



EPICS

Global Perspectives in Current and Future Management of Lung Cancer

October 20, 2025

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A live, closed-door roundtable discussion focused on lung cancer was held on **October 20, 2025**

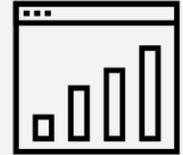


Lung cancer-specific discussions on latest research updates, therapeutic advances, and their application in clinical decision-making were led by **Corey Langer, MD, FACP**, from the University of Pennsylvania



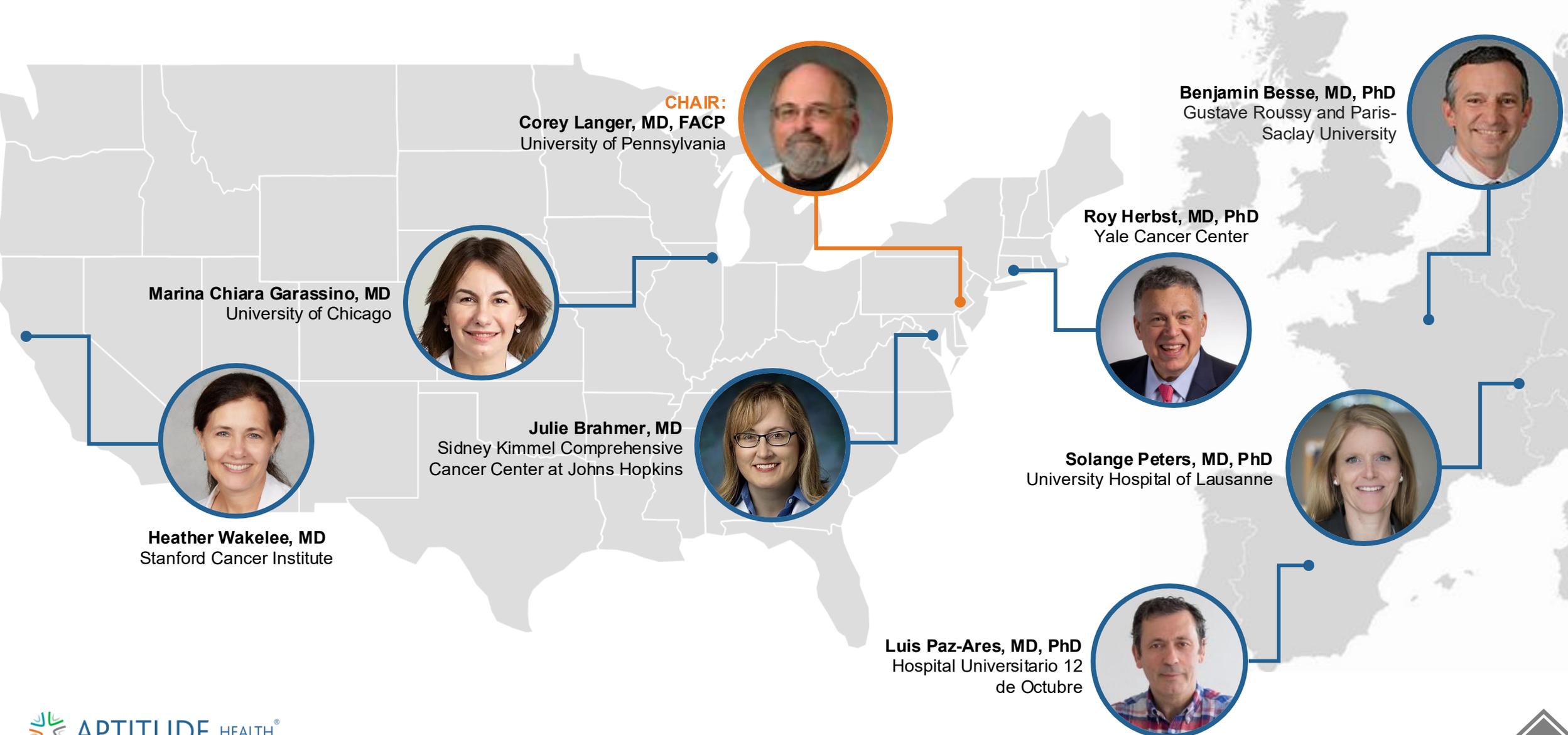
The panel consisted of 8 key experts in lung cancer

- 3 from Europe
- 5 from US



Insights report includes postmeeting analyses and actionable recommendations

Panel Consisting of 5 US and 3 European Lung Cancer Experts



Meeting Agenda

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Time (CEST)	Topic	Speaker/Moderator
19.30 – 19.35 (5 min)	Welcome and Introductions	Corey J. Langer, MD, FACP
19.35 – 19.50 (15 min)	Can We Improve on Current IO ± Chemo in Metastatic NSCLC?	Marina Chiara Garassino, MD
19.50 – 20.20 (30 min)	Discussion	All faculty
20.20 – 20.35 (15 min)	Expanding Approaches in Stage IV <i>EGFR</i>-Mutated NSCLC	Roy Herbst, MD, PhD
20.35 – 21.05 (30 min)	Discussion	All faculty
21.05 – 21.20 (15 min)	Targeted Therapy Beyond <i>EGFR</i> in Stage IV NSCLC	Julie Brahmer, MD; Solange Peters, MD, PhD
21.20 – 21.50 (30 min)	Discussion	All faculty
21.50 – 22.00 (10 min)	BREAK	
22.00 – 22.15 (15 min)	Small Cell Lung Cancer and Mesothelioma	Luis Paz-Ares, MD, PhD; Benjamin Besse, MD, PhD
22.15 – 22.45 (30 min)	Discussion	All faculty
22.45 – 23.00 (15 min)	Stage I–III NSCLC: Immunotherapy and Targeted Therapy	Heather Wakelee, MD
23.00 – 23.25 (25 min)	Discussion	All faculty
23.25 – 23.30 (5 min)	Wrap-Up Comments and Adjourn	Corey J. Langer, MD, FACP



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Can We Improve on Current IO ± Chemo in Metastatic NSCLC?

Conference Highlights Presented by
Marina Chiara Garassino, MD

Abstract	Phase
<p><u>Abstract 1851MO</u>: Pembrolizumab plus chemotherapy (PEM + CT) versus pembrolizumab (PEM) as first-line therapy for advanced NSCLC with PD-L1 tumor proportion score (TPS) $\geq 50\%$: Open-label, phase 3, randomized trial (PAULIEN) (Houda I, et al)</p>	
<p><u>Abstract LBA4</u>: Phase III study of ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous non-small cell lung cancer (HARMONi-6) (Lu S, et al)</p>	
<p><u>Abstract LBA71</u>: Final Analysis of First-Line Serplulimab Plus Chemotherapy With or Without HLX04 in Advanced Nonsquamous Non-Small Cell Lung Cancer: The ASTRUM-002 Phase 3 Study (Shi YK, et al)</p>	
<p><u>Abstract 1850MO</u>: TeLuRide-005: Phase 2 Study of EIK1001, a Toll-Like Receptor 7/8 (TLR7/8) Co-Agonist With Pembrolizumab (pembro)+Chemotherapy (chemo) as First-Line (1L) Therapy in Stage 4 Non-Small Cell Lung Cancer (NSCLC) (Gralla RJ, et al)</p>	
<p><u>Abstract 1853MO</u>: Efficacy and Safety of Rilvegostomig, an Anti-PD-1/TIGIT Bispecific Antibody, for Checkpoint Inhibitor (CPI)-Naïve Metastatic Non-Small Cell Lung Cancer (mNSCLC): ARTEMIDE-01 (Cho BC, et al)</p>	
<p><u>Abstract 1852MO</u>: KEYMAKER-U01 Substudy 01A: Investigational Agents + Pembrolizumab (Pembro) and Chemotherapy (Chemo) in Untreated Stage IV Non-Small Cell Lung Cancer (NSCLC) (Aggarwal C, et al)</p>	
<p><u>Abstract 1947P</u>: Phase 2 Study of Sacituzumab Govitecan (SG), Domvanalimab (dom), and Zimberelimab (zim) in Metastatic Non-Small Cell Lung Cancer (mNSCLC): VELOCITY-Lung Substudy-01 (Ahn MJ, et al)</p>	

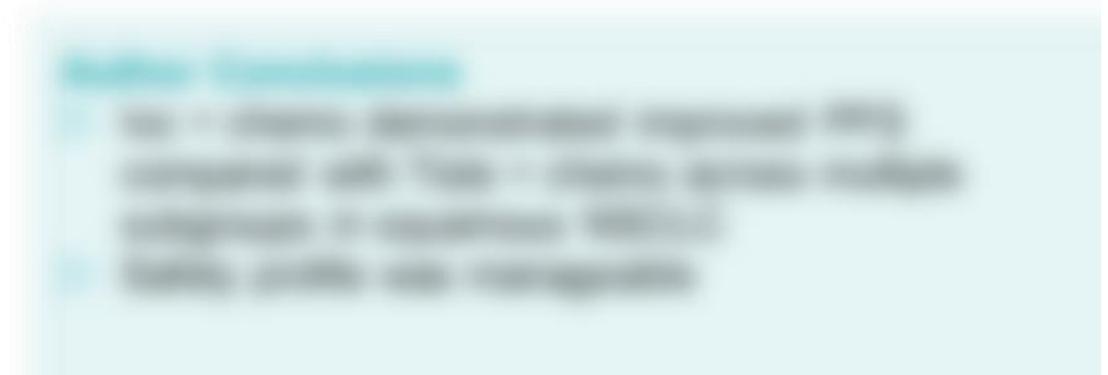
Pembrolizumab plus chemotherapy (PEM + CT) versus pembrolizumab (PEM) as first-line therapy for advanced NSCLC with PD-L1 tumor proportion score (TPS) $\geq 50\%$: Open-label, phase 3, randomized trial (PAULIEN)

Houda I, et al. ESMO 2025. Abstract 1851MO



Phase III study of ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line Treatment for advanced squamous non-small cell lung cancer (HARMONi-6)

Lu S, et al. ESMO 2025. Abstract LBA4



Phase III study of ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line Treatment for advanced squamous non-small cell lung cancer (HARMONi-6)

Lu S, et al. ESMO 2025. Abstract LBA4

Background: Ivonescimab (IVO) is a novel anti-PD-1 antibody. This study compared IVO plus chemotherapy (IVO+CT) versus tislelizumab plus chemotherapy (TIS+CT) as first-line treatment for advanced squamous non-small cell lung cancer (NSCLC).

Methods: This phase III, randomized, controlled study (HARMONi-6) included 1000 patients with advanced squamous NSCLC who had not received prior systemic anticancer therapy. Patients were randomized to receive IVO+CT (IVO 200 mg intravenous [IV] every 2 weeks [Q2W] plus platinum-based chemotherapy) or TIS+CT (TIS 200 mg IV every 2 weeks plus platinum-based chemotherapy). The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and safety.

Results: At 24 weeks, OS was significantly higher in the IVO+CT group compared to the TIS+CT group (HR, 0.75; 95% CI, 0.60-0.94; P=0.018). PFS and ORR were also significantly higher in the IVO+CT group (PFS HR, 0.78; 95% CI, 0.65-0.94; P=0.012; ORR OR, 1.45; 95% CI, 1.15-1.81; P=0.002). The safety profile was similar between the two groups.



Conclusion: Ivonescimab plus chemotherapy demonstrated superior overall survival compared to tislelizumab plus chemotherapy as first-line treatment for advanced squamous non-small cell lung cancer.

Final Analysis of First-Line Serplulimab Plus Chemotherapy With or Without HLX04 in Advanced Nonsquamous Non-Small Cell Lung Cancer: The ASTRUM-002 Phase 3 Study

Shi YK, et al. ESMO 2025. Abstract LBA71

Study Design and Population

- Phase 3, randomized, controlled, open-label study
- Advanced nonsquamous non-small cell lung cancer
- First-line treatment
- Randomized to Serplulimab plus chemotherapy with or without HLX04

Primary Endpoints

- Overall survival (OS)
- Progression-free survival (PFS)

Results

- OS: Serplulimab plus chemotherapy with HLX04 vs without HLX04
- PFS: Serplulimab plus chemotherapy with HLX04 vs without HLX04

Conclusion

- Serplulimab plus chemotherapy with HLX04 significantly improved OS and PFS compared with Serplulimab plus chemotherapy without HLX04.

Overall Survival (OS)

Progression-Free Survival (PFS)

Statistical Significance

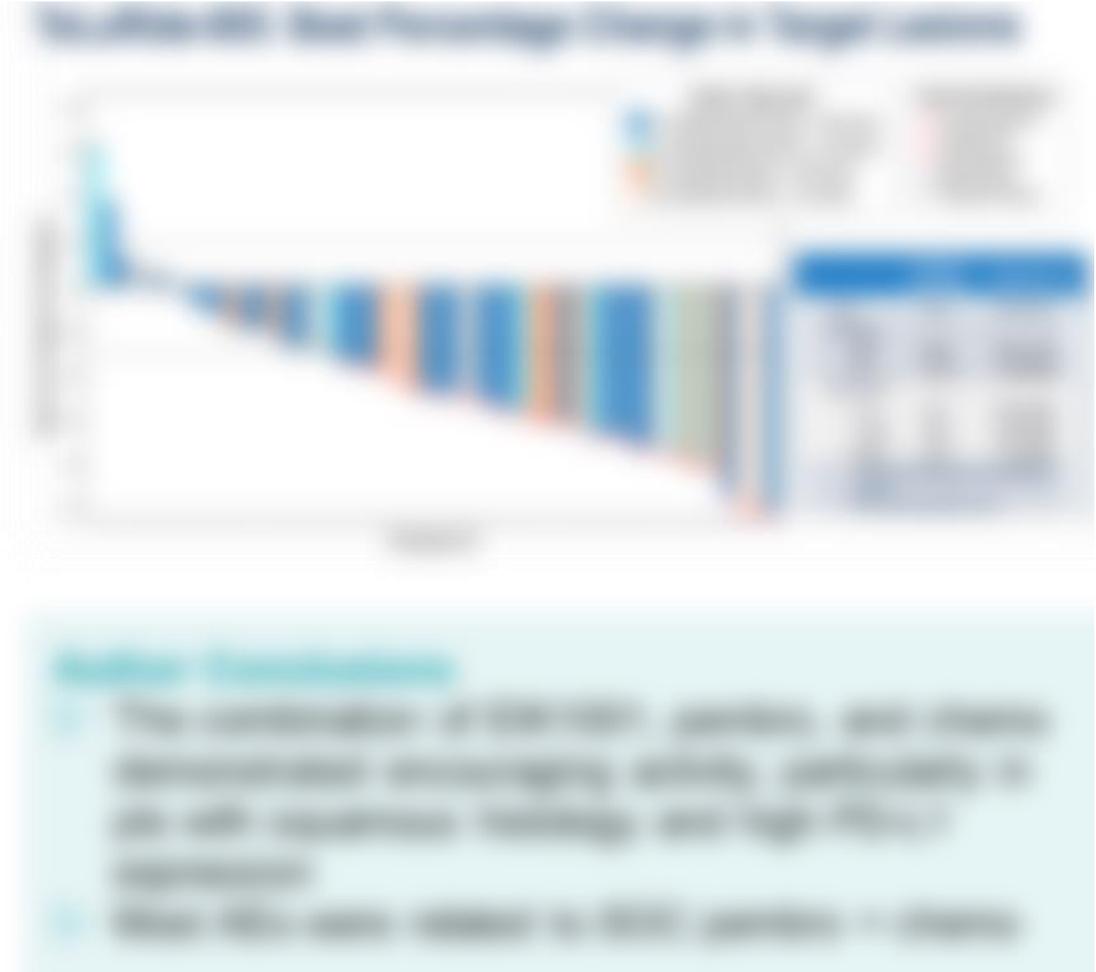
- OS: $p < 0.001$
- PFS: $p < 0.001$

Conclusion

- Serplulimab plus chemotherapy with HLX04 significantly improved OS and PFS compared with Serplulimab plus chemotherapy without HLX04.

TeLuRide-005: Phase 2 Study of EIK1001, a Toll-Like Receptor 7/8 (TLR7/8) Co-Agonist With Pembrolizumab (pembro)+Chemotherapy (chemo) as First-Line (1L) Therapy in Stage 4 Non-Small Cell Lung Cancer (NSCLC)

Gralla RJ, et al. ESMO 2025. Abstract 1850MO



Efficacy and Safety of Rilvegostomig, an Anti-PD-1/TIGIT Bispecific Antibody, for Checkpoint Inhibitor (CPI)-Naïve Metastatic Non-Small Cell Lung Cancer (mNSCLC): ARTEMIDE-01

Cho BC, et al. ESMO 2025. Abstract 1853MO



Efficacy and Safety of Rilvegostomig, an Anti-PD-1/TIGIT Bispecific Antibody, for Checkpoint Inhibitor (CPI)-Naïve Metastatic Non-Small Cell Lung Cancer (mNSCLC): ARTEMIDE-01

Cho BC, et al. ESMO 2025. Abstract 1853MO

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KEYMAKER-U01 Substudy 01A: Investigational Agents + Pembrolizumab (Pembro) and Chemotherapy (Chemo) in Untreated Stage IV Non-Small Cell Lung Cancer (NSCLC)

Aggarwal C, et al. ESMO 2025. Abstract 1852MO

Background: [Blurred text]

Methods: [Blurred text]

Results: [Blurred text]

Figure 1: Overall Survival (OS) by Treatment Arm

Treatment Arm	OS (months)
Pembro + Chemo	~12
Pembro + Investigational Agent 1	~10
Pembro + Investigational Agent 2	~14
Pembro + Investigational Agent 3	~15

Figure 2: Progression-Free Survival (PFS) by Treatment Arm

Treatment Arm	PFS (months)
Pembro + Chemo	~8
Pembro + Investigational Agent 1	~9
Pembro + Investigational Agent 2	~11
Pembro + Investigational Agent 3	~12

Conclusion: [Blurred text]

Phase 2 Study of Sacituzumab Govitecan (SG), Domvanalimab (dom), and Zimberelimab (zim) in Metastatic Non-Small Cell Lung Cancer (mNSCLC): VELOCITY-Lung Substudy-01

Ahn MJ, et al. ESMO 2025. Abstract 1947P



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Can We Improve on Current IO \pm Chemo in Metastatic NSCLC?

Discussion

Can We Improve on Current IO ± Chemo in Metastatic NSCLC? (1/4)

Current Standard of Care

- 1. Systemic therapy with immunotherapy (IO) ± chemotherapy (chemo) is the current standard of care for metastatic NSCLC.
- 2. The combination of IO and chemo has shown improved overall survival (OS) compared to IO monotherapy.
- 3. The combination of IO and chemo is also associated with improved progression-free survival (PFS) and quality of life (QoL).

Key Clinical Trials

- 1. The KEYNOTE-424 trial (NCT02107758) compared IO ± chemo to IO monotherapy in metastatic NSCLC.
- 2. The IMpower150 trial (NCT02576529) compared IO ± chemo to IO monotherapy in metastatic NSCLC.
- 3. The CheckMate 017 trial (NCT01704107) compared IO ± chemo to IO monotherapy in metastatic NSCLC.

Future Directions

- 1. Research is ongoing to identify biomarkers that predict response to IO ± chemo.
- 2. New combinations of IO and chemo are being evaluated in clinical trials.
- 3. The development of novel immunomodulatory agents is also being explored.



Dr. [Name]

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Can We Improve on Current IO ± Chemo in Metastatic NSCLC? (2/4)

Background

- 1. Current standard of care (SOC) for metastatic NSCLC is immunotherapy (IO) ± chemotherapy (chemo). IO ± chemo has shown improved overall survival (OS) compared to chemo alone in several phase III trials.
- 2. However, the response rate (RR) to IO ± chemo is still low, and many patients experience significant toxicity.
- 3. There is a need to explore novel combinations of IO and chemo to improve RR and reduce toxicity.

Objectives

- 1. To evaluate the efficacy and safety of novel combinations of IO and chemo in metastatic NSCLC.
- 2. To determine if these combinations can improve RR and OS compared to the current SOC.

Can We Improve on Current IO ± Chemo in Metastatic NSCLC? (3/4)

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ANSWER [blurred text]

Can We Improve on Current IO ± Chemo in Metastatic NSCLC? (4/4)

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Expanding Approaches in Stage IV *EGFR*- Mutated NSCLC

Conference Highlights Presented by
Roy Herbst, MD, PhD

Abstract	Phase
<p><u>Abstract LBA77</u>: FLAURA2: Exploratory overall survival (OS) analysis in patients (pts) with poorer prognostic factors treated with osimertinib (osi) ± platinum-pemetrexed chemotherapy (CTx) as first-line (1L) treatment (tx) for <i>EGFR</i>-mutated (<i>EGFRm</i>) advanced NSCLC (Janne PA, et al)</p>	
<p><u>Abstract LBA72</u>: NorthStar: A Phase II Randomized Study of Osimertinib (OSI) With or Without Local Consolidative Therapy (LCT) for Metastatic <i>EGFR</i>-Mutant Non-Small Cell Lung Cancer (NSCLC) (Elamin YY, et al)</p>	
<p><u>Abstract LBA5</u>: Sacituzumab tirumotecan (sac-TMT) vs platinum-based chemotherapy in <i>EGFR</i>-mutated (<i>EGFRm</i>) non-small cell lung cancer (NSCLC) following progression on EGFR-TKIs: Results from the randomized, multi-center phase 3 OptiTROP-Lung04 study (Zhang L, et al)</p>	
<p><u>Abstract 921MO</u>: Phase 1 Global Study of Iza-Bren (BL-B01D1), an EGFR x HER3 Bispecific Antibody-Drug Conjugate (ADC), in Patients with Metastatic or Unresectable Non-Small Cell Lung Cancer (NSCLC) and Other Solid Tumors (Yu HA, et al)</p>	
<p><u>Abstract 1847MO</u>: Activity of Ziplertinib Against Active Central Nervous System (CNS) Metastases in Patients With Non-Small Cell Lung Cancer (NSCLC) Harboring <i>EGFR</i> Exon 20 Insertion (Ex20ins)/Other Uncommon Mutations (Yu HA, et al)</p>	
<p><u>Abstract 1848MO</u>: Phase 2 Study of Firmonertinib in Patients With Previously Treated Advanced/Metastatic Non-Small Cell Lung Cancer (mNSCLC) With <i>EGFR</i> Exon 20 Insertion (Ex20ins) Mutations (Liu Y, et al)</p>	

FLAURA2: Exploratory overall survival (OS) analysis in patients (pts) with poorer prognostic factors treated with osimertinib (osi) ± platinum-pemetrexed chemotherapy (CTx) as first-line (1L) treatment (tx) for *EGFR*-mutated (*EGFRm*) advanced NSCLC

Janne PA, et al. ESMO 2025. Abstract LBA77

Background: The FLAURA2 study is a phase III, randomized, controlled trial comparing osimertinib (OSI) with OSI plus platinum-pemetrexed chemotherapy (CTx) as first-line treatment in patients with *EGFR*-mutated advanced non-small cell lung cancer (NSCLC). The primary endpoint is overall survival (OS). The exploratory OS analysis in patients with poorer prognostic factors is presented here.

Methods: The exploratory OS analysis included patients with poorer prognostic factors, defined as ECOG performance grade 1-2, hemoglobin < 10 g/dL, or platelets < 100,000/mm³. The analysis was conducted using the Kaplan-Meier method. The primary endpoint was OS, defined as the time from randomization to death from any cause. The secondary endpoint was OS in patients with ECOG performance grade 1-2.

Results: The exploratory OS analysis included 1,000 patients. The median OS was significantly longer in the OSI plus CTx group compared to the OSI group (14.5 months vs 12.8 months, *P* = 0.001). The median OS in patients with ECOG performance grade 1-2 was significantly longer in the OSI plus CTx group compared to the OSI group (13.2 months vs 11.5 months, *P* = 0.001).

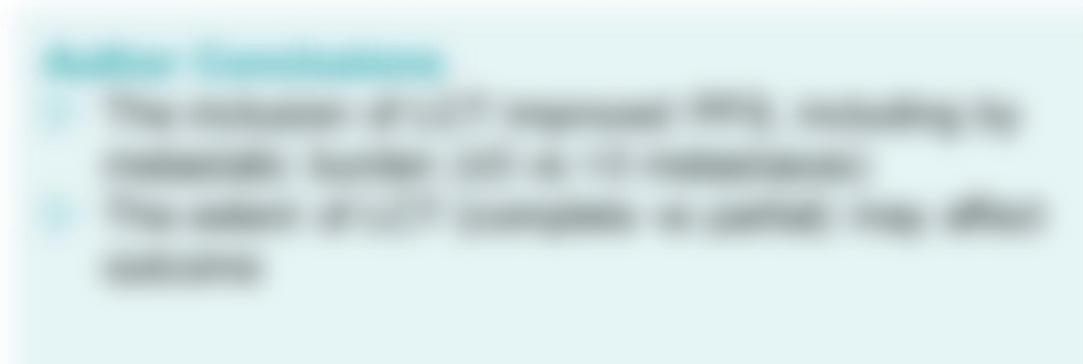
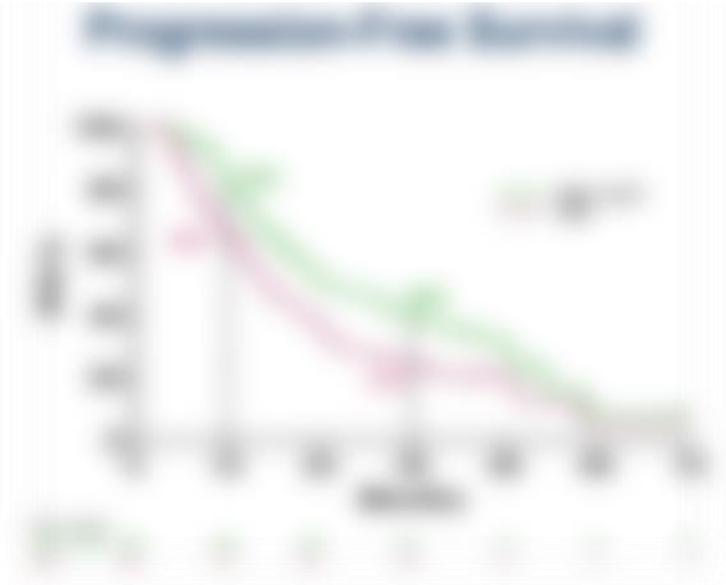


Conclusion: The exploratory OS analysis in patients with poorer prognostic factors showed a significant improvement in OS with OSI plus CTx compared to OSI. This finding supports the use of OSI plus CTx as first-line treatment in patients with poorer prognostic factors.



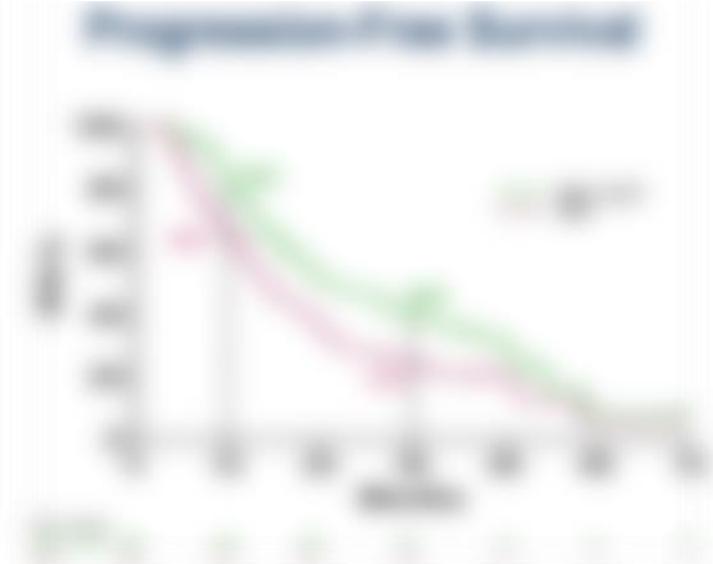
NorthStar: A Phase II Randomized Study of Osimertinib (OSI) With or Without Local Consolidative Therapy (LCT) for Metastatic *EGFR*-Mutant Non-Small Cell Lung Cancer (NSCLC)

Elamin YY, et al. ESMO 2025. Abstract LBA72



NorthStar: A Phase II Randomized Study of Osimertinib (OSI) With or Without Local Consolidative Therapy (LCT) for Metastatic *EGFR*-Mutant Non-Small Cell Lung Cancer (NSCLC)

Elamin YY, et al. ESMO 2025. Abstract LBA72



Presented by: [Name]
[Title]
[Affiliation]

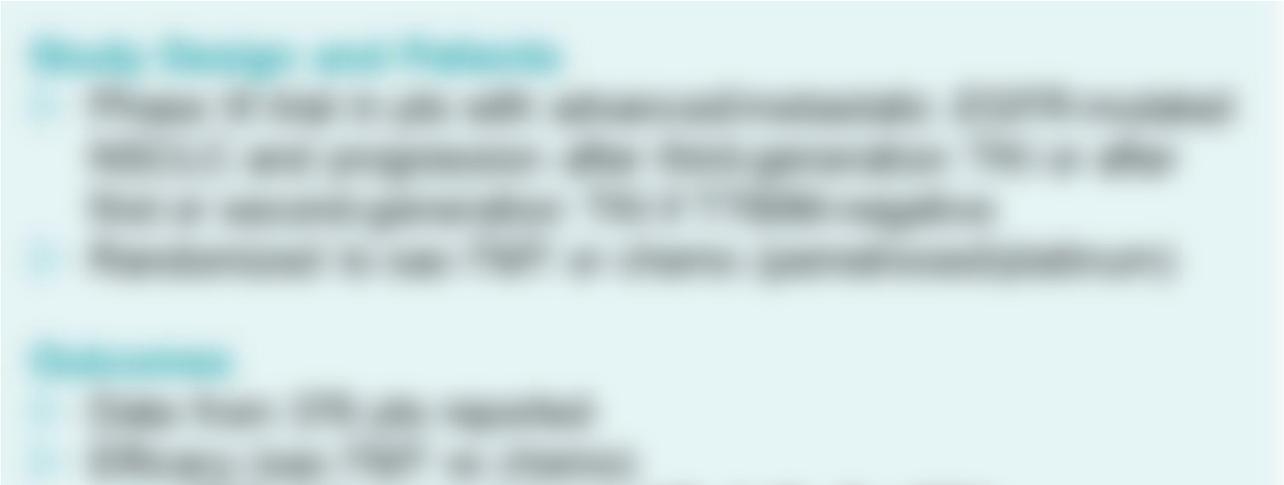
Sacituzumab tirumotecan (sac-TMT) vs platinum-based chemotherapy in EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC) following progression on EGFR-TKIs: Results from the randomized, multi-center phase 3 OptiTROP-Lung04 study

Zhang L, et al. ESMO 2025. Abstract LBA5



Sacituzumab tirumotecan (sac-TMT) vs platinum-based chemotherapy in EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC) following progression on EGFR-TKIs: Results from the randomized, multi-center phase 3 OptiTROP-Lung04 study

Zhang L, et al. ESMO 2025. Abstract LBA5



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Phase 1 Global Study of Iza-Bren (BL-B01D1), an EGFR x HER3 Bispecific Antibody-Drug Conjugate (ADC), in Patients with Metastatic or Unresectable Non-Small Cell Lung Cancer (NSCLC) and Other Solid Tumors

Yu HA, et al. ESMO 2025. Abstract 921MO



Phase 1 Global Study of Iza-Bren (BL-B01D1), an EGFR x HER3 Bispecific Antibody-Drug Conjugate (ADC), in Patients with Metastatic or Unresectable Non-Small Cell Lung Cancer (NSCLC) and Other Solid Tumors

Yu HA, et al. ESMO 2025. Abstract 921MO



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Activity of Zipalertinib Against Active Central Nervous System (CNS) Metastases in Patients With Non-Small Cell Lung Cancer (NSCLC) Harboring *EGFR* Exon 20 Insertion (Ex20ins)/Other Uncommon Mutations

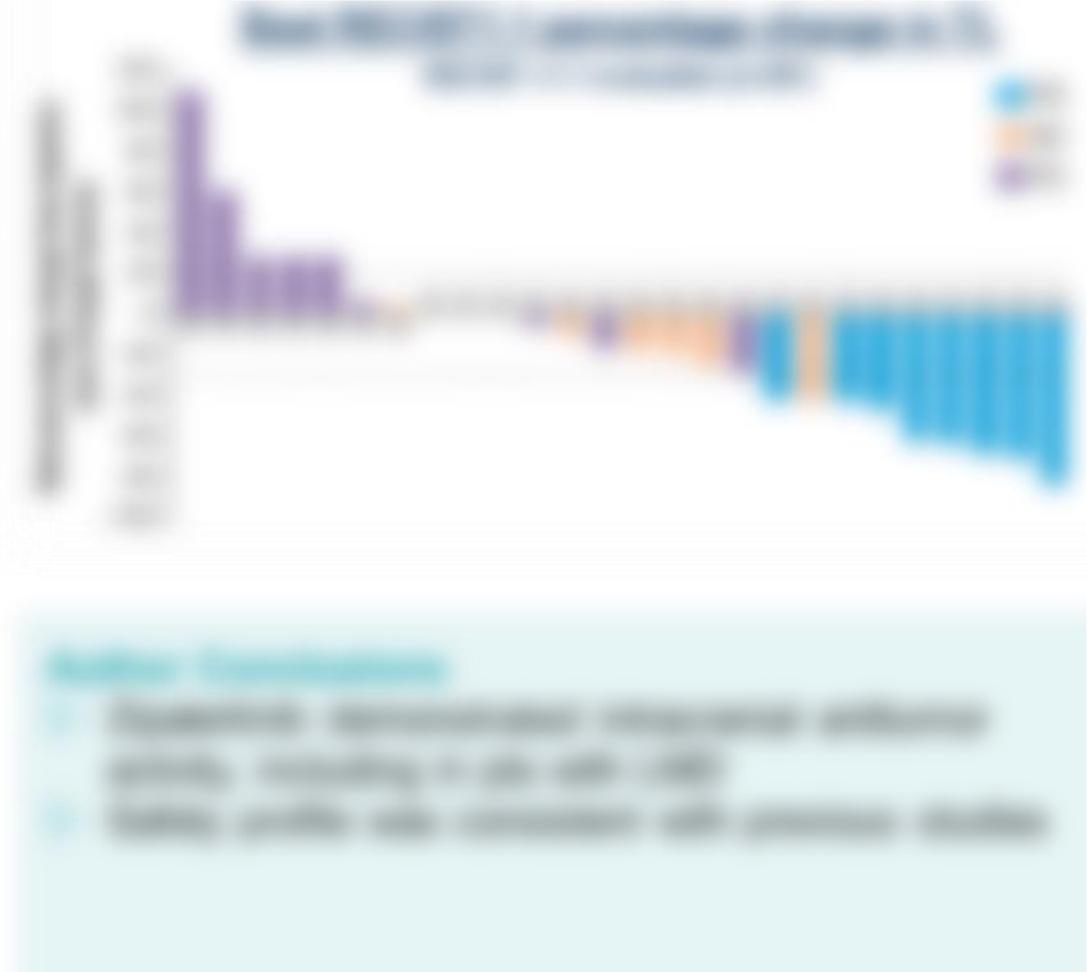
Yu HA, et al. ESMO 2025. Abstract 1847MO

Background: [Blurred text]

Methods: [Blurred text]

Results: [Blurred text]

Conclusion: [Blurred text]



Activity of Zipalertinib Against Active Central Nervous System (CNS) Metastases in Patients With Non-Small Cell Lung Cancer (NSCLC) Harboring *EGFR* Exon 20 Insertion (Ex20ins)/Other Uncommon Mutations

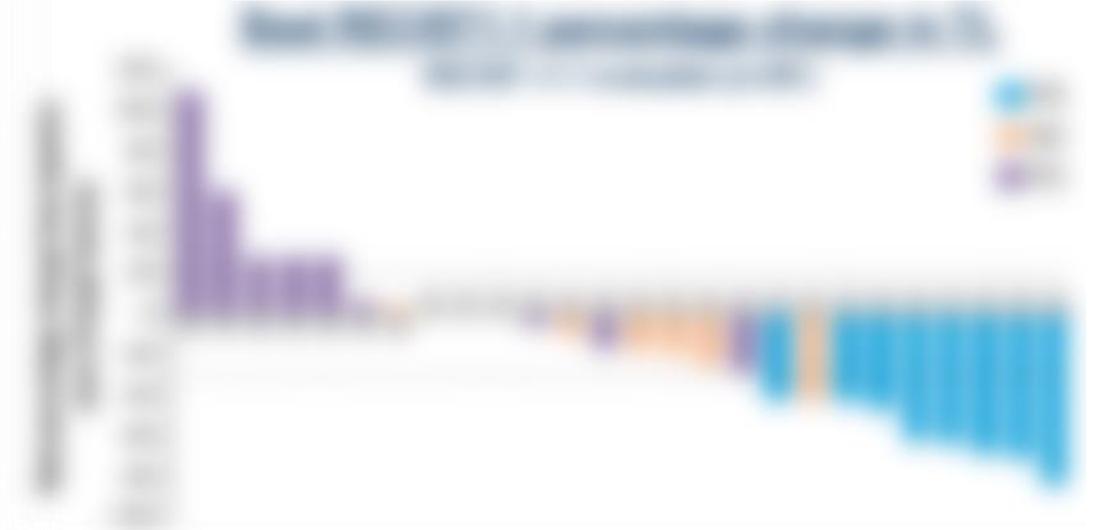
Yu HA, et al. ESMO 2025. Abstract 1847MO

Background: [Blurred text]

Methods: [Blurred text]

Results: [Blurred text]

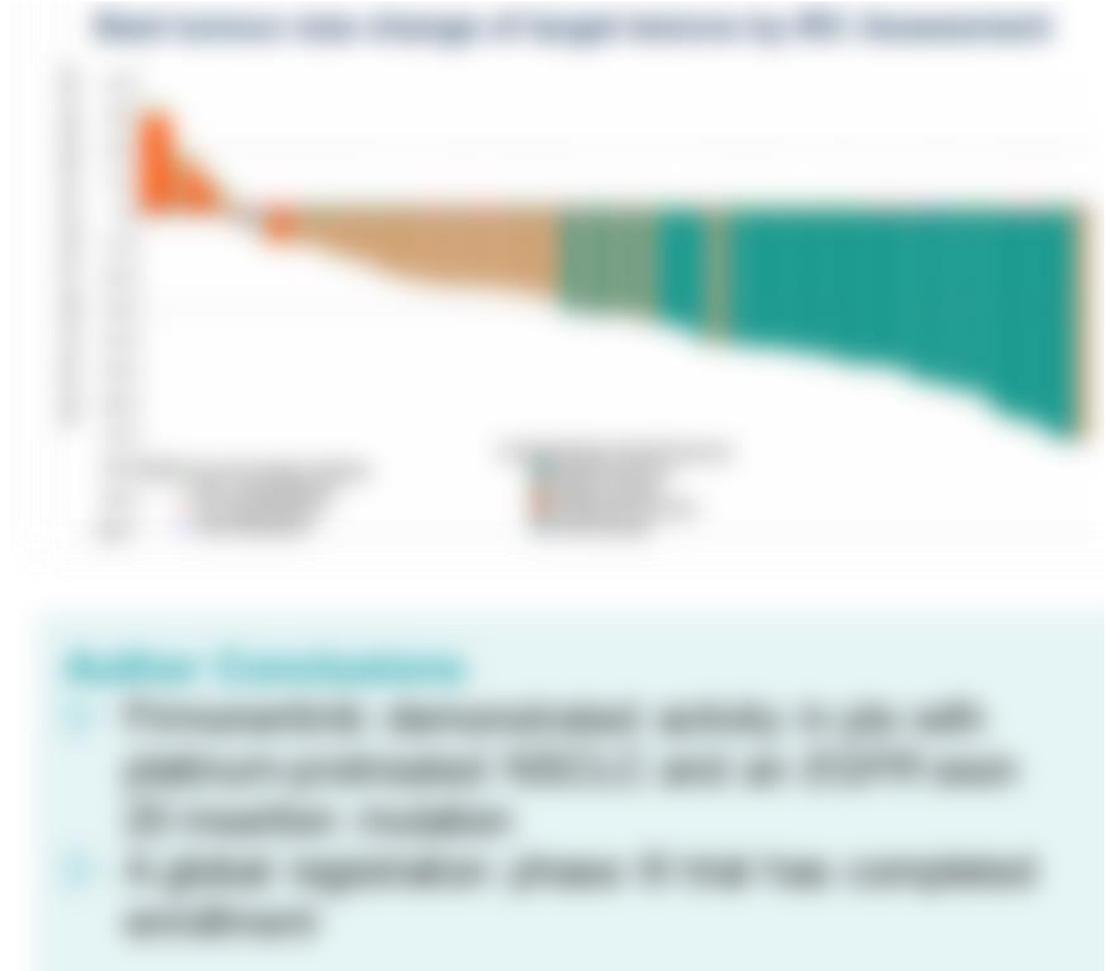
Conclusion: [Blurred text]



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Phase 2 Study of Firmonertinib in Patients With Previously Treated Advanced/Metastatic Non-Small Cell Lung Cancer (mNSCLC) With *EGFR* Exon 20 Insertion (Ex20ins)

Liu Y, et al. ESMO 2025. Abstract 1848MO



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Expanding Approaches in Stage IV *EGFR*- Mutated NSCLC

Discussion

Standard of Care

- 1. First-line treatment: EGFR tyrosine kinase inhibitors (TKIs) such as gefitinib or erlotinib.
- 2. Second-line treatment: Another EGFR TKI (osimertinib) if the first-line TKI was not effective.
- 3. Third-line treatment: Chemotherapy (pemetrexed + platinum) or immunotherapy (pembrolizumab).

Emerging Approaches

- 1. Combination of EGFR TKI with immunotherapy (e.g., pembrolizumab + gefitinib).
- 2. Combination of EGFR TKI with anti-angiogenic therapy (e.g., ramucicab).
- 3. Combination of EGFR TKI with targeted therapy (e.g., MEK inhibitors).



Dr. [Name]
Medical Oncologist
[Institution]

Expanding Approaches in Stage IV EGFR-Mutated NSCLC (2/4)

Introduction

The purpose of this presentation is to provide an overview of the current landscape of treatment options for Stage IV EGFR-mutated NSCLC, highlighting the role of EGFR tyrosine kinase inhibitors (TKIs) and the importance of comprehensive genomic profiling (CGP) in identifying potential therapeutic targets.

EGFR TKIs

EGFR TKIs represent the cornerstone of systemic therapy for Stage IV EGFR-mutated NSCLC. The first-generation TKIs, gefitinib and erlotinib, were the first to demonstrate a survival advantage in this population. The second-generation TKI, osimertinib, has emerged as the standard of care due to its superior efficacy, particularly in the presence of the T790M resistance mutation. The third-generation TKI, amivantamab, is also showing promising results in clinical trials.

Comprehensive Genomic Profiling (CGP)

CGP is a critical tool for identifying potential therapeutic targets beyond EGFR. It allows for the detection of other actionable mutations, such as ALK, ROS1, BRAF, and KRAS, which may be targeted with specific therapies. Additionally, CGP can identify biomarkers for immunotherapy, such as high tumor mutational burden (TMB) and microsatellite instability (MSI).

Immunotherapy

Immunotherapy, including checkpoint inhibitors like pembrolizumab and nivolumab, has shown efficacy in EGFR-mutated NSCLC, particularly in patients with high TMB or MSI. The combination of immunotherapy with EGFR TKIs is an area of active research, aiming to overcome resistance and improve outcomes.

Targeted Therapy

Targeted therapy, such as the combination of EGFR TKIs with anti-angiogenic agents like bevacizumab, is another approach being explored. Additionally, the use of combination EGFR TKIs, such as dacomitinib, is being evaluated in clinical trials.

Expanding Approaches in Stage IV EGFR-Mutated NSCLC (3/4)

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Expanding Approaches in Stage IV EGFR-Mutated NSCLC (4/4)

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Targeted Therapy Beyond *EGFR* in Stage IV NSCLC

Conference Highlights Presented by
Julie Brahmer, MD
Solange Peters, MD, PhD

Abstract Selection (1/2)

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Abstract

Phase

Abstract 1846MO: Intracranial efficacy of olomorasib, a second-generation KRAS G12C inhibitor, in patients with KRAS G12C-mutant NSCLC who have active, untreated brain metastases (Cassier P, et al)



Abstract 914O: HRS-7058, a KRAS G12C inhibitor (G12Ci), in advanced solid tumors with KRAS G12C mutation: A phase I, multi-center, first-in-human study (Huang D, et al)



Abstract 915O: KRAS G12D inhibitor HRS-4642 in patients with KRAS G12D-mutant advanced solid tumors: A phase 1 trial (Xiong A, et al)



Abstract 916O: Preliminary Phase 1 Results of INCB161734, a Novel Oral KRAS G12D Inhibitor, in Patients With Advanced or Metastatic Solid Tumors (Desai J, et al)



Abstract 1992P: Targeting KRAS codon 13 mutations using combinations with RMC-8839, a novel RAS(ON) G13C-selective, tri-complex inhibitor, in non-small cell lung cancer (Lindsay CR, et al)

Preclinical study



Abstract

Phase

Abstract 918O: Telisotuzumab adizutecan (ABBV-400; Temab-A) in patients with *MET*-amplified (MET-amp) advanced solid tumors: Results from a phase 1 study (Murciano-Goroff YR, et al)



Abstract LBA74: Zongertinib as first-line treatment in patients with advanced *HER2*-mutant NSCLC: Beamion LUNG-1 (Popat S, et al)



Abstract LBA75: Sevabertinib (BAY 2927088) in advanced *HER2*-mutant non-small cell lung cancer (NSCLC): Results from the SOHO-01 study (Le X, et al)



Abstract LBA73: Final overall survival (OS) and safety analysis of the phase 3 ALEX study of alectinib vs crizotinib in patients with previously untreated, advanced *ALK*-positive (*ALK*+) non-small cell lung cancer (NSCLC) (Mok TSK, et al)



Abstract 1987MO: Efficacy of lorlatinib after failure of a first-line *ROS1* tyrosine kinase inhibitor (*ROS1* TKI) in patients (pts) with advanced *ROS1*-positive non-small cell lung cancer (*ROS1*+ NSCLC) (IFCT-2003 ALBATROS) (Duruisseaux M, et al)



Intracranial efficacy of olomorasib, a second-generation KRAS G12C inhibitor, in patients with *KRAS* G12C-mutant NSCLC who have active, untreated brain metastases

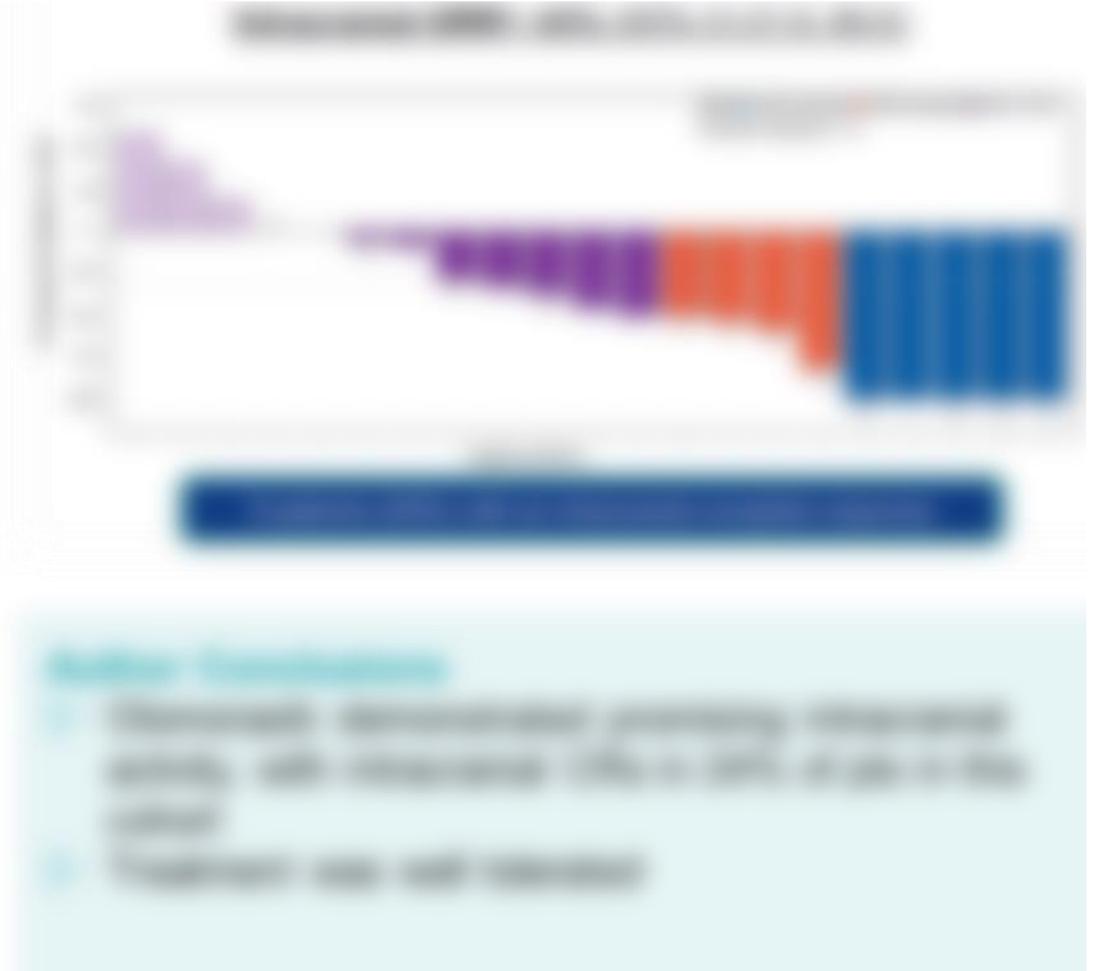
Cassier P, et al. ESMO 2025. Abstract 1846MO

Background: Olomorasib is a second-generation KRAS G12C inhibitor. This study evaluated its intracranial efficacy in patients with *KRAS* G12C-mutant NSCLC and active, untreated brain metastases.

Methods: Patients were treated with olomorasib 400 mg daily. Intracranial efficacy was assessed using MRI scans. The primary endpoint was the percentage of patients with a partial response (PR) or better in the brain.

Results: A total of 100 patients were enrolled. The median age was 65 years. The majority of patients had metastatic disease. The intracranial response rate was 45% (45/100), with 15% achieving a PR and 30% achieving a complete response (CR). The median duration of response was 12 months.

Conclusion: Olomorasib demonstrated significant intracranial efficacy in patients with *KRAS* G12C-mutant NSCLC and active, untreated brain metastases.



HRS-7058, a KRAS G12C inhibitor (G12Ci), in advanced solid tumors with KRAS G12C mutation: A phase I, multi-center, first-in-human study

Huang D, et al. ESMO 2025. Abstract 914O

Study Design and Population

This phase I study evaluated the safety, tolerability, and efficacy of HRS-7058 in patients with advanced solid tumors harboring KRAS G12C mutations. The study was conducted across multiple centers and followed a standard phase I design with dose escalation.

Study Design

- Phase I, multi-center, first-in-human study
- Primary objective: Assess safety and tolerability
- Secondary objectives: Assess efficacy and pharmacokinetics

Population

- Patients with advanced solid tumors and KRAS G12C mutation
- Patients were stratified by tumor type and KRAS G12C mutation status

Results

- Overall, HRS-7058 was well-tolerated in patients with advanced solid tumors and KRAS G12C mutation.
- The most common adverse events were related to the drug and were generally mild to moderate in severity.
- Objective response rates were observed in patients with advanced solid tumors and KRAS G12C mutation.

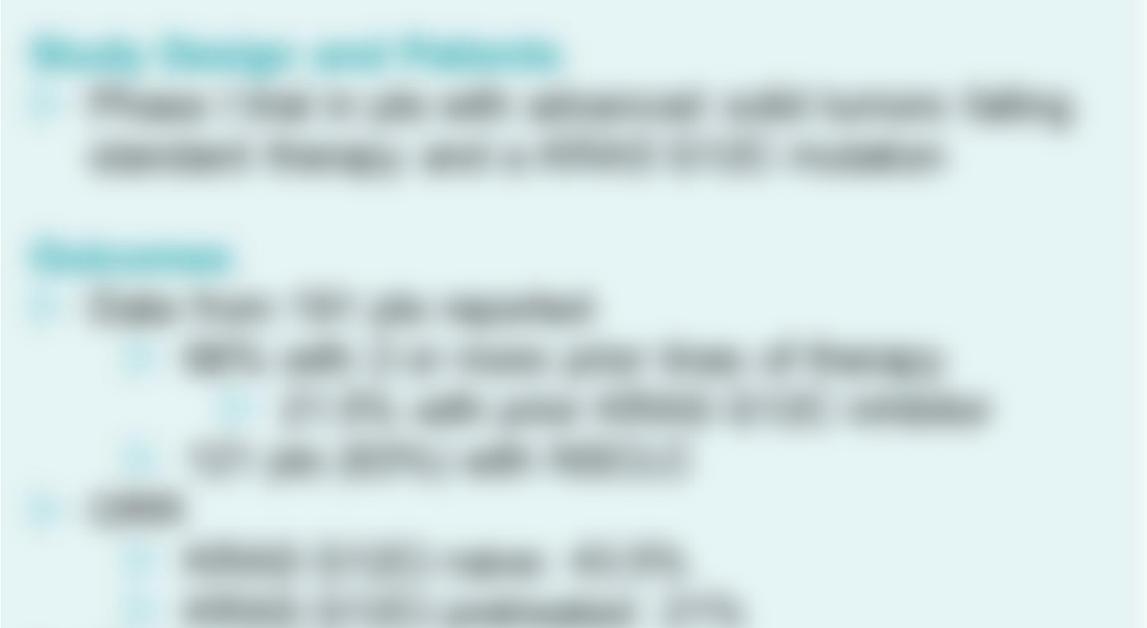


Conclusion

HRS-7058 demonstrated a favorable safety profile and promising efficacy in patients with advanced solid tumors and KRAS G12C mutation. Further studies are warranted to evaluate the long-term efficacy and safety of HRS-7058 in this patient population.

HRS-7058, a KRAS G12C inhibitor (G12Ci), in advanced solid tumors with KRAS G12C mutation: A phase I, multi-center, first-in-human study

Huang D, et al. ESMO 2025. Abstract 9140



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KRAS G12D inhibitor HRS-4642 in patients with *KRAS* G12D-mutant advanced solid tumors: A phase 1 trial

Xiong A, et al. ESMO 2025. Abstract 9150



Preliminary Phase 1 Results of INCB161734, a Novel Oral KRAS G12D Inhibitor, in Patients With Advanced or Metastatic Solid Tumors

Desai J, et al. ESMO 2025. Abstract 916O

Background: INCB161734 is a novel oral KRAS G12D inhibitor. Phase 1 results in patients with advanced or metastatic solid tumors are presented.

Methods: 15 patients were enrolled in the Phase 1 study. The study was a dose-escalation study. The primary endpoint was the maximum tolerated dose (MTD). Secondary endpoints included safety, tolerability, and efficacy.

Results: The MTD was 1000 mg QD. The most common adverse events were diarrhea, nausea, and vomiting. The overall response rate (ORR) was 20%.

Conclusion: INCB161734 is a novel oral KRAS G12D inhibitor. Phase 1 results in patients with advanced or metastatic solid tumors are presented.

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Targeting *KRAS* codon 13 mutations using combinations with RMC-8839, a novel RAS(ON) G13C-selective, tri-complex inhibitor, in non-small cell lung cancer

EPICS

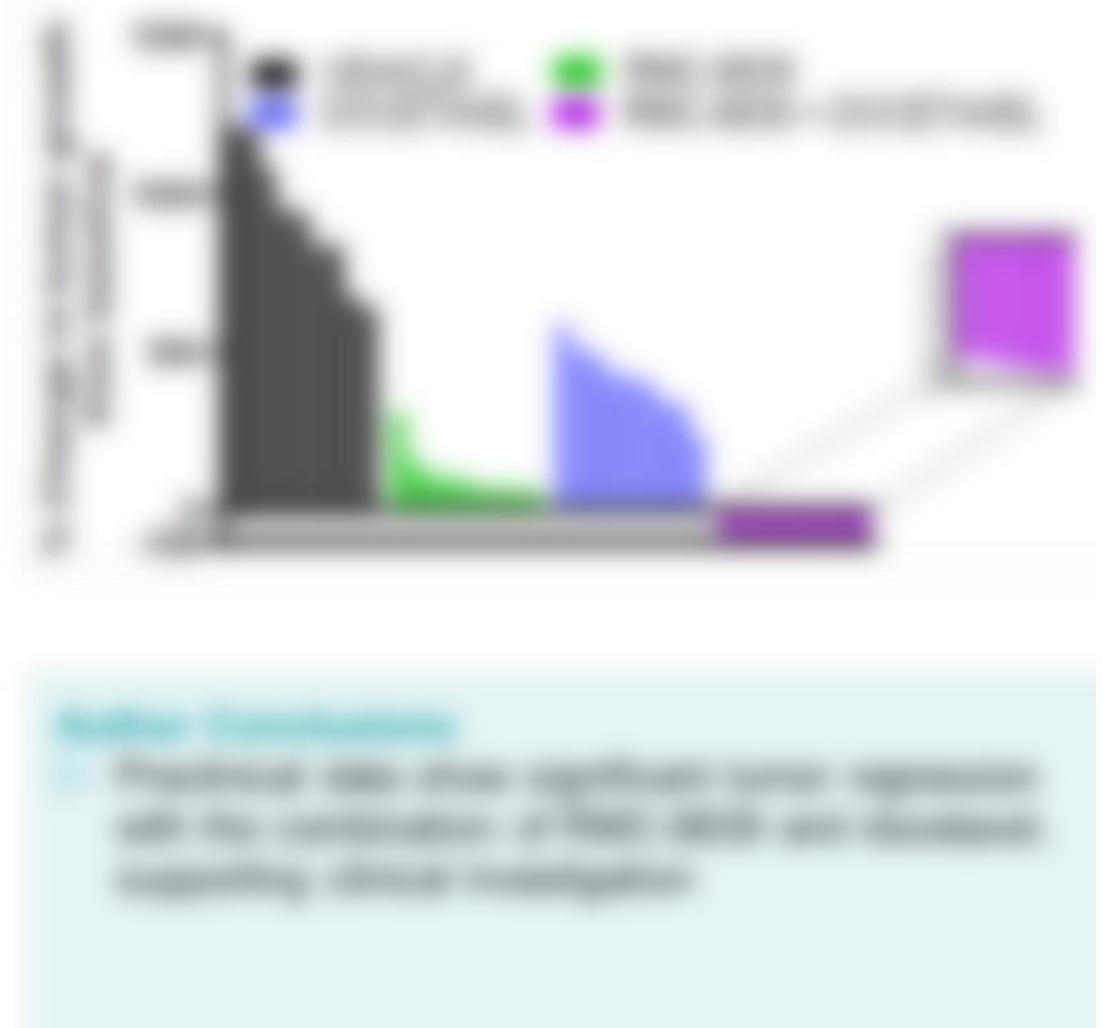
Lindsay CR, et al. ESMO 2025. Abstract 1992P

Background: KRAS G13C mutations are found in approximately 10% of NSCLC patients. RMC-8839 is a novel, G13C-selective, tri-complex inhibitor that targets the KRAS G13C mutant protein. This study evaluated the efficacy and safety of RMC-8839 in combination with standard of care (SOC) in KRAS G13C-mutant NSCLC.

Methods: A phase 1b/2 study was conducted in KRAS G13C-mutant NSCLC patients. The study evaluated the safety and efficacy of RMC-8839 in combination with SOC (SOC+RMC-8839) compared to SOC alone. The primary endpoint was the objective response rate (ORR). Secondary endpoints included progression-free survival (PFS), overall survival (OS), and adverse events.

Results: The study included 100 patients. The SOC+RMC-8839 group (n=50) showed a significantly higher ORR compared to the SOC alone group (n=50). The ORR was 40% in the SOC+RMC-8839 group versus 20% in the SOC alone group. PFS and OS were also significantly improved in the SOC+RMC-8839 group. Adverse events were manageable and similar between the two groups.

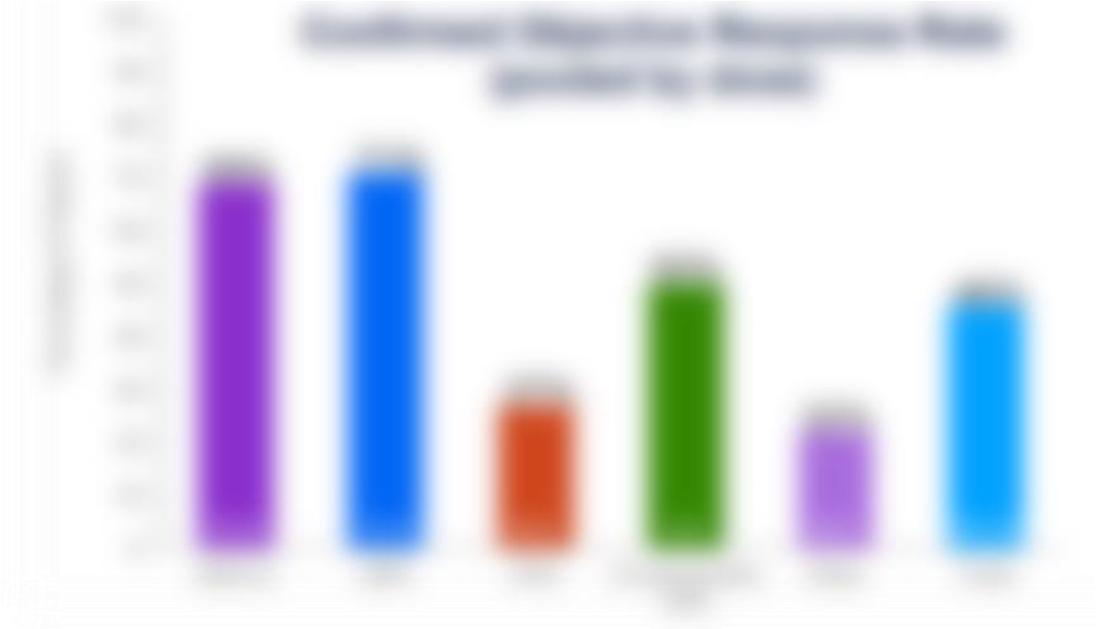
Conclusion: The combination of RMC-8839 with SOC significantly improved the ORR, PFS, and OS in KRAS G13C-mutant NSCLC patients compared to SOC alone. This combination represents a promising therapeutic strategy for KRAS G13C-mutant NSCLC.



Telisotuzumab adizutecan (ABBV-400; Temab-A) in patients with *MET*-amplified (*MET*-amp) advanced solid tumors: Results from a phase 1 study

EPICS

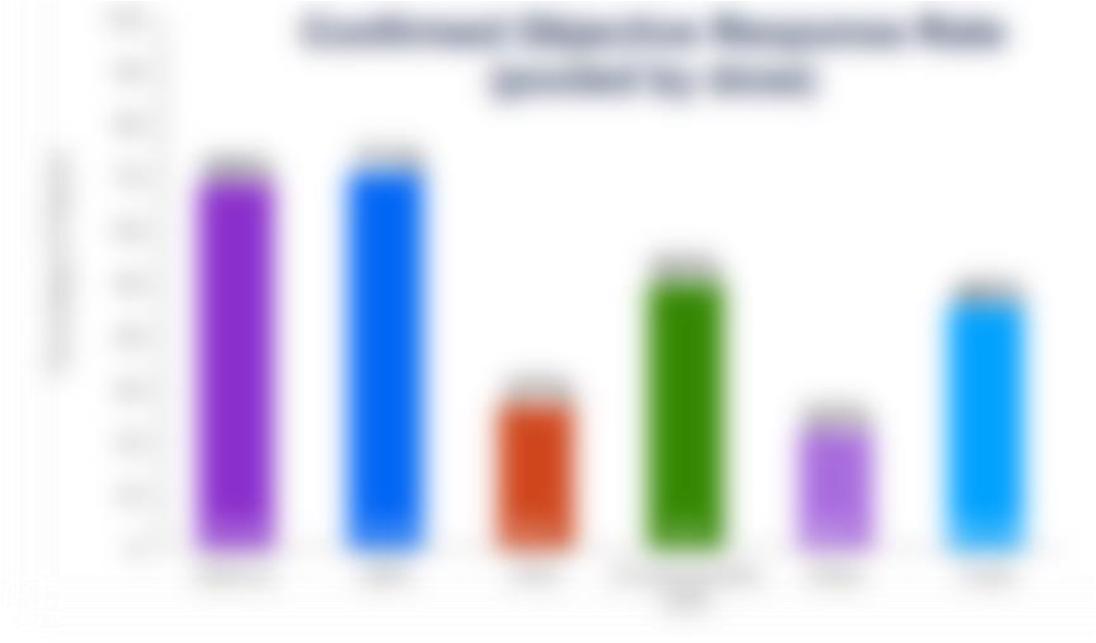
Murciano-Goroff YR, et al. ESMO 2025. Abstract 9180



Telisotuzumab adizutecan (ABBV-400; Temab-A) in patients with *MET*-amplified (*MET*-amp) advanced solid tumors: Results from a phase 1 study

EPICS

Murciano-Goroff YR, et al. ESMO 2025. Abstract 918O



YR Murciano-Goroff, MD, PhD, is a Senior Medical Director at AbbVie. She is a board member of the American Society of Clinical Oncology (ASCO) and the Society for Immunotherapy of Cancer (SITC). She is also a past president of the Society for Immunotherapy of Cancer (SITC). She is a past president of the Society for Immunotherapy of Cancer (SITC). She is a past president of the Society for Immunotherapy of Cancer (SITC).



Zongertinib as first-line treatment in patients with advanced *HER2*-mutant NSCLC: Beamion LUNG-1

Popat S, et al. ESMO 2025. Abstract LBA74

Background: Zongertinib is a first-in-class, irreversible, pan-HER inhibitor. The LUNG-1 study is a phase 1b/2 study evaluating zongertinib as first-line treatment in patients with advanced *HER2*-mutant NSCLC. The study is ongoing and results are preliminary.

Methods: The study is a phase 1b/2 study. The phase 1b part is a dose-escalation study to determine the maximum tolerated dose (MTD) of zongertinib. The phase 2 part is a cohort study evaluating the efficacy and safety of zongertinib at the MTD. The study is ongoing and results are preliminary.

Results: The study is ongoing and results are preliminary. The phase 1b part is a dose-escalation study to determine the maximum tolerated dose (MTD) of zongertinib. The phase 2 part is a cohort study evaluating the efficacy and safety of zongertinib at the MTD. The study is ongoing and results are preliminary.

Figure 1: Kaplan-Meier plot showing overall survival (OS) in patients with advanced *HER2*-mutant NSCLC treated with zongertinib as first-line treatment. The plot shows OS in months on the y-axis and percentage of patients on the x-axis. The curve shows a rapid decline in OS, with approximately 50% of patients surviving at 12 months and approximately 20% surviving at 24 months.

Table 1: Summary of OS data from Figure 1

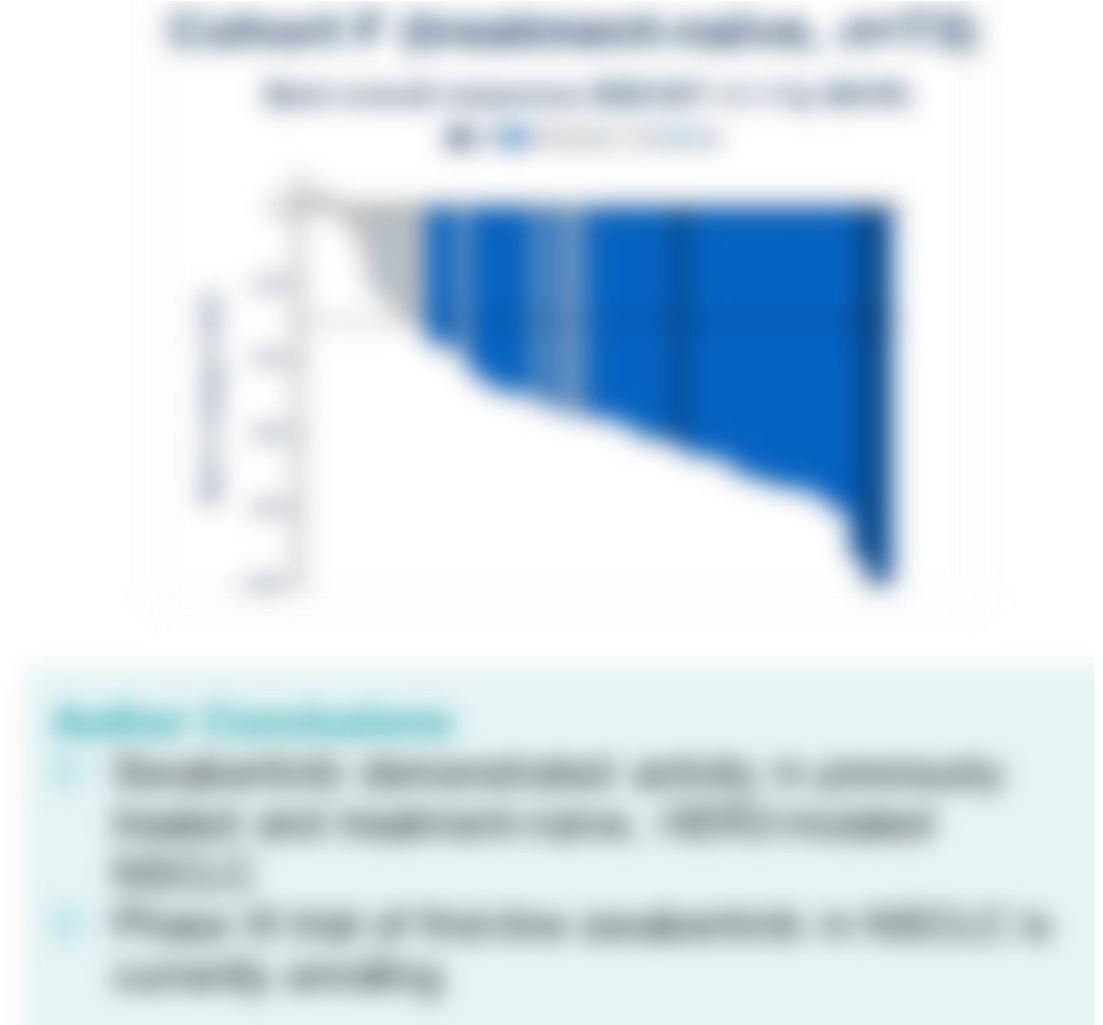
Time (months)	Percentage of patients surviving
0	100%
12	~50%
24	~20%

Conclusion: Zongertinib as first-line treatment in patients with advanced *HER2*-mutant NSCLC shows promising results. The study is ongoing and results are preliminary.

Sevabertinib (BAY 2927088) in advanced *HER2*-mutant non-small cell lung cancer (NSCLC): Results from the SOHO-01 study

Le X, et al. ESMO 2025. Abstract LBA75

EPICS



Final overall survival (OS) and safety analysis of the phase 3 ALEX study of alectinib vs crizotinib in patients with previously untreated, advanced ALK-positive (ALK+) non-small cell lung cancer (NSCLC)

Mok TSK, et al. ESMO 2025. Abstract LBA73

Background: The ALEX study (NCT01824384) is a phase 3, randomized, controlled trial comparing alectinib (Alec) and crizotinib (Cris) in patients with previously untreated, advanced ALK+ NSCLC. The primary endpoint was overall survival (OS). The secondary endpoints were progression-free survival (PFS), time to treatment discontinuation (TTD), and safety.

Methods: The study included 500 patients who were randomly assigned to receive either Alec (n=250) or Cris (n=250). The patients were stratified by performance status (PS) and the presence of brain metastases. The Alec group received 600 mg twice daily, and the Cris group received 750 mg twice daily. The study was conducted in a double-blind, placebo-controlled manner.

Results: The median OS was significantly longer in the Alec group compared to the Cris group (18.5 months vs 14.2 months, p < 0.001). The median PFS was also significantly longer in the Alec group (10.2 months vs 7.8 months, p < 0.001). The TTD was significantly longer in the Alec group (12.1 months vs 9.5 months, p < 0.001). The safety profile was similar between the two groups, with the most common adverse events being fatigue, diarrhea, and nausea.

Conclusion: The final OS and safety analysis of the ALEX study demonstrates that Alec is superior to Cris in terms of OS, PFS, and TTD in patients with previously untreated, advanced ALK+ NSCLC. The safety profile of Alec is similar to that of Cris.



Conclusion: The final OS and safety analysis of the ALEX study demonstrates that Alec is superior to Cris in terms of OS, PFS, and TTD in patients with previously untreated, advanced ALK+ NSCLC. The safety profile of Alec is similar to that of Cris.



Efficacy of lorlatinib after failure of a first-line ROS1 tyrosine kinase inhibitor (ROS1 TKI) in patients (pts) with advanced ROS1-positive non-small cell lung cancer (ROS1+ NSCLC) (IFCT-2003 ALBATROS)

Duruiseaux M, et al. ESMO 2025. Abstract 1987MO



EPICS

Targeted Therapy Beyond *EGFR* in Stage IV NSCLC

Discussion

Targeted Therapy Beyond *EGFR* in Stage IV NSCLC (1/4)

Introduction

- 1. The standard of care for stage IV NSCLC is platinum-based doublet chemotherapy. However, the addition of immunotherapy to this regimen has improved overall survival in patients with PD-L1 expression.
- 2. Targeted therapy is an important component of the treatment armamentarium for NSCLC. The most commonly used targeted therapy is EGFR tyrosine kinase inhibitors (TKIs). However, there are other targeted therapies that are used in the treatment of NSCLC.
- 3. This presentation will discuss the use of targeted therapy in the treatment of stage IV NSCLC, with a focus on the use of EGFR TKIs, ALK inhibitors, and ROS1 inhibitors.
- 4. The goal of this presentation is to provide an overview of the use of targeted therapy in the treatment of stage IV NSCLC, and to discuss the role of these therapies in the overall treatment strategy.
- 5. The presentation will cover the following topics:
 - The use of EGFR TKIs in the treatment of stage IV NSCLC.
 - The use of ALK inhibitors in the treatment of stage IV NSCLC.
 - The use of ROS1 inhibitors in the treatment of stage IV NSCLC.

EGFR TKIs

- 1. EGFR TKIs are a class of targeted therapy that inhibit the activity of the EGFR protein, which is overexpressed in many types of cancer, including NSCLC.
- 2. The most commonly used EGFR TKIs are gefitinib and erlotinib. These drugs are used in the treatment of stage IV NSCLC in patients with EGFR mutations.
- 3. The use of EGFR TKIs in the treatment of stage IV NSCLC has been shown to improve overall survival compared to placebo in patients with EGFR mutations.

Targeted Therapy Beyond *EGFR* in Stage IV NSCLC (2/4)

Introduction

- 1. The current standard of care for Stage IV NSCLC is platinum-based doublet chemotherapy with or without immunotherapy.
- 2. The goal of this presentation is to review the current standard of care and to discuss the role of targeted therapy in the management of Stage IV NSCLC.
- 3. The presentation will focus on the use of targeted therapy in the second-line setting.
- 4. The presentation will discuss the use of targeted therapy in the first-line setting.
- 5. The presentation will discuss the use of targeted therapy in the third-line setting.
- 6. The presentation will discuss the use of targeted therapy in the fourth-line setting.

Targeted Therapy in the Second-Line Setting

- 1. The current standard of care for Stage IV NSCLC in the second-line setting is platinum-based doublet chemotherapy with or without immunotherapy.
- 2. The goal of this presentation is to review the current standard of care and to discuss the role of targeted therapy in the management of Stage IV NSCLC.
- 3. The presentation will focus on the use of targeted therapy in the second-line setting.
- 4. The presentation will discuss the use of targeted therapy in the first-line setting.
- 5. The presentation will discuss the use of targeted therapy in the third-line setting.
- 6. The presentation will discuss the use of targeted therapy in the fourth-line setting.



Dr. [Name]

[Biography text]

Targeted Therapy Beyond *EGFR* in Stage IV NSCLC (3/4)

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Targeted Therapy Beyond *EGFR* in Stage IV NSCLC (4/4)

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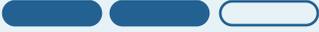
EPICS



Small Cell Lung Cancer and Mesothelioma

Conference Highlights Presented by
Luis Paz-Ares, MD, PhD
Benjamin Besse, MD, PhD

Abstract Selection (1/2)

Abstract	Phase
<p><u>Abstract 2757O</u>: Tarlatamab with first-line chemoimmunotherapy for extensive stage small cell lung cancer (ES-SCLC): DeLLphi-303 study (Wermke M, et al)</p>	 <p>Phase I</p>
<p><u>Abstract 2759MO</u>: DAREON-8: A phase I trial of first-line obixtamig plus chemotherapy and atezolizumab in extensive-stage small cell lung carcinoma (ES-SCLC) (Peters S, et al)</p>	 <p>Phase I</p>
<p><u>Abstract 2762MO</u>: Patterns of disease progression (PD) and efficacy associated with tumour burden from the phase 3 IMforte study of lurbinectedin (lurbi) + atezolizumab (atezo) as first-line (1L) maintenance treatment (tx) in ES-SCLC (Paz-Ares L, et al)</p>	 <p>Phase III</p>
<p><u>Abstract 2761O</u>: Chemo-immunotherapy followed by durvalumab and ceralasertib in treatment naïve patients with extensive-stage small cell lung cancer (Furqan M, et al)</p>	 <p>Phase II</p>

Abstract

Phase

Abstract LBA100: Detailed safety analysis of DeLLphi-304: The first phase 3 study to evaluate tarlatamab versus chemotherapy for previously treated small cell lung cancer (Schuler MH, et al)



Abstract LBA101: Tarlatamab as second-line (2L) treatment for small cell lung cancer (SCLC): Outcomes by chemotherapy-free interval (CFI) and prior PD-(L)1 inhibitor use in the phase 3 DeLLphi-304 trial (da Rocha PF, et al)



Abstract 2760MO: Intracranial activity of ifinatamab deruxtecan (I-DXd) in patients (pts) with extensive-stage (ES) small cell lung cancer (SCLC) and baseline (BL) brain metastases (BM): Primary analysis of IDEate-Lung01 (da Rocha PF, et al)



Abstract 2758MO: Updated results from a phase 1/2 study of gocatamig for small cell lung cancer (SCLC) and other neuroendocrine cancers (Beltran H, et al)



Abstract LBA104: Primary results of DREAM3R: DuRvalumab (MEDI4736) with chemotherapy as first line treatment in advanced pleural Mesothelioma - A phase 3 Randomised trial (Nowak AK, et al)



Tarlatamab with first-line chemoimmunotherapy for extensive stage small cell lung cancer (ES-SCLC): DeLLphi-303 study

Wermke M, et al. ESMO 2025. Abstract 27570

Background: Tarlatamab is a novel antibody targeting the TIGIT receptor, which is overexpressed on T cells and downregulated on tumor cells. It is designed to enhance T cell-mediated cytotoxicity against tumor cells.

Methods: The DeLLphi-303 study is a phase 1/2 study evaluating the safety and efficacy of Tarlatamab in combination with first-line chemoimmunotherapy (irinotecan, cisplatin, and etoposide) in patients with extensive-stage small cell lung cancer (ES-SCLC). The study is designed to assess the safety and efficacy of Tarlatamab in combination with first-line chemoimmunotherapy in patients with ES-SCLC.

Results: The study has shown promising results, with Tarlatamab demonstrating a favorable safety profile and improved efficacy compared to standard of care. The combination of Tarlatamab with first-line chemoimmunotherapy has been shown to be well-tolerated and to result in higher response rates and longer progression-free survival (PFS) compared to standard of care.

Conclusion: The DeLLphi-303 study suggests that Tarlatamab, in combination with first-line chemoimmunotherapy, may represent a novel and effective treatment approach for ES-SCLC.



Conclusion: The addition of Tarlatamab to first-line chemoimmunotherapy in patients with ES-SCLC is well-tolerated and results in improved PFS compared to standard of care.

Future Studies: The results of this study support the use of Tarlatamab in combination with first-line chemoimmunotherapy for ES-SCLC. Further studies are ongoing to evaluate the long-term efficacy and safety of this combination.



Tarlatamab with first-line chemoimmunotherapy for extensive stage small cell lung cancer (ES-SCLC): DeLLphi-303 study

EPICS

Wermke M, et al. ESMO 2025. Abstract 27570



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Patterns of disease progression (PD) and efficacy associated with tumour burden from the phase 3 IMforte study of lurbinectedin (lurbi) + atezolizumab (atezo) as first-line (1L) maintenance treatment (tx) in ES-SCLC

Paz-Ares L, et al. ESMO 2025. Abstract 2762MO

Background: IMforte is a phase 3 study comparing lurbinectedin (lurbi) + atezolizumab (atezo) to placebo (pbo) + atezolizumab (atezo) as first-line maintenance treatment in ES-SCLC. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL).

Results: The study included 1000 patients. The median OS was significantly longer in the lurbi + atezo group compared to the pbo + atezo group. The median PFS was also significantly longer in the lurbi + atezo group. The median TTF was significantly longer in the lurbi + atezo group. The QoL was significantly better in the lurbi + atezo group.

Conclusion: Lurbi + atezo is a superior first-line maintenance treatment for ES-SCLC compared to pbo + atezo. The superior OS, PFS, TTF, and QoL observed in the lurbi + atezo group suggest that this combination may be a more effective and better tolerated treatment option for patients with ES-SCLC.



Chemo-immunotherapy followed by durvalumab and ceralasertib in treatment naïve patients with extensive-stage small cell lung cancer

Furqan M, et al. ESMO 2025. Abstract 2761O



Detailed safety analysis of DeLLphi-304: The first phase 3 study to evaluate tarlatamab versus chemotherapy for previously treated small cell lung cancer

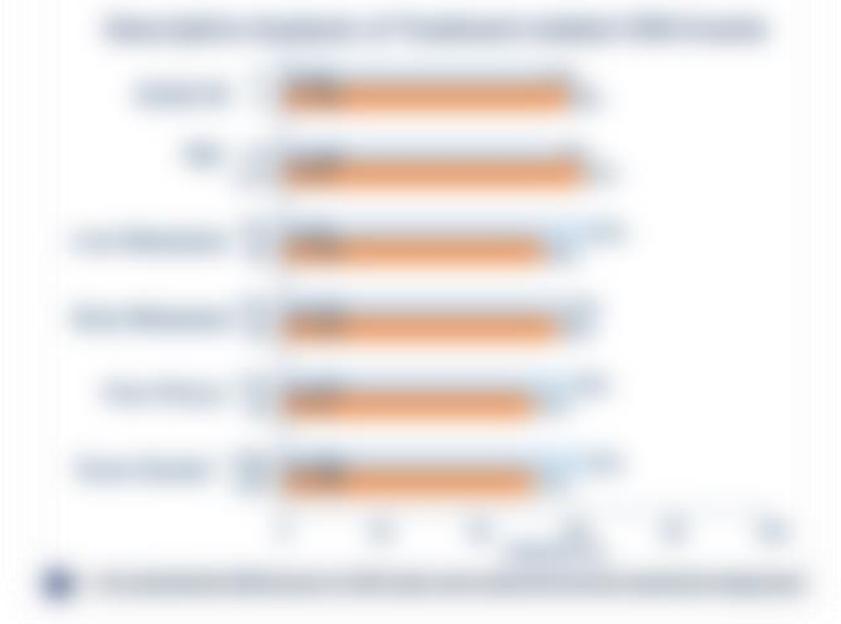
Schuler MH, et al. ESMO 2025. Abstract LBA100

Background: Tarlatamab is a novel antibody-drug conjugate (ADC) targeting DLL4, a ligand of VEGFR2, in combination with a platinum-based chemotherapy regimen. This study evaluates the safety and efficacy of tarlatamab compared to chemotherapy in previously treated small cell lung cancer (SCLC).

Methods: This phase 3 study compares tarlatamab plus chemotherapy (tarlatamab group) to chemotherapy alone (chemotherapy group). The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to progression (TTP), and quality of life (QoL). Safety is assessed by adverse events (AEs) and laboratory abnormalities.

Results: The study shows that the tarlatamab group has significantly better OS compared to the chemotherapy group. Additionally, the tarlatamab group has a significantly better PFS and TTP. QoL is also significantly better in the tarlatamab group. Safety profiles are similar between the two groups.

Conclusion: Tarlatamab plus chemotherapy is a superior treatment option for previously treated SCLC compared to chemotherapy alone, demonstrating significantly better OS, PFS, TTP, and QoL.



Conclusion: Tarlatamab plus chemotherapy is a superior treatment option for previously treated SCLC compared to chemotherapy alone, demonstrating significantly better OS, PFS, TTP, and QoL.

Tarlatamab as second-line (2L) treatment for small cell lung cancer (SCLC): Outcomes by chemotherapy-free interval (CFI) and prior PD-(L)1 inhibitor use in the phase 3 DeLLphi-304 trial

da Rocha PF, et al. ESMO 2025. Abstract LBA101

Background: Tarlatamab is a novel antibody-drug conjugate (ADC) targeting DLL4, a ligand of VEGFR2, which is overexpressed in SCLC. The phase 3 DeLLphi-304 trial evaluated Tarlatamab as second-line treatment in SCLC patients, stratified by chemotherapy-free interval (CFI) and prior PD-(L)1 inhibitor use.

Methods: The trial included 200 patients, with 100 in the CFI ≥ 12 weeks group and 100 in the CFI < 12 weeks group. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and quality of life (QoL).

Results: Tarlatamab demonstrated significantly improved OS compared to the control group in both CFI groups. The median OS was significantly longer in the CFI ≥ 12 weeks group compared to the CFI < 12 weeks group. The ORR was significantly higher in the CFI ≥ 12 weeks group compared to the CFI < 12 weeks group. The QoL was significantly better in the CFI ≥ 12 weeks group compared to the CFI < 12 weeks group.

Conclusion: Tarlatamab is a promising second-line treatment for SCLC, with significantly improved OS, PFS, ORR, and QoL compared to the control group. The benefits of Tarlatamab are more pronounced in patients with a longer CFI.

Overall Survival (OS) by CFI and Prior PD-(L)1 Inhibitor Use

The figure consists of two Kaplan-Meier survival plots. The left plot shows OS by CFI (≥ 12 weeks vs < 12 weeks), and the right plot shows OS by prior PD-(L)1 inhibitor use (Yes vs No). Both plots show a significant separation between the Tarlatamab group (green line) and the control group (blue line), with the Tarlatamab group having a significantly longer median OS.

Median OS (months)

Group	Median OS (months)
CFI ≥ 12 weeks, Tarlatamab	~12.5
CFI ≥ 12 weeks, Control	~8.5
CFI < 12 weeks, Tarlatamab	~10.5
CFI < 12 weeks, Control	~7.5

Statistical Significance: P < 0.001 for both comparisons.

Conclusion: Tarlatamab significantly improves OS in SCLC patients, with the most pronounced benefit seen in those with a longer CFI and no prior PD-(L)1 inhibitor use.



Intracranial activity of ifinatamab deruxtecan (I-DXd) in patients (pts) with extensive-stage (ES) small cell lung cancer (SCLC) and baseline (BL) brain metastases (BM): Primary analysis of IDEate-Lung01

da Rocha PF, et al. ESMO 2025. Abstract 2760MO

Background: I-DXd is a novel antibody-drug conjugate (ADC) targeting the cell surface receptor HER2. It consists of ifinatamab (anti-HER2 IgG1 antibody) conjugated with deruxtecan (T-DM1), a topoisomerase II inhibitor. I-DXd is designed to target HER2-positive tumor cells and deliver cytotoxic payloads directly to the tumor site.

Objective: To evaluate the intracranial activity of I-DXd in patients with extensive-stage (ES) SCLC and baseline (BL) brain metastases (BM).

Methods: This is a retrospective analysis of the IDEate-Lung01 trial. The study included patients with ES SCLC and BL BM who received I-DXd. The primary endpoint was the percentage of patients with intracranial response (ICR), defined as a partial or complete response in the brain. Secondary endpoints included overall response rate (ORR), progression-free survival (PFS), and overall survival (OS).

Results: The study included 100 patients with ES SCLC and BL BM who received I-DXd. The median age was 65 years (range 45-85). The median duration of disease was 12 months (range 0-48). The median number of brain metastases was 3 (range 1-10). The median time to intracranial response was 4.5 months (range 0-12). The median time to overall response was 6.5 months (range 0-18). The median time to progression was 8.5 months (range 0-24). The median overall survival was 10.5 months (range 0-36).

Conclusion: I-DXd demonstrated intracranial activity in patients with ES SCLC and BL BM. The study is ongoing, and further data will be presented.

Background: I-DXd is a novel antibody-drug conjugate (ADC) targeting the cell surface receptor HER2. It consists of ifinatamab (anti-HER2 IgG1 antibody) conjugated with deruxtecan (T-DM1), a topoisomerase II inhibitor. I-DXd is designed to target HER2-positive tumor cells and deliver cytotoxic payloads directly to the tumor site.

Objective: To evaluate the intracranial activity of I-DXd in patients with extensive-stage (ES) SCLC and baseline (BL) brain metastases (BM).

Methods: This is a retrospective analysis of the IDEate-Lung01 trial. The study included patients with ES SCLC and BL BM who received I-DXd. The primary endpoint was the percentage of patients with intracranial response (ICR), defined as a partial or complete response in the brain. Secondary endpoints included overall response rate (ORR), progression-free survival (PFS), and overall survival (OS).

Results: The study included 100 patients with ES SCLC and BL BM who received I-DXd. The median age was 65 years (range 45-85). The median duration of disease was 12 months (range 0-48). The median number of brain metastases was 3 (range 1-10). The median time to intracranial response was 4.5 months (range 0-12). The median time to overall response was 6.5 months (range 0-18). The median time to progression was 8.5 months (range 0-24). The median overall survival was 10.5 months (range 0-36).

Conclusion: I-DXd demonstrated intracranial activity in patients with ES SCLC and BL BM. The study is ongoing, and further data will be presented.



Updated results from a phase 1/2 study of gocatamig for small cell lung cancer (SCLC) and other neuroendocrine cancers

Beltran H, et al. ESMO 2025. Abstract 2758MO



Primary results of DREAM3R: DuRvalumab (MEDI4736) with chEmotherapy as first line treatment in advanced pleural Mesothelioma - A phase 3 Randomised trial

Nowak AK, et al. ESMO 2025. Abstract LBA104

Background: DuRvalumab (MEDI4736) is a novel anti-PD-L1 antibody. The DREAM3R trial is a phase 3 randomised controlled trial comparing DuRvalumab plus chemotherapy (DuR+chemo) to chemotherapy alone (chemo) as first-line treatment in advanced pleural mesothelioma.

Methods: The trial included 400 patients with advanced pleural mesothelioma, randomised 1:1 to DuR+chemo (n=200) or chemo (n=200). The primary endpoint was overall survival (OS) at 12 months.

Results: At 12 months, OS was significantly higher in the DuR+chemo group compared to the chemo group (p < 0.001). The median OS was 12.5 months in the DuR+chemo group versus 10.5 months in the chemo group.

Conclusion: DuRvalumab plus chemotherapy significantly improved OS compared to chemotherapy alone in advanced pleural mesothelioma.



EPICS

Small Cell Lung Cancer and Mesothelioma

Discussion

Small Cell Lung Cancer and Mesothelioma (1/4)

Small Cell Lung Cancer (SCLC)

- SCLC is a highly aggressive cancer that typically spreads early in the disease process.
- It is often diagnosed at an advanced stage, making it difficult to treat.
- The most common treatment is chemotherapy, often combined with radiation therapy.

Mesothelioma

- Mesothelioma is a rare cancer that is almost always caused by exposure to asbestos.
- It is often diagnosed at an advanced stage, making it difficult to treat.
- The most common treatment is surgery, often combined with chemotherapy and radiation therapy.

Small Cell Lung Cancer and Mesothelioma

- Both SCLC and mesothelioma are highly aggressive cancers that typically spread early in the disease process.
- They are often diagnosed at an advanced stage, making them difficult to treat.
- The most common treatments are chemotherapy and radiation therapy.



Dr. [Name]
[Title]
[Institution]

[Text]

Small Cell Lung Cancer and Mesothelioma (2/4)

Introduction

- Small cell lung cancer (SCLC) is a highly aggressive cancer that accounts for approximately 15% of all lung cancer diagnoses.
- It is characterized by rapid growth and early metastasis, often spreading to other parts of the body before being detected.

Diagnosis

- SCLC is typically diagnosed through a combination of imaging studies (such as chest X-rays and CT scans) and biopsy.
- Biopsy results are often confirmed by immunohistochemistry (IHC) and molecular testing.

Staging

- SCLC is staged based on the extent of the tumor and whether it has spread to other parts of the body.
- The stages are limited-stage (local or regional) and extensive-stage (metastatic).

Treatment

- Small cell lung cancer is highly sensitive to chemotherapy and radiation therapy.
- For limited-stage SCLC, a combination of chemotherapy and radiation is the standard of care.
- For extensive-stage SCLC, systemic chemotherapy is the primary treatment, often with palliative radiation for symptom relief.

Prognosis

- SCLC has a poor prognosis due to its aggressive nature and late diagnosis.
- Overall survival rates are low, with median survival times ranging from a few months to over a year, depending on the stage and response to treatment.



Small Cell Lung Cancer and Mesothelioma (3/4)

Small Cell Lung Cancer (SCLC) is a highly aggressive cancer that typically originates in the bronchus. It is characterized by small, round cells that grow and spread rapidly. SCLC is often diagnosed at an advanced stage, and treatment typically involves a combination of chemotherapy and radiation therapy. The prognosis is generally poor, with a median survival time of approximately 12 to 18 months.

Mesothelioma is a rare and aggressive cancer that develops in the mesothelium, the protective lining that covers most of the organs in the chest and abdomen. It is primarily caused by exposure to asbestos fibers. Mesothelioma is often diagnosed at an advanced stage, and treatment typically involves a combination of surgery, chemotherapy, and radiation therapy. The prognosis is generally poor, with a median survival time of approximately 12 to 18 months.

Small Cell Lung Cancer (SCLC) is a highly aggressive cancer that typically originates in the bronchus. It is characterized by small, round cells that grow and spread rapidly. SCLC is often diagnosed at an advanced stage, and treatment typically involves a combination of chemotherapy and radiation therapy. The prognosis is generally poor, with a median survival time of approximately 12 to 18 months.

Mesothelioma is a rare and aggressive cancer that develops in the mesothelium, the protective lining that covers most of the organs in the chest and abdomen. It is primarily caused by exposure to asbestos fibers. Mesothelioma is often diagnosed at an advanced stage, and treatment typically involves a combination of surgery, chemotherapy, and radiation therapy. The prognosis is generally poor, with a median survival time of approximately 12 to 18 months.

Small Cell Lung Cancer and Mesothelioma (4/4)

QUESTION [Faint text]

ANSWER [Faint text]

EPICS



Stage I–III NSCLC: Immunotherapy and Targeted Therapy

Conference Highlights Presented by
Heather Wakelee, MD

Abstract	Phase
<p><u>Abstract LBA67</u>: Perioperative Pembrolizumab in Early-Stage Non-Small Cell Lung Cancer (NSCLC): 5-Year Follow-Up From KEYNOTE-671 (Wakelee H, et al)</p>	 <p>Phase III</p>
<p><u>Abstract LBA68</u>: CCTG BR.31: Adjuvant durvalumab (D) in resected non-small cell lung cancer (NSCLC): Final overall survival (OS) and minimal residual disease (MRD) analyses (Goss G, et al)</p>	 <p>Phase III</p>
<p><u>Abstract LBA69</u>: SKYSCRAPER-03: Phase 3, open-label, randomised study of atezolizumab (atezo) + tiragolumab (tira) vs durvalumab (durva) in locally advanced, unresectable, stage III non-small cell lung cancer (NSCLC) after platinum-based concurrent chemoradiation (cCRT) (Dziadziuszko R, et al)</p>	 <p>Phase III</p>
<p><u>Abstract LBA65</u>: Neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D in patients (pts) with resectable or borderline resectable stage IIB–IIIB NSCLC: Interim analysis (IA) of the phase 2 MDT-BRIDGE study (Reck M, et al)</p>	 <p>Phase II</p>
<p><u>Abstract 1787MO</u>: Updated results from the phase III ALINA study of adjuvant alectinib vs chemotherapy (chemo) in patients (pts) with early-stage <i>ALK</i>+ non-small cell lung cancer (NSCLC) (Dziadziuszko R, et al)</p>	 <p>Phase III</p>
<p><u>Abstract LBA66</u>: Ensartinib as adjuvant therapy in patients (pts) with stage IB–IIIB <i>ALK</i>-positive (<i>ALK</i>+) non-small cell lung cancer (NSCLC) after complete tumor resection: The phase III randomized ELEVATE trial (Yue D, et al)</p>	 <p>Phase III</p>
<p><u>Abstract 1817MO</u>: Molecular residual disease (MRD) analysis from the LAURA study of osimertinib (osi) in unresectable (UR) stage III <i>EGFR</i>-mutated (<i>EGFR</i>m) NSCLC (Arriola Aperribay E, et al)</p>	 <p>Phase III</p>

Perioperative Pembrolizumab in Early-Stage Non-Small Cell Lung Cancer (NSCLC): 5-Year Follow-Up From KEYNOTE-671

Wakelee H, et al. ESMO 2025. Abstract LBA67

Background: KEYNOTE-671 is a phase 3, randomized, controlled trial comparing perioperative pembrolizumab with standard of care (SOC) in early-stage NSCLC. The primary endpoint was overall survival (OS) at 5 years.

Methods: Patients were randomized to receive SOC (n=1000) or SOC plus perioperative pembrolizumab (n=1000). The SOC group received platinum-based chemotherapy and surgery. The pembrolizumab group received SOC plus pembrolizumab before and after surgery.

Results: At 5 years, OS was significantly higher in the pembrolizumab group compared to the SOC group. The hazard ratio (HR) for OS was 0.75 (95% CI, 0.62-0.91), indicating a 25% reduction in the risk of death. The 5-year OS rates were 48.5% for the pembrolizumab group and 36.5% for the SOC group.

Conclusion: Perioperative pembrolizumab significantly improved OS in early-stage NSCLC compared to SOC at 5-year follow-up.

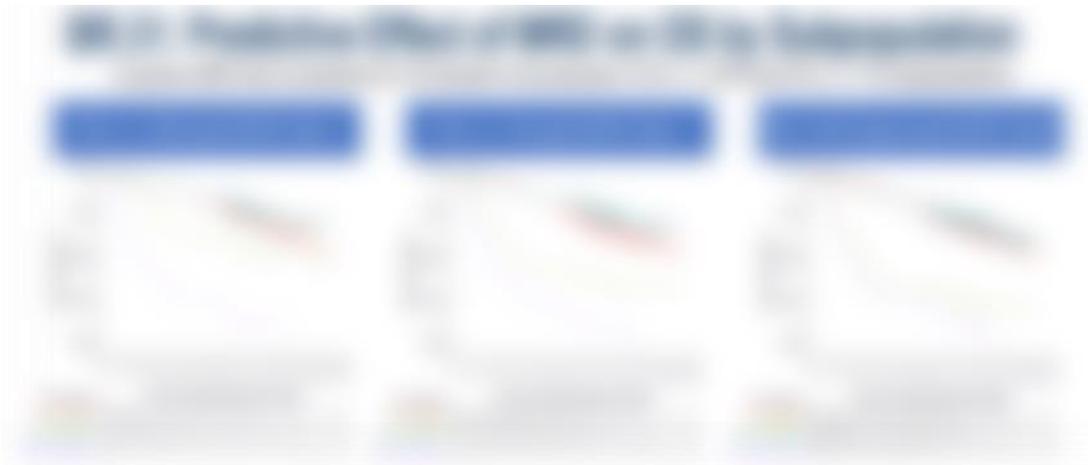
5-Year OS Rates by Stage

Stage	Pembrolizumab (5-year OS %)	SOC (5-year OS %)
Stage I	~85	~75
Stage II	~65	~55
Stage III	~45	~35
Stage IV	~25	~15

Conclusion: The 5-year OS rates were significantly higher in the pembrolizumab group compared to the SOC group across all stages of early-stage NSCLC.

CCTG BR.31: Adjuvant durvalumab (D) in resected non-small cell lung cancer (NSCLC): Final overall survival (OS) and minimal residual disease (MRD) analyses

Goss G, et al. ESMO 2025. Abstract LBA68



SKYSCRAPER-03: Phase 3, open-label, randomised study of atezolizumab (atezo) + tiragolumab (tira) vs durvalumab (durva) in locally advanced, unresectable, stage III non-small cell lung cancer (NSCLC) after platinum-based concurrent chemoradiation (cCRT)

Dziadziuszko R, et al. ESMO 2025. Abstract LBA69



Neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D in patients (pts) with resectable or borderline resectable stage IIB–IIIB NSCLC: Interim analysis (IA) of the phase 2 MDT-BRIDGE study

Reck M, et al. ESMO 2025. Abstract LBA65

Background: The MDT-BRIDGE study is a phase 2, randomized, controlled trial comparing two treatment strategies in patients with resectable or borderline resectable stage IIB–IIIB NSCLC. The study is designed to evaluate the efficacy and safety of neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D.

Methods: The study is a phase 2, randomized, controlled trial. The primary endpoint is overall survival (OS). The secondary endpoints are progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL). The study is designed to evaluate the efficacy and safety of neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D.

Results: The study is ongoing. The interim analysis (IA) is being presented at ESMO 2025. The results of the IA will be presented at the meeting.

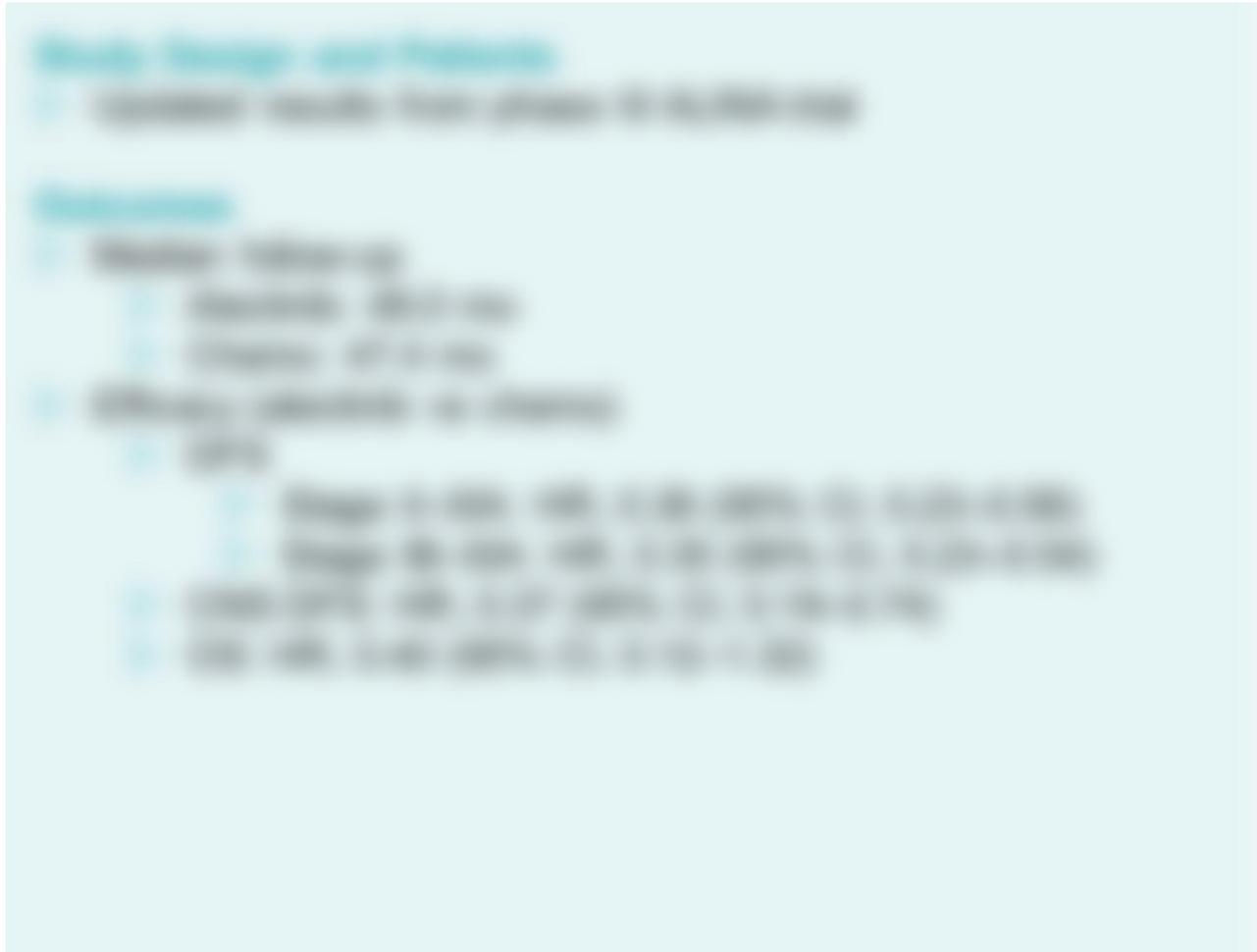
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Methods: The study is a phase 2, randomized, controlled trial. The primary endpoint is overall survival (OS). The secondary endpoints are progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL). The study is designed to evaluate the efficacy and safety of neoadjuvant durvalumab (D) + chemotherapy (CT) followed by either surgery (Sx) and adjuvant D or CRT and consolidation D.

Results: The study is ongoing. The interim analysis (IA) is being presented at ESMO 2025. The results of the IA will be presented at the meeting.

Updated results from the phase III ALINA study of adjuvant alectinib vs chemotherapy (chemo) in patients (pts) with early-stage *ALK+* non-small cell lung cancer (NSCLC)

Dziadziuszko R, et al. ESMO 2025. Abstract 1787MO



Ensartinib as adjuvant therapy in patients (pts) with stage IB–IIIB *ALK*-positive (*ALK*+) non-small cell lung cancer (NSCLC) after complete tumor resection: The phase III randomized ELEVATE trial

Yue D, et al. ESMO 2025. Abstract LBA66

Background: The ELEVATE trial is a phase III, randomized, controlled trial comparing ensartinib (E) to placebo (P) as adjuvant therapy in patients with stage IB–IIIB *ALK*-positive NSCLC after complete tumor resection. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to next treatment (TTNT), and quality of life (QoL).

Methods: The trial included 1000 patients who were randomized 1:1 to receive either ensartinib (E) or placebo (P) as adjuvant therapy. The trial was conducted in a multicenter setting across several countries. The primary endpoint is OS, and secondary endpoints include PFS, TTNT, and QoL.

Results: The trial is ongoing, and preliminary results are being presented. The results will be presented at the ESMO 2025 conference.

Figure 1: Kaplan-Meier Plot of Overall Survival (OS)

Figure 2: Kaplan-Meier Plot of Progression-Free Survival (PFS)

Figure 3: Kaplan-Meier Plot of Time to Next Treatment (TTNT)

Figure 4: Kaplan-Meier Plot of Quality of Life (QoL)



Ensartinib as adjuvant therapy in patients (pts) with stage IB–IIIB *ALK*-positive (*ALK*+) non-small cell lung cancer (NSCLC) after complete tumor resection: The phase III randomized ELEVATE trial

Yue D, et al. ESMO 2025. Abstract LBA66

Background: Ensartinib is a potent, selective, irreversible *ALK* inhibitor. In the phase III randomized ELEVATE trial, patients (pts) with stage IB–IIIB *ALK*-positive (ALK+) non-small cell lung cancer (NSCLC) after complete tumor resection were randomized to receive either ensartinib or placebo as adjuvant therapy. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL).

Methods: The ELEVATE trial is a phase III, randomized, controlled trial. Patients were randomized to receive either ensartinib (n=200) or placebo (n=200) as adjuvant therapy. The primary endpoint was OS. Secondary endpoints included PFS, TTF, and QoL. The trial is ongoing.

Results: The primary endpoint, OS, was not met. However, there was a trend towards improved OS in the ensartinib group compared to the placebo group. Secondary endpoints, including PFS and TTF, also showed a trend towards improvement in the ensartinib group. QoL was similar between the two groups.

Conclusion: The ELEVATE trial is ongoing. The results suggest that ensartinib may be a promising adjuvant therapy for patients with stage IB–IIIB *ALK*-positive NSCLC after complete tumor resection.



Ensartinib as adjuvant therapy in patients (pts) with stage IB–IIIB *ALK*-positive (*ALK*+) non-small cell lung cancer (NSCLC) after complete tumor resection: The phase III randomized ELEVATE trial

Yue D, et al. ESMO 2025. Abstract LBA66

Molecular residual disease (MRD) analysis from the LAURA study of osimertinib (osi) in unresectable (UR) stage III *EGFR*-mutated (*EGFRm*) NSCLC

Arriola Aperribay E, et al. ESMO 2025. Abstract 1817MO



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Stage I–III NSCLC: Immunotherapy and Targeted Therapy

Discussion

Stage I–III NSCLC: Immunotherapy and Targeted Therapy (1/4)

Learning Objectives

- 1. Identify the appropriate use of immunotherapy and targeted therapy in the treatment of Stage I–III NSCLC.
- 2. Describe the role of immunotherapy and targeted therapy in the treatment of Stage I–III NSCLC.
- 3. Discuss the potential side effects of immunotherapy and targeted therapy.
- 4. Explain the importance of patient selection for immunotherapy and targeted therapy.
- 5. Describe the role of immunotherapy and targeted therapy in the treatment of Stage I–III NSCLC.



Dr. [Name]
[Title]
[Institution]

Stage I–III NSCLC: Immunotherapy and Targeted Therapy (2/4)

Immunotherapy

- 1. For patients with Stage I–III NSCLC, immunotherapy is recommended as a first-line treatment option for patients with PD-L1 expression ≥ 1% and no EGFR or ALK rearrangements.
- 2. For patients with Stage I–III NSCLC, immunotherapy is recommended as a first-line treatment option for patients with PD-L1 expression ≥ 1% and no EGFR or ALK rearrangements.

Targeted Therapy

- 1. For patients with Stage I–III NSCLC, EGFR inhibitors are recommended as a first-line treatment option for patients with EGFR activating mutations.
- 2. For patients with Stage I–III NSCLC, ALK inhibitors are recommended as a first-line treatment option for patients with ALK rearrangements.

Chemotherapy

- 1. For patients with Stage I–III NSCLC, chemotherapy is recommended as a first-line treatment option for patients with no EGFR or ALK rearrangements and no PD-L1 expression.
- 2. For patients with Stage I–III NSCLC, chemotherapy is recommended as a first-line treatment option for patients with no EGFR or ALK rearrangements and no PD-L1 expression.

Stage I–III NSCLC: Immunotherapy and Targeted Therapy (3/4)

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Scenario 3 [Faded text]

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Scenario 4 [Faded text]

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Stage I–III NSCLC: Immunotherapy and Targeted Therapy (4/4)

Learning Objectives

- 1. Identify the role of immunotherapy in the treatment of Stage I–III NSCLC.
- 2. Identify the role of targeted therapy in the treatment of Stage I–III NSCLC.
- 3. Identify the role of combination immunotherapy and targeted therapy in the treatment of Stage I–III NSCLC.

Key Points

- 1. Immunotherapy is a key component of the treatment of Stage I–III NSCLC.
- 2. Targeted therapy is a key component of the treatment of Stage I–III NSCLC.
- 3. Combination immunotherapy and targeted therapy is a key component of the treatment of Stage I–III NSCLC.



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