Novedades & Claves en CÁNCER de PULMÓN 2025

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13 Enero 2026
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 Dr. Paula Espinosa Hospital General Univ. de Valencia
16:30 - 16:50	Estadios iniciales y enfermedad localmente avanzada Dr. Patricia Cruz Hospital General Univ. de Ciudad Real
16.50 - 17:10	Enfermedad metastática (incluyendo inmunoterapia) Dr. Begoña Campos Hospital Univ. Lucus Augusti, Lugo
17:10 - 17:30	Cáncer de pulmón microcítico y otros tumores Dr. Andrés Barba Hospital Santa Creu I Sant Pau, Barcelona
17:30 - 17:45	Debate/preguntas
17:45 - 18:00	Conclusiones Dr. Jose Luís González Larriba Hospital Clínico San Carlos, Madrid

Organizado por:

GECP lung cancer research

Patrocinado por:

Bristol Myers Squibb™

REGENERON SCIENCE TO MEDICINE®

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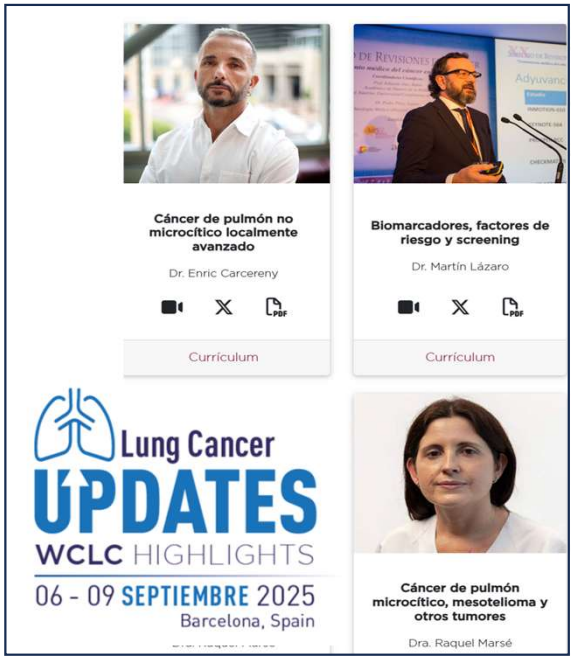
- **Speaker & Advisor:**
- BMS, Roche, MSD, Astra Zeneca, Novartis, Pierre Fabre, Sanofi, Rovi, Leo Pharma

- **Travel and educational expenses:**
- BMS, Roche, MSD, Lilly, Astra Zeneca, Novartis, Sanofi, Pierre Fabre, Rovi, Leo Pharma, Janssem

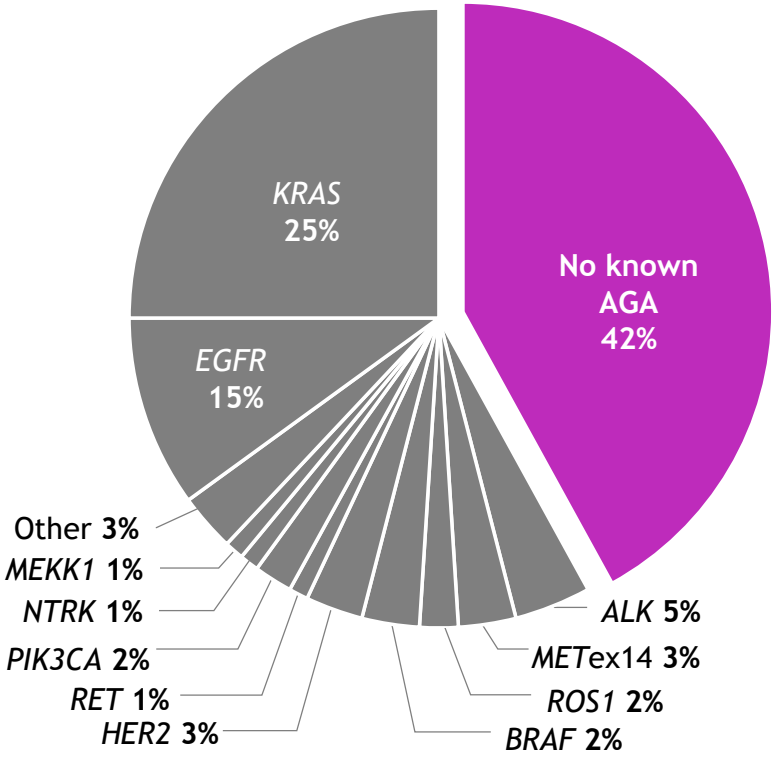
Las fuentes



elcc European Lung Cancer Congress 2025

Consideration of tumor PD-L1 expression is vital for making treatment decisions for patients with mNSCLC[1,2]

Diversity of biomarker expression in patients with NSQ NSCLC[1]



- NSCLC accounts for nearly 90% of lung-cancer cases
- Most patients present with metastatic disease at time of diagnosis
- Diverse biomarkers expressed in NSCLC allow for targeted therapy use where available
- In patients with no known AGA, as well as in those with AGAs for which there is no approved treatment in 1L (eg, *KRAS*), tumor PD-L1 expression is key to informing treatment decisions in 1L mNSCLC

Abbreviations in speaker notes.

1. Bubendorf L et al. *Eur Respir Rev*. 2017. doi:10.1183/1600617.0007-2017. 2. Goldschmidt JH et al. *Drugs Real World Outcomes*. 2024;11(3):425-439.

Rosalyn Juergens, MD, PhD (Chair)
Medical Oncology, Juravinski Cancer Centre
Hamilton, Ontario, Canada

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ESMO 2025 Industry Satellite Symposium

Navigating a dynamic treatment landscape: established therapies and emerging modalities for patients with lung cancer

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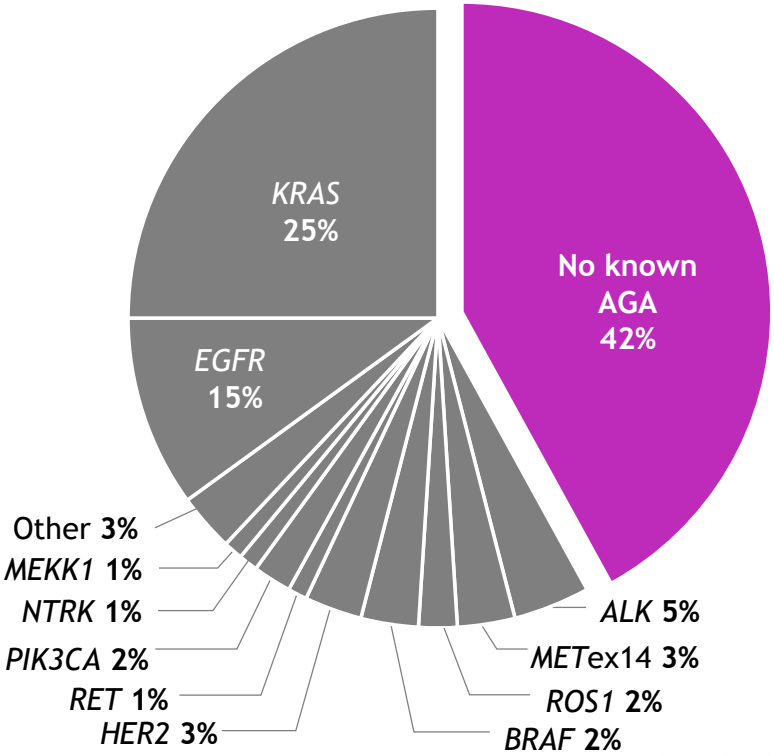
Consideration of tumor PD-L1 expression is vital for making treatment decisions for patients with mNSCLC[1,2]

Diversity of biomarker expression in patients with NSQ NSCLC[1]



Rosalyn Juergens, MD, PhD (Chair)
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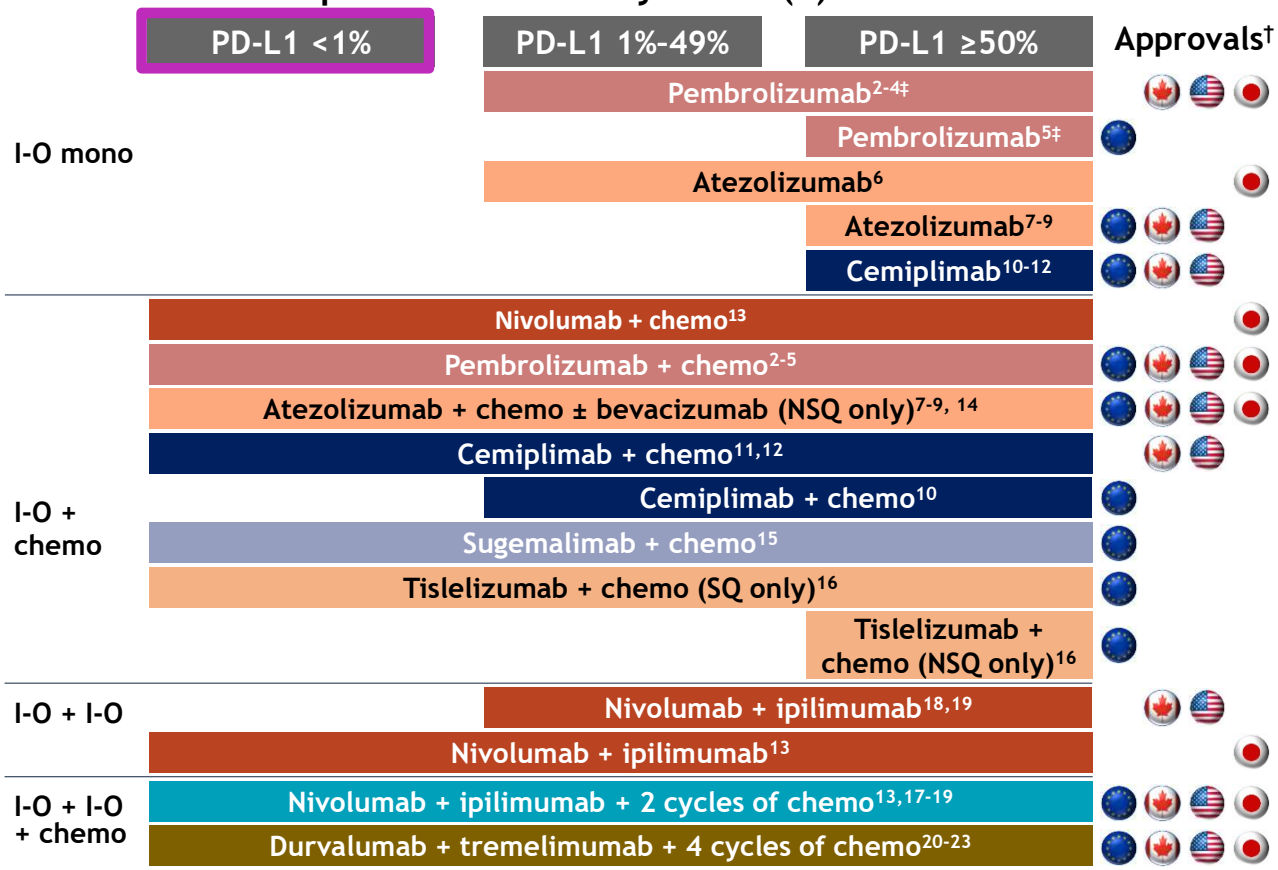
Hamilton, Ontario, Canada

Landscape overview of key 1L PD-(L)1-based I-O*



*This diagram is intended for educational and illustrative purposes only. It reflects the views of the presenter, and the treatment algorithm may vary by region. †Refer to local materials such as the prescribing information and/or the Summary of Product Characteristics (SmPC). ‡ESMO guidelines indicate that benefit is driven mostly by high-expressors.

References and abbreviations in speaker notes.

En España, ¿qué hacemos?: estudio REVEAL

Estudio retrospectivo y multicéntrico sobre tendencias en la práctica clínica real en el tratamiento de primera línea del cáncer de pulmón no microcítico metastásico en España: análisis intermedio del estudio REVEAL

Nº de Póster: 51

Juan Coves[1], Francisco de A. Aparisi[2], Ana Cardeña-Gutiérrez[3], Bartomeu Massutí[4], Victoria E. Castellón[5], Juan Verdún[6], Ana Cobo Rodríguez[7], Luis Cabezón-Gutiérrez[8], Javier Garde-Noguera[9], Sergio Vázquez[10], Alejandro Navarro[11], Soledad Medina[12], Esperanza Arriola[13], Carmen Areses[14], Ana Laura Ortega Granados[15], Manuel Cobo[16], Néstor Álvarez[17], David Vilanova[17], Carlos Aguado[18]

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Introducción

- El cáncer de pulmón no microcítico (CPNM) representa el 85% de los casos, dividido en histología escamosa (30%) y no escamosa (70%)[1].
- El 80% se diagnostica en estadios avanzados (IIIB-IV), con una supervivencia a 5 años menor al 5%[2].
- La quimioterapia basada en platino fue el tratamiento estándar hasta la llegada de la inmunoterapia[3,4], que ha mejorado significativamente la supervivencia, especialmente en pacientes con PD-L1 <50%[5-8].

Objetivo

- El propósito del estudio REVEAL es recoger y analizar datos de la práctica clínica en España para caracterizar a los pacientes en 1L de CPNM metastásico, así como describir su perfil clínico y el uso de recursos sanitarios asociados.

Métodos

- Estudio observacional, retrospectivo y multicéntrico realizado en los Servicios de Oncología de 17 centros en España.
- Pacientes adultos con CPNM metastásico sin mutaciones en *EGFR/ALK*, con PD-L1 <50 % o desconocido, que iniciaron tratamiento de 1L según práctica clínica entre enero 2022 y marzo 2023. La población incluía pacientes con distintos tipos histológicos (escamoso y no escamoso) y estrategias terapéuticas aprobadas (escamosos: doblete de QT y QT+IM; no escamosos: doblete de platino, QT+IM y QT+doble IM).
- El objetivo principal del estudio es la supervivencia global. Entre los objetivos secundarios se incluyen los resultados clínicos (según histología, PD-L1 y tratamiento), perfil clínico y uso de recursos sanitarios. En esta comunicación presentamos las características sociodemográficas y clínicas de los pacientes y utilización de recursos sanitarios.

Resultados

Características de los pacientes

- Las características sociodemográficas y clínicas de la población global y por grupo histológico y de tratamiento se describen en la **Tabla 1**.
- La mediana de edad al diagnóstico fue de 65 años (rango: 33-86), con un 15,3% de los pacientes ≥75 años. Se observaron diferencias de edad entre los grupos, destacando el subgrupo escamoso/QT, cuya mediana de edad fue de 78 años (rango: 57-85) (Tabla 1). Sólo el 6,6% de los pacientes eran no fumadores.
- Las metástasis más frecuentes fueron las óseas (34,1%), aunque en los subgrupos tratados sólo con QT fueron las hepáticas (escamoso: 26,7%/no escamoso: 32,6%). Las metástasis cerebrales fueron más comunes en el grupo no escamoso/QT+doble IM (29,3 %) (**Tabla 1**).

Tabla 1. Características sociodemográficas y clínicas

Tipo histológico	Escamoso		No escamoso			Total
Grupo de tratamiento	QT	QT + IM	QT	QT + IM	QT + doble IM	Total
Número de pacientes	N=15	N=48	N=43	N=99	N=82	N=287
Edad al diagnóstico (años), mediana (rango)	78,0 (57-85)	67,0 (46-86)	67,0 (44-84)	66,0 (43-86)	62,0 (33-78)	65,0 (33-86)
≥75 años, n (%)	10 (66,7)	2 (4,2)	9 (20,9)	15 (15,2)	8 (9,8)	44 (15,3)
Hombres, n (%)	14 (93,3)	38 (79,2)	35 (81,4)	67 (67,7)	53 (64,6)	207 (72,1)
Fumador/exfumador, n (%)	13 (86,7)	48 (100,0)	38 (88,4)	92 (93,9)	77 (93,9)	268 (93,4)
Adenocarcinoma, n (%)	0 (0,0)	0 (0,0)	40 (93,0)	89 (89,9)	78 (96,3)	207 (92,8)
CPNM en estadios tempranos, n (%)	3 (20,0)	13 (27,1)	8 (18,6)	14 (14,1)	16 (19,5)	54 (18,8)
ECOG	[14]	[45]	[38]	[90]	[73]	[260]
0-1	7 (50,0)	39 (86,7)	26 (68,4)	83 (92,2)	72 (98,6)	227 (87,3)
≥2	7 (50,0)	6 (13,3)	12 (31,6)	7 (7,8)	1 (1,4)	33 (12,7)
Estadio al diagnóstico de la enfermedad metastásica, n (%)						
IV A	12 (80,0)	27 (56,3)	17 (39,5)	41 (41,4)	32 (39,0)	129 (44,9)
IV B	3 (20,0)	21 (43,8)	26 (60,5)	58 (58,6)	50 (61,0)	158 (55,1)
Metástasis a distancia [#], n (%)						
Ósea	3 (20,0)	10 (20,8)	15 (34,9)	45 (45,5)	25 (30,5)	98 (34,1)
Cerebral	0 (0,0)	2 (4,2)	7 (16,3)	19 (19,2)	24 (29,3)	52 (18,1)
Hepática	4 (26,7)	6 (12,5)	14 (32,6)	13 (13,1)	11 (13,4)	48 (16,7)
Adrenal	0 (0,0)	6 (12,5)	5 (11,6)	22 (22,2)	10 (12,2)	43 (15,0)
Linfadenopatía no torácica	0 (0,0)	7 (14,6)	4 (9,3)	11 (11,1)	15 (18,3)	37 (12,9)
Otras	3 (20,0)	9 (18,8)	3 (7,0)	14 (14,1)	18 (22,0)	47 (16,4)
Tratamiento en estadios tempranos [#], n (%)	[3]	[13]	[8]	[14]	[16]	[54]
Cirugía	1 (33,3)	5 (38,5)	4 (50,0)	7 (50,0)	3 (18,8)	20 (37,0)
Radioterapia	2 (66,7)	7 (53,8)	4 (50,0)	6 (42,9)	12 (75,0)	31 (57,4)
Tratamiento sistémico con QT	2 (66,7)	5 (38,5)	2 (25,0)	7 (50,0)	13 (81,3)	29 (53,7)
Tiempo diagnóstico a 1ªL CPNM metastásico (meses)	[3]	[12]	[7]	[14]	[14]	[50]
Mediana (rango)	22,21 (20,2-45,9)	12,95 (3,6-190,3)	21,83 (5,6-33,3)	20,70 (6,4-100,5)	14,71 (5,5-101,3)	16,51 (3,6-190,3)

En los casos en el que el número de pacientes con dato disponible no coincide con la N total, se ha indicado entre corchetes. CPNM, cáncer de pulmón no microcítico; DE, desviación estándar; ECOG, *Eastern Cooperative Oncology Group*; INM, inmunoterapia; QT, quimioterapia.
[#] Un paciente puede presentar más de una localización metastásica / haber recibido más de un tratamiento.

Perfil de biomarcadores del tumor

- El estudio de biomarcadores se realizó principalmente en muestras de biopsia (66,9%) y bloque celular (22,6%). En menor proporción, se utilizaron muestras obtenidas mediante citología (10,5%) y biopsia líquida (2,4%).
- La expresión de PD-L1 fue <1% para el 61,3% de los pacientes y entre 1-49% para el 31,7%, de acuerdo con el criterio de inclusión. **(Tabla 2).**

Tabla 2. Perfil molecular de los pacientes con CPNM

Biomarcador	n	Mutado n (%)	No mutado n (%)	Desconocido n (%)
KRAS	117	44 (37,6)	71 (60,7)	2 (1,7)
STK11	31	7 (22,6)	20 (64,5)	4 (12,9)
LKB1	29	1 (3,4)	8 (27,6)	20 (69,0)
BRAF	114	10 (8,8)	102 (89,5)	2 (1,8)
HER-2	76	5 (6,6)	68 (89,5)	3 (3,9)
MET	99	4 (4,0)	93 (93,9)	2 (2,0)
RET	100	1 (1,0)	96 (96,0)	3 (3,0)
ROS1	151	1 (0,7)	147 (97,4)	3 (2,0)

n, número total de pacientes con dato disponible.
BRAF, v-raf murine sarcoma viral oncogene homolog B; CPNM, cáncer de pulmón no microcítico; HER2, human epidermal receptor 2; KRAS, Kirsten rat sarcoma virus; LKB1, liver kinase B1; MET, c-MET proto-oncogene; ti; RET, rearranged during transfection; ROS1, ROS proto-oncogene 1; STK11, serine/threonine kinase 11.

Uso de recursos

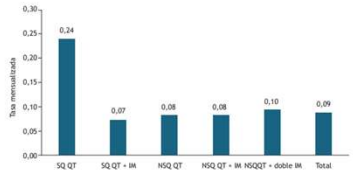
- La mediana de tiempo de seguimiento fue de 9,8 meses (rango intercuartílico: 4,3-17,9) para los pacientes tratados solo con QT y de 14,8 meses (RIC: 6,7-24,0) para los pacientes que recibieron cualquier combinación con IM.
- La mediana de tiempo en tratamiento con doblete de platino fue de 2,1 meses (RIC: 0,8-2,3), mientras que la mediana de tiempo en tratamiento con inmunoterapia fue de 6 meses (RIC: 2,7-11,7). La mediana de ciclos recibidos de inmunoterapia fue de 8 (RIC: 4,0-15,0), con valores similares entre los distintos grupos de tratamiento.
- Desde el diagnóstico de enfermedad metastásica hasta la progresión a 1L, el 50,2 % de los pacientes (n=144) presentaron al menos una hospitalización relacionada con el cáncer, con una duración media de 15,2 ± 14,6 días **(Tabla 3)**. La tasa prorrateada mensualmente de hospitalizaciones fue mayor en pacientes con histología escamosa tratados únicamente con QT (0,24) que en aquellos con histología no escamosa (0,08). En los pacientes con carcinoma escamoso tratados con IM se observó una reducción de la tasa de hospitalizaciones (0,07), mientras que en los no escamosos no se observó un efecto relevante **(Figura 1)**.

Tabla 3. Hospitalizaciones y visitas realizadas relacionadas con el CPNM

Tipo histológico	Escamoso		No escamoso			Total
Grupo de tratamiento	QT	QT + IM	QT	QT + IM	QT + doble IM	Total
Número de pacientes	N=15	N=48	N=43	N=99	N=82	N=287
Pacientes hospitalizados, n (%)	8 (53,3)	24 (50,0)	15 (34,9)	50 (50,5)	47 (57,3)	144 (50,2)
Media (DE)	2,4 (2,8)	1,5 (0,7)	1,7 (1,3)	1,7 (1,1)	1,9 (1,3)	1,8 (1,3)
Pacientes con visitas a consultas externas/hospital de día, n (%)	15 (100,0)	47 (97,9)	36 (83,7)	94 (94,5)	76 (92,7)	268 (93,4)
Media (DE)	12,6 (8,5)	17,3 (15,3)	11,8 (11,5)	18,8 (13,7)	17,8 (12,9)	17,0 (13,4)
Pacientes con visitas a urgencias, n (%)	10 (66,7)	27 (56,3)	23 (53,5)	67 (67,7)	50 (61,0)	177 (61,7)
Media (DE)	3,2 (3,5)	3,2 (5,2)	1,91 (1,4)	2,9 (2,6)	2,8 (2,0)	2,8 (2,9)
Pacientes con visitas a otros servicios, n (%)	6 (40,0)	16 (33,3)	21 (48,8)	37 (37,4)	35 (42,7)	115 (40,1)
Media (DE)	2,3 (1,0)	2,7 (1,7)	4,9 (5,4)	5,7 (6,6)	6,7 (6,8)	5,2 (6,0)

CPNM, cáncer de pulmón no microcítico; DE, desviación estándar.

Figura 1. Tasas prorrateadas mensualmente de las hospitalizaciones relacionadas con el CPNM



CPNM, cáncer de pulmón no microcítico; IM, inmunoterapia; QT, quimioterapia; NSQ, no escamoso; SQ, escamoso

- Las analíticas (98,6 %) y los TACs (91,3 %) fueron las pruebas más frecuentes, con una media de 17,1 ± 13,9 y 4,4 ± 3,1 por paciente, respectivamente **(Tabla 4)**.

Tabla 4. Pruebas diagnósticas realizadas relacionadas con el CPNM

Tipo histológico	Escamoso		No escamoso			Total
Grupo de tratamiento	QT	QT + IM	QT	QT + IM	QT + doble IM	Total
Número de pacientes	N=15	N=48	N=43	N=99	N=82	N=287
Analíticas, n%	15 (100,0)	48 (100,0)	41 (95,3)	99 (100,0)	80 (97,6)	283 (98,6)
Media (DE)	12,9 (15,1)	15,6 (15,0)	11,2 (6,6)	19,0 (15,7)	19,6 (12,5)	17,1 (13,9)
Mediana (RIC)	6 (4-15)	10,5 (6-19,5)	10 (6-15)	15 (8-27)	16,5 (11-25,5)	14 (7-24)
TAC, n%	15 (100,0)	42 (87,5)	36 (83,7)	91 (91,9)	78 (95,1)	262 (91,3)
Media (DE)	2,8 (1,9)	4,3 (3,0)	3,4 (2,7)	4,8 (3,4)	4,8 (3,0)	4,4 (3,1)
Radiografías, n%	12 (80,0)	34 (70,8)	26 (60,5)	83 (83,8)	60 (73,2)	215 (74,9)
Media (DE)	3,4 (2,6)	4,1 (5,1)	4,2 (3,3)	4,3 (3,8)	4,0 (3,0)	4,1 (3,7)
RM, n%	3 (20,0)	19 (39,6)	19 (44,2)	48 (48,5)	50 (61,0)	139 (48,4)
Media (DE)	1,7 (1,2)	1,3 (0,5)	1,6 (1,6)	2,3 (1,9)	2,5 (2,1)	2,1 (1,8)
PET/TAC, n%	7 (46,7)	27 (56,3)	13 (30,2)	47 (47,5)	44 (53,7)	138 (48,1)
Media (DE)	1,3 (0,5)	1,3 (0,7)	1,6 (1,2)	1,4 (1,0)	1,3 (0,8)	1,4 (0,9)
Ecografías, n%	3 (20,0)	12 (25,0)	7 (16,3)	27 (27,3)	24 (29,3)	73 (25,4)
Media (DE)	1,3 (0,6)	1,6 (0,9)	1,7 (1,0)	1,9 (1,5)	1,4 (0,8)	1,7 (1,1)
Endoscopias digestivas, n%	2 (13,3)	3 (6,3)	1 (2,3)	8 (8,1)	10 (12,2)	24 (8,4)
Media (DE)	1,5 (0,7)	1,7 (0,6)	1,0 (-)	1,1 (0,4)	1,3 (0,5)	1,3 (0,5)

CPNM, cáncer de pulmón no microcítico; DE, desviación estándar; IM, inmunoterapia; PET, positron emission tomography; QT, quimioterapia; RIC, rango intercuartílico; RM, resonancia magnética; TAC, tomografía axial computarizada.

Conclusiones

- En el estudio REVEAL, aunque se predefinieron 5 subgrupos según histología y tratamiento, los de QT exclusiva no llegaron a completarse, lo que refleja la amplia adopción de regímenes con IM en 1L en pacientes con CPNM metastásico, en consonancia con las recomendaciones de las guías ESMO[9] y SEOM[10], independientemente de la histología tumoral.
- Un aspecto relevante de esta población es la presencia de metástasis óseas (34,1%), cerebrales (18,1 %) y hepáticas (16,7 %) y con ECOG ≥2 (12,7%), que habitualmente se encuentran poco representados en ensayos clínicos, mostrando así el perfil de pacientes en la práctica clínica. Señalar también la baja presencia de pacientes no fumadores (6.6%) con respecto a otros estudios[11].
- Destaca la alta carga asistencial asociada a la enfermedad, con elevadas tasas de hospitalización y un número considerable de visitas y pruebas diagnósticas, lo que refleja el impacto clínico del CPNM en estadio avanzado.
- Además, los pacientes tratados con IM presentaron una mayor utilización de recursos sanitarios, posiblemente asociada a un seguimiento más prolongado, atribuible a su vez, a la mejora observada en la supervivencia con este tipo de tratamiento, y a la necesidad de un control clínico más frecuente. Por el contrario, el grupo escamoso tratado con QT mostró la mayor media de hospitalizaciones, lo que podría reflejar una mayor fragilidad clínica.

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- **Objetivo**:
  - Recoger y analizar datos de la práctica clínica en España para caracterizar a los pacientes en 1L de CPNM metastásico, así como describir su perfil clínico y el uso de recursos sanitarios asociados
- **18 hospitales españoles:**
  - **287 pacientes** adultos con CPNM metastásico sin mutaciones en EGFR/ALK, con PD-L1 <50% o desconocido, reclutados entre enero 2022 y marzo 2023
- **Conclusiones:**
  - Alta carga de enfermedad
    - Metástasis óseas (34,1%), cerebrales (18,1 %) y hepáticas (16,7 %) y con ECOG ≥2 (12,7%)
  - Alta carga asistencial
  - Mayor utilización de recursos sanitarios si empleamos inmunoterapia

Seguimos en España…

Retrospective and multicenter study of real-world first-line treatment patterns in metastatic non-small cell lung cancer in spain: analysis of effectiveness from the REVEAL study

Nº de Póster: 20
16th Congress on Lung Cancer (GECP)

Carlos Aguado[1], Francisco de A. Aparisi[2], Ana Cardeña-Gutiérrez[3], Bartomeu Massuti[4], Victoria E. Castellón[5], Juan Verdún[6], Ana Cobo Rodriguez[7], Luis Cabezón-Gutiérrez[8], Javier Garde-Noguera[9], Sergio Vázquez[10], Alejandro Navarro[11], Soledad Medina[12], Esperanza Arriola[13], Carmen Areses[14], Ana Laura Ortega Granados[15], Manuel Cobo[16], Néstor Álvarez[17], David Vilanova[17], Juan Coves[18].

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Introduction

- Immunotherapy (IO) has transformed metastatic NSCLC (mNSCLC) treatment, improving survival over platinum chemotherapy (CT)[1-3]. Most approved IO combination regimens target patients with PD-L1 expression ≥50%[4-6].
- IO-based regimens have shown better outcomes than CT in clinical trials, but trial populations often do not reflect real-world patients due to strict eligibility criteria[3,6].

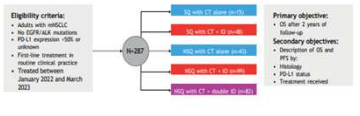
Objective

- The aim of this study was to collect real-world clinical data on the treatment and management of patients receiving first-line therapy for mNSCLC in Spain, including hard-to-treat patient populations such as those with SQ histology, PD-L1-negative tumors, or brain metastases.

Methods

- REVEAL was a non-interventional, multicentric, and retrospective chart review study conducted in Oncology Departments of 18 Spanish hospitals (**Figure 1**).

Figure 1. Study design



Results

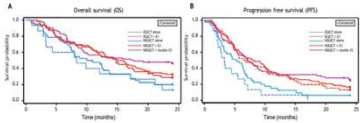
Patients' characteristics

- The median (interquartile range [IQR]) age at diagnosis was 65 years (59.0-72.0), with 15.3% of patients being ≥75 years old. Most patients (87.3%) presented an ECOG of 0-1. Regarding PD-L1 expression, 61.3% were negative and 31.7% had 1-49% PD-L1 expression, while for 7.0% PD-L1 expression was unknown. The sociodemographic and clinical characteristics of the study population have been presented previously[7].

Overall survival and progression-free survival in the overall population

- At database lock (June 2025), 70.7% of patients were no longer under follow-up, with death being the main reason in 95.1% of cases. Disease progression was the leading cause of death (82.9%).
- The median (IQR) follow-up time for patients treated with CT (n=57) was 9.8 (4.3-17.9) months, while it was 14.8 (6.7-24.0) months for those treated with any combination of CT + IO (n=229).
- The median OS and PFS for the entire population were 13.6 months (95% CI: 11.7-16.5), and 6.5 months (95% CI: 5.6-7.6) respectively. Analyses by histology and PD-L1 status are highlighted in **Table 1**. In patients with SQ and NSQ, treated with CT alone exhibited the poorest OS and PFS compared with those treated with any IO combination (**Figure 2A and 2B**).

Figure 2. OS (A) and PFS (B) of patients with mNSCLC included in the study according to the histology and treatment received



Treatment strategy	N	Median OS, months (95% CI)	OS (2 years), n (%)	N	Median PFS, months (95% CI)	PFS (2 years), n (%)
SQ/CT alone	15	8.30 (2.83-17.10)	2 (13.3)	15	3.30 (1.97-5.52)	0 (0.0)
SQ/CT + IO	48	14.78 (10.61-17.78)	11 (22.9)	48	6.59 (4.78-10.47)	6 (12.5)
NSQ/CT alone	42	10.45 (7.40-13.61)	8 (18.6)	43	5.25 (3.20-6.60)	2 (4.7)
NSQ/CT + IO	99	15.77 (11.61-18.30)	29 (29.3)	98	8.10 (5.45-10.10)	15 (15.0)
NSQ/CT + double IO	82	17.63 (9.48-NA)	34 (41.5)	80	7.16 (5.68-8.86)	18 (22.5)

OS: SQ p-value: 0.128; NSQ p-value: 0.023; **PFS**: SQ p-value: 0.003; NSQ p-value: 0.00
CI, confidence interval; CT, chemotherapy; IO, immunotherapy; mNSCLC metastatic non-small cell lung cancer; N, total number of patients; NA, not available; NSQ, non-squamous; OS, overall survival; PFS, progression-free survival; SQ, squamous.

Table 1. Median OS and PFS of the study population according to histology and PD-L1 expression

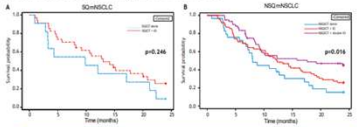
	N	OS: Median OS, months (95% CI)	OS: p-value	N	PFS: Median PFS, months (95% CI)	PFS: p-value
Histology			0.220			0.176
SQ	63	13.00 (9.19-17.10)		63	5.58 (4.57-8.00)	
NSQ	223	13.71 (11.61-17.16)		221	6.65 (5.78-8.00)	
PD-L1			<0.001			0.009
Negative	176	14.13 (10.84-17.63)		174	6.62 (5.61-8.07)	
1%-49%	90	16.65 (12.43-NA)		90	7.13 (5.25-8.79)	
Unknown	20	4.13 (2.83-7.90)		20	2.82 (1.87-5.71)	

CI, confidence interval; N, total number of patients; NSQ, non-squamous; OS, overall survival; PFS: progression-free survival; SQ, squamous.

Effectiveness in PD-L1 unknown/negative patients

- In patients with unknown/negative tumor PD-L1 expression, analyzed by histology and treatment choice, an OS increase was observed in NSQ patients treated with CT + double IO compared with those treated with CT or CT+IO. In SQ population, CT+IO showed a better OS compared with those treated with CT (**Figure 3**).

Figure 3. Overall survival in patients with SQ (A) and NSQ (B) mNSCLC and unknown/negative PD-L1 expression according to the histology and treatment received



Treatment strategy	N	Median (95% CI)	OS (2 years), n (%)
SQ/CT alone	11	9.84 (2.83-21.17)	1 (9.1)
SQ/CT + IO	34	13.00 (7.93-20.00)	7 (20.6)
NSQ/CT alone	29	8.00 (6.29-13.61)	4 (13.8)
NSQ/CT + IO	62	12.29 (8.19-16.84)	16 (25.8)
NSQ/CT + double IO	60	17.63 (9.29-NA)	22 (36.7)

CI, confidence interval; CT, chemotherapy; IO, immunotherapy; mNSCLC metastatic non-small cell lung cancer; N, total number of patients; NA, not available; NSQ, non-squamous; OS, overall survival; SQ, squamous.

Safety

- A total of 92 treatment-related adverse events (TRAE) leading to treatment temporary/definitive discontinuation or dose reduction were recorded in 69 patients. Details of the adverse events occurring in at least 5 patients are shown in **Table 2**.

Table 2. Treatment-related events reported in patients included in the study

	SQ histology, n (%)		NSQ histology, n (%)			All patients
	CT alone N=15	CT + IO N=48	CT alone N=43	CT + IO N=99	CT + double IO N=82	N=287
Number of patients with at least one TRAE leading to discontinuation or dose reduction	-	6 (12.5)	11 (25.6)	24 (24.2)	28 (34.1)	69 (24.0)
Blood and lymphatic system disorders	-	2 (4.2)	6 (14.0)	12 (12.1)	4 (4.9)	24 (8.4)
Gastrointestinal disorders	-	1 (2.1)	1 (2.3)	5 (5.1)	8 (9.8)	15 (5.2)
Renal and urinary disorders	-	-	1 (2.3)	6 (6.1)	2 (2.4)	9 (3.1)
Respiratory, thoracic and mediastinal disorders	-	2 (4.2)	-	1 (1.0)	4 (4.9)	7 (2.4)
Hepatobiliary disorders	-	-	-	1 (1.0)	4 (4.9)	5 (1.7)
Skin and subcutaneous tissue disorders	-	-	-	-	5 (6.1)	5 (1.7)

CT, chemotherapy; IO, immunotherapy; NSQ, non-squamous; SQ, squamous.

Conclusions

- OS and PFS in the overall population were higher in patients treated with CT + IO compared with those who only received CT, showing an association between IO and improved survival outcomes. Further analyses are needed to identify which patients still receive CT alone.
- Overall, our findings suggest that in NSQ patients with PD-L1 negative or unknown status, CT + double IO, may offer better survival benefits in real-world patients.
- The rate and profile of treatment-related adverse events leading to discontinuation were consistent with registrational trial[3,4]. However, retrospective data may underreport some events.
- Longer follow-up and deeper analysis will help clarify real-world long-term outcomes and identify long-term survivors among first-line mNSCLC patients.

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4. Paz-Ares L, et al. N Engl J Med. 2018 Nov 22;379(21):2040-2051.
5. Paz-Ares L, et al. Lancet Oncol. 2021 Feb;22(2):198-211.
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Acknowledgments

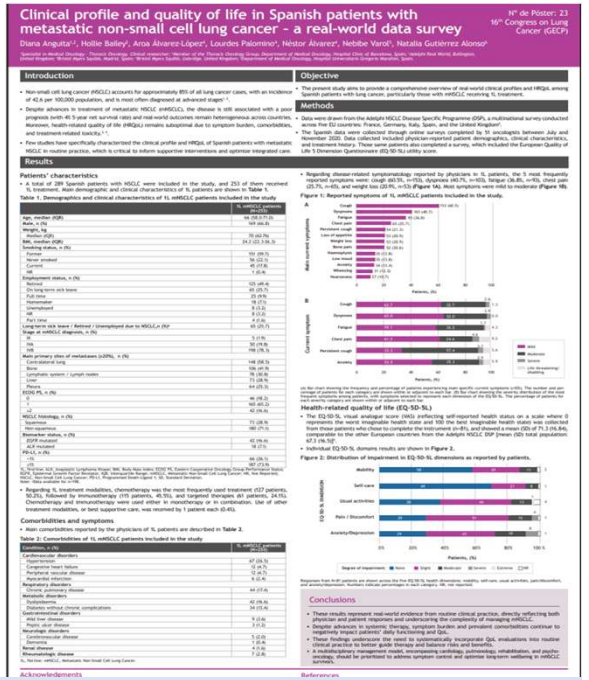
The clinical study teams who participated. The study was funded by Bristol Mayers Squibb. All authors contributed to and approved the presentation; writing and editorial assistance were provided by Víctor Latorre, PhD (Evidenze Health España S.L.U.), funded by Bristol Mayers Squibb.

- Se presentan **los primeros datos de SG y SLP en vida real**, diferenciados por histología, tratamiento recibido y subgrupos de PD-L1
  - En el subgrupo NSQ con PD-L1 negativo/unknown, **la combinación CT+ doble IO en NSQ mostró la mejor supervivencia mediana de OS en CM9LA: 17.6 meses**; CT sola: 8.0 meses; CT+IO: 12.3 meses
- Perfil de seguridad:
  - El porcentaje de pacientes con eventos adversos que llevaron a discontinuación o reducción de dosis fue del 24% (CT sola: 12.5%; **CT+IO: 25.6%; CM9LA: 34.1%)**
  - Consistente con los ensayos pivotales, sin datos nuevos relevantes tras el seguimiento

Clinical profile and quality of life in Spanish patients with metastatic non-small cell lung cancer – a real-world data survey

Nº de Póster: 23
16º Congreso en Lung Cancer (GECP)

Diana Angulta[1,2], Hollie Bailey[1], Aroa Álvarez-López[2], Lourdes Palomino[3], Néstor Álvarez[4], Nebibe Varol[5], Natalia Gutiérrez Alonso[6]



El estudio recoge datos de **289 pacientes** y aporta información relevante sobre comorbilidades, síntomas y el impacto en la vida diaria, reforzando la necesidad de incorporar la evaluación sistemática de QoL en la práctica clínica.

Comorbilidades:

Alta prevalencia de HTA (26.5%), EPOC (17.4%), diabetes (13.4%) y dislipidemia (16.6%).

El 25.7% de los pacientes estaban en situación de baja laboral prolongada o jubilación por el cáncer.

Síntomas predominantes:

Tos (60.5%), disnea (40.7%), fatiga (36.8%), dolor torácico (25.7%) y pérdida de peso (20.9%).

La mayoría de los síntomas fueron de intensidad leve a moderada, pero con impacto significativo en la funcionalidad diaria.

Calidad de vida (QoL):

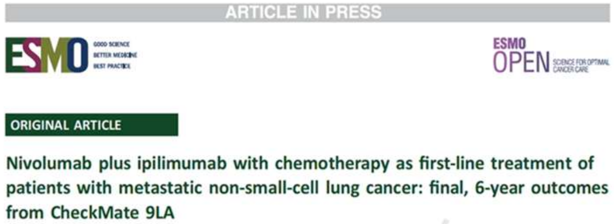
El EQ-5D-5L mostró una puntuación media de 71.3 (SD 16.8), comparable a otros países europeos, pero inferior a la población general.

Los dominios más afectados fueron movilidad, actividades habituales y dolor/disconfort.

El impacto psicológico también es relevante: ansiedad y bajo estado de ánimo presentes en más del 13% de los pacientes.

Inmunoterapia “clásica”

Inmunoterapia con datos robustos: 6 años de CM9LA



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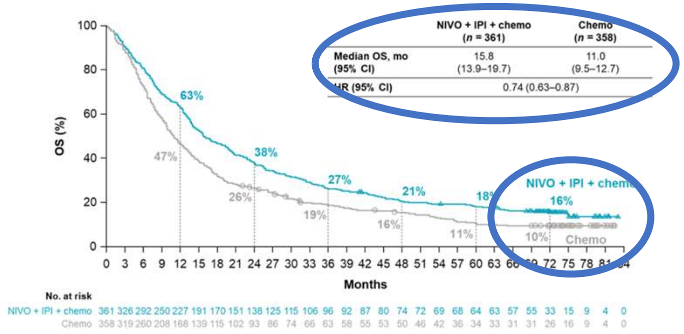
ORIGINAL ARTICLE

Nivolumab plus ipilimumab with chemotherapy as first-line treatment of patients with metastatic non-small-cell lung cancer: final, 6-year outcomes from CheckMate 9LA

OS in all randomized patients - Fig 1



Minimum/median follow-up for OS: 68.6/75.8 months.

Inmunoterapia con datos robustos: 6 años de CM9LA

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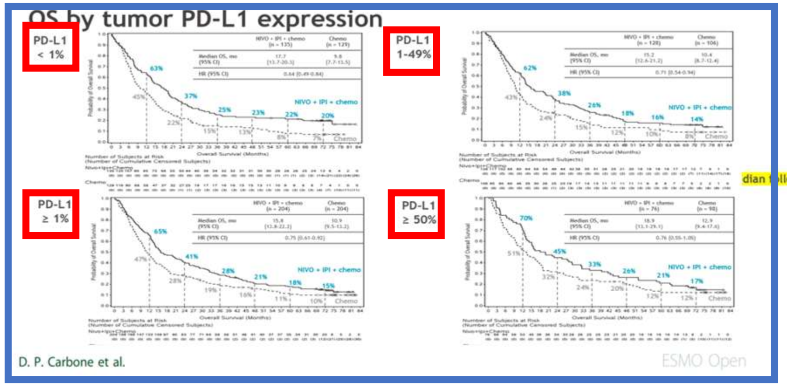
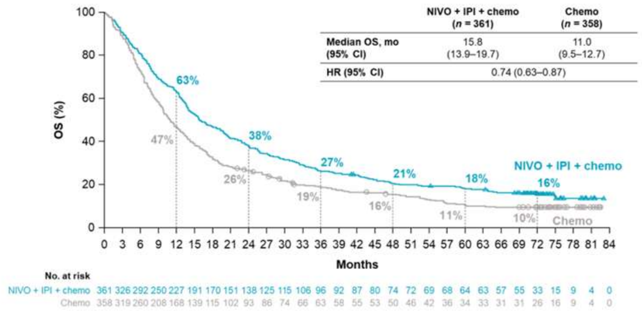
ORIGINAL ARTICLE

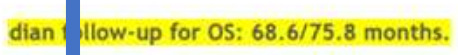
Nivolumab plus ipilimumab with chemotherapy as first-line treatment of patients with metastatic non-small-cell lung cancer: final, 6-year outcomes from CheckMate 9LA

OS by tumor PD-L1 expression



OS in all randomized patients - Fig 1





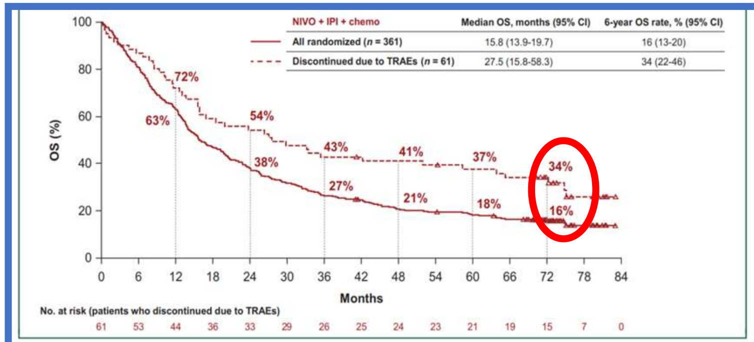
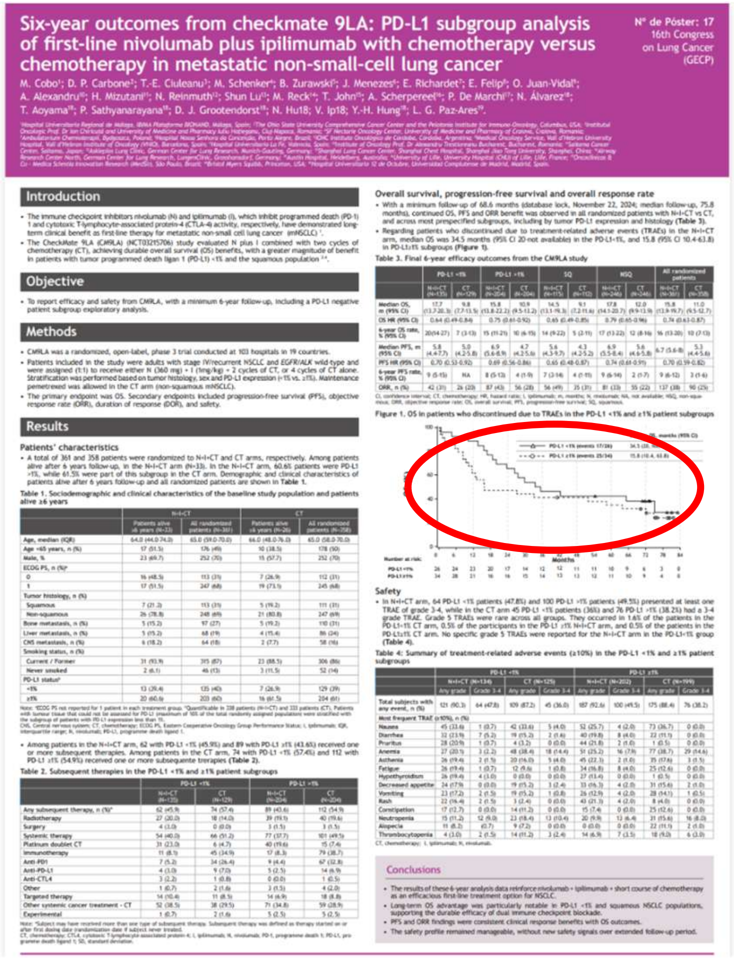


Figure 3. OS in patients who discontinued due to TRAEs. Adverse events were reported between the first dose and 30 days after the last dose of study treatment and led to discontinuation of all components of study treatment. Minimum follow-up for OS was 68.6 months.



Inmunoterapia con datos robustos: 6 años de CM9LA

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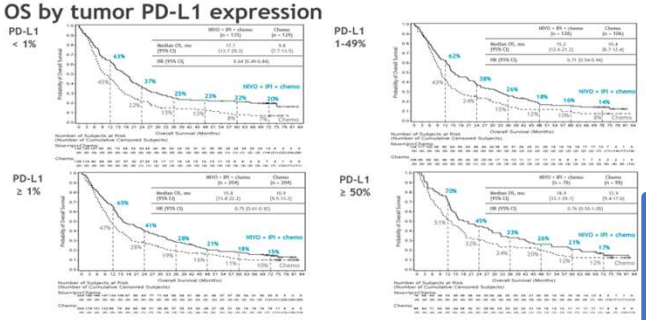
ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

ORIGINAL ARTICLE

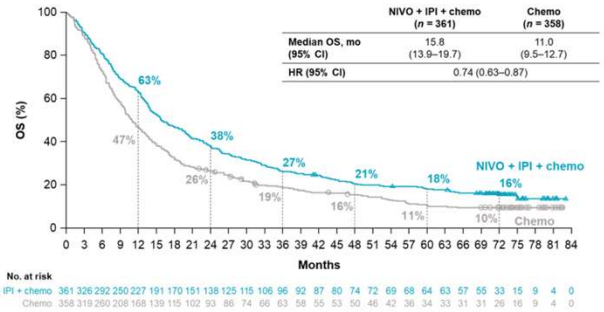
Nivolumab plus ipilimumab with chemotherapy as first-line treatment of patients with metastatic non-small-cell lung cancer: final, 6-year outcomes from CheckMate 9LA

D. P. Carbone et al.

OS by tumor PD-L1 expression



OS in all randomized patients - Fig 1



Minimum/median follow-up for OS: 68.6/75.8 months.

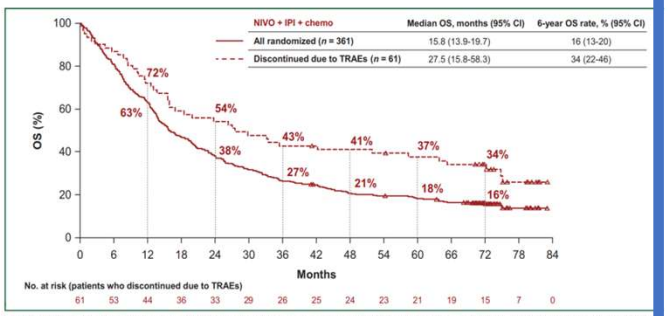
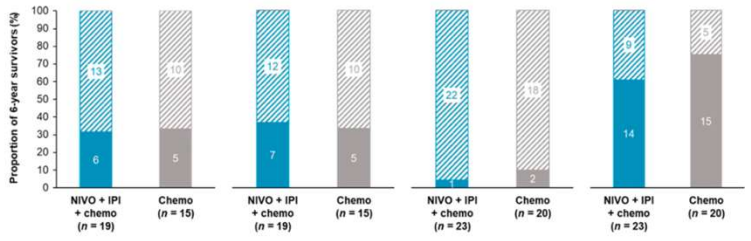


Figure 3. **OS in patients who discontinued due to TRAEs.** Adverse events were reported between the first dose and 30 days after the last dose of study treatment led to discontinuation of all components of study treatment. Minimum follow-up for OS was 68.6 months.

Genomic mutation status in long-term (≥6-year) survivors



Data within the bars represent the number of patients with wild-type or mutant tumors.

Harboring these mutations does not negatively impact long-term OS in patients receiving nivolumab plus ipilimumab with chemotherapy given that 32%, 37%, and 61% of 6-year survivors with mutation-evaluable tissue had *KRAS*-, *STK11*-, or *TP53*-mutant NSCLC, respectively.

Six-year outcomes from checkmate 9LA: PD-L1 subgroup analysis of first-line nivolumab plus ipilimumab with chemotherapy versus chemotherapy in metastatic non-small-cell lung cancer

Nº de Póster: 17
16th Congress on Lung Cancer (GECP)

M. Cobo[1]; D. P. Carbone[2]; T.-E. Ciuleanu[3]; M. Schenker[4]; B. Zurawski[5]; J. Menezes[6]; E. Richardet[7]; E. Felip[8]; O. Juan-Vidal[9]; A. Alexandru[10]; H. Mizutani[11]; N. Reinmuth[12]; Shun Lu[13]; M. Reck[14]; T. John[15]; A. Scherpereel[16]; P. De Marchi[17]; N. Álvarez[18]; T. Aoyama[19]; P. Sathyanarayana[20]; D. J. Grootendorst[21]; N. Hui8; V. Ip18; Y.-H. Hung[22]; L. G. Paz-Ares[23].

Introduction

- The immune checkpoint inhibitors nivolumab (N) and ipilimumab (I), which inhibit programmed death (PD-1) and cytotoxic T-lymphocyte-associated protein-4 (CTLA-4) activity, respectively, have demonstrated long-term clinical benefit as first-line therapy for metastatic non-small cell lung cancer (mNSCLC)[1].
- The CheckMate 9LA (CA9LA) (NCT03215706) study evaluated N plus I combined with two cycles of chemotherapy (CT), achieving durable overall survival (OS) benefits, with a greater magnitude of benefit in patients with tumor programmed death ligan 1 (PD-L1) <1% and the squamous population [1,2].

Objective

- To report efficacy and safety from CA9LA, with a minimum 6-year follow-up, including a PD-L1 negative patient subgroup exploratory analysis.

Methods

- CA9LA was a randomized, open-label, phase 3 trial conducted at 103 hospitals in 19 countries.
- Patients included in the study were adults with stage IV/recurrent NSCLC and *EGFR*/*ALK* wild-type and were assigned (1:1) to receive either N (360 mg) + I (1mg/kg) + 2 cycles of CT, or 4 cycles of CT alone. Stratification was performed based on tumor histology, sex and PD-L1 expression (<1% vs. ≥1%). Maintenance pemetrexed was allowed in the CT arm (non-squamous mNSCLC).
- The primary endpoint was OS. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), duration of response (DOR), and safety.

Results

Patients' characteristics

- A total of 361 and 358 patients were randomized to N+I+CT and CT arms, respectively. Among patients alive after 6 years follow-up, in the N+I+CT arm (N=13), in the N+I+CT arm, 60.6% patients were PD-L1 <1%, while 61.5% were part of this subgroup in the CT arm. Demographic and clinical characteristics of patients alive after 6 years follow-up and all randomized patients are shown in Table 1.

Table 1. Sociodemographic and clinical characteristics of the baseline study population and patients

Overall survival, progression-free survival and overall response rate

- With a minimum follow-up of 68.6 months (database lock, November 22, 2024; median follow-up, 75.8 months), continued OS, PFS and ORR benefit was observed in all randomized patients with N+I+CT vs CT, and across most prespecified subgroups, including by tumor PD-L1 expression and histology (**Table 3**).
- Regarding patients who discontinued due to treatment-related adverse events (TRAEs) in the N+I+CT arm, median OS was 34.5 months (95% CI 20-not available) in the PD-L1<1%, and 15.8 (95% CI 10.4-63.8) in PD-L1≥1% subgroups (**Figure 1**).

Table 3. Final 6-year efficacy outcomes from the CM9LA study

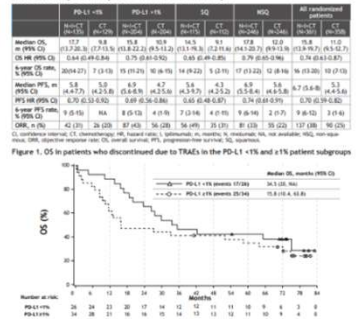
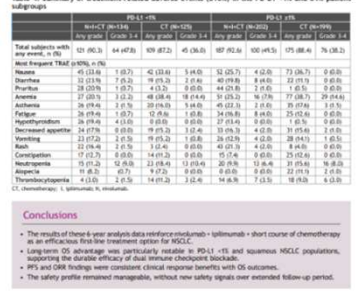


Figure 1. OS in patients who discontinued due to TRAEs in the PD-L1 <1% and ≥1% patient subgroups

Safety

- In N+I+CT arm, 64 PD-L1 <1% patients (47.8%) and 100 PD-L1 ≥1% patients (49.5%) presented at least one TRAE of grade 3-4, while in the CT arm 45 PD-L1 <1% patients (36%) and 76 PD-L1 ≥1% (38.2%) had a 3-4 grade TRAE. Grade 5 TRAEs were rare across all groups. They occurred in 1.6% of the patients in the PD-L1<1% CT arm, 0.5% of the participants in the PD-L1 ≥1% N+I+CT arm, and 0.5% of the patients in the PD-L1≥1% CT arm. No specific grade 5 TRAEs were reported for the N+I+CT arm in the PD-L1<1% group (**Table 4**).

Table 4: Summary of treatment-related adverse events (≥10%) in the PD-L1 <1% and ≥1% patient subgroups



Conclusions

- The results of these 6-year analysis data reinforce nivolumab + ipilimumab + short course of chemotherapy as an efficacious first-line treatment option for NSCLC.
- Long-term OS advantage was particularly notable in PD-L1 <1% and squamous NSCLC populations, supporting the durable efficacy of dual immune checkpoint blockade.
- PFS and ORR findings were consistent clinical response benefits with OS outcomes.
- The safety profile remained manageable, without new safety signals over extended follow-up period.

¿En qué momento del día la administramos?

Study design

A Phase 3, randomized, open-label study (Clinicaltrials.gov: NCT05549037)

Key eligibility criteria

- Stage IIIC-IV NSCLC
- More than 18 years old
- Driver gene negative
- PS 0-1
- ≥1 measurable lesion (RECIST 1.1)
- Clinical stable brain metastasis

N=210, R 1:1

Early ToD group

Standard chemotherapy* in combination with standard ICI** with first 4 cycles starting and completed before 15:00hr

Late ToD group

Standard chemotherapy* in combination with standard ICI** with first 4 cycles starting after 15:00hr

Endpoints

Primary endpoint:
- PFS by BIRC

Secondary endpoint:
- OS
- ORR by BIRC
- Whole blood lymphocyte subset analysis***

Stratification factor: None

*(for details of chemotherapy: carboplatin (AUC of 5 mg/ml/min) and nab-paclitaxel (200 mg/m²), pemetrexed (500 mg/m²)
**(details of ICI: 200 mg of pembrolizumab or sintilimab)
***T cells (CD3⁺), CD4⁺ T cells (CD3⁺, CD4⁺), CD8⁺ T cells (CD3⁺, CD8⁺), B cells (CD3⁻, CD20⁺), and NK cells (CD16⁺, CD56⁺)

2025 ASCO ANNUAL MEETING

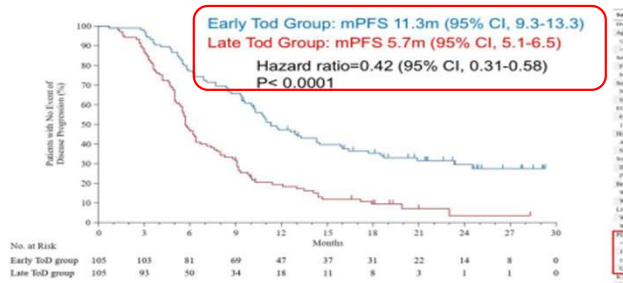
Randomized trial of Time-of-Day immunochemotherapy on Survival in Non-Small Cell Lung Cancer

Zhe Huang[1,2*], Liang Zeng[1*], Zhaohui Ruan[1*], Qun Zeng[3*], Huan Yan[1], Wenjuan Jiang[1], Yi Xiong[1], Chunhua Zhou[1], Haiyan Yang[1], Li Liu[1], Jiacheng Dai[1], Nachuan Zou[1], Shidong Xu[1,2], Ya Wang[1], Zhan Wang[1], Jun Deng[4], Xue Chen[4], Jing Wang[5], Hua Xiang[5], Xiaomei Li[6], Boris Duchemann[6,7], Guoqiang Chen[8,9], Christoph Scheiermann[3,11,12,13†], Francis Lévi[6,10†], Nong Yang[14†], Yongchang Zhang[1,2,4,15†]

Presenter: Yongchang Zhang, MD, PhD, Hunan Cancer Hospital, zhangyongchang@csu.edu.cn

Results: PFS

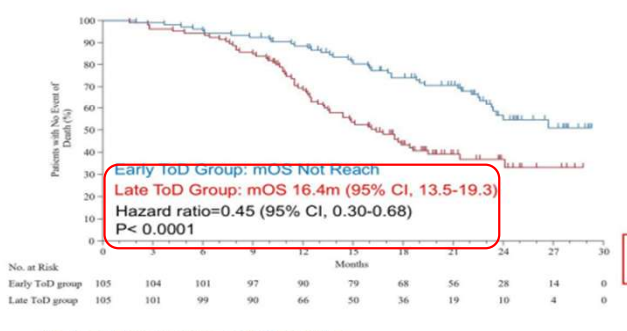
Statistically significant improvement in PFS comparing early with late ToD group



Median follow-up time: 23.2 months.

Results: OS

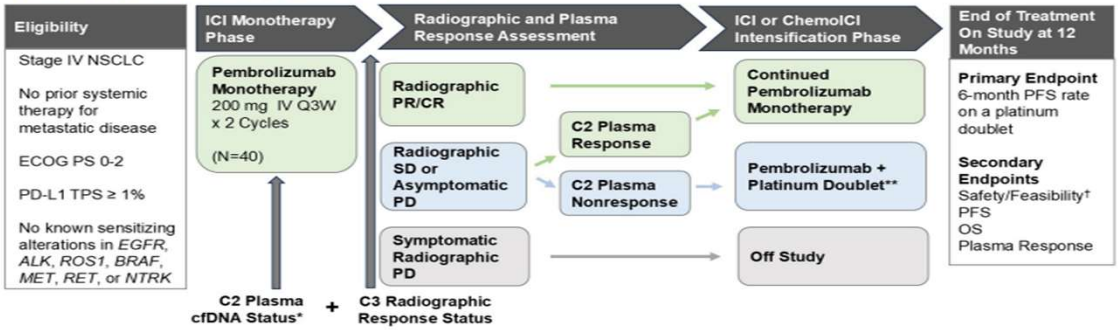
Statistically significant improvement in OS comparing early with late ToD group



Median follow-up time: 23.2 months.

¿Evaluamos bien la respuesta?

Plasma response-guided adaptive treatment of advanced NSCLC receiving first-line pembrolizumab



*Plasma Response defined as ≥50% reduction in plasma ctDNA max AF for patients with high shed [≥0.5% max AF] at baseline or continued low shed [<0.5% max AF] for patients with low shed at baseline, as measured by amplicon-based plasma NGS

**NSQ: Carboplatin AUC 5 + Pemetrexed 500 mg/m2 Q3W x 4 cycles followed by Pemetrexed 500 mg/m2 Q3W; SQ: Carboplatin AUC 6 + Paclitaxel 200 mg/m2 Q3W x 4 cycles, with concurrent pembrolizumab 200 mg IV Q3W to end of study treatment

†Feasibility defined as completion of the integrated plasma response and C3 imaging assessment, with one-sided upper 90% binomial confidence interval >82.5%

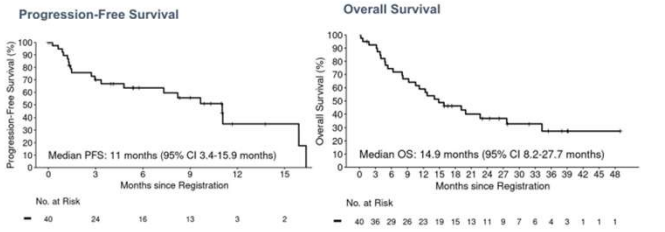
2025 ASCO ANNUAL MEETING

Plasma-guided adaptive first-line chemoimmunotherapy for non-small cell lung cancer (NSCLC)

Julia K. Rotow, Grace Heavey, Mizuki Nishino, Shail Maingi, Christopher S. Lathan, Umit Tapan, Alexandra S. Bailey, Zihan Wei, Emanuele Mazzola, Diandra Ocot, Geoffrey R. Oxnard, David A. Barbie, Pasi A. Jänne, Cloud P. Paweletz, Michael L. Cheng

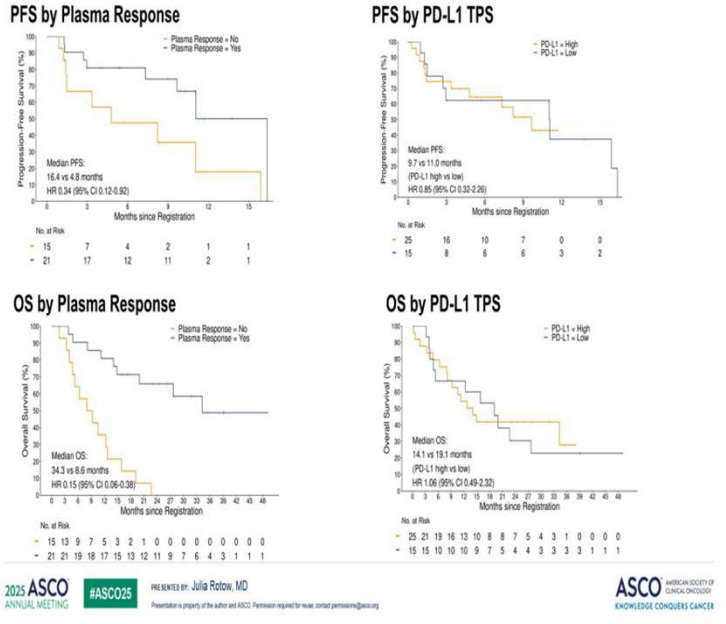
Julia Rotow, MD
Clinical Director, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute
Assistant Professor, Harvard Medical School

Survival Outcomes to an Adaptive Treatment Strategy



Survival outcomes were calculated for all enrolled patients from date of registration to date of progression or death inclusive of pembrolizumab monotherapy and, if indicated per protocol, adaptive pembrolizumab plus platinum doublet

Survival by PD-L1 TPS and by Plasma Response



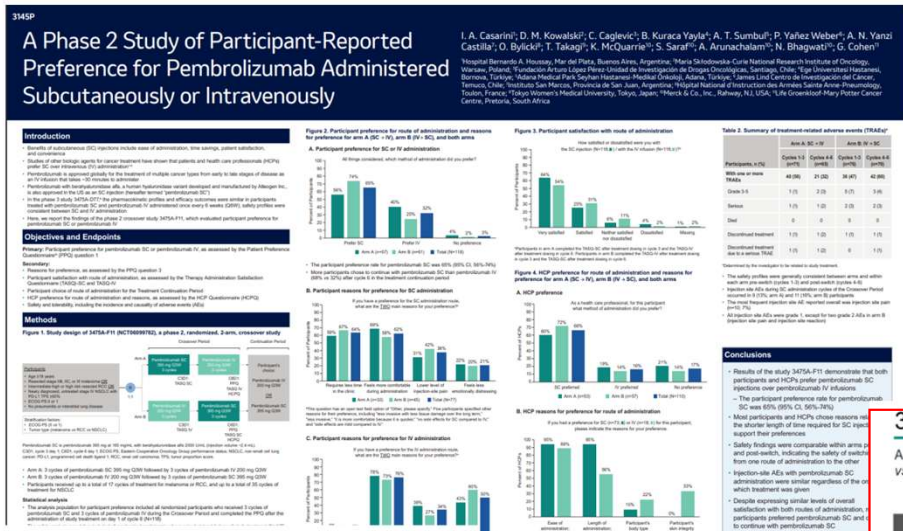
Key Conclusions

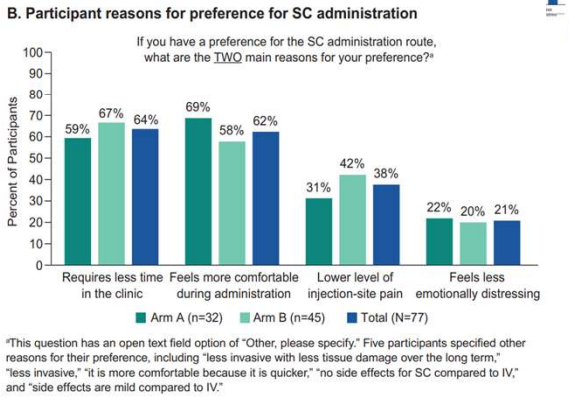
Plasma-guided intensification from first-line pembrolizumab monotherapy to platinum doublet/pembrolizumab is feasible in metastatic NSCLC

A plasma-guided strategy resulted in a median PFS of 11.0 months with fewer patients receiving first-line platinum doublet chemotherapy than would be predicted by PD-L1 TPS

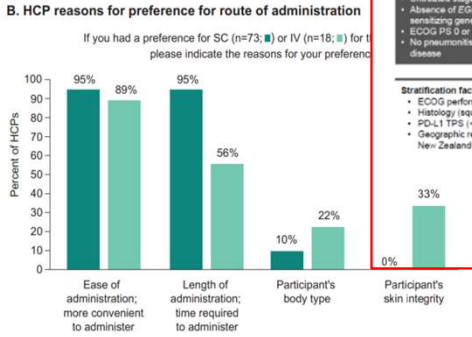
As a dynamic biomarker, ctDNA kinetics are an important emerging tool to guide clinical decision making in NSCLC. Further validation within a randomized study is needed to clarify implications for clinical practice

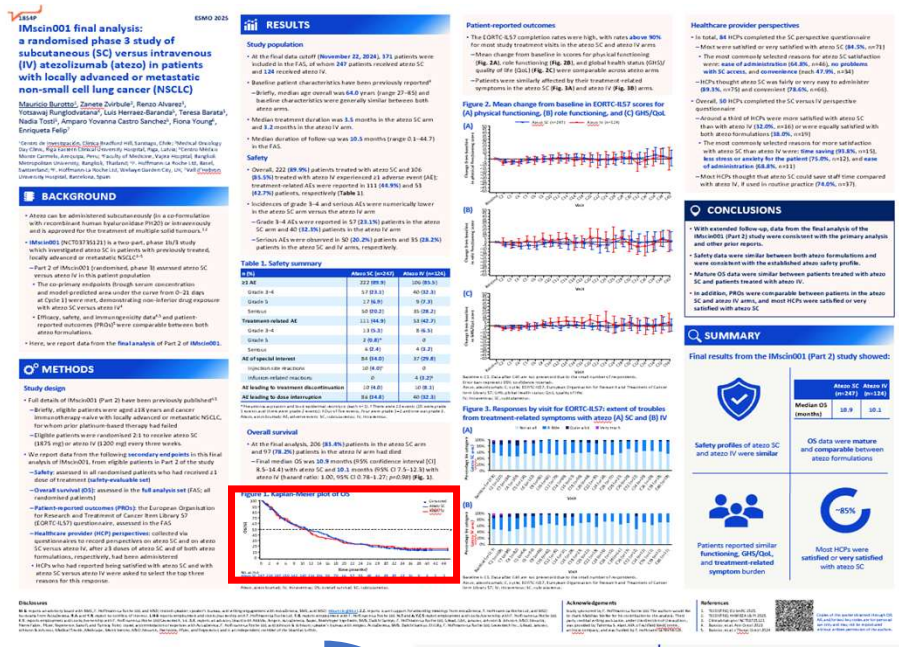
Intravenosa o subcutánea?

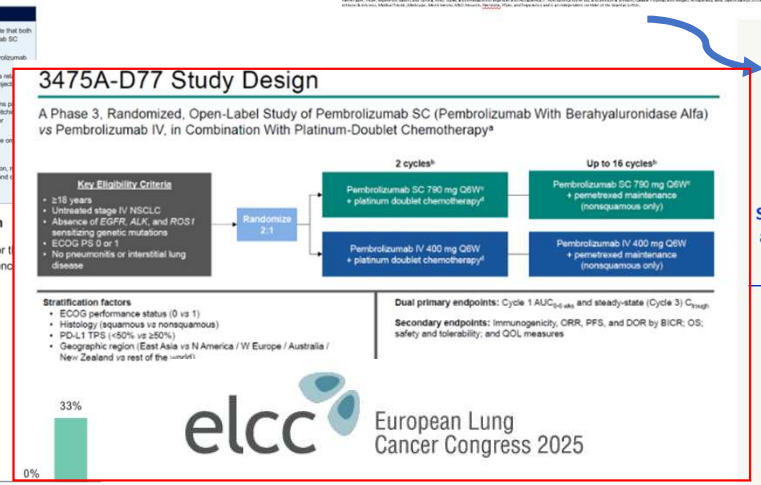


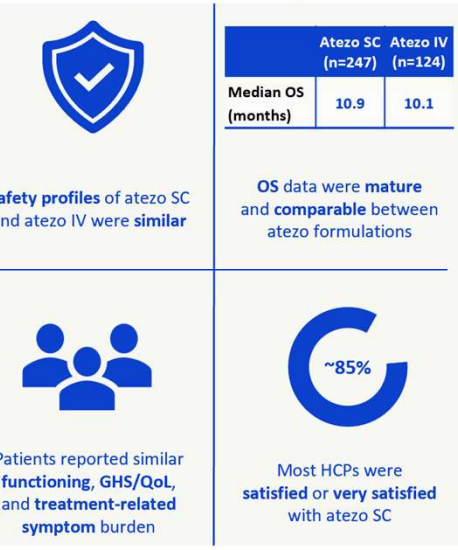


[a]This question has an open text field option of "Other, please specify." Five participants specified other reasons for their preference, including "less invasive with less tissue damage over the long term," "less invasive," "it is more comfortable because it is quicker," "no side effects for SC compared to IV," and "side effects are mild compared to IV."









En ancianos…

First-line atezolizumab plus chemotherapy in elderly patients with advanced NSCLC
IFCT-1805 ELDERLY: a randomized, multicenter, open-label, phase 3 trial

Key eligility criteria
NSCLC
Stage IIIB, IIIC non irradiable or IV (8th classification)
Age 70 - 89
PS 0 -1
MMS ≥ 24
EGFR, ALK wild type

R 2:1
N=510

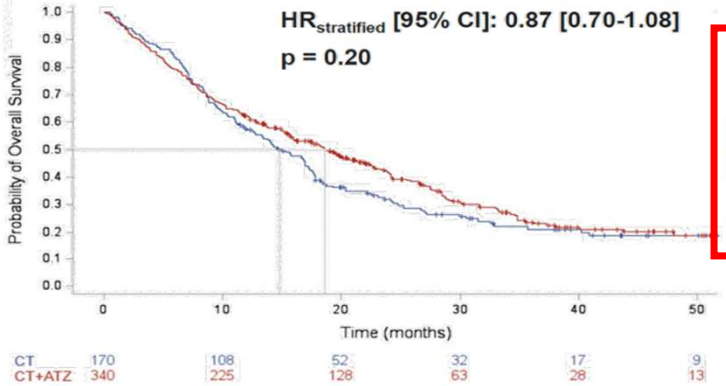
Carboplatin Q4W - weekly paclitaxel (4 cycles) + Atezolizumab Q3W (max 2 years) (CT + ATZ arm)
until progression or unacceptable toxicity

Carboplatin Q4W - weekly paclitaxel (4 cycles) (CT arm)
until progression or unacceptable toxicity

Stratification factors
- histology (squamous vs non squamous),
- age (70-79 vs 80-89),
- expression of PDL1 (0 vs ≥ 1 vs unknown)

Primary endpoint	Overall survival (OS)*
Secondary endpoints	Progression-Free Survival (PFS)* Best response rate* Duration of response* Safety**

Overall survival



	CT (N=170)	CT+ ATZ (N=340)
Median OS: months [95% CI]	15.0 [11.8-17.5]	18.6 [15.5-22.4]
6-m OS: % [95% CI]	83.5 [77-88.3]	79.1 [74.4-83.1]
12-m OS: % [95% CI]	57.6 [49.8-64.7]	62.3 [57-67.3]

Median FU: 38.0 months (IC95%: [33.6; 39.4])
27 november 2024

The addition of ATZ to CT significantly improved PFS, ORR, DOR, independently of PDL1 expression.

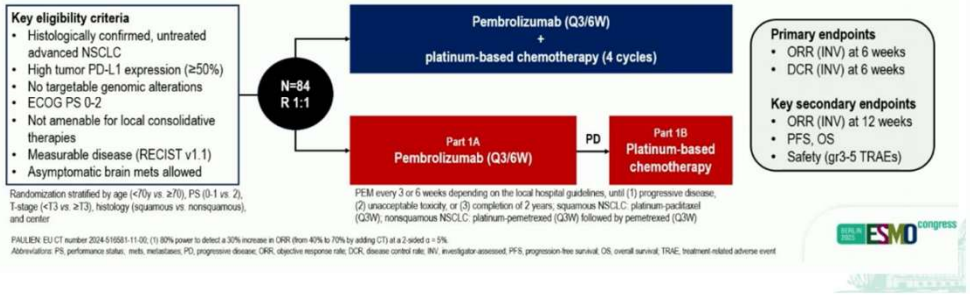
A significantly higher toxicity was seen with the addition of ATZ to CT for elderly patients.

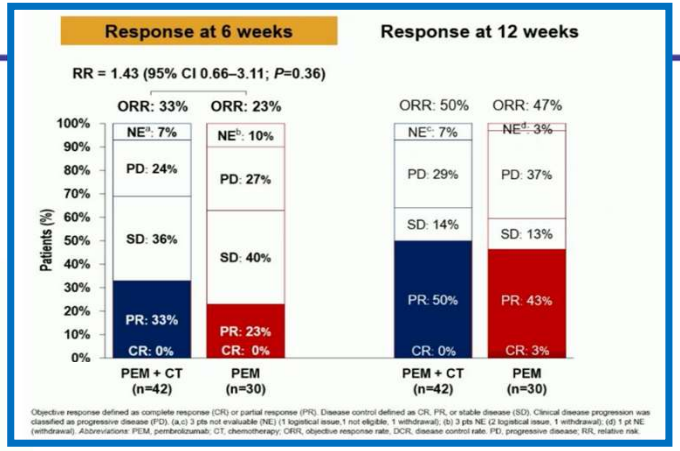
En altos expresores añadir QT aporta?

Pembrolizumab plus chemotherapy vs pembrolizumab as first-line therapy for advanced NSCLC with PDL1 (TPS) ≥ 50%: open-label, phase 3, randomized trial (PAULIEN)

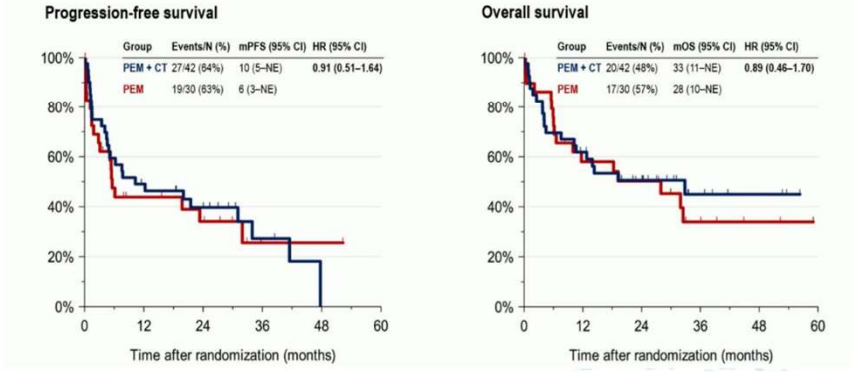
Study rationale and design

- Pembrolizumab (PEM) is the standard first-line therapy for advanced NSCLC with high tumor PD-L1 expression (TPS ≥50%) and no targetable genomic alterations.
- However, in those cases where an urgent tumor response is needed, chemotherapy (CT) is often added to PEM, though its benefit is unclear.
- PAULIEN is a multicenter (eight Dutch sites), open-label, phase III, randomized controlled, superiority trial comparing **PEM + CT** with **PEM** to assess **tumor responses at 6 weeks**.
- Hypothesis: adding CT to PEM will result in a 30% increase[1] in objective tumor response (ORR) at 6 weeks.





Progression-free survival and overall survival



Inmunoterapia “clásica” y algo más o comparada con otras combinaciones…

IO clásica + otras IO

IO clásica frente a otras IO

IO clásica + ADCs

ADCs + nuevas IO

Antiangiogénicos + IO clásica…

Overall survival with nivolumab plus relatlimab with platinum-doublet chemotherapy in metastatic non-small cell lung cancer from RELATIVITY-104

Luis G. Paz-Ares,[1] Manuel Cobo-Dols,[2] Mauricio Burotto,[3] Michael Schenker,[4] Alejo Lingua,[5] Jarushka Naidoo,[6,7] Francisco Orlandi,8 Emma K. Beardsley,[9] Vamsidhar Velcheti,[10] Martin Reck,[11] Gaston Lucas Martinengo,[12] Enriqueta Felip,[13] Eniola Yeates,[14] Priyanka Kasbekar,[14] Srijata Samanta,[14] Satyendra Suryawanshi,[14] Annie Yu,[14] Laura McDonald,[14] Jaclyn Neely,[14] Nicolas Girard[15]

[1]Hospital Universitario 12 de Octubre, Universidad Complutense de Madrid, Madrid, Spain; [2] Hospital Regional Universitario de Málaga, Málaga, Spain; [3] Bradford Hill Centro de Investigación Clínica, Santiago, Chile; [4] SF Nectarie Oncology Center, Craiova, Romania; [5] Instituto Médico Río Cuarto, Río Cuarto, Argentina; [6] Beaumont Hospital, Dublin, Ireland; [7] RCSI University of Medicine and Health Sciences, Dublin, Ireland; [8] Orlandi Oncología, Providencia, Chile; [9] Frankston Hospital – Peninsula Health, Frankston, VIC, Australia; [10]Mayo Clinic Comprehensive Cancer Center, Jacksonville, FL, USA; [11]Airway Research Center North, German Center for Lung Research, LungClinic, Grosshansdorf, Germany; [12]Sanatorio Parque SA, Rosario, Argentina; [13]Vall d'Hebron Barcelona Hospital Campus, Vall d'Hebron Institute of Oncology, Universitat Autonoma de Barcelona, Barcelona, Spain; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]Institut du Thorax Curie-Montsouris, Institut Curie, Paris, France

P1.11.85

Nivolumab + Relatlimab + doblete de platino

Key eligibility criteria
- 1L stage IV/recurrent NSCLC
- No prior systemic therapy for metastatic disease
- No *EGFR*, *ALK*, or *ROS-1* alterations[a]
- ECOG PS 0-1

N = 309, R 1:1

NIVO 360 mg + RELA 360 mg Q3W + PDCT[c] (4 cycles)
Prophylactic myeloid growth factor was mandatory for patients aged ≥ 60 years[d] according to guidelines[3,4]

NIVO 360 mg Q3W + PDCT[c] (4 cycles)

Stratified by tumor PD-L1[b] (≥ 1% vs < 1%), histology (NSQ vs SQ), and ECOG PS (0 vs 1)

Primary endpoint
- ORR (BICR)

Secondary endpoints
- PFS (BICR)
- Safety
- ORR and PFS by PD-L1
- DOR (BICR)

Exploratory endpoints
- OS*
- Biomarker analysis
- PROs

	NIVO + RELA + PDCT (n = 158)		NIVO + PDCT (n = 149)[b]	
Ongoing treatment,[c] (%)	22 (14)		25 (17)	
Safety	**Any grade**	**Grade 3-4**	**Any grade**	**Grade 3-4**
All-cause AEs, n (%)	158 (100)	114 (72)	148 (99)	111 (74)
TRAEs, n (%)	147 (93)	86 (54)	138 (93)	86 (58)
Serious TRAEs	37 (23)	33 (21)	37 (25)	33 (22)
TRAEs leading to discontinuation	26 (16)	13 (8)	24 (16)	14 (9)
TRAEs leading to death	6 (4)		3 (2)	

PD-L1 ≥ 1%

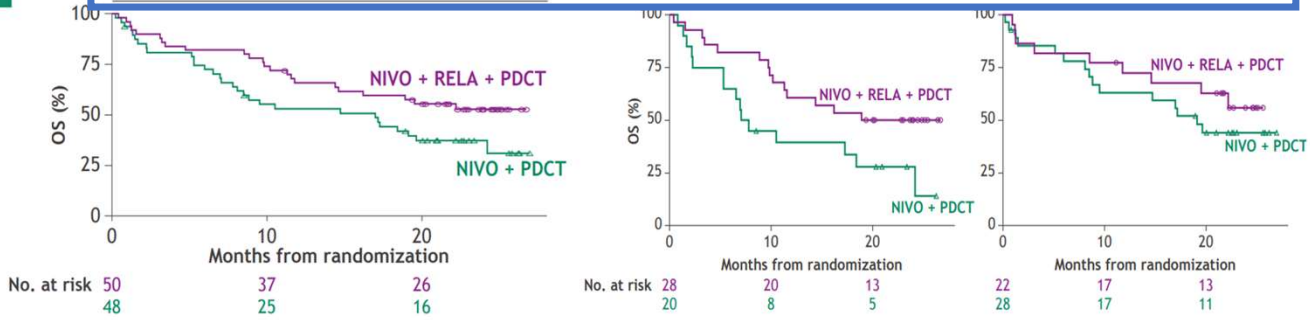
	NIVO + RELA + PDCT (n = 50)	NIVO + PDCT (n = 48)
Median OS, mo (90% CI)	NR (14.6-NR)	17.0 (8.1-19.6)
HR (90% CI)	0.60 (0.38-0.94)	

PD-L1 1%-49%

	NIVO + RELA + PDCT (n = 28)	NIVO + PDCT (n = 20)
Median OS, mo (90% CI)	18.9 (11.3-NR)	7.4 (5.3-18.4)
HR (90% CI)	0.46 (0.25-0.86)	

PD-L1 ≥ 50%

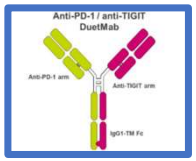
	NIVO + RELA + PDCT (n = 22)	NIVO + PDCT (n = 28)
Median OS, mo (90% CI)	NR (14.6-NR)	19.1 (8.8-NR)
HR (90% CI)	0.67 (0.34-1.35)	

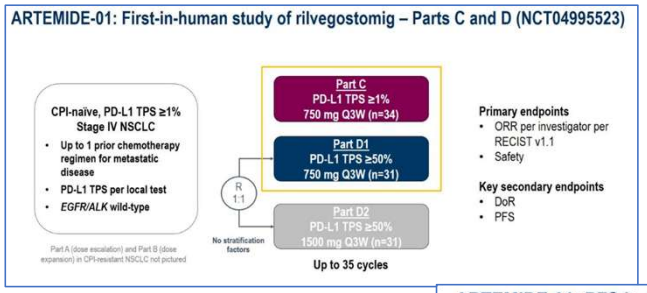


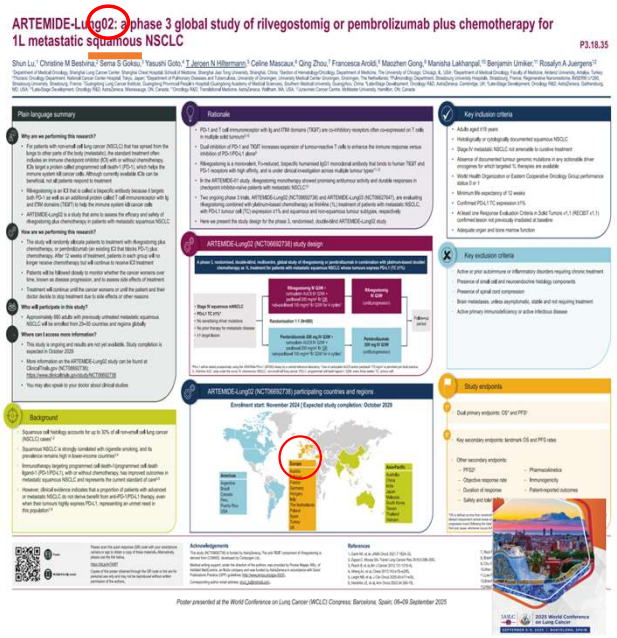
Median follow-up (range) for Part 2: 12.6 (0.0-28.4) months. NR, not reached.

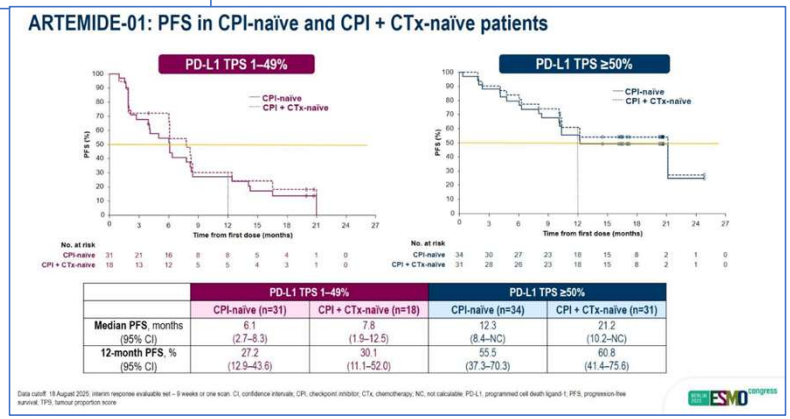
Luis G. Paz-Ares et al. Poster presented at WCLC Congress, September 6-9, 2025. Barcelona, Spain. P1.11.85

Rilvesgotomig vs Pembrolizumab en 1ª línea de CPNCP con doblete de platino

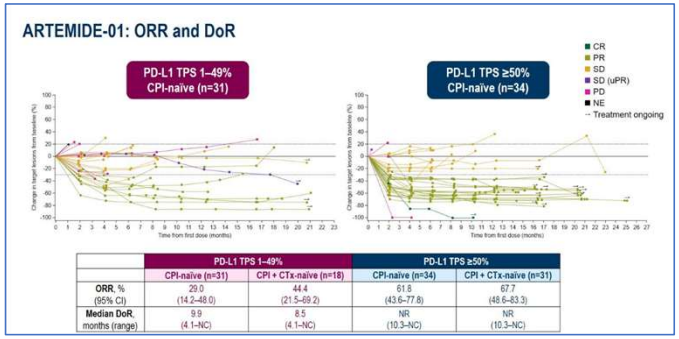




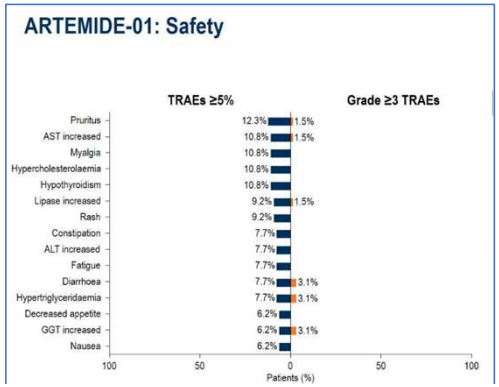




	PD-L1 TPS 1–49%		PD-L1 TPS ≥50%	
	CPI-naïve (n=31)	CPI + CTx-naïve (n=18)	CPI-naïve (n=34)	CPI + CTx-naïve (n=31)
Median PFS, months (95% CI)	6.1 (2.7–8.3)	7.8 (1.9–12.5)	12.3 (8.4–NC)	21.2 (10.2–NC)
12-month PFS, % (95% CI)	27.2 (12.9–43.6)	30.1 (11.1–52.0)	55.5 (37.3–70.3)	60.8 (41.4–75.6)



	PD-L1 TPS 1–49%		PD-L1 TPS ≥50%	
	CPI-naïve (n=31)	CPI + CTx-naïve (n=18)	CPI-naïve (n=34)	CPI + CTx-naïve (n=31)
ORR, % (95% CI)	29.0 (14.2–48.0)	44.4 (21.5–69.2)	61.8 (43.6–77.8)	67.7 (48.6–83.3)
Median DoR, months (range)	9.9 (4.1–NC)	8.5 (4.1–NC)	NR (10.3–NC)	NR (10.3–NC)



Phase 3 eVOLVE-Lung02 trial of volrustomig plus chemotherapy versus pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer with PD-L1 tumor cell expression <50%

Melissa Johnson,[1] Edurne Arriola,[2] Terufumi Kato,[3] Nicolas Girard,[4] Shirish Gadgeel,[5] Margarita Majem Tarruella,[6] Thomas Newsom-Davis,[7] Mateusz Polaczek,[8] Xin Chen,[9] Kamil Stefaniak,[10] Caitlin Lowery,[11] Natasha Angra,[11] Gary Doherty,[12] Myung-Ju Ahn[13]

[1]Sarah Cannon Research Institute, Nashville, TN, USA; [2]Medical Oncology Department, Hospital del Mar-CIBERONC, Barcelona, Spain; [3]Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; [4]Department of Thoracic Oncology, Institute Curie, Paris, France; [5]Division of Hematology and Oncology, Department of Internal Medicine, Henry Ford Health, Detroit, MI, USA; [6]Medical Oncology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [7]Chelsea and Westminster Hospital NHS Foundation Trust, London, UK; [8]III Department of Lung Diseases and Oncology, The Institute of Tuberculosis and Lung Diseases, Warsaw, Poland; [9]AstraZeneca, Wilmington, DE, USA; [10]AstraZeneca, Warsaw, Poland; [11]AstraZeneca, Gaithersburg, MD, USA; [12]AstraZeneca, Cambridge, UK; [13]Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Poster P3.18

Plain language summary

Why are we performing this research?

Immuno-oncology (IO) treatments (given alone or with chemotherapy) are widely used as the first treatment (first-line [1L] treatment) given to patients with non-small-cell lung cancer (NSCLC) that has spread to other parts of the body (metastatic NSCLC).

While 1L IO treatments improve survival in many patients with metastatic NSCLC, other patients, such as those with low expression of a protein called PD-L1 on the tumour cell surface (i.e., PD-L1 tumour cell [TC] <50%), do not respond as well.

Volrustomig is a potential new IO treatment that binds two different proteins, PD-1 and CTLA-4, and that activates a particular type of immune cells, called T cells, to attack cancer cells.

The combination of 1L volrustomig and chemotherapy has shown encouraging clinical activity and acceptable tolerability in patients with NSCLC, including those with low levels of PD-L1.[5,6]

The phase 3 eVOLVE-Lung02 study aims to evaluate if the combination of 1L volrustomig and chemotherapy improves the length of time participants with metastatic NSCLC and low levels of PD-L1 live for without their disease progressing, and live for overall, compared with similar participants receiving 1L standard-of-care pembrolizumab plus chemotherapy. The study will also look at how the cancer responds to 1L volrustomig and chemotherapy, as well as the side effects of treatment and how well it is tolerated by the participants.

How are we performing this research?

Eligible participants will be randomly assigned in equal numbers to either of the following two groups:

- Volrustomig in combination with chemotherapy.
- Pembrolizumab in combination with chemotherapy.

All participants will receive the study treatment for a maximum of 24 months. Both the participants and their physicians will be aware of which group the participant is assigned to.

Who will participate in this study?

We aim to recruit approximately 1200 patients with metastatic NSCLC with low or absent levels of PD-L1 (PD-L1 TC <50%). To be eligible, study participants must not have received any prior 1L IO treatment, chemotherapy or any other systemic therapy for metastatic NSCLC.

Where can I access more information?

This study is ongoing and is expected to complete in April 2028; no results are currently available. More information about this study can be found at https://clinicaltrials.gov/study/NCT05984277. You may also speak to your doctor about clinical studies.

(5) Ahn M, et al. Ann Oncol 2023;33(suppl_7):S1403.
(6) Spigel DR, et al. J Thorac Oncol 2024;19(suppl):S33-4.

Background

- Immunotherapies targeting PD-1 or its ligand PD-L1 have transformed the treatment of 1L mNSCLC and are now routinely used alone or combined with chemotherapy (CT) and/or other agents in clinical practice.[1–5]
  - However, in a subset of patients with PD-L1-low (i.e. PD-L1 TC <50%) or PD-L1-negative (i.e. TC <1%) disease, such therapies are associated with shorter OS than in patients with PD-L1 TC ≥50% disease regardless of NSCLC histology.[1]
  - This indicates a significant unmet medical need for additional treatment options that improve clinical outcomes in this patient population.
- Dual inhibition of PD-(L)1 and CTLA-4, with or without chemotherapy, has shown clinical activity, including survival benefit, in patients with PD-L1-low and PD-L1-negative mNSCLC and is used in clinical practice to address the poorer prognosis of these patients.[9–15]
- Achieving further efficacy improvements with monospecific CTLA-4 inhibitors at higher treatment doses is clinically restrained by toxicity.[16–19]

Volrustomig and rationale

- Volrustomig (MEDI5752) is a monovalent, PD-1/CTLA-4 bispecific, humanised IgG1 monoclonal antibody engineered to specifically inhibit PD-1 with increased CTLA-4 blockade on PD-1-positive activated T cells compared with PD-1-negative T cells.[20]
  - This mode of action may facilitate enhanced CTLA-4 inhibition at tolerable doses beyond those achievable with current PD-1/CTLA-4 combinations.
- Data from the first-in-human phase 1/2 study of volrustomig (NCT03530397) have shown evidence of T-cell activation and expansion of new and existing T-cell clones at pharmacodynamic levels exceeding those clinically feasible with coadministered anti-PD-1 and anti-CTLA-4 monospecific antibodies.[21]
  - Encouraging antitumor activity and a manageable safety profile were reported in patients with mNSCLC who received 1L volrustomig with pemetrexed plus carboplatin every 3 weeks (Q3W), including those with PD-L1 TC <1% disease.[22,23]
- The phase 3, two-arm, randomised, multicentre, open-label eVOLVE-Lung02 trial (NCT05984277) will evaluate the efficacy and safety of 1L volrustomig plus histology-specific CT versus pembrolizumab plus histology-specific CT in patients with PD-L1 TC <50% mNSCLC.

eVOLVE-Lung02 (NCT05984277) study design: phase 3, two-arm, parallel, randomised, multicentre, open-label trial

Patients with squamous or non-squamous stage IV NSCLC
~N=1200

- PD-L1 TC <50%
- *EGFR, ALK & ROS1* wild-type
- Absence of genomic alterations in other actionable driver oncogenes (e.g. *NTRK, BRAF, RET, MET*)*
- ECOG PS 0 or 1
- No prior systemic therapy for mNSCLC; no prior immunotherapy

R† 1:1

- Volrustomig‡ + histology-specific CT§ Q3W x 4 → Volrustomig Q3W¶ until completion of 24 months of treatment or disease progression, or other discontinuation criteria are met
- Pembrolizumab‡ 200 mg + histology-specific CT§ Q3W x 4 → Pembrolizumab Q3W/Q6W¶# until completion of 24 months of treatment or disease progression, or other discontinuation criteria are met

*Absence of documented tumour genomic alteration results from tests conducted as part of standard local practice in any other actionable driver oncogenes for which there are locally approved targeted 1L therapies.
†Randomisation will be stratified according to histology (squamous vs non-squamous), PD-L1 expression (TC <1% vs TC 1–49%), smoking status (never vs former/current), and geographic region (Asia vs Rest of the World).
‡Treatment with volrustomig or pembrolizumab is given intravenously.
§CT regimen for squamous histology is paclitaxel + carboplatin; CT regimen for non-squamous histology is pemetrexed + carboplatin (+ pemetrexed maintenance therapy, per investigator discretion).
¶Plus pemetrexed maintenance therapy, if applicable.
#200 mg Q3W or 400 mg Q6W where locally approved.

Study status

- **eVOLVE-Lung02** is currently enrolling at approximately 265 sites in 25 countries/regions; approximately 1200 patients will be recruited.
- Enrolment began in October 2023, and primary completion is anticipated in April 2028.

Key inclusion criteria

- Age ≥18 years.
- Histologically or cytologically documented squamous or non-squamous stage IV NSCLC (according to Version 8 of the IASLC Staging Manual in Thoracic Oncology 2016) not amenable to curative surgery or radiation.
- PD-L1 TC <50% as determined using the VENTANA PD-L1 (SP263) assay by a central reference laboratory; tumour tissue samples for PD-L1 testing must be acquired ≤3 months prior to screening.
- Absence of sensitising EGFR mutations and ALK and ROS1 rearrangements.
- Absence of documented tumour genomic alteration results from tests conducted as part of standard local practice in any other actionable driver oncogenes (e.g. NTRK, BRAF, RET, MET) for which there are locally approved targeted 1L therapies.
- At least one measurable lesion not previously irradiated.
- ECOG PS 0 or 1; life expectancy ≥12 weeks.
- Adequate organ and marrow function.

Key exclusion criteria

- Any prior 1L CT or any other systemic therapy for Stage IV NSCLC.
- Prior treatment with immunotherapy.
- Persistent toxicities of Grade ≥2 (as assessed by NCI CTCAE v5.0) caused by previous anticancer therapy, excluding alopecia. (Participants with irreversible toxicity that is not reasonably expected to be exacerbated by study intervention in the opinion of the investigator may be included).
- Mixed SCLC and NSCLC histology or sarcomatoid variant. Rare subtypes are excluded.
- Cardiac disease including but not limited to cardiomyopathy, heart failure, and uncontrolled hypertension.
- Spinal cord compression.
- Symptomatic brain metastases; a brain scan with IV contrast is mandatory at screening/baseline.

Study endpoints

1°
- **BICR-assessed PFS** (per RECIST v1.1) in patients with PD-L1 TC <1%.
- **OS** in patients with PD-L1 TC <1%.

2° **Key:**
- **BICR-assessed PFS** (per RECIST v1.1) in all randomised patients (i.e., PD-L1 TC <50%; ITT population).
- **OS** in all randomised patients.

Other:
- **BICR-assessed PFS** (per RECIST v1.1) landmarks (at 6, 12, 18, and 24 months) in patients with PD-L1 TC <1% and in all randomised patients.
- **OS** landmarks (at 12, 18, 24, and 36 months) in patients with PD-L1 TC <1% and in all randomised patients.
- **Investigator-assessed PFS** (per RECIST v1.1) in patients with PD-L1 TC <1% and in all randomised patients.
- **BICR-assessed ORR and DoR** (per RECIST v1.1) in patients with PD-L1 TC <1% and in all randomised patients.
- **PFS2** (progression after starting first subsequent therapy or death) in patients with PD-L1 TC <1% and in all randomised patients.
- **Safety and tolerability**.
- **Pharmacokinetics and immunogenicity of volrustomig**.
- **Patient-reported outcomes** (including NSCLC Symptom Assessment Questionnaire on disease-related symptoms).

Poster

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Abbreviations

1L, first-line; ALK, anaplastic lymphoma kinase; BICR, blinded independent central review; CT, chemotherapy; CTLA-4, cytotoxic T-lymphocyte associated antigen-4; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; IASLC, International Association for the Study of Lung Cancer; IO, immuno-oncology; ITT, intent-to-treat; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NSCLC, non-small-cell lung cancer; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed death-(ligand-) 1; PFS, progression-free survival; PFS2, time to second progression or death; PS, performance status; Q3/6W, every 3/6 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; SCLC, small-cell lung cancer; TC, tumour cell.

Acknowledgements

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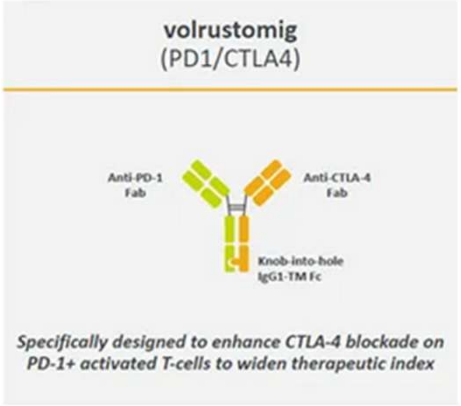
Poster presented at the IASLC World Congress on Lung Cancer (WCLC); Barcelona, Spain; 6–9 September, 2025

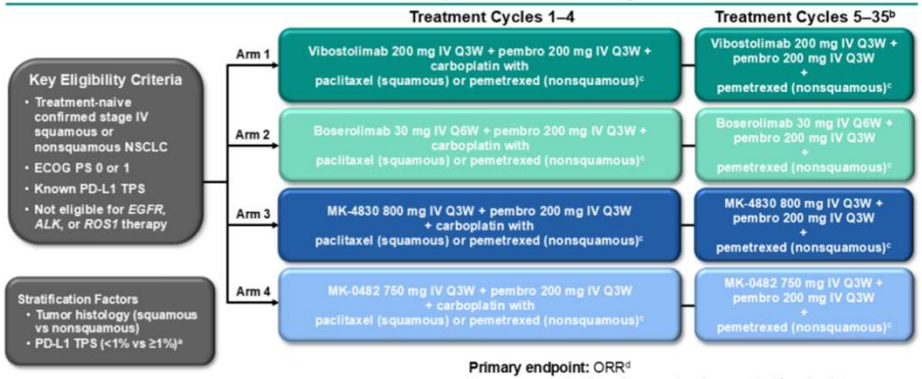
Volrustomig + QT vs Pembrolizumab + QT



Doblete de platino + Pembrolizumab + nuevas IO

KEYMAKER-U01 substudy 01: investigational agents + pembrolizumab and chemotherapy in untreated stage IV NSCLC

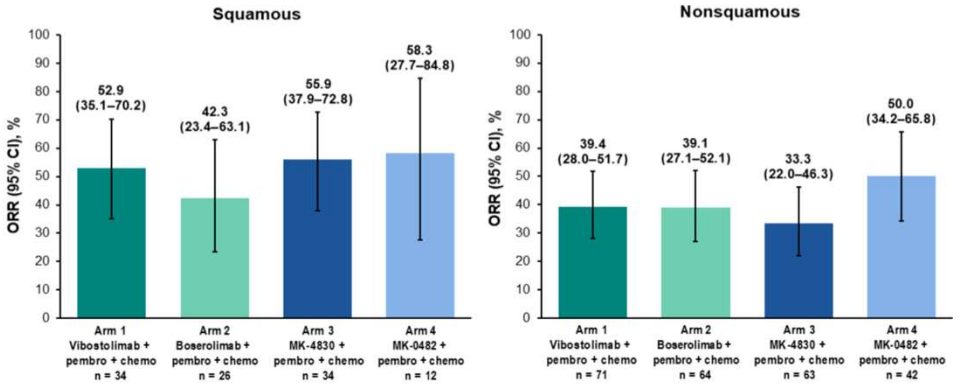
KEYMAKER-U01 Substudy 01A Design



Primary endpoint: ORR[d]
Secondary endpoints: Progression-free survival[d] and safety

- Vibostolimab, a TIGIT antagonist mAb (arm 1)
- Boserolimab, a CD27 agonist mAb (arm 2)
- MK-4830, an ILT4 antagonist mAb (arm 3)
- MK-0482, an ILT3 antagonist mAb (arm 4)

Efficacy: Investigator-Assessed ORR per RECIST v1.1



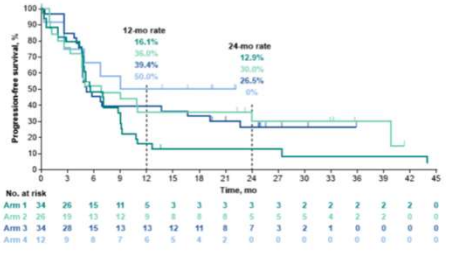
Efficacy: Investigator-Assessed PFS per RECIST v1.1

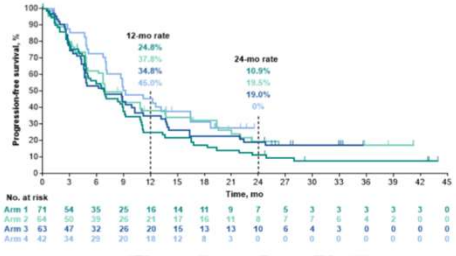
Squamous

	Events/N	Median (95% CI), mo
Arm 1: vibostolimab + pembro + chemo	30/34	5.6 (4.8–9.0)
Arm 2: boserolimab + pembro + chemo	18/26	6.8 (4.6–24.0)
Arm 3: MK-4830 + pembro + chemo	24/34	5.2 (4.7–16.7)
Arm 4: MK-0482 + pembro + chemo	6/12	NR (2.6–NE)

Nonsquamous

	Events/N	Median (95% CI), mo
Arm 1: vibostolimab + pembro + chemo	61/71	6.9 (4.8–9.0)
Arm 2: boserolimab + pembro + chemo	49/64	6.9 (5.0–11.0)
Arm 3: MK-4830 + pembro + chemo	50/63	6.8 (4.6–10.3)
Arm 4: MK-0482 + pembro + chemo	28/42	9.2 (7.1–16.4)





BERLIN GERMANY 17-21 OCTOBER 2025
BERLIN 2025 ESMO congress

ZEAL-1L

Study design

- Phase 3, multicenter, randomized, double-blind study

Inclusion

- Histologically or cytologically confirmed diagnosis of NSCLC without known targetable driver alteration (squamous or non-squamous; mixed histology allowed)
- Advanced (Stage IIIB not amenable to definitive chemoradiotherapy) or metastatic (Stage IV) NSCLC
- Completed 4–6 cycles of pembrolizumab + platinum-based 1L induction chemo and achieved SD, PR, or CR
- ECOG score of 0 to 1; adequate organ function
- Asymptomatic brain metastases permitted

Exclusion

- Mixed small cell lung cancer or sarcomatoid variant NSCLC
- Receipt of prior PARP inhibitor(s) in prior lines of treatment
- Known history of MDS or AML or active tuberculosis
- Systolic BP >140 mmHg and/or diastolic BP >90 mmHg

Experimental: Niraparib + Pembrolizumab

Comparator: Placebo + Pembrolizumab

Stratification

- Histology Squamous vs. Non-SQ
- Response SD vs CR/PR
- PD-L1 Status TPS <1% vs >=1%

Dosing

- **Niraparib**: 100-mg tablets or matched placebo orally QD, continuously (200 or 300 mg starting dose)
- **Pembrolizumab**: 200 mg IV Q3W

Endpoints

Primary:

1. PFS by BICR in the CR/PR population

Key Secondary/Other:

2. PFS by BICR in the ITT population
3. OS in the CR/PR population
4. OS in the ITT population
5. Time to progression in the CNS (assessed by BICR using RANO-BM)
- Safety

Hierarchical Testing

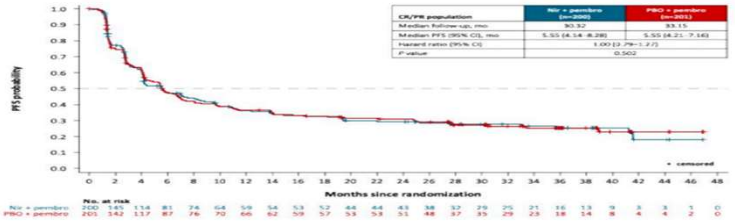
- The 5 efficacy endpoints will be tested in the pre-specified sequential order.
- If any endpoint fails to reach statistical significance, formal testing will stop and all subsequent endpoints will not be formally tested.

Pembrolizumab +/- Niraparib de mantenimiento

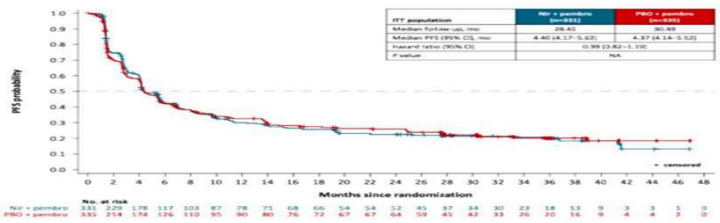
Ramalingam WCLC 2025

PFS in the CR/PR or ITT population

CR/PR



ITT

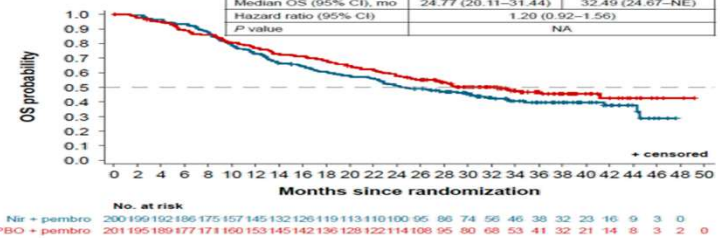


- PFSm:
  - CR/PR: 5,55-5,55m (HR 1)
  - ITT: 4,4-4,37m (HR 0,99)
- OSm:
  - CR/PR: 24,77-32,49m (HR 1,2)
  - ITT: 21,36-25,26m (HR 1,16)

Key secondary endpoint: Overall Survival

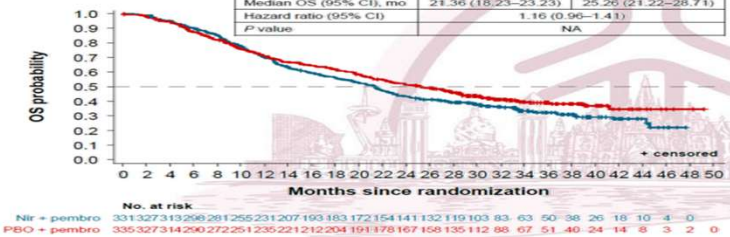
CR/PR population

CR/PR population	Nir + pembro (n=200)	PBO + pembro (n=201)
Median follow-up, mo	34.66	34.43
Median OS (95% CI), mo	24.77 (20.11–31.44)	32.49 (24.67–NE)
Hazard ratio (95% CI)	1.20 (0.92–1.56)	
P value	NA	



ITT population

ITT population	Nir + pembro (n=331)	PBO + pembro (n=336)
Median follow-up, mo	34.30	33.45
Median OS (95% CI), mo	21.36 (18.23–23.23)	25.26 (21.22–28.71)
Hazard ratio (95% CI)	1.16 (0.96–1.41)	
P value	NA	



ADCs anti-TROP2

2025 ASCO ANNUAL MEETING

TROPION-Lung02: Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab (pembro) with or without platinum chemotherapy (Pt-CT) as first-line (1L) therapy for advanced non-small cell lung cancer (aNSCLC)

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2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Benjamin P. Levy, MD, FASCO

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ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

TROPION-Lung02

- Phase 1b study of Dato-DXd + pembrolizumab ± Pt-CT in a/mNSCLC without actionable genomic alterations[a]

Key eligibility criteria

- a/mNSCLC
- Dose escalation[b]: ≤2 lines of prior therapy[c]
- Dose expansion
  - ≤1 line of Pt-CT (cohorts 1 and 2)[c]
  - Treatment-naive (cohort 2)[c,d]
  - Treatment-naive (cohorts 3–6)[c]

1L patients only	Dato-DXd IV Q3W	+ Pembrolizumab IV Q3W	+ Pt-CT IV Q3W	
Cohort 1 (n=2):	4 mg/kg	+ 200 mg		Doublet
Cohort 2 (n=40):	6 mg/kg	+ 200 mg		Doublet
Cohort 3 (n=14):	4 mg/kg	+ 200 mg	+ Carboplatin AUC 5	Triplet
Cohort 4 (n=26):	6 mg/kg	+ 200 mg	+ Carboplatin AUC 5	Triplet
Cohort 5 (n=8):	4 mg/kg	+ 200 mg	+ Cisplatin 75 mg/m²	Triplet
Cohort 6 (n=6):	6 mg/kg	+ 200 mg	+ Cisplatin 75 mg/m²	Triplet

Objectives

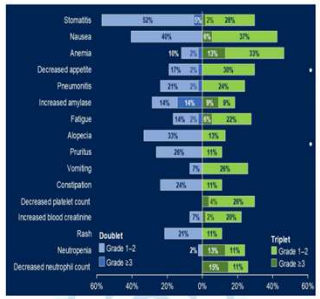
Primary: Safety and tolerability

Secondary: Efficacy

Data cutoff: April 29, 2024. Median study duration was 18.7 months (range, 11–33.8) for doublet and 24.6 months (range, 15.4–32.4) for triplet combinations.

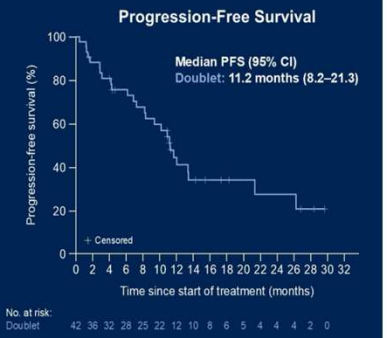
RO ~55%
PFSm: 11,2m (doblete) – 6,8m (triplete)
OSm: NE (doblete) – 17,4m (triplete)

Event, n (%)	All 1L (N=96)	
	Doublet (n=42)	Triplet (n=54)
TRAEs	39 (92.9)	54 (100)
Grade ≥3	17 (40.5)	30 (55.6)
Associated with death	0	0
TRAEs associated with dose modifications		
Dose reduction of any drug	8 (19.0)	14 (25.9)
Dose reduction of Dato-DXd	8 (19.0)	7 (13.0)
Discontinuation of any drug	14 (33.3)	20 (37.0)
Discontinuation of Dato-DXd	13 (31.0)	16 (29.6)
Serious TRAEs	5 (11.9)	12 (22.2)
Grade ≥3	4 (9.5)	9 (16.7)
AESIs		
Oral mucositis/stomatitis	26 (61.9)	22 (40.7)
Grade 3	2 (4.8)	1 (1.9)
Adjudicated drug-related ILD/pneumonitis	11 (26.2)	14 (25.9)
Grade 3	2 (4.8)	1 (1.9)
Ocular surface events	9 (21.4)	18 (33.3)
Grade 3	1 (2.4)	2 (3.7)

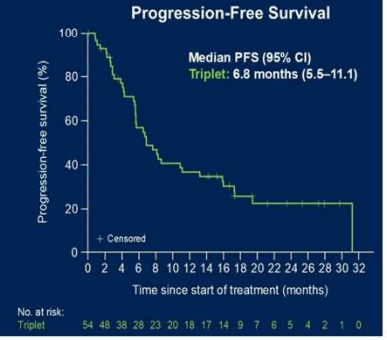


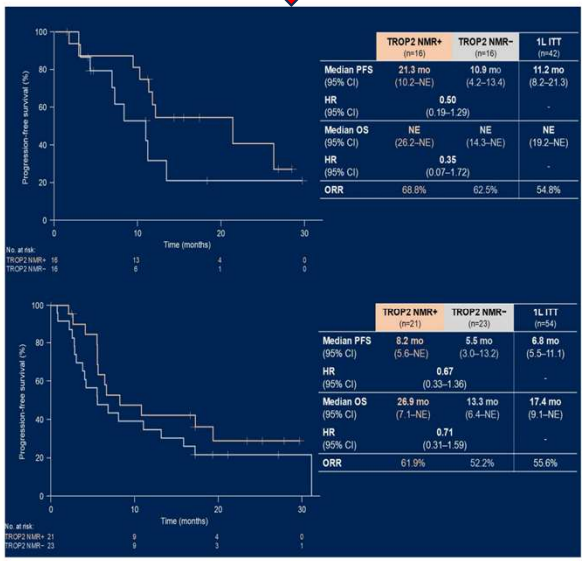
Mediana duración tto:
9.7 meses Dato-Dx-Pembro
5.3 meses Dato-Dx-Pembro-QT

	Doublet (n=42)
Confirmed ORR*, n (%)	23 (54.8)
95% CI	38.7–70.2
Median DOR, months	20.1
95% CI	9.7–NE
DCR, n (%)	37 (88.1)
95% CI	74.4–96.0
Median TTR, months	1.4
Range	1.2–7.0
Median PFS, months	11.2
95% CI	8.2–21.3
Median OS, months	NE
95% CI	19.2–NE



	Triplet (n=54)
Confirmed ORR*, n (%)	30 (55.6)
95% CI	41.4–69.1
Median DOR, months	13.7
95% CI	5.7–NE
DCR, n (%)	48 (88.9)
95% CI	77.4–95.8
Median TTR, months	1.4
Range	1.2–9.6
Median PFS, months	6.8
95% CI	5.5–11.1
Median OS, months	17.4
95% CI	9.1–NE





	TROP2 NMR+ (n=16)	TROP2 NMR− (n=16)	1L ITT (n=42)
Median PFS (95% CI)	21.3 mo (10.2–NE)	10.9 mo (4.2–13.4)	11.2 mo (8.2–21.3)
HR (95% CI)	0.50 (0.19–1.29)		-
Median OS (95% CI)	NE (26.2–NE)	NE (14.3–NE)	NE (19.2–NE)
HR (95% CI)	0.35 (0.07–1.72)		-
ORR	68.8%	62.5%	54.8%

	TROP2 NMR+ (n=21)	TROP2 NMR− (n=23)	1L ITT (n=54)
Median PFS (95% CI)	8.2 mo (5.6–NE)	5.5 mo (3.0–13.2)	6.8 mo (5.5–11.1)
HR (95% CI)	0.67 (0.33–1.36)		-
Median OS (95% CI)	26.9 mo (7.1–NE)	13.3 mo (6.4–NE)	17.4 mo (9.1–NE)
HR (95% CI)	0.71 (0.31–1.59)		-
ORR	61.9%	52.2%	55.6%

EE CC activos en 1L con ADCs anti-TROP2

Lung Cancer UPDATES ASCO HIGHLIGHTS 30 MAYO - 03 JUNIO 2025 Chicago, USA

GECP lung cancer research

Clinical Trial Name	Phase	Treatment	Status
TROPION-Lung07	3	Dato-DXd Plus Pembro +/-Chemo in 1L nonsquamous NSCLC	Recruiting
TROPION-Lung08	3	Dato-DXd Plus Pembro vs. Pembro in 1L nonsquamous NSCLC with PD-L1 ≥50%	Recruiting
EVOKE-03	3	Pembro vs. Sacituzumab Govitecan Plus Pembro in 1L NSCLC with PD-L1 ≥50%	Recruiting
TroFuse-007	3	Sacituzumab Tirumotecan (Sac-TMT) Plus Pembro vs. Pembro Alone in 1L NSCLC with PD-L1 ≥ 50%	Recruiting
TroFuse-023	3	Pembro +/- Sac-TMT in 1L maintenance for squamous NSCLC	Recruiting

Dato_DXd + Rilvesgotomig en CPNCP no escamoso PDL1>50%, no AGAs

TROPION-Lung10: Phase 3 study of datopotamab deruxtecan plus rilvegostomig in non-squamous advanced or metastatic non-small cell lung cancer with high PD-L1 expression and without actionable genomic alterations

Thomas Newsom-Davis,[1] Benjamin Solomon,[2] Barbara Melosky,[3] Rebecca S. Heist,[4] Shun Lu,[5] Giulia Pasello,[6] Julia Niewczas,[7] Marta Stachowiak,[8] Pavlo Lyfar,[9] Xiaojin Shi,[10] Suresh S. Ramalingam[11]

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Poster 122TiP

Plain language summary

Why are we performing this research?

- Non-small cell lung cancer (NSCLC) is the most common type of lung cancer.[1] For patients with NSCLC that has spread to nearby tissue or lymph nodes (advanced) or from its original site (metastatic), and who have expression of a protein called PD-L1 on at least 50% of their tumour cells, 1L treatment options include immunotherapy, given with or without chemotherapy.[2–6]
- Immunotherapy targets the immune system to help the body fight cancer. However, some patients don't respond to immunotherapy, or the treatment stops working, and new treatment options are needed.[7]
- Datopotamab deruxtecan (Dato-DXd) is an antibody-drug conjugate that consists of an antibody (datopotamab) and an anticancer drug (DXd), joined via a plasma-stable cleavable linker.[8] Dato-DXd has shown promising efficacy in previous studies in patients with advanced or metastatic NSCLC, either when given alone or in combination with immunotherapy and/or chemotherapy.[9–12]
- Rilvegostomig is a drug that blocks proteins called PD-1 and TIGIT on the surface of immune cells, which helps the immune system kill cancer cells.[13]
- TROPION-Lung10 is evaluating if the combination of Dato-DXd and rilvegostomig can improve outcomes for patients with advanced or metastatic NSCLC.

How are we performing this research?

Approximately 675 patients will be randomised to receive either Dato-DXd in combination with rilvegostomig, rilvegostomig alone, or pembrolizumab, which is the current standard of care treatment.

Who will participate in this study?

Eligible patients:

- Have a type of NSCLC called non-squamous that is advanced or metastatic
- Do not have tumours with genetic changes for which there are approved targeted therapies
- Have tumours that express a protein called PD-L1 on at least 50% of tumour cells
- Have not received any treatment for advanced or metastatic NSCLC

Where can I access more information?

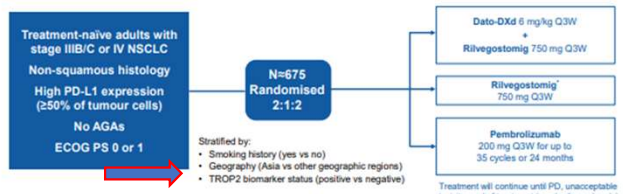
For more information about TROPION-Lung10, please visit https://clinicaltrials.gov/study/NCT06357533. You may also speak to your doctor about clinical studies.

1. Duma N, et al. Mayo Clin Proc 2019;94:1623–40; 2. Gandhi L, et al. N Eng J Med 2018;378:2078–92; 3. Johnson ML, et al. J Clin Oncol 2022;41:1213–27; 4. de Castro G, et al. J Clin Oncol 2022;41:1986–91; 5. Reck M, et al. N Eng J Med 2016;375:1823–33; 6. Hendriks LE, et al. Ann Oncol 2023;34:358–76; 7. Memon D, et al. Cancer Cell 2024;42:209–24; 8. Okajima D, et al. Mol Cancer Ther 2021;20:2329–40; 9. Ahn M-J, et al. J Clin Oncol 2025;43:260–72; 10. Garassino MC, et al. J Thorac Oncol 2024;19(suppl):2–3; 11. Levy BP, et al. J Clin Oncol 2024;42(suppl 16):8617 (abstr); 12. Papadopoulos K.P, et al. J Thorac Oncol 2023;18(suppl 11):S55; 13. Hiltermann TJN, et al. J Thorac Oncol 2024;19(suppl):S33.

Background

- 1L immunotherapy targeting the PD-1/PD-L1 pathway, with or without chemotherapy, has improved outcomes for patients with advanced/metastatic NSCLC without AGAs;[1–3] however, some patients may not respond or may develop resistance, meaning new treatment strategies and approaches to identifying patients who may respond are needed.[4,5]
- TROP2 is a transmembrane glycoprotein that is highly expressed in several solid tumours, including lung cancers.[3–11]
- Dato-DXd is a TROP2-directed ADC composed of a humanised anti-TROP2 IgG1 monoclonal antibody conjugated to a highly potent topoisomerase I inhibitor payload via a plasma-stable tetrapeptide-based tumour selective cleavable linker.[7]
- Dato-DXd alone or in combination with anti-PD-1/PD-L1 therapy ± chemotherapy has shown activity as 1L+ treatment in patients with advanced or metastatic NSCLC.[12–15]
  - In the phase 3 TROPION-Lung01 study, Dato-DXd monotherapy significantly improved PFS compared with docetaxel (median PFS: 4.4 vs 3.7 months; HR 0.75 [95% CI: 0.62–0.91]) in patients with pretreated advanced/metastatic NSCLC with and without AGAs, which was driven by patients with non-squamous histology.[12]
  - In an exploratory analysis of TROPION-Lung01, the use of a computational pathology-based approach showed that patients receiving Dato-DXd who had TROP2 QCS-NMR-positive tumours had increased ORR and longer PFS than those with TROP2 QCS-NMR-negative tumours.[13]
  - In the phase 1b TROPION-Lung02 study in patients who received doublet and triplet combinations of 1L Dato-DXd plus pembrolizumab ± chemotherapy, ORRs were 52% and 56%, DCRs were 88% and 89%, and median DoRs were NE and 12.9 months, respectively.[14]
  - In the phase 1b TROPION-Lung04 study, 1L Dato-DXd demonstrated promising efficacy in combination with durvalumab ± carboplatin, with no new safety signals identified, in patients with advanced or metastatic NSCLC (ORR: 50% and 77%; DCR: 93% and 92%, respectively[15] and is also being investigated in combination with rilvegostomig.[16]
- Rilvegostomig (AZD2936) is an Fc-reduced, monovalent, bispecific, humanised monoclonal IgG1 antibody targeting both PD-1 and TIGIT receptors.[17]
- Rilvegostomig has shown preliminary efficacy, with an ORR of 62%, and an acceptable safety profile in patients with advanced/metastatic NSCLC with ≥50% PD-L1 expression on tumour cells and who were naïve to immune checkpoint inhibitors.[17]
- TROPION-Lung10 (NCT06357533) is evaluating the potential of the directed cytotoxicity of Dato-DXd, combined with the immune checkpoint inhibition of rilvegostomig as 1L treatment for patients with advanced/metastatic non-squamous NSCLC versus the current standard of care pembrolizumab.

TROPION-Lung10 (NCT06357533): A phase 3, randomised, open-label, global study



*The rilvegostomig monotherapy arm will be used to assess the contribution of components of the experimental arm.

Enrolment start: April 2024 | Enrolment is ongoing

Countries and regions with participating study sites

Australia, Austria, Belgium, Brazil, Canada, China, Germany, Hungary, India, Italy, Japan, Republic of Korea, Poland, Spain, Taiwan, Türkiye, United States of America, United Kingdom

Key inclusion criteria

- Age ≥18 years
- Histologically or cytologically documented non-squamous NSCLC
- Stage IIIB/C or stage IV NSCLC (based on the AJCC edition 8) not amenable to curative surgery or definitive chemoradiation
- Absence of sensitising *EGFR* mutations, *ALK* and *ROS1* rearrangements and negative results for any other known genomic alteration for which there are locally approved and available targeted 1L therapies
- ≥50% PD-L1 expression on tumour cells
- No prior chemotherapy or other systemic therapy for stage IIIB, IIIC or IV NSCLC
- Measurable disease per RECIST version 1.1
- ECOG PS 0 or 1
- Provision of a tumour sample to determine PD-L1 status, TROP2 status and other biomarkers prior to randomisation

Key exclusion criteria

- History of another primary malignancy within 3 years
- Severe or uncontrolled systemic diseases, including active bleeding diseases, active infection, and cardiac disease, or active or prior documented autoimmune or inflammatory disorders
- Clinically significant third-space fluid retention not amenable to repeated drainage
- History of non-infectious ILD/pneumonitis that required steroids, or current or suspected ILD/pneumonitis
- Significantly compromised pulmonary function
- Spinal cord compression, or brain metastases unless treated, no longer symptomatic and radiologically stable
- History of leptomeningeal carcinomatosis
- Clinically significant corneal disease
- Active infection with TB, HBV, HCV, HAV, or uncontrolled HIV infection
- History of active primary immunodeficiency

Key study endpoints

1° **Dual-primary endpoints:**

- PFS* and OS in the TROP2 QCS-NMR-positive population for Dato-DXd + rilvegostomig vs pembrolizumab

2°

		Dato-DXd + rilvegostomig vs pembrolizumab	Rilvegostomig monotherapy vs pembrolizumab	Dato-DXd + rilvegostomig vs rilvegostomig monotherapy
Secondary Endpoints	TROP2+ population	ORR* DoR* PFS2 Patient-reported outcomes	PFS* OS ORR* DoR*	
	Full analysis set	PFS* OS ORR* DoR* PFS2 Patient-reported outcomes		
	Safety analysis set	Safety and tolerability		-
		PK and immunogenicity of Dato-DXd + rilvegostomig and rilvegostomig monotherapy		

*Assessed by BICR per RECIST v1.1.
TROP2 biomarker status will be assessed using the TROP2 QCS-NMR assay. The full analysis set will include all randomised patients. The safety analysis set will include all randomised patients who have received ≥1 dose of study intervention and for whom any post-dose data are available. PK and immunogenicity analysis will be conducted in those in the safety analysis set who have ≥1 reportable PK concentration or ≥1 non-missing Dato-DXd or rilvegostomig ADA result at any time, respectively.

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Poster

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Abbreviations

1L, first line; ADA, anti-drug antibody; ADC, antibody-drug conjugate; AGA, actionable genomic alterations; AJCC, American Joint Committee on Cancer; ALK, anaplastic lymphoma kinase; BICR, blinded independent central review; CI, confidence interval; Dato-DXd, datopotamab deruxtecan; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; HAV/HBV/HCV, hepatitis A/B/C virus; HIV, human immunodeficiency virus; HR, hazard ratio; IgG1, immunoglobulin G1; ILD, interstitial lung disease; NE, not evaluable; NMR, normalised membrane ratio; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, disease progression; PD-(L)1, programmed cell death (ligand) 1; PFS, progression-free survival; PFS2, second PFS; PK, pharmacokinetics; PS, performance status; QCS, quantitative continuous scoring; Q3W, every 3 weeks; RECIST v1.1; Response Evaluation Criteria in Solid Tumors version 1.1; TB, tuberculosis; TIGIT, T cell immunoglobulin and ITIM domain; TROP2, trophoblast cell surface antigen-2.

Acknowledgments

The anti-TIGIT component of rilvegostomig is derived from COM902 developed by Compugen Ltd. This study (NCT06357533) is sponsored by AstraZeneca. In July 2020, Daiichi-Sankyo entered into a global development and commercialisation collaboration with AstraZeneca for datopotamab deruxtecan (Dato-DXd). Medical writing support for the development of this poster, under the direction of the authors, was provided by Ella Spencer, MSci, of Ashfield MedComms (London, UK), an Inizio Company, and was funded by AstraZeneca in accordance with Good Publication Practice (GPP) guidelines (http://www.ismpp.org/gpp-2022).

Disclosures

Thomas Newsom-Davis reports advisory board participation with AbbVie, Amgen, AstraZeneca, Bayer, Bristol-Myers Squibb, Boehringer Ingelheim, Daiichi-Sankyo, EQRx, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Merck Sharpe Dohme, Novartis, Novocure, Pfizer, Regeneron, Roche, Sanofi and Takeda, has been an invited speaker for Amgen, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, EQRx, Gilead, GlaxoSmithKline, Janssen, Lilly, Novartis, Roche and Takeda and a steering committee member for AstraZeneca, Merck Sharpe Dohme and Roche. For co-author disclosures, please refer to the abstract.

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17. Hiltermann TJN,

Poster presented at the European Lung Cancer Congress (ELCC) 2025; Paris, France; March 26–29 2025 by Thomas Newsom-Davis.
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elcc European Lung Cancer Congress 2025

Antiangiogénicos vs IO

Lung Cancer UPDATES ESMO HIGHLIGHTS 17 - 21 OCTUBRE 2025 Berlin, Germany

Phase III study of Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous NSCLC (HARMONi-6)

Study Design

A multicenter, randomized, double-blind, parallel-controlled phase III study

Key Eligibility Criteria
- Pathologically confirmed sq-NSCLC
- Stage IIIB-IV
- No prior systemic therapy
- No EGFR mutations or ALK rearrangements
- ECOG PS 0 or 1

R 1:1 N=532

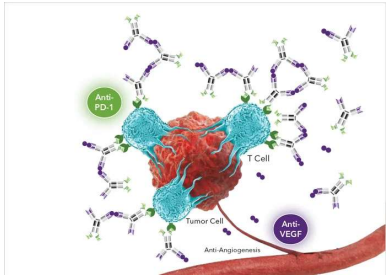
- Ivonescimab (20 mg/kg, Q3W) + Carboplatin (AUC 5, Q3W) + Paclitaxel (175 mg/m², Q3W) up to 4 cycles → Ivonescimab (20 mg/kg, Q3W) up to 24 months or unacceptable toxicity
- Tislelizumab (200 mg, Q3W) + Carboplatin (AUC 5, Q3W) + Paclitaxel (175 mg/m², Q3W) up to 4 cycles → Tislelizumab (200 mg, Q3W) up to 24 months or unacceptable toxicity

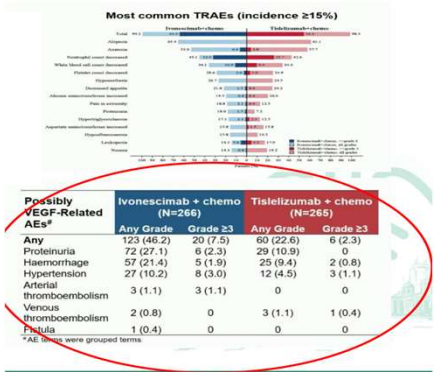
Stratification Factors:
- Stage: IIIB/IIIC vs. IV
- PD-L1 TPS: ≥1% vs. <1%

Endpoints:
- **Primary endpoint: PFS by IRRC per RECIST v1.1**
- Key secondary endpoint: OS
- Secondary endpoints: PFS by INV, ORR, DCR, DoR, TTR and safety

Data cutoff date: February 28, 2025

Mediana de seguimiento de 10 meses



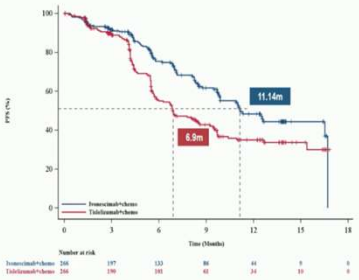


Possibly VEGF-Related AEs#	Ivonescimab + chemo (N=266)		Tislelizumab + chemo (N=265)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any	123 (46.2)	20 (7.5)	60 (22.6)	6 (2.3)
Proteinuria	72 (27.1)	6 (2.3)	29 (10.9)	0
Haemorrhage	57 (21.4)	5 (1.9)	25 (9.4)	2 (0.8)
Hypertension	27 (10.2)	8 (3.0)	12 (4.5)	3 (1.1)
Arterial thromboembolism	3 (1.1)	3 (1.1)	0	0
Venous thromboembolism	2 (0.8)	0	3 (1.1)	1 (0.4)
Fistula	1 (0.4)	0	0	0

#AE terms were grouped terms

Primary endpoint: PFS by IRRC

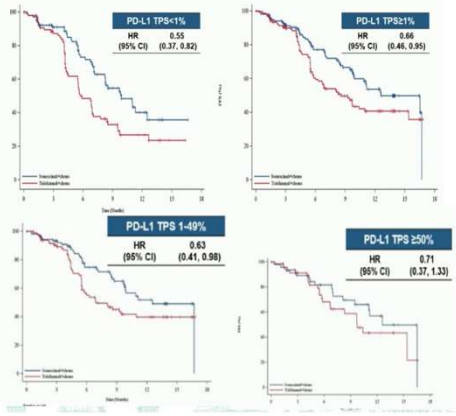
Ivonescimab+chemo demonstrated a statistically significant improvement in PFS vs. tislelizumab+chemo with HR=0.60, representing a 4.2 months improvement in mPFS.



	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
mPFS, months (95% CI)	11.14 (9.86, NE)	6.90 (5.82, 8.57)
Stratified HR (95% CI)	0.60 (0.46, 0.78)	
p-value	<0.0001	

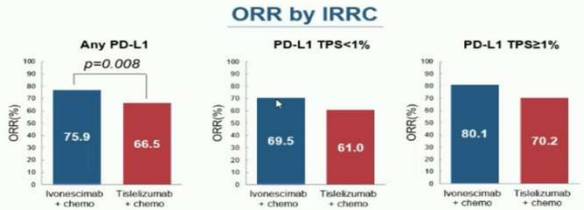
Median Follow-up: 10.28 months

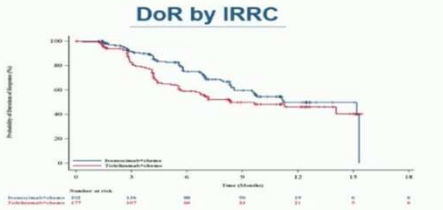
Consistent PFS benefit by investigator-assessment: HR = 0.64 (95% CI: 0.50, 0.84)



ORR and DoR by IRRC

Tumor response was higher and more durable in the ivonescimab arm.



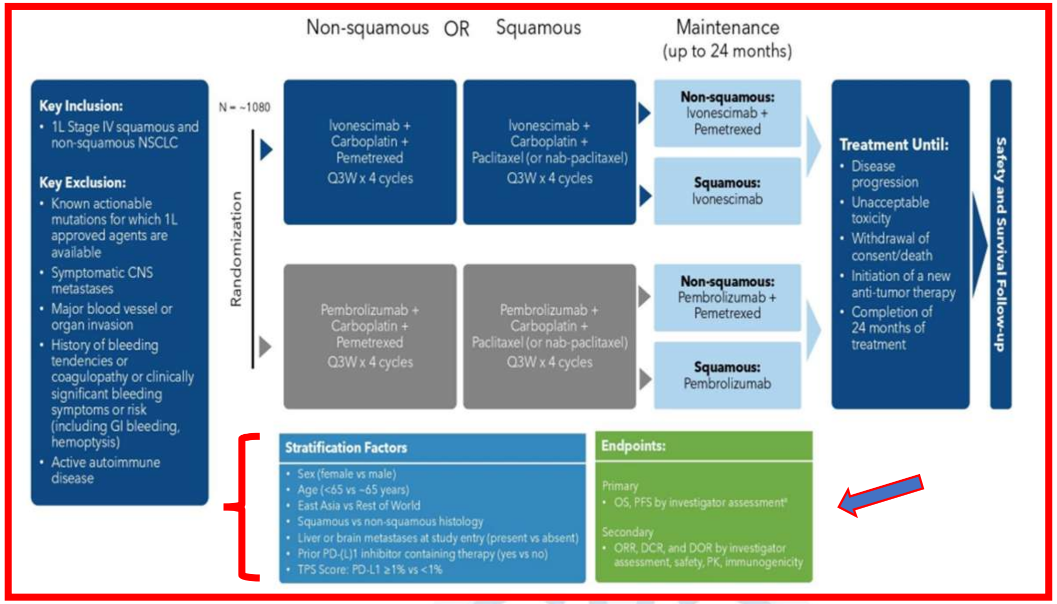


	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
BOR, n (%)		
CR	1 (0.4)	0
PR	201 (75.6)	177 (66.5)
SD	39 (14.7)	60 (22.6)
PD	6 (2.3)	15 (5.6)

	Ivonescimab + chemo (N=202)	Tislelizumab + chemo (N=177)
mDoR, months (95% CI)	11.20 (8.54, NE)	8.38 (5.72, NE)
p-value	0.0219	

Pendiente resultados…

Poster Bd#135b: HARMONi-3



Lung Cancer UPDATES
ASCO HIGHLIGHTS
30 MAYO - 03 JUNIO 2025
Chicago, USA

Antiangiogénicos + IO

2025 ASCO ANNUAL MEETING

CAMPASS: Benmelstobart in combination with anlotinib vs pembrolizumab in the first-line treatment of PD-L1 positive, advanced non-small cell lung cancer (aNSCLC): A randomized, blind, multicenter phase 3 study

Authors: Baohui Han[1], Kai Li[2], Runxiang Yang[3], Yongzhong Luo[4], Wei Zuo[5], Chao Xie[6], Qingshan Li[7], Xingxiang Xu[8], Qiang Liu[9], Yan Yu[10], Qiming Wang[11], Tienan Yi[12], Yongxing Chen[13], Hongmei Sun[14], Xuhong Min[15], Huaqiu Shi[16], Hualin Chen[17], Jianhua Shi[18], Jinsheng Shi[19], Junzhen Gao[20]

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Baohui Han MD
Shanghai Chest Hospital, Shanghai, China

Randomized, blind, multicenter phase 3 study (NCT04964479)

Key enrollment criteria

- Locally advanced or recurrent/metastatic NSCLC
- TPS ≥ 1%
- Age: 18-75; ECOG PS: 0-1
- Previous systemic treatment naïve
- No EGFR mutations, no ALK or ROS1 rearrangements
- No prior exposure of anti-angiogenic agents or immune checkpoint inhibitors

2:1
N = 531

- Benmelstobart 1200mg iv D1
- Anlotinib 12mg po, QD D1~D14
- 3 weeks / cycle

- Pembrolizumab 200mg iv D1
- Placebo 0mg po, QD D1~D14
- 3 weeks / cycle

Primary endpoint
- Progression-free survival (PFS) per RECIST 1.1 assessed by IRC

Secondary endpoints
- Overall survival (OS)
- Objective response rate (ORR)
- PFS per RECIST 1.1 by INV
- Disease control rate (DCR)
- Safety

Stratification factors:
- Histology: squamous vs. non-squamous
- Brain metastases: yes vs. no
- PD-L1 expression (TPS): ≥ 50% vs. 1-49%

Brazo comparador adecuado??

Abbreviation: IRC: independent review committee, INV: investigator, TPS: tumor proportion score

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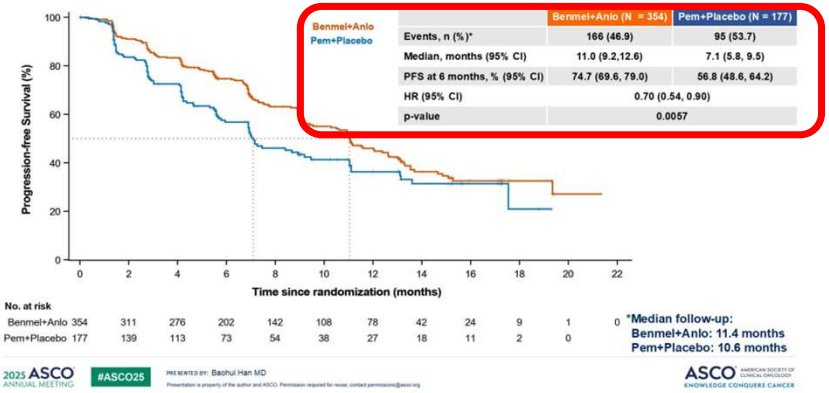
Results — Primary endpoint: PFS by IRC



	Benmel+Anlo (N = 354)	Pem+Placebo (N = 177)
Events, n (%)*	166 (46.9)	95 (53.7)
Median, months (95% CI)	11.0 (9.2,12.6)	7.1 (5.8, 9.5)
PFS at 6 months, % (95% CI)	74.7 (69.6, 79.0)	56.8 (48.6, 64.2)
HR (95% CI)	0.70 (0.54, 0.90)	
p-value	0.0057	

*Median follow-up:
Benmel+Anlo: 11.4 months
Pem+Placebo: 10.6 months

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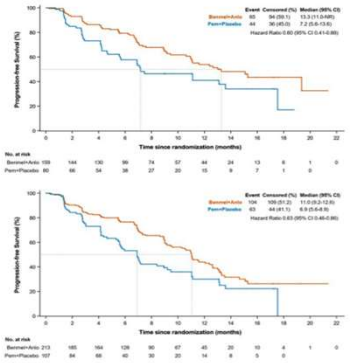
Key Pre-specified PFS Subgroup Analyses



TPS ≥ 50%	Benmel+Anlo	Pem+Placebo
N (%)	159 (44.9)	80 (45.2)
Median, months (95% CI)	13.3 (11.0, NE)	7.2 (5.6, 13.6)
HR (95% CI)	0.60 (0.41, 0.88)	

Squamous	Benmel+Anlo	Pem+Placebo
N (%)	213 (60.2)	107 (60.5)
Median, months (95% CI)	11.0 (9.2, 12.6)	6.9 (5.6, 8.9)
HR (95% CI)	0.63 (0.46, 0.86)	

Benmelstobart in combination with anlotinib vs pembrolizumab in the 1L

- **Key findings: Efficacy & Safety**
  - mPFS subgroup analysis: Squamous mPS 11 mo (HR 0.6); PD-L1 ≥ 50% 13.3 mo (HR 0.63)
  - Higher ORR 57 vs 40%
  - Safety: higher rates of grade ≥ 3 toxicities, but no increased rates of IRAEs or discontinuation

Antiangiogénico de mantenimiento tras QT + IO

2025 ASCO ANNUAL MEETING

Phase 3 study of benmelstobart in combination with chemotherapy followed by sequential combination with anlotinib for the first-line treatment of locally advanced or metastatic squamous non-small cell lung cancer (sq-NSCLC)

Yuankai Shi[1], Longhua Sun[2], Runxiang Yang[3], Dingzhi Huang[4], Yongzhong Luo[5], Haichuan Su[6], Qiang Liu[7], Peng Zhang[8], XingYa Li[9], Xiangjiao Meng[10], Yu Yao[11], Lingfeng Min[12], Yan Wang[13], Lei Yang[14], Conghua Xie[15], Junquan Yang[16], Jianhua Shi[17], Zhi Xu[18], Hongbo Wu[19], Honghai Wang[20]

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Yuankai Shi, Cancer Hospital, Chinese Academy of Medical Sciences

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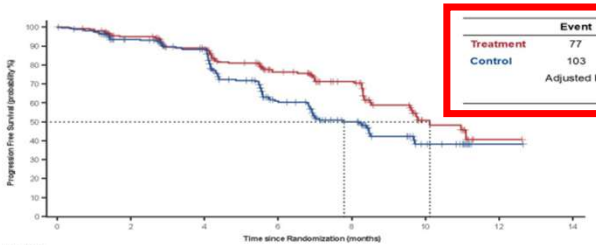
PFS (per RECIST version 1.1 by IRC, ITT), Interim Analysis



	Event	Censor (%)	Median (95 CI%)
Treatment	77	201 (72.30)	10.12 (8.54-NE)
Control	103	181 (63.73)	7.79 (6.87-9.69)
Adjusted Hazard Ratio 0.64 (98.35% CI 0.45-0.93)			
Stratified Log-rank P=0.0038			

a: Superiority boundary α=0.0165; Data cutoff date for this interim analysis: March 1, 2024. Median follow-up of PFS: 6.97 months (95%CI: 5.78, 7.62) vs. 6.87 months (95%CI: 5.62, 7.29).

Abbreviation: PFS, progression free survival; RECIST, Response Evaluation Criteria in Solid Tumors; IRC, Independent Review Committee; ITT, intent to treatment; NE, not estimated.

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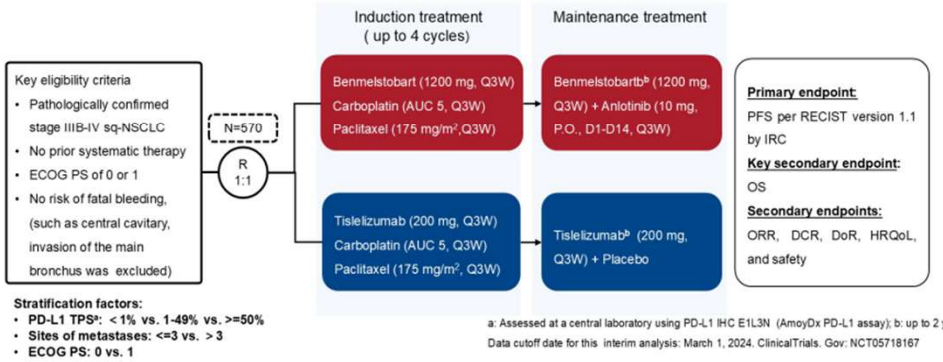
Study Design

TQB2450-III-12 is multicenter, randomized, double-blind, parallel-controlled phase III study



Stratification factors:

- **PD-L1 TPS[a]: < 1% vs. 1-49% vs. >=50%**
- **Sites of metastases: <=3 vs. > 3**
- **ECOG PS: 0 vs. 1**

a: Assessed at a central laboratory using PD-L1 IHC E1L3N (AmoyDx PD-L1 assay); b: up to 2 years;

Data cutoff date for this interim analysis: March 1, 2024. ClinicalTrials. Gov: NCT05718167

Abbreviation: sq, squamous; NSCLC, non-small cell lung cancer; ECOG, Eastern Cooperative Oncology Group, PS, Performance Status; PD-L1, programmed death ligand 1; TPS, , tumor proportion score; AUC, area under the curve; PFS, progression free survival; RECIST, Response Evaluation Criteria in Solid Tumors; IRC, Independent Review Committee; OS, overall survival; ORR, objective response rate; DCR, disease control rate; DoR, duration of response; HRQoL, health related quality of life.

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Conclusions

- Benmelstobart in combination with chemotherapy followed by sequential combination with anlotinib demonstrated a significantly improvement in PFS compared with tislelizumab plus chemotherapy for locally advanced or metastatic sq-NSCLC.
  - Median PFS: 10.12 (95% CI: 8.54, NE) vs. 7.79 (95% CI: 6.87, 9.69) months, HR 0.64 (98.35% CI: 0.45, 0.93), P=0.0038.
  - PFS benefit favored benmelstobart in combination with anlotinib group in almost all subgroups.
- Improvements in ORR, DCR, and a more durable tumor response were observed.
- OS was not matured at this interim analysis.
- Benmelstobart in combination with chemotherapy followed by sequential combination with anlotinib showed a manageable safety profile.

Benmelstobart in combination with chemotherapy followed by sequential combination with anlotinib might be a new first-line treatment option for sq-NSCLC.

Abbreviation: PFS, progression free survival; sq, squamous; NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval; NE, not estimated; ORR, objective response rate; DCR, disease control rate; OS, overall survival

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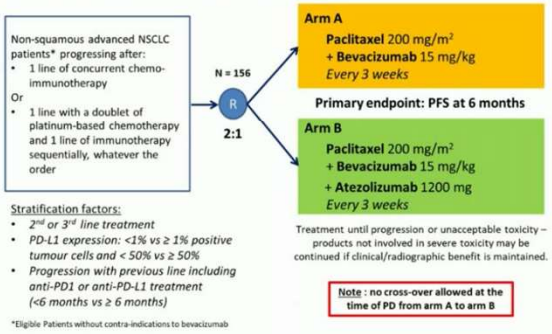
Antiangiogénicos +/- IO tras PD a QT + IO

Lung Cancer UPDATES ESMO HIGHLIGHTS 17 - 21 OCTUBRE 2025 Berlin, Germany

Paclitaxel-bevacizumab +/- atezolizumab in advanced non-squamous NSCLC progressing after chemo-immunotherapy

Trial design

- Open-label, randomized (2:1), non-comparative, multicenter phase II trial



- Primary endpoint : progression-free survival (PFS) rate at 6 months, assessed by independent review committee (IRC).
- Secondary endpoints : PFS by investigators, objective response rate (ORR), overall survival (OS), safety and quality of life.

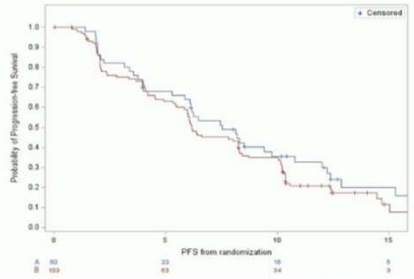
Primary endpoint: 6-month PFS rate by IRC in eligible pts

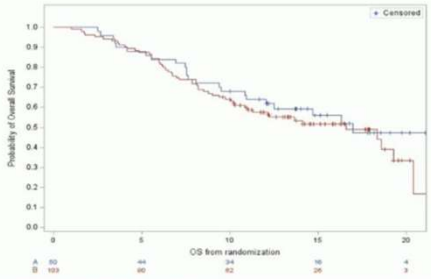
In eligible patients	A: paclitaxel + bevacizumab (N=50)	B: paclitaxel + bevacizumab + atezolizumab (N=103)
	6-month PFS rate: % [95% CI]	6-month PFS rate: % [95% CI]
By IRC	**52.0% [38.2-65.9]**	**40.8% [31.3-50.3]**
By Investigators	52.0% [38.2-65.9]	42.7% [33.2-52.3]

Reminder: NON COMPARATIVE trial design

Secondary endpoints :

- **ORR similar in both arms:** 42.0% in arm A, and 41.7% in arm B; **DCR:** 82.0% in arm A, and 76.7% in arm B.
- **Median PFS [95% CI]:** 7.5 [5.8-9.8] months in arm A, and 6.2 [5.5-8.2] months in arm B.
- **Median OS [95% CI]:** 17.0 [10.9-NR] months in arm A, and 16.6 [10.8-19.3] months in arm B





Metástasis en SNC

Mtx en SNC: QT + IO? ADCs?

NIVIPI-Brain

Treatment naïve patients with stage IV NSCLC with untreated brain metastases not amenable for SRS, *EGFR/ALK/ROS1* negative, any PD-L1, ECOG PS 0-1, measurable systemic and brain lesions

COHORT A (n=44)
Asymptomatic brain metastases and not receiving steroids
COHORT B (n=27)
Oligosymptomatic brain metastases controlled with low dose steroids (dexa ≤ 4mg qd)

Tumor evaluation by body CT scan and brain MRI
Q6W until the 12th week and thereafter Q9W until disease progression

NIVO 360mg Q3W + IPI 1mg/kg Q6W
+
Chemotherapy Q3W (2 cycles)*

Until disease progression#, unacceptable toxicity or a maximum of 2 years

*Non-squamous: CDDP or CBDCA + pemetrexed; squamous:CBDCA + paclitaxel

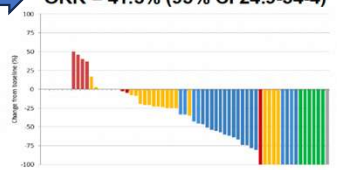
Primary endpoint:
Intracranial disease control rate (icDCR): percentage of patients without progression for at least 6 months, as asssessed by RANO-BM

Secondary endpoints:
- Intracranial and systemic ORR & PFS by RANO-BM and by RECIST v1.1 respectively
- Safety by CTCAE v5.0
- Overall Survival
- Time to brain RT and quality of life

#Patients with exclusive CNS PD were allowed to continue within the study after brain RT
CBDCA: carboplatin; CDDP: cisplatin; CT: computerized tomography; CTCAE: common toxicity criteria for adverse events; IPI: ipilimumab; MRI: magnetic resonance imaging; NIVO: nivolumab; ORR: overall response rate; PD: progression disease; RANO-BM: response assessment in neuro-oncology brain metastases; RECIST: response evaluation criteria in solid tumors; RT: radiotherapy

CNS Best ORR (by RANO-BM)

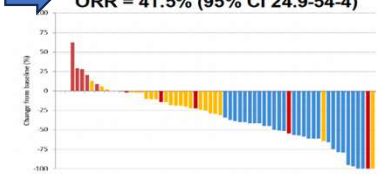
ORR = 41.5% (95% CI 24.9-54-4)



Clinical Benefit Rate (CBR) = 73.8%
6 CR, 21 RP and 21 SD

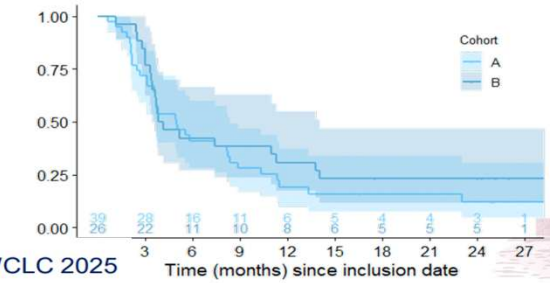
Systemic Best ORR (by RECIST)

ORR = 41.5% (95% CI 24.9-54-4)



Clinical Benefit Rate (CBR) = 78.4%
27 RP and 24 SD

Primary Endpoint: Intracranial DCR (by RANO-BM)



Cohort	Intracranial DCR
A	At 6 months 41% (95% CI 28-60)
B	At 5 months 46% (95% 31-79)

As the intracranial DCR is below 50%, the study did not achieve the expected efficacy

TROPION-Lung01

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

Key eligibility criteria

- NSCLC (stage IIIB, IIIC, or IV)
- ECOG PS 0 or 1
- No prior docetaxel
- **Patients with clinically inactive, asymptomatic brain metastases were eligible**

Without actionable genomic alterations:[a]
- 1–2 prior lines, including Pt-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*
- 1–2 prior approved targeted therapies + Pt-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

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

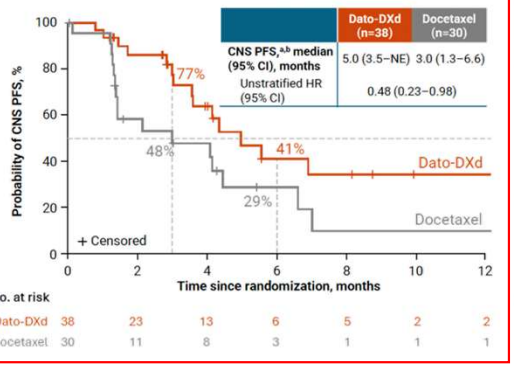
Dual primary end points:
- PFS by BICR per RECIST 1.1
- OS

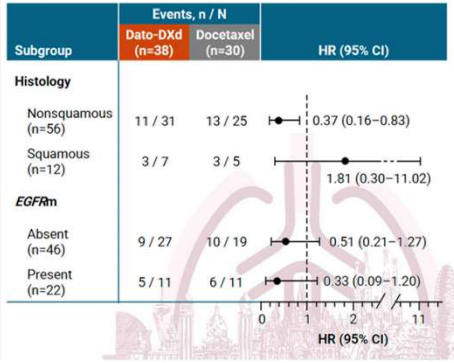
Post hoc analysis (intracranial activity):
- CNS ORR, DCR, and PFS, assessed by CNS BICR per CNS RECIST
- Percentage change from baseline in SOD in measurable brain metastases

	Dato-DXd (n=16)	Docetaxel (n=11)
CNS confirmed ORR,[a] % (95% CI)	38 (15–65)	0 (0–29)
CNS confirmed DCR,[a] % (95% CI)	88 (62–98)	36 (11–69)

CNS PFS

All Patients With Untreated BM or Progression After RT





Mtx en SNC: los chinos apuestan por los antiangiogénicos

BAP BRAIN

GECP lung cancer research

➢ Randomized, multi-center phase 3 study conducted across 11 centers in China (NCT01951482)

Main inclusion criteria:
- Non-squamous NSCLC
- EGFR-wild type and ALK negative
- Treatment naive
- Confirmed brain metastases by enhanced MRI
- Number of intracranial lesion either ≥ 3 or 1-2 unapplicable for local treatment
- At least one intracranial lesion ≥ 5mm

N=160

R 1：1

Experimental arm (BAP)
Bevacizumab 7.5mg/kg + pemetrexed-platinum[a] (IV, Q3W, 4-6 cycles) (N=80)

CR/PR/SD → Bevacizumab 7.5mg/kg + pemetrexed[a] (Q3W)

Control arm (AP)
Pemetrexed-platinum[a] (IV, Q3W, 4-6 cycles) (N=80)

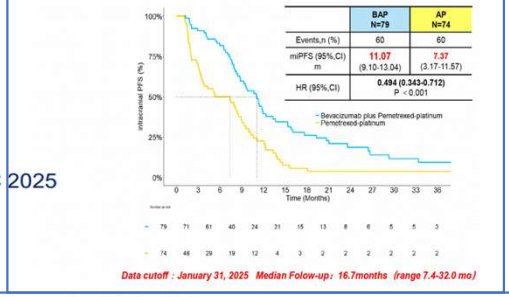
CR/PR/SD → Pemetrexed[a] (Q3W)

Until PD or intolerable toxicity

Primary endipoint: iPFS by INV (modified RECIST v1.1)

Secondary endpoints: PFS[b]、OS[b]、iORR[b]、iDCR[b]、ORR[b]、DCR[b]

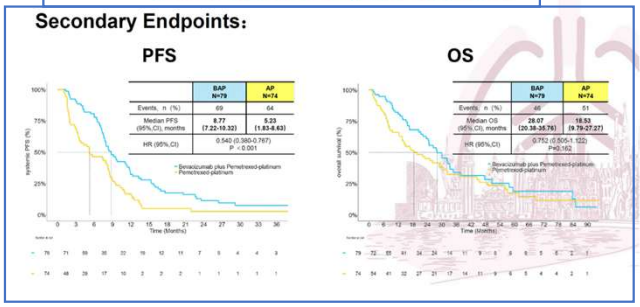
Primary Endpoint：iPFS



Data cutoff：January 31, 2025 Median Folow-up：16.7months (range 7.4-32.0 mo)

Chen WCLC 2025

Secondary Endpoints：



iPFSm: 11 vs 7m
PFSm: 8,7 vs 5,2m
OSm: 28 vs 18,5m
Folow Upm: 16,7m

SUPER BRAIN

GECP lung cancer research

Study Design (NCT05807893)

Study Design

Inclusion Criteria
- 18 to 75 years;
- Stage IV non-squamous NSCLC with untreated BMs confirmed by histopathology or cytology;
- MRI-confirmed brain parenchymal metastasis with ≥3 lesions; or 1-2 lesions unsuitable for or refused local treatment;
- ≥ 1 measurable lesion with a diameter ≥5mm in the brain;
- No EFGR sensitive gene mutation, no ALK/ROS1 gene fusion;
- ECOG PS score is 0-1;
- ...

Until PD, unacceptable toxicity, or death, for up to 2 years

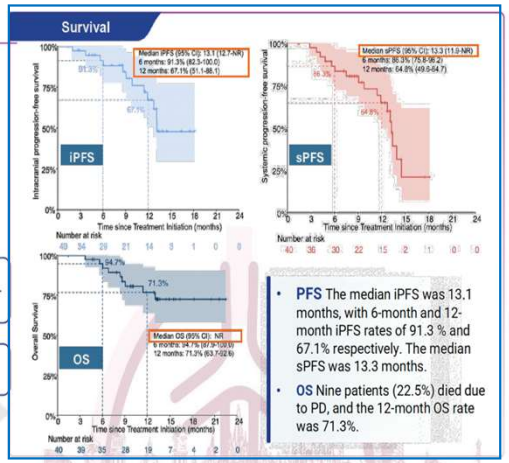
Patients accessed for eligibility → **40 enrolled** → **First line treatment** serplulimab combined with bevacizumab, pemetrexed, and carboplatin → 4-6 cycles → **maintenance therapy** serplulimab plus bevacizumab and pemetrexed

→ **Primary endpoint** intracranial progression-free survival (iPFS)

→ **Secondary endpoint** PFS, OS, ORR, Safety

median follow-up time: 13.3 months (95% CI: 13.0–13.5) 17 February 2025

Survival



- **PFS** The median iPFS was 13.1 months, with 6-month and 12-month iPFS rates of 91.3 % and 67.1% respectively. The median sPFS was 13.3 months.
- **OS** Nine patients (22.5%) died due to PD, and the 12-month OS rate was 71.3%.

ORR intracraneal: 84%
ORR extracraneal: 64%

Yu WCLC 2025

iPFSm: 13,1m
PFSm: 13,3m
OSm: NA; 71,3% vivos a 12m
Follow Upm: 13,3m

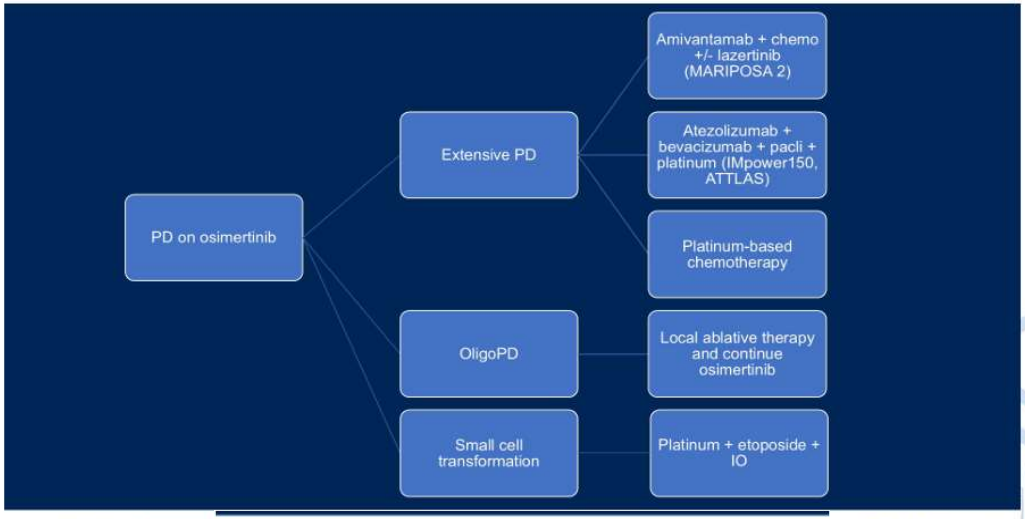
- Adenocarcinoma con Mtx SNC (RM)
  - >3 ó 1-2 no subsidiarias de tto local
  - Al menos 1 > 5 mm
- No mutados (EGFR, ALK)
- 1ª línea

Terapias dirigidas

EGFRm

EGFR

Tratamiento a la progresion



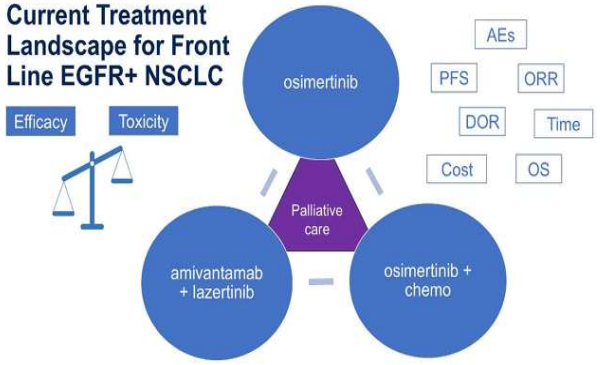
2025 ASCO ANNUAL MEETING #ASCO25

Prof Vanita Noronha, Mumbai (India)

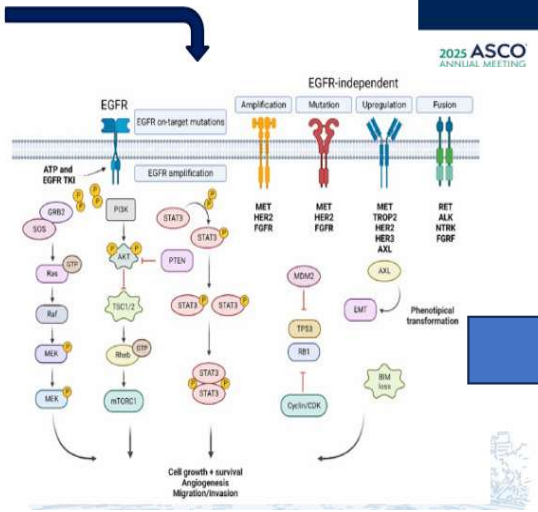
EGFR

Decision

Current Treatment Landscape for Front Line EGFR+ NSCLC



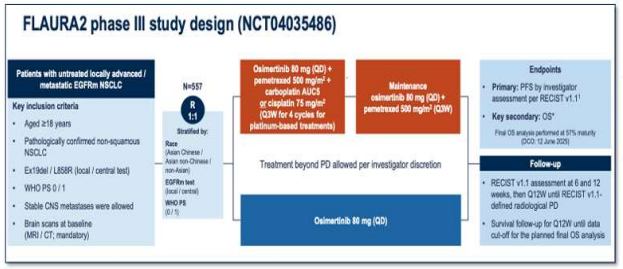
Baumann ASCO 2025



2025 ASCO ANNUAL MEETING

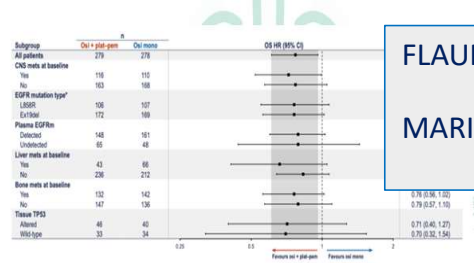
EGFRm: FLAURA 2 vs MARIPOSA

FLAURA 2: exploratory OS analyses in patients with poorer prognostic factors treated with Osimertinib +/- platinum-pemetrexed as first line treatment for EGFR-mutated advanced NSCLC



Exploratory OS analyses were based on the following baseline prognostic factors:

- CNS metastases (yes vs no)
- Bone metastases (yes vs no)
- Liver metastases (yes vs no)
- EGFR L858R mutation (vs Ex19del)
- Tissue TP53 alteration (vs wild-type)
- Plasma EGFRm ctDNA (detected vs undetected)

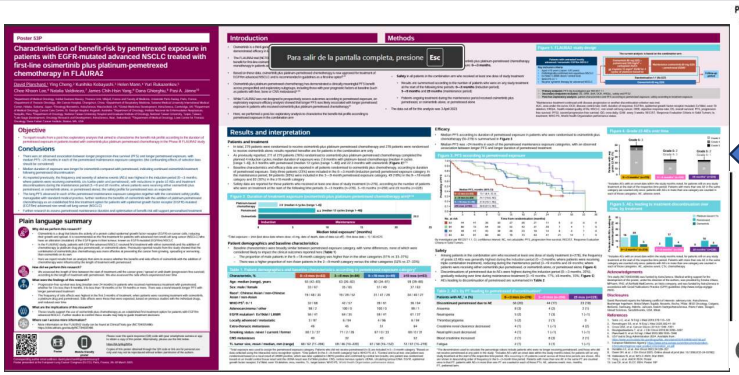


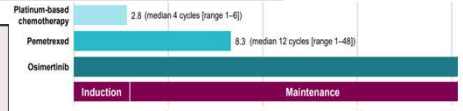
FLAURA:

- SG a 48m: 49 vs 41%

MARIPOSA:

- SG a 42m: 56 vs 44%





Median PFS, months (95% CI)

0–<3 mos (n=63)	13.1 (8.4, 22.2)
3–<9 mos (n=84)	24.7 (19.6, NC)
9–<18 mos (n=49)	27.6 (16.7, NC)
≥18 mos (n=83)	30.6 (27.4, NC)

elcc European Lung Cancer Congress 2025

Phase 3 MARIPOSA Study Design

MARIPOSA Ami + Laz in 1L EGFR+ NSCLC

Focus of this presentation

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 (yes or no)

2:2:1 Randomization (N=1074)

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

Lazertinib monotherapy arm was included to assess the contribution of components

Primary endpoint:

- PFS by BICR per RECIST v1.1

Key secondary endpoint:

- Protocol-specified final overall survival[b]

Other endpoints reported in this presentation:

- Intracranial PFS (icPFS)
- Intracranial ORR (icORR)
- Intracranial DoR (icDoR)
- Time to symptomatic progression (TTSP)
- Safety

Serial brain MRIs were required for all participants
MARIPOSA did not allow treatment crossover[a]

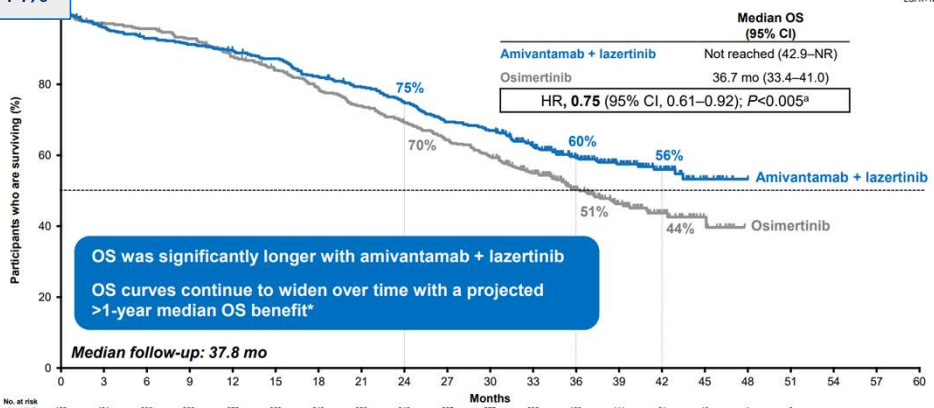
OS was a key secondary endpoint with prespecified alpha to assess significance

MARIPOSA: Overall Survival

MARIPOSA Ami + Laz in 1L EGFR+ NSCLC

Median OS (95% CI)	
Amivantamab + lazertinib	Not reached (42.9–NR)
Osimertinib	36.7 mo (33.4–41.0)

HR, **0.75** (95% CI, 0.61–0.92); *P*<0.005[a]



OS was significantly longer with amivantamab + lazertinib

OS curves continue to widen over time with a projected >1-year median OS benefit*

Median follow-up: 37.8 mo

*Based on an exponential distribution assumption of OS in both arms, the improvement in median OS is projected to exceed 1 year.

Note: Last participant was enrolled in May 2022. Clinical cutoff date was December 4, 2024. In total, 390 deaths had occurred in the amivantamab + lazertinib (173 deaths) and osimertinib (217 deaths) arms.

[a]P-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified Cox regression model.

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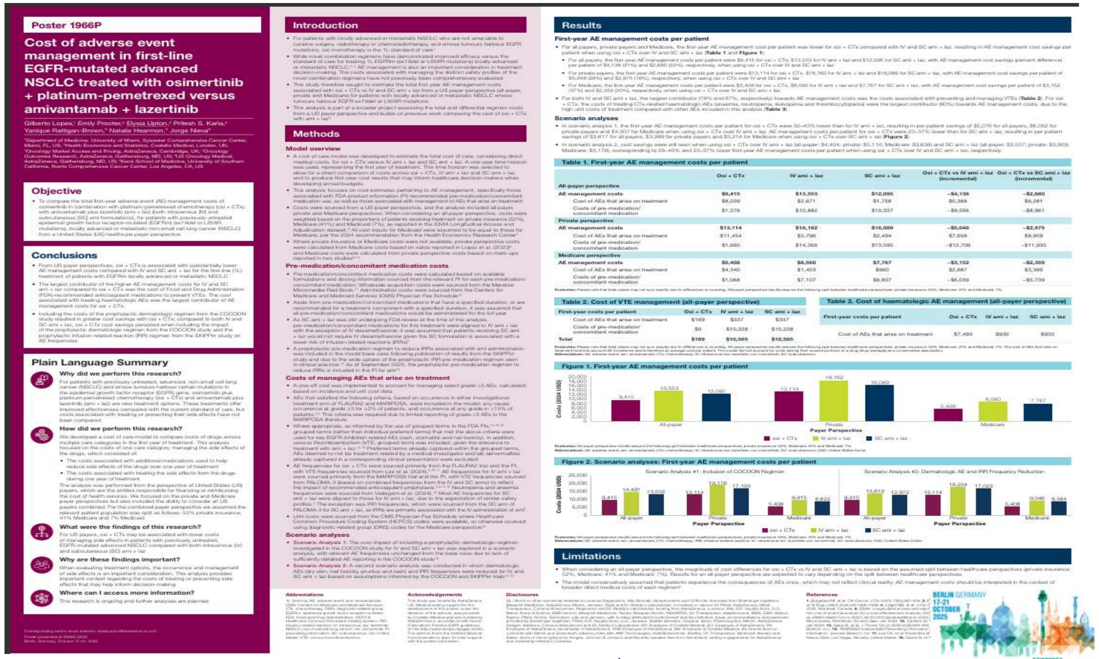
EGFRm

EGFR mutations

FLAURA vs FLAURA 2 vs MARIPOSA trial

	Osimertinib	Osimertinib-Pemetrexed-carboplatin	Amivantamab-Lazertinib
Study	FLAURA	FLAURA2	MARIPOSA
Efficacy	PFS 18.9 m **OS 38.6 m v 31.8 m**	PFS 25.5 m **Δ 9.9 m** **OS 47.5 m v 37.6 m (HR 0.77)**	PFS 23.7 m **Δ12 m+** **OS Not reached v 36.7 m (HR 0.75)**
Side effects (all grades)	Diarrhoea 42% Rash 22% Paronychia 27% Neutropenia 4% Neutrophil count decreased 7% Anaemia 11%	Diarrhoea 46% Rash 30% Paronychia 26% Neutropenia 25% Neutrophil count decreased 24% Anaemia 48% (G3 20%) Creatinine increase 14%	Diarrhoea 32% Rash 64% Paronychia 69% Infusion related reaction 65% Peripheral edema 38% Venous thromboembolism 40% Anaemia 27%
Supportive care	Emollient cream, steroid creams	Emollient cream, steroid creams Cytopenias/ mouthwashes	Emollient cream, steroid creams Prophylactic antibiotics, anticoagulation
Schedule	Daily oral tablet Visit every 2-3 months	Daily oral tablet, Iv Infusion once every 3 weeks	Daily oral tablet, Infusion/ subcut once per week for first 4 weeks; once every 2 weeks thereafter
Financial	$	$$	$$$$

David Planchard et al WCLC 2025 , Soria JC et al N Engl J Med. 2018, Cho BC et al N Engl J Med. 2024



COCOON Study Conclusions

- At the first pre-planned interim analysis, **the primary endpoint was met: The prophylactic COCOON DM regimen significantly reduced the incidence of grade ≥2 dermatologic AEs**[a] vs SoC DM in the first 12 weeks
  - Incidence of **grade ≥2 dermatologic AEs was reduced by 50%** with COCOON DM vs SoC DM (*P*<0.0001)
  - **Grade 3 dermatologic AEs were reduced by >50%** with COCOON DM vs SoC DM
  - **>3-fold reduction in moderate to severe scalp dermatologic AEs** with COCOON DM compared with SoC DM
- **~50% reduction in discontinuations due to AEs** with COCOON DM vs SoC DM allows participants to remain on treatment
- The COCOON DM and SoC DM arms are fully enrolled (N=201) with additional results planned at upcoming congresses[b]

The prophylactic COCOON DM regimen, with widely available and easy-to-use agents, significantly reduced the incidence and severity of dermatologic AEs with amivantamab + lazertinib

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Preventing AEs with Amivantamab + Lazertinib

Begin Amivantamab + Lazertinib

IRR Prophylactic Regimen (SKIPPirr)[1]	VTE Prophylactic Regimen (PALOMA-2, PALOMA-3)[2,3]
2 Days to 1 hour before start Oral 8-mg dexamethasone BID 2 days and 1 day prior and 8-mg 1 hour before first infusion[a]	First 4 months Oral anticoagulants as per NCCN or local guidelines

Dermatologic Prophylactic Regimen (COCOON)[b]

Antibiotic prophylaxis	Weeks 1–12 100-mg BID doxycycline or minocycline	Weeks 13+ 1% Topical clindamycin lotion on the scalp daily
Nail cleaning agent	Weeks 1+ 4% Chlorhexidine on the fingernails and toenails daily for 12 months	
Long-acting skin hydration	Weeks 1+ Ceramide-based moisturizer at least daily for 12 months[c]	

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Conclusions

- From US payer perspectives, osi + CTx is associated with substantially lower AE management costs compared with IV and SC ami + laz for the first-line (1L) treatment of patients with EGFRm locally advanced or metastatic NSCLC
- The largest contributor of the higher AE management costs for IV and SC ami + laz compared to osi + CTx was the cost of Food and Drug Administration (FDA)-recommended anticoagulant medications to prevent VTEs. The cost associated with treating haematologic AEs was the largest contributor of AE management costs for osi + CTx
- Including the costs of the prophylactic dermatologic regimen from the COCOON study resulted in greater cost savings with osi + CTx; compared to both IV and SC ami + laz, osi + CTx cost savings persisted when including the impact of the prophylactic dermatologic regimen from the COCOON study and the prophylactic infusion-related reaction (IRR) regimen from the SKIPPirr study on AE frequencies

Alternativas terapéuticas en 2L EGFR mut+

Study	Regimen	Phase	PFS	HR for PFS	OS	Gr ≥ 3 tox	Remarks
MARIPOSA-2	**Amivantamab + chemo**	III	6.3 vs 4.2	0.48 (0.36-0.64); P < 0.001	17.7 vs 15.3; HR=0.73, P=0.039	72% vs 48%	Approved in US, EU, Japan, China, etc; OS data still immature
	Amivantamab + lazertinib + chemo		8.3 vs 4.2	0.44 (0.35-0.56); P < 0.001	NA	92% vs 48%	
HARMONi (Global)	**Ivonescimab + chemo vs chemo (Press release!)**	III	Not disclosed (HARMONi-A: 7.1 vs 4.8)	0.52 (0.41-0.66); P<0.00001	16,8 vs14; HR 0,78 (0,62-0,98); p=0,0332	56% vs 50%	OS immature. Drug approved in China
IMpower150	**Atezo + bev + pacli + carbo (ABCP vs BCP)**	III (subset)	NR	NR	27.8 vs 18.1; HR, 0.74 (0.38-1.46)	52.1% vs 54.5%	Exploratory subset analysis
ATTLAS	**Atezo + bev + pacli + carbo (ABCP) vs chemo**	III	8.5 vs 5.6	0.62 (0.45-0.86); P=0.004	20.6 vs 20.2; HR. 2.02 (0.69-1.46), P=0.975	40.4% vs 21.6%	PFS positive, OS negative
SACHI (*MET*amp)	**Osi + savolitinib vs chemo**	III	8.2 vs 4.5	0.34 (0.23-0.49); P<0.0001	22.9 vs 17.7; HR, 0.84 (0.55-1.29)	57% vs 57%	Only available in China
HERTHENA-Lung02	**HER3-DXd vs chemo**	III	5.8 vs 5.4	0.77 (0.63-0.94); P=0.011	16.0 vs 15.9; HR, 0.98 (0.79-1.22)	57.9% vs 46.1%	Drug will not be marketed
OptiTROP-Lung03	**Sacituzumab tirumotecan vs docetaxel**	II	6.9 vs 2.8	0.30 (0.20-0.46); P<0.0001	NR vs NR; HR, 0.49 (0.27-0.88); P=0.0070	56% vs 71.7%	FDA breakthroug therapy designation
OptiTROP-Lung 04	**Saci-TMT vs platino +pemetrexed**	III	8,3 vs 4,3	0,6 (0,39-0,62); p<0,0001	NR vs 17,4; HR 0,6		

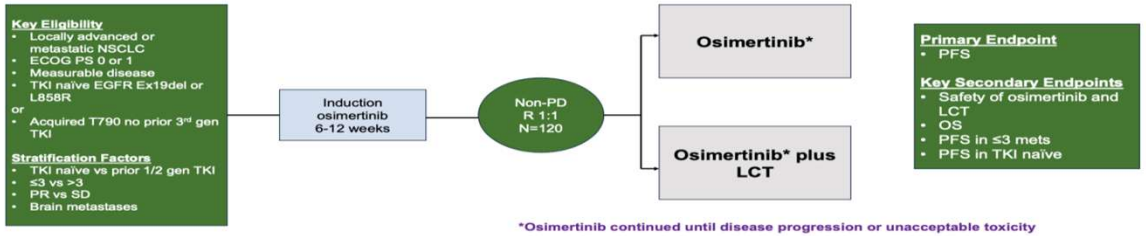
Name	Design	N	Inclusion criteria	Endpoints	Results
SAVANNAH	Phase 2 study of osimertinib + savolitinib	172	PD post 1-3 cycles of EGFR TKI, METamp (IHC 90%, FISH 10+)	1º: ORR	ORR: 55% mPFS: 7.5 mths (6.4-11.3) Grade≥3 AEs: 56.4%
ORCHARD	Phase 2 platform trial evaluating resistance to osi	30 (interim-20)	PD on 1L osimertinib with MET alterations on NGS	1º: ORR	ORR: 41% Grade≥3 AEs: 30%
SAFFRON	Phase 3 comparing osimertinib + savolitinib vs pem + carbo	324	Chemo naïve, PS 0-1, received osimertinib as 1st or 2nd line therapy	1º: PFS	NA
FLOWERS/CTONG2008	Ph 2 RCT comparing osi +/- savolitinib	44	Chemo naïve, EGFRm and METamp (IHC/NGS)	1º: ORR	ORR: 90.5% vs 60.9% mPFS: 19.6 vs 9.3; HR=0.8 (0.19-1.81); Gr≥3 AEs: 57.1% vs 8.7%

NORTHSTAR: a phase II randomized study of Osimertinib with or without local consolidative therapy for metastatic EGFR mutant NSCLC

Lung Cancer UPDATES ESMO HIGHLIGHTS 17 - 21 OCTUBRE 2025 Berlin, Germany

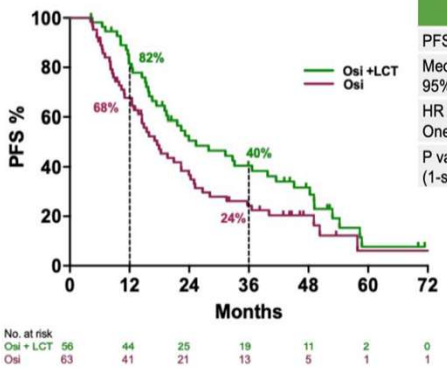
NorthStar Study Design

Randomized, multicenter, phase II trial, NCT03410043



*Osimertinib continued until disease progression or unacceptable toxicity

Progression Free Survival



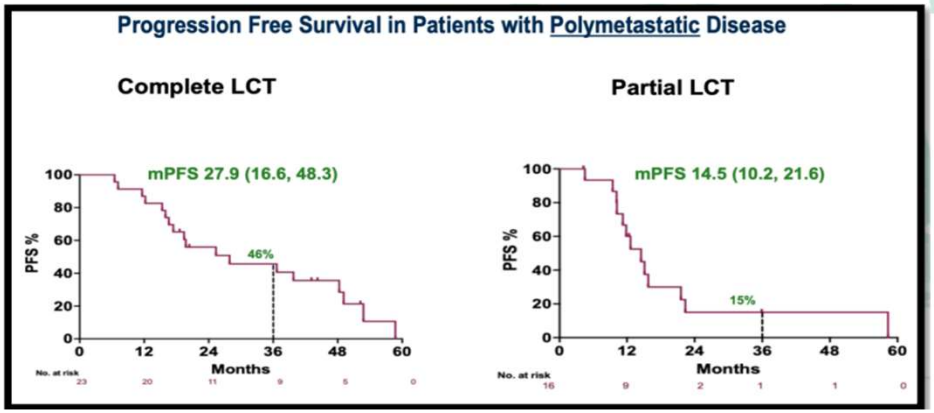
	Osimertinib (n=63)	Osimertinib plus LCT (n=56)
PFS events, n (%)	50 (79.3%)	42 (75%)
Median PFS month 95% CI	17.5 (14.5, 24.3)	25.3 (19.4, 45.0)
HR One-sided 90% CI	0.66 0.50 - 0.87	
P value (1-sided log rank)	0.025	

Demographics and Baseline Characteristics

Characteristics	Osimertinib (n=63)	Osimertinib plus LCT (n=56)
Age, median (range), y	64 (31-82)	66 (40-88)
Women	42 (66.7%)	37 (66.1%)
***EGFR* mutation subtype**		
Ex19del	42 (66.7%)	32 (57.1%)
L858R	18 (28.5%)	22 (39.3%)
T790M (with L858R or Ex19del)	3 (4.8%)	2 (3.6%)
No of Metastases at baseline		
greater than 3	45 (71.4%)	39 (69.6%)
less than or equal 3	18 (28.6%)	17 (30.30%)
No of metastases at randomization*		
greater than 3	37 (58.7%)	32 (57.1%)
less than or equal 3	26 (41.3%)	24 (42.9%)
Brain metastasis*		
yes	23 (36.5%)	21 (37.5%)
no	40 (63.5%)	35 (62.5%)
Response to induction osimertinib*		
PR	43 (68.3%)	40 (71.4%)
SD	20 (31.7%)	16 (28.6%)
Prior Therapy*		
TKI naïve	60 (95.2%)	54 (96.4%)
1st or 2nd generation TKI	3 (4.8%)	2 (3.6%)

	n (%)
LCT modality n=56	
Radiation	33 (58.9%)
Surgery	17 (32.1%)
Surgery and radiation	6 (9%)
Type of surgery n=23	
Lobectomy	18 (78.3%)
Lobectomy and wedge resection	1 (4.3%)
Wedge resection	2 (8.7%)
Segmentectomy	1 (4.3%)
Adrenalectomy	1 (4.3%)
Radiation modality n=50, 39 patients	
VMAT or IMRT	28 (56%)
SBRT	15 (30%)
3D conformal or 2D conformal	7 (14%)

Progression Free Survival in Patients with Polymetastatic Disease



Adverse Event	Osimertinib plus LCT (n=56)		
	Grade 1	Grade 2	Grade 3
Pneumonitis	1 (1.8%)	5 (8.9%)	1 (1.8%)

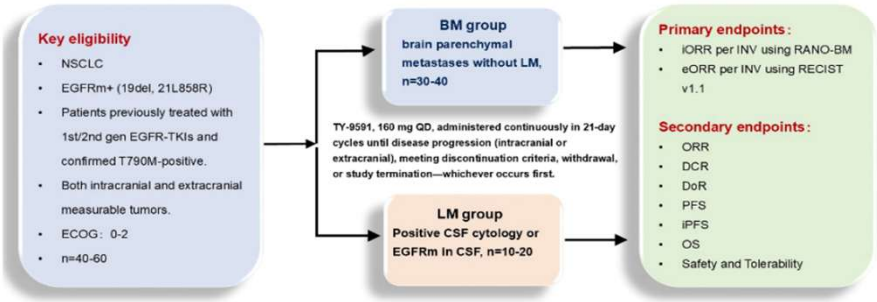
EGFRm con Mtx en SNC tras PD a TKI

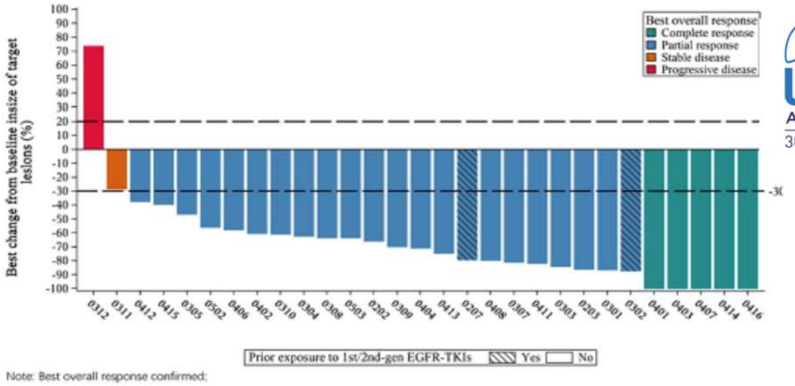
EGFR. Brain mets after 1-2G TKI

Oral abstract 2004. Asandeurtenib TY 9591 Phase 1

Significantly Reduces Toxic Metabolites of Osimertini via Deuteration Technology

- Structural similarity to osimertinib, with comparable efficacy and development potential.
- Deuteration technology enhances metabolic stability by blocking key metabolic sites, thus significantly **reduces formation of the toxic metabolite TY-9591-D1 (AZ5104).**
- Potential for improved efficacy and lower toxicity, leading to a broader therapeutic window.





Lung Cancer UPDATES ASCO HIGHLIGHTS 30 MAYO - 03 JUNIO 2025 Chicago, USA

Figure 2. Waterfall plot of the best variation of the sum of the longest diameters of intracranial target lesions from baseline

- Asandeutertinib treatment showed improvement in ORR, DCR, iPFS and PFS.
- Median iPFS, DOR, and OS were not reached when the trial was completed.

Table 3. Secondary Efficacy Results

	ORR (%; 95%CI)	DCR (%; 95%CI)	PFS (months; 95%CI)	iPFS (months; 95%CI)	12m-iPFS (%; 95%CI)
All patients (n=29)	82.8 (64.2 - 94.2)	96.6 (82.2 - 99.9)	13.5 (12.5 - NA)	NA (14.7 - NA)	96.6 (77.9 - 99.5)
Treatment naïve (n=27)	81.5 (61.9 - 93.7)	96.3 (81.0 - 99.9)	15.1 (12.5 - NA)	NA	96.3 (76.5-99.5)

FASE III VS OSIMERTINIB EN BM

ALEX: randomised, open-label, Phase 3 multicentre study

Key eligibility criteria

- Histologically/cytologically confirmed advanced *ALK*-positive NSCLC (by Ventana IHC)
- Aged ≥18 years
- ECOG PS 0–2
- No prior systemic therapy for advanced disease

R 1:1

Alectinib (600 mg BID)

Imaging every eight weeks until PD/death

Crizotinib (250 mg BID)

Treat until PD, unacceptable toxicity, withdrawal or death

No crossover permitted before PD

Stratification factors

- ECOG PS (0 or 1 vs 2)
- Race (Asian vs non-Asian)
- Baseline CNS metastases (yes vs no)

Primary endpoint

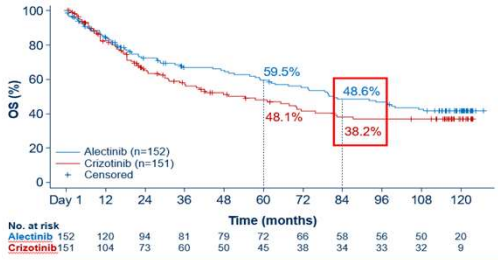
- PFS per investigator using RECIST v1.1

Secondary endpoints

- PFS by IRC
- Time to CNS progression
- ORR
- DoR
- OS; safety

OS in the ITT population

- Median follow-up was 53.5 months with alectinib and 23.3 months with crizotinib
- 7-year OS rate: 48.6% with alectinib vs 38.2% with crizotinib



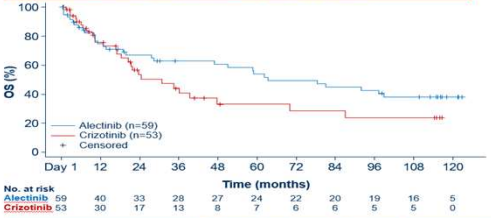
	Alectinib (n=152)	Crizotinib (n=151)
Patients with event, n (%)	76 (**50.0**)	73 (**48.3**)
Median, months (95% CI)	**81.1** (62.3–NE)	**54.2** (34.6–75.6)
Stratified HR (95% CI)	**0.78** (0.56–1.08)	
p-value (stratified log-rank)	0.1320	

Alectinib induced a clinically meaningful **OS benefit** compared with **crizotinib**

OS by CNS metastases* at baseline

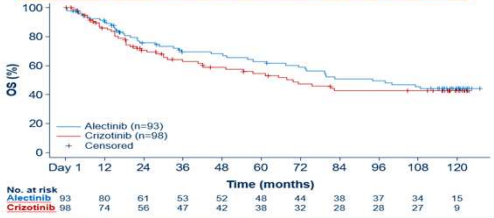
Patients with CNS metastases at baseline

- Median OS: 63.4 months with alectinib vs 30.9 months with crizotinib (HR 0.68; 95% CI 0.40–1.15)



Patients without CNS metastases at baseline

- Median OS: 94.0 months with alectinib vs 69.8 months with crizotinib (HR 0.87; 95% CI 0.58–1.32)



Alectinib induced a clinically meaningful **OS benefit** compared with **crizotinib** in patients both **with** and **without CNS metastases**

NCT02075840. Data cut-off date: 28 April 202
*Assessed by investigato

Prof. Tony Mok

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ESMO congress

ALK+

Abstract 8589

Depth of response and progression-free survival in patients with advanced *ALK*-positive non-small cell lung cancer treated with lorlatinib

Conclusions

- With lorlatinib treatment, 80% of patients experienced >50% shrinkage in target lesion, and 34% had >75% shrinkage in target lesion
- Greater depth of response (DepOR) was associated with longer progression-free survival (PFS) in patients with advanced anaplastic lymphoma kinase (*ALK*)-positive non-small cell lung cancer (NSCLC) treated with lorlatinib
  - The probability of remaining progression free at 5 years was 75% in patients with DepOR of >75%-100%, compared with 37% in patients with DepOR of 0%-50%
- No differences were observed in *ALK* fusion variants in the DepOR groups
- No association was observed between DepOR and circulating tumor DNA (ctDNA) clearance status

Rosario García Campelo,[1]

Abstract 8590

Impact of lorlatinib dose modifications on adverse event outcomes in the phase 3 CROWN study

Conclusions

- In the phase 3 CROWN study, about one-third of the patients treated with lorlatinib had 1 or 2 dose reductions
- Median time to dose reduction to the 75-mg dose was 7.1 months, and median time to dose reduction to the 50-mg dose was 11.3 months
- Dose reductions enabled patients to continue treatment with a median duration post reduction of 42.2 months for the duration on 75-mg dose and 20.7 months for the duration on 50-mg dose
- This post hoc analysis showed that dose reductions were effective in managing AEs associated with lorlatinib, with most evaluable events partially or completely resolved with 1 or 2 dose reductions
- These findings show the importance of dose modifications to mitigate toxicity and continue lorlatinib treatment for prolonged periods of time in patients with advanced *ALK*-positive NSCLC

Geoffrey Liu,[1] E

2025 ASCO ANNUAL MEETING

KRYSTAL 7

KRAS

Key eligibility criteria
- Advanced, unresectable or metastatic NSCLC with *KRAS*^{G12C} mutation[b]
- No prior systemic therapy for locally advanced/metastatic disease[c]
- Known PD-L1 TPS (local or central testing)[d]
- Treated, neurologically stable brain metastases allowed

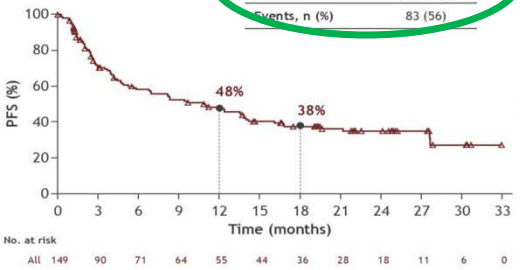
ADA 400 mg PO BID + PEMBRO 200 mg IV Q3W[e,f]

Primary endpoint
- ORR per investigator assessment (RECIST v1.1)

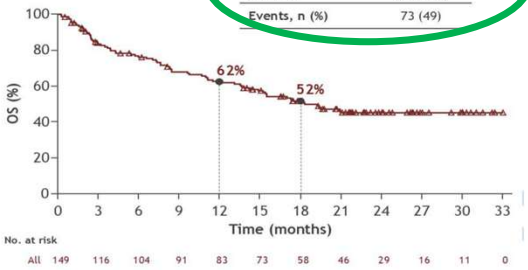
Secondary endpoints
- DOR and PFS per investigator assessment
- OS
- Safety

PFS[a] and OS[b] in all patien

PFS	All patients (N = 149)
Median PFS, mo (95% CI)	11.0 (5.8-14.0)
Events, n (%)	83 (56)



OS	All patients (N = 149)
Median OS, mo (95% CI)	18.3 (14.3-NE)
Events, n (%)	73 (49)



- A total of 45 (30%) patients received subsequent anticancer therapy, the most common being chemotherapy (n = 21) and chemotherapy with checkpoint inhibitor therapy (n = 9)

Rapid oral Abstract 8519. Olomorasib + Pembrolizumab all PDL1 levels

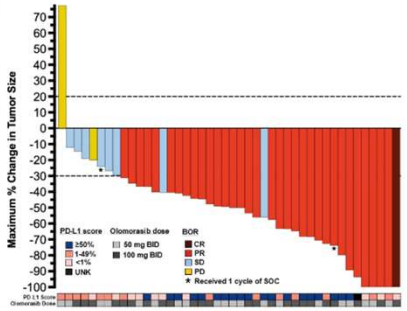
Part G: 1L NSCLC
Olomorasib + pembrolizumab[a]
Randomized 1:1[b]
(n=43)

Part G Eligibility
- No prior therapy for metastatic disease[c]
- All PD-L1 expression permitted

Key objectives
- Safety and Tolerability
- Determine MTD and R2PD
- Pharmacokinetics
- ORR, DCR, PFS and DoR per RECIST v1.1

Efficacy of 1L Olomorasib + Pembrolizumab

ORR 90% PDL1 > 50%



Efficacy Evaluable Patients[a]	Olomorasib + Pembrolizumab All n=46	Olomorasib + Pembrolizumab PD-L1 ≥50% n=20
BOR, n (%)		
CR	1 (2)	0 (0)
PR	33 (72)	18 (90)
SD	8 (17)	1 (5)
PD	3 (7)[b]	1 (5)[b]
NE	1 (2)	0 (0)
ORR, % (95% CI)[c]	**74 (58.9-85.7)**	**90 (68.3-98.8)**
DCR, % (95% CI)	91 (79.2-97.6)	95 (75.1-99.9)
Median DOR, months (95% CI)	NE (10.5-NE)	NE (10.5-NE)
Median PFS, months (95% CI)	NE (12.0-NE)	NE (12.0-NE)
6-month PFS rate, % (95% CI)	80.2 (64.1-89.6)	89.7 (64.8-97.3)
12-month PFS rate, % (95% CI)	66.7 (40.9-83.2)	59.8 (8.2-90.0)

Oral Abstract 8500. KRYSTAL 7 Phase 2 . Adagrasib 400mg + Pembrolizumab all PDL1

Toxicity

Patients, n (%)	PD-L1 < 50% (n = 95)	PD-L1 ≥ 50% (n = 54)	All patients (N = 149)
TRAEs			
Any grade	91 (96)	50 (93)	141 (95)
Grade 3	54 (57)	32 (59)	86 (58)
Grade 4	13 (14)	3 (6)	16 (11)
Grade 5	3 (3)	0	3 (2)[b]
TRAEs leading to			
ADA dose interruption	65 (68)	35 (65)	100 (67)
ADA dose reduction[c]	50 (53)	22 (41)	72 (48)
ADA discontinuation only	5 (5)	5 (9)	10 (7)
PEMBRO discontinuation only	19 (20)	6 (11)	25 (17)
ADA and PEMBRO discontinuation[d]	7 (7)	3 (6)	10 (7)
Any grade immune-related AEs	23 (24)	10 (19)	33 (22)

TRAEs G1-2 : Nausea, Diarrhea
iAEs: Pneumonitis 12%

Futuro: KRYSTAL 7 (en solo PDL1 > 50%)
KRYSTAL 4 + QT

Patients, n (%)	All patients (N = 149)				
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4
Any hepatic TRAEs	88 (59)	25 (17)	20 (13)	41 (28)	2 (1)
Most frequent hepatic TRAEs[b]					
ALT increase	59 (40)	23 (15)	19 (13)	16 (11)	1 (< 1)
AST increase	53 (36)	20 (13)	12 (8)	19 (13)	2 (1)

Lung Cancer UPDATES
ASCO HIGHLIGHTS
30 MAYO - 03 JUNIO 2025
Chicago, USA

Safety Profile: 1L Olomorasib + Pembrolizumab

SLP a 1 año, ~60%

Parameter n (%)	Olomorasib (50 or 100 mg BID) + Pembrolizumab (n=48)						
	TEAEs (≥10%)		TRAEs[a]				
	Any Grade	Grade ≥ 3	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4[b]
Any AE	45 (93.8)	26 (54.2)	43 (89.6)	9 (18.8)	15 (31.3)	17 (35.4)	2 (4.2)
Diarrhea	20 (41.7)	4 (8.3)	17 (35.4)	8 (16.7)	5 (10.4)	4 (8.3)	-
ALT increased	16 (33.3)	11 (22.9)	14 (29.2)	1 (2.1)	2 (4.2)	11 (22.9)	-
AST increased	14 (29.2)	7 (14.6)	14 (29.2)	2 (4.2)	5 (10.4)	7 (14.6)	-
Nausea	13 (27.1)	-	9 (18.8)	6 (12.5)	3 (6.3)	-	-
Fatigue	11 (22.9)	-	7 (14.6)	2 (4.2)	5 (10.4)	-	-
Vomiting	10 (20.8)	-	6 (12.5)	3 (6.3)	3 (6.3)	-	-
Decreased appetite	8 (16.7)	1 (2.1)	6 (12.5)	4 (8.3)	2 (4.2)	-	-
Pruritis	9 (18.8)	-	7 (14.6)	6 (12.5)	1 (2.1)	-	-
Abdominal pain	9 (18.8)	-	3 (6.3)	2 (4.2)	1 (2.1)	-	-
Peripheral oedema	8 (16.7)	1 (2.1)	2 (4.3)	-	-	-	-
Constipation	7 (14.6)	1 (2.1)	1 (2.1)	1 (2.1)	-	-	-

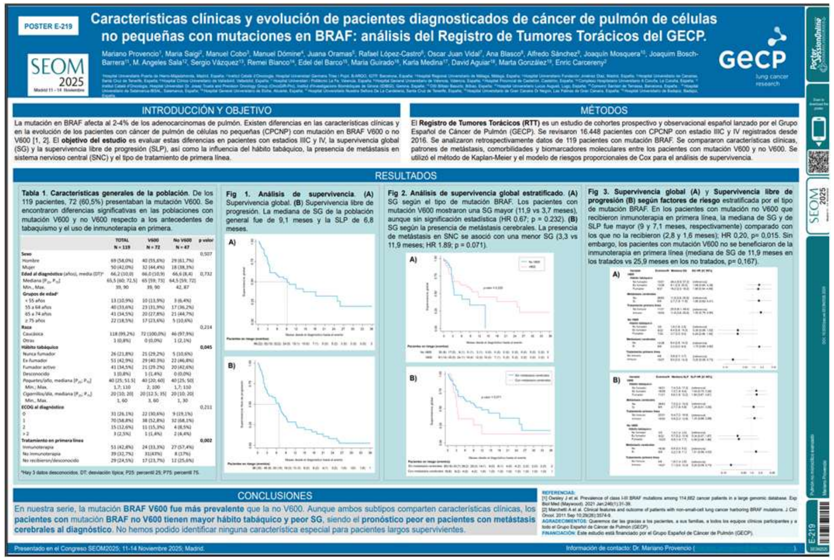
Dose modifications due to TRAEs

TRAEs led to dose reductions of olomorasib in 11 patients (23%)

TRAEs[c] led to discontinuation of the treatment regimen in 2 patients (4%)

- Hepatotoxicidad y diarrea
- Solo 2 pacientes discontinuaron el tratamiento por EA

BRAF



POSTER E-219
Características clínicas y evolución de pacientes diagnosticados de cáncer de pulmón de células no pequeñas con mutaciones en BRAF: análisis del Registro de Tumores Torácicos del GECP.
Mariano Provencio, Maria Saigí, Manuel Cobo, Manuel Dómine, Juana Oramas, Rafael López-Castro, Oscar Juan Vidal, Ana Blasco, Alfredo Sánchez, Joaquín Mosquera, Joaquim Bosch-Barrera, M. Angeles Sala, Sergio Vázquez, Remei Blanco, Edel del Barco, Maria Guirado, Karla Medina, David Aguiar, Marta González, Enric Carcereny
SEOM 2025
GECP
INTRODUCCIÓN Y OBJETIVO
La mutación en BRAF afecta al 2-4% de los adenocarcinomas de pulmón. Existen diferencias en las características clínicas y en la evolución de los pacientes con cáncer de pulmón de células no pequeñas (CPCNP) con mutación en BRAF V600 o no V600 [1, 2]. El objetivo del estudio es evaluar estas diferencias en pacientes con estadios IIIC y IV, la supervivencia global (SG) y la supervivencia libre de progresión (SLP), así como la influencia del hábito tabáquico, la presencia de metástasis en sistema nervioso central (SNC) y el tipo de tratamiento de primera línea.
MÉTODOS
El Registro de Tumores Torácicos (RTT) es un estudio de cohortes prospectivo y observacional español lanzado por el Grupo Español de Cáncer de Pulmón (GECP). Se revisaron 16.448 pacientes con CPCNP con estadio IIIC y IV registrados desde 2016. Se analizaron retrospectivamente datos de 119 pacientes con mutación BRAF. Se compararon características clínicas, patrones de metástasis, comorbilidades y biomarcadores moleculares entre los pacientes con mutación V600 y no V600. Se utilizó el método de Kaplan-Meier y el modelo de riesgos proporcionales de Cox para el análisis de supervivencia.
RESULTADOS
CONCLUSIONES

119 pacientes

- 72 (60,5%) presentaban la mutación V600

CONCLUSIONES

En nuestra serie, la mutación **BRAF V600 fue más prevalente** que la no V600. Aunque ambos subtipos comparten características clínicas, los **pacientes con** mutación **BRAF no V600 tienen mayor hábito tabáquico y peor SG**, siendo el **pronóstico peor en pacientes con metástasis cerebrales al diagnóstico**. No hemos podido identificar ninguna característica especial para pacientes largos supervivientes.

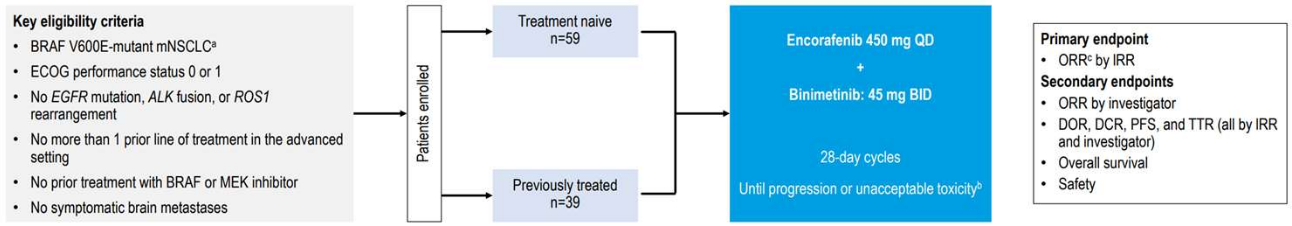
BERLIN 2025 ESMO congress

Updated overall survival analysis from the phase 2 PHAROS study of encorafenib plus binimetinib in patients with BRAF V600E-mutant metastatic NSCLC (mNSCLC)

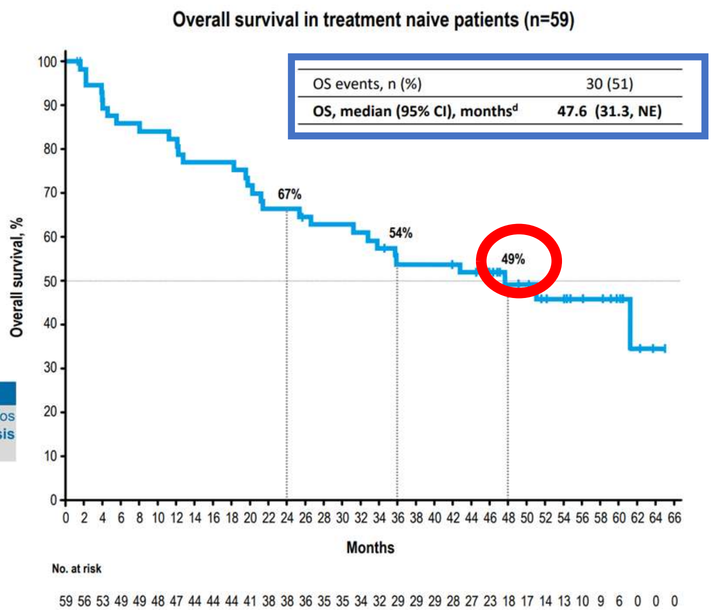
Melissa L. Johnson,[1] Egbert F. Smit,[2] Enriqueta Felip,[3] Suresh S. Ramalingam,[4] Myung-Ju Ahn,[5] Anne Tsao,[6] Bruce E. Johnson,[7] Michael Offin,[8] Maen Hussein,[9] Ibiayi Dagogo-Jack,[10] Jonathan W. Goldman,[11] Jeffrey M. Clarke,[12] Marcelo V. Negrao,[6] Rachel E. Sanborn,[13] Daniel Morgensztern,[14] Tiziana Usari,[15] Keith Wilner,[16] Linh Alejandro,[16] Xiaosong Zhang,[17] Gregory J. Riely[8]

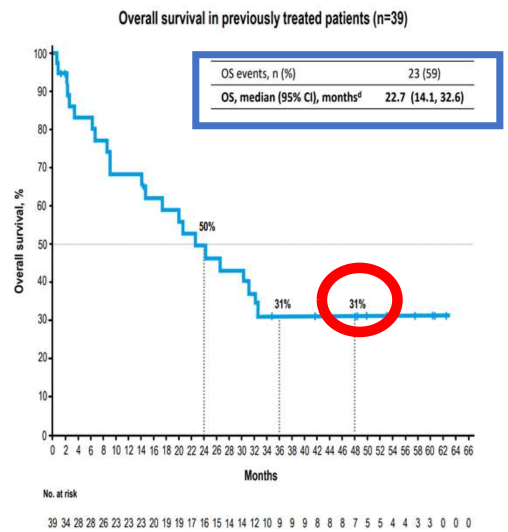
RO: 75% -- 49%
DRO: 40m – 16,7m
SLP: 30,4m –9,3m
SG: 47,6m – 22,7m

PHAROS (NCT03915951): a single-arm, open-label, multicenter, phase 2 study[5-7]

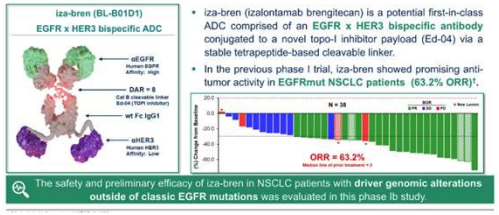


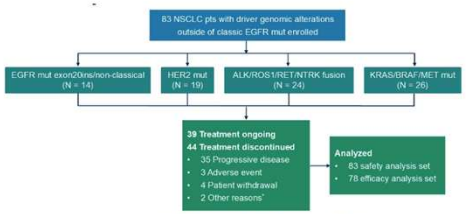
Key eligibility criteria
BRAF V600E-mutant mNSCLC[a]
ECOG performance status 0 or 1
No EGFR mutation, ALK fusion, or ROS1 rearrangement
No more than 1 prior line of treatment in the advanced setting
No prior treatment with BRAF or MEK inhibitor
No symptomatic brain metastases
Patients enrolled
Treatment naive n=59
Previously treated n=39
Encorafenib 450 mg QD
+
Binimetinib: 45 mg BID
28-day cycles
Until progression or unacceptable toxicity[b]
Primary endpoint
ORR[c] by IRR
Secondary endpoints
ORR by investigator
DOR, DCR, PFS, and TTR (all by IRR and investigator)
Overall survival
Safety

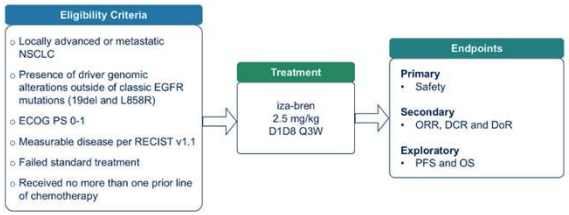


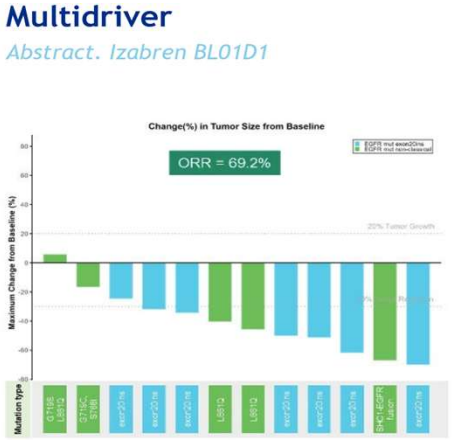


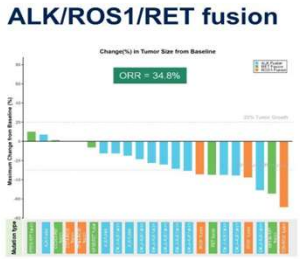
Otras mutaciones, y nuevos estudios….

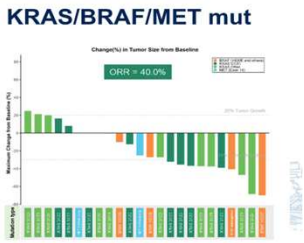












- **EGFR deleción exón 20**
  - Zipalertinib y Firmonertinib presentan datos esperanzadores de eficacia tanto a nivel sistémico intracraneal en población pre-tratada, con un perfil de toxicidad favorable
- **ROS1**
  - Zidesamtinib es una potencial nueva opción de tratamiento en CPNCP ROS1+ que ha progresado a línea
- **HER2:**
  - DESTINY-LUNG 03: T-DXd + rilvegostomig ± platino 1ª línea, CPNCP con sobreexpresión HER2
  - DESTINY-LUNG 05: T-DXd en CPNCP HER2 mutados chinos pretratados (SLP 9,9m; SG 21m)
  - DESTINY-LUNG 06: T-DXd + pembrolizumab en 1ª línea, CPNCP con sobreexpresión HER2 y PDL1 < 50%
- **Met-exón14:**
  - Savolitinib (1ª línea—posteriores): SG: 28,3m — 25,3m; SG mtx SNC: 25,3m – 15,3m
- **Deleción de MTAP:**
  - Antitumor activity with BMS-986504 was also observed in patients with *MTAP*-del NSCLC irrespective of alterations in *EGFR*, *ALK*, and *KRAS*
    - ORR was 57%, median DOR was 8.6 months in the *EGFR*-positive population (n = 7)
    - ORR was 50%, median DOR was 7.1 months in the *ALK*-positive population (n = 4)
    - ORR was 25%, median DOR was 11.3 months in the *KRAS*-positive population (n = 8)

Pasi A. Jänne et al. Oral Communication presented at WCLC Congress, September 6-9, 2025. Barcelona, Spain. Presentation number OA08.01

Conclusiones

Conclusiones

- Es **fundamental** el **estudio molecular y de PDL1** del CPNCP al diagnóstico para poder seleccionar adecuadamente el tratamiento de cada paciente en concreto
- La **inmunoterapia** ha llegado al CPNCP para quedarse
  - Tanto por eficacia (datos de EC a largo plazo)
  - Como por calidad de vida para nuestros pacientes (iv, sc)
  - Pero…
    - Aún muchas dudas: ¿Cuándo administrarla?, ¿en ancianos también?, ¿adecuada evaluación de respuesta?
- Surgen **múltiples combinaciones** con otras opciones de tratamiento
  - Mejoraremos resultados combinando distintas inmunoterapias, o con ADCs, o con antiangiogénicos?
    - Pendientes de muchos resultados de los nuevos estudios en marcha e ilusionados con ellos
    - **España está presente en toda esta investigación**
- Y en pacientes con **mutaciones** seguimos mejorando resultados en salud…
  - Hemos de realizar estudios adaptados para obtener la mayor información posible
  - Ojo con las comutaciones