org

DeLLphi-303: Tarlatamab with PD-L1 Inhibitor as 1LM

Phase 1b, multicenter, open-label study (NCT05361395)



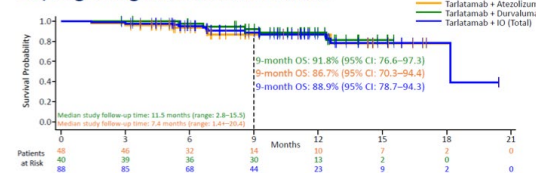
Must initiate CID1 of maintenance phase within 8 weeks of the start of the last cycle of 1L chemo-immunotherapy
Median follow-up time (N = 88): 10.0 months (range: 1.4–20.4)

Primary Endpoints*: Dose-limiting toxicities, treatment-emergent / treatment-related adverse events (TEAEs, TRAEs)
Secondary Endpoints*: Disease control and PFS per local RECIST 1.1 assessment, OS



2024 World Conference on Lung Cancer SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA #WCLC24 wclc2024.lasinc.org

OS, beginning from 1L maintenance

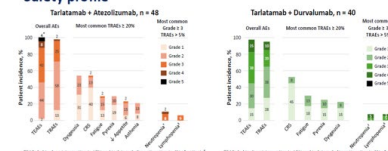


After a median time from 1L chemoimmunotherapy to 1LM of 3.6 months, tarlatamab with a PD-L1 inhibitor as 1LM showed a 9-month OS of 89%.

These results demonstrate a favorable benefit-to-risk profile and support a randomized controlled study of tarlatamab with durvalumab as 1L maintenance, which is underway (Phase 3 DeLLphi-305; NCT06211036)

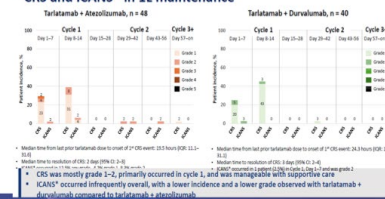


Safety profile



* Tarlatamab with a PD-L1 inhibitor as 1LM had a manageable safety profile with no OLCs and no fatal TRAEs
* There were no new or unexpected toxicities, and immune related adverse events (IRAEs) were rare

CRS and ICANS* in 1L maintenance



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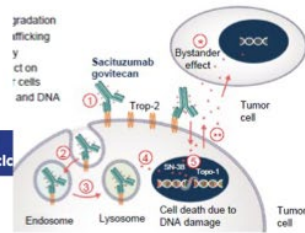


Cáncer de Pulmón Microcítico y otros tumores (Dr. Martí)

Nuevos fármacos

Sacituzumab Govitecan as Second-Line Treatment in Patients With Extensive-Stage Small Cell Lung Cancer

Afshin Dowlati¹, Anne C. Chiang², Andrés Cervantes³, Sunil Babu⁴, Erika Hamilton⁵, Shu Fen Wong⁶.



2024 World Conference on Lung Cancer SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA

TROPiCS-03 Study Design

- The ongoing, open-label, multicohort, phase 2 TROPiCS-03 study (NCT03964727) is evaluating SG in patients with metastatic or locally advanced solid tumors
- A preliminary analysis showed SG has promising antitumor activity and a manageable safety profile in an extensive-stage small cell lung cancer (ES-SCLC) cohort¹
- Here, we report updated results with additional patients and longer follow-up from the ES-SCLC cohort

Key eligibility criteria

- Histologically confirmed ES-SCLC
- Disease progression after no more than 1 prior line of platinum-based chemo and anti-PD-(L)-1 therapy
- Measurable disease per RECIST v1.1
- ECOG PS 0-1
- Stable, treated brain metastases allowed^a

ES-SCLC cohort (N = 43)

SG 10 mg/kg IV on D1 and D8 21-day cycles (until PD or unacceptable toxicity)

Survival follow-up

- Primary end points**
- ORR (INV^b)
- Secondary end points**
- DOR, CBR, PFS (INV^b)
 - ORR, DOR, CBR, PFS (BICR^b)
 - OS
 - Safety

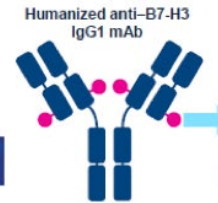
- At data cutoff (8 March 2024), median follow-up was 12.3 (range, 8.1–20.1) months



^aPatients with stable CNS disease for 24 weeks prior to the first study dose and all neurologic symptoms returned to baseline may be included in the study. All patients with carcinomatous meningitis are excluded from the study, regardless of clinical stability. ^bPer RECIST v1.1. BICR, blinded independent central review; CBR, clinical benefit rate; chemo, chemotherapy; CNS, central nervous system; D, day; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; INV, investigator-assessed; IV, intravenous; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SG, sacituzumab govitecan. 1. Dowlati A, et al. Oral presentation ESMO 2023, Abstract #1066AC.

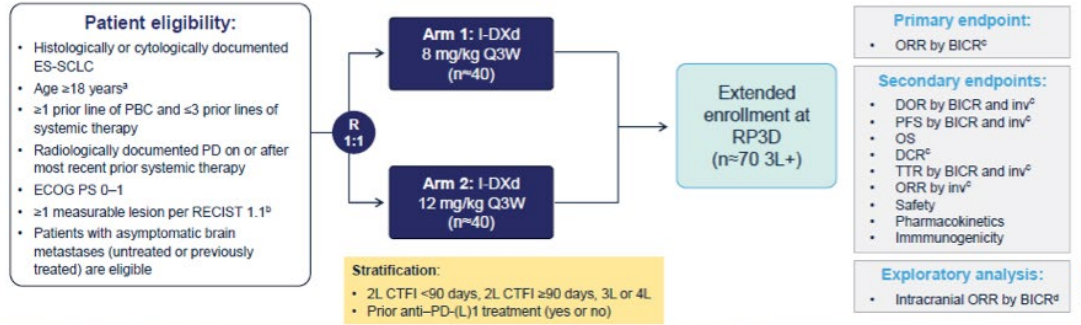
Ifinatamab deruxtecan (I-DXd) in extensive-stage small cell lung cancer (ES-SCLC): interim analysis of IDEate-Lung01

Charles M. Rudin,¹ Myung-Ju Ahn,² Melissa Johnson,³ Christine L. Hann,⁴ Nicolas Girard,⁵



2024 World Conference on Lung Cancer SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA

Phase 2 IDEate-Lung01 study (NCT05280470)



Cáncer de Pulmón Microcítico y otros tumores (Dr. Martí)

Mesotelioma

Extended pleurectomy decortication and chemotherapy versus chemotherapy alone for pleural mesothelioma (MARS 2): a phase 3 randomised controlled trial

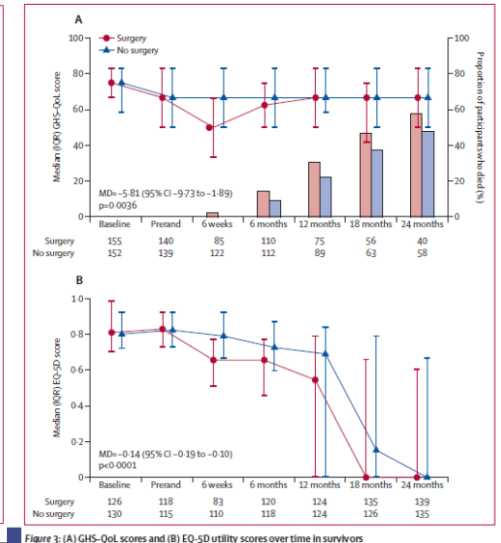
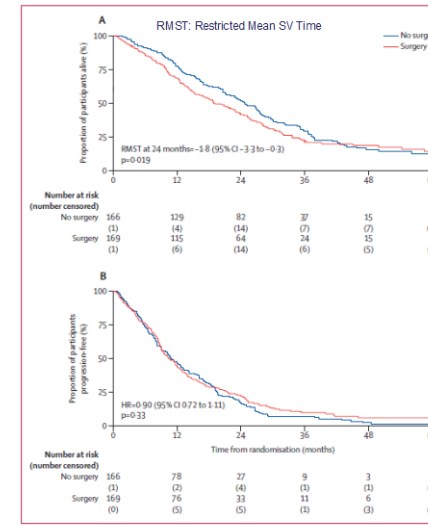
Eric Lim, David Waller, Kelvin Lau, Jeremy Steele, Anthony Pope, Clinton Ali, Rocco Bilancia, Manjusha Keni, Sanjay Popat, Mary O'Brien, Nadza Tokaca, Nick Maskell, Louise Staddon, Dean Fennell, Louise Nelson, John Edwards, Sara Tenconi, Laura Socci, Robert C Rintoul, Kelly Wood, Amanda Stone, Dakshinamoorthy Muthukumar, Charlotte Ingle, Paul Taylor, Laura Cove-Smith, Raffaele Califano, Yvonne Summers, Zacharias Tasigiannopoulos, Andrea Bille, Riyaz Shah, Elizabeth Fuller, Andrew Macnair, Jonathan Shamash, Talal Mansy, Richard Milton, Pek Koh, Andreea Alina Ionescu, Sarah Treece, Amy Roy, Gary Middleton, Alan Kirk, Rosie A Harris, Kate Ashton, Barbara Warnes, Emma Bridgeman, Katherine Joyce, Nicola Mills, Daisy Elliott, Nicola Famar, Elizabeth Stokes, Vikki Hughes, Andrew G Nicholson, Chris A Rogers, on behalf of the MARS 2 Investigators*

Summary

Background Extended pleurectomy decortication for complete macroscopic resection for pleural mesothelioma has never been evaluated in a randomised trial. The aim of this study was to compare outcomes after extended pleurectomy decortication plus chemotherapy versus chemotherapy alone.



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Novedades y Claves en Cáncer de Pulmón 2024

Comentarios finales

- 2024 ha sido un año muy productivo e inspirador para nuevas estrategias en el diagnóstico y tratamiento del Cáncer de Pulmón
- Un mejor conocimiento de la biología del Cáncer de Pulmón ha permitido trabajar con nuevos biomarcadores predictivos y pronósticos
- Se ha establecido como estándar el uso de las combinaciones de QT + ITP en la aproximación terapéutica del Cáncer de Pulmón Localmente Avanzada
- Los ADC y Ac biespecíficos tienen un futuro prometedor en la enfermedad metastásica, a confirmar su utilidad en 1ª o 2ª línea
- Las combinaciones de anti EGFR de 3ª G y Ac biespecíficos frente a EGFR, pendiente de optimizar su tolerancia, es activa CPCNP con mutaciones habituales de EGFR y en las atípicas (distintas de los exones 19, 20 y 21)
- Se consolidan los excelentes resultados de Lorlatinib en ALK + y aparecen nuevas moléculas que podrían tener un papel en las resistencias y refractariedad al tratamiento estándar
- Asimismo, en CPCP podemos decir que la inmunoterapia, tanto en estadios localizados como diseminados, produce un beneficio limitado pero significativo en nuestros pacientes
- Nuevos agentes, como Tarlatamab y Lurbinectidina, permiten ser optimistas en los progresos terapéuticos de los enfermos con CPCP
- Ha quedado demostrado la no utilidad de grandes cirugías en los Mesoteliomas

Novedades & Claves en CÁNCER de PULMÓN 2024

Añade esta fecha
a tu calendario

21 Enero 2025
16:00h-18:00h

FORMATO **VIRTUAL**

ACCEDER

Programa científico

- 16:00 - 16:10 **Introducción**
Dr. Jose Luís González Larriba
Hospital Clínico San Carlos, Madrid
- 16:10 - 16:30 **Biomarcadores pronósticos**
Dra. Ana Cardeña
Hospital Univ. Nuestra Señora de Candelaria, Santa Cruz de Tenerife
- 16:30 - 16:50 **Estadios iniciales y enfermedad localmente avanzada**
Dr. Eider Akcona
Hospital Univ. de Cruces, Baracaldo, Vizcaya
- 16:50 - 17:10 **Enfermedad metastática (incluyendo inmunoterapia)**
Dra. Noelia Vilarriño
ICO, Hospital Duran i Reynals, L'Hospitalet de Llobregat, Barcelona
- 17:10 - 17:30 **Cáncer de pulmón microcítico y otros tumores**
Dr. Juan Luis Martí
Hospital General Univ. Dr. Balmis, Alicante
- 17:30 - 17:45 **Debate**
- 17:45 - 18:00 **Conclusiones**
Dr. Jose Luís González Larriba
Hospital Clínico San Carlos, Madrid

Muchas gracias

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