COMMENTARY

A Landmark Year for Lung Cancer Research at ASCO 2025

Roy Herbst[1a]

[1] Yale Cancer Center and Smilow Cancer Hospital, Yale University, New Haven, CT, United States

Keywords: editorial, lung, lungcancer, asco, asco2025

https://doi.org/10.36000/HBT.OH.2025.24.177

healthbook TIMES Oncology Hematology

Vol. 24, Issue 2, 2025

Attending the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting feels like stepping into a new era of lung cancer research. Reflecting on nearly 30 years of participation, the transformation is nothing short of extraordinary. I remember a time when ASCO lung cancer sessions offered little more than incremental changes in chemotherapy, long-term survival was rare and multimodality therapy was just beginning to emerge. Today, we are witnessing breakthroughs in novel approaches, such as targeted therapy and immunotherapy, for both non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).

One of the most striking updates this year is the neoadjuvant use of osimertinib, building on the foundational success of the ADAURA trial.[1,2] I had the privilege of presenting ADAURA at a plenary lecture in the past years, and it is inspiring to see its ongoing impact. At ASCO 2025, Dr Jamie Chaft from the Memorial Sloan Kettering Cancer Center presented results of the NeoADAURA study, showing that osimertinib yields a major pathologic response in 25% of patients with early-stage *EGFR*-mutant NSCLC.[3] These data provide clear evidence of growing paradigm shift toward earlier intervention with precision therapies. We will continue to build on the success of the ADAURA trials, and for patients with *EGFR* driver mutations, this will enable benefit from targeted therapy earlier in their disease course.

In SCLC, a notable advancement was presented in the phase III trial DeLLphi-304 trial, in which tarlatamab, a delta-like ligand 3 (DLL3) × CD3 T-cell engager, demonstrated superiority over standard chemotherapy in recurrent disease.[4] Dr Charles Rudin from the Fiona and Stanley Druckenmiller Center for Lung Cancer Research and Memorial Sloan Kettering Cancer Center reported this pivotal data, marking it is as a cornerstone of this year's lung cancer track.

a Roy S. Herbst, MD, PhD
Ensign Professor of Medicine and Pharmacology
Deputy Director and Chief of Medical Oncology and Hematology
Yale Cancer Center and Smilow Cancer Hospital
Yale University
New Haven, CT, United States
Email: roy.herbst@yale.edu

Further presentations in the lung cancer session highlighted promising data on combination strategies, including KRAS inhibitors such as adagrasib in combination with immunotherapy in the phase III KRYSTAL-7 trial.[5] While not all trials were positive, such as the phase III HERTHENA-Lung02 study of a new HER3-directed antibody-drug conjugate patritumab deruxtecan in resistant *EGFR*-mutant advanced NSCLC presented by Dr Tony Mok from the State Key Laboratory of Translational Oncology, Chinese University of Hong Kong, which failed to show overall survival benefit,[6] others brought encouraging news. Specifically, novel approaches to overcome EGFR resistance, including c-Met-directed agents or small molecules such as savolitinib, demonstrated clinical benefit. The phase III SACHI trial reported improved progression-free survival when savolitinib was combined with osimertinib in patients with *EGFR*-mutant, *MET*-amplified, pretreated NSCLC.[7]

What resonates most is that this progress is deeply patient-centered. Each new agent and strategy brings us a step closer to tailored, effective and earlier treatment. What was once a field with limited options is now at the forefront of precision oncology. It is a thrilling time to be part of this transformative journey.

Sincerely,

Roy S. Herbst, MD, PhD
Ensign Professor of Medicine and Pharmacology
Deputy Director and Chief of Medical Oncology and Hematology
Yale Cancer Center and Smilow Cancer Hospital
Yale University
New Haven, CT, United States
Email: roy.herbst@yale.edu

Conflict of interest

The author reported ownership of stocks and shares from Normunity, Checkpoint Therapeutics, Bolt Biotherapeutics and Immunocore; reports consulting and advisory roles for AstraZeneca, Genentech/Roche, Merck, Pfizer, AbbVie, Bristol Myers Squibb, Lilly, EMD Serono, Junshi Pharmaceuticals, Loxo, NextCure, Novartis, Sanofi, Bolt Biotherapeutics, I-Mab, Mirati Therapeutics, Cybrexa Therapeutics, eFFECTOR Therapeutics, Candel Therapeutics, Oncternal Therapeutics, Xencor, Checkpoint

Therapeutics, DynamiCure Biotechnology, Gilead/Forty-Seven, HiberCell, Immune-Onc Therapeutics, Johnson & Johnson, Ocean Biomedical, OncoCyte, Refactor Health, Ribon Therapeutics, Janssen, NextCure, Normunity, Regeneron and Revelar; leadership roles for Junshi Pharmaceuticals, Immunocore, American Association for Cancer Research, IASLS, Society for Immunotherapy of Cancer and SWOG; research funding from AstraZeneca, Merck, Lilly and Genentech/Roche; and travel expenses from American Cancer Society, IASLC, and SWOG. These funding entities did not play a role in the development of the manuscript and did not influence its content in any way.

Funding

The author has declared that no financial support was received from any organization for the submitted manuscript.

Author contributions

The author has created and approved the final manuscript.

Published: June 20, 2025 CEST.

REFERENCES

1. Tsuboi M, Herbst RS, John T, et al. Overall Survival with Osimertinib in Resected EGFR-Mutated NSCLC. *N Engl J Med*. 2023;389(2):137-147. doi:10.1056/NEJMoa2304594

2. Wu YL, Tsuboi M, He J, et al. Osimertinib in Resected EGFR-Mutated Non-Small-Cell Lung Cancer. *N Engl J Med*. 2020;383(18):1711-1723. doi:10.1056/NEJMoa2027071

3. Chaft JE, Weder W, He J, et al. Neoadjuvant osimertinib ± chemotherapy (CT) vs CT alone in resectable epidermal growth factor receptor-mutated (EGFRm) NSCLC: NeoADAURA. Presented at: 2025 ASCO Annual Meeting; 30 May–3 June 2025. Chicago, IL, USA. Oral presentation 8001. doi:10.1200/JCO.2025.43.16_suppl.8001

4. Rudin CM, Mountzios GS, Sun L, et al. Tarlatamab versus chemotherapy (CTx) as second-line (2L) treatment for small cell lung cancer (SCLC): Primary analysis of Ph3 DeLLphi-304. Presented at: 2025 ASCO Annual Meeting; 30 May–3 June 2025. Chicago, IL, USA. Oral presentation LBA8008. doi:10.1200/JCO.2025.43.17_suppl.LBA8008

5. Jänne PA, Theelen WS, Garassino MG, et al. First-line adagrasib with pembrolizumab in patients with advanced/metastatic KRASG12C-mutated non-small cell lung cancer (NSCLC) from the phase 2 portion of the KRYSTAL-7 study. Presented at: 2025 ASCO Annual Meeting; 30 May–3 June 2025. Chicago, IL, USA. Oral presentation 8500. doi:10.1200/JCO.2025.43.16_suppl.8500

6. Mok T, Yu H, Lim SM, et al. Patritumab deruxtecan (HER3-DXd) in resistant EGFR-mutated (EGFRm) advanced non-small cell lung cancer (NSCLC) after a third-generation EGFR TKI: The phase 3 HERTHENA-Lung02 study. Presented at: 2025 ASCO Annual Meeting; 30 May–3 June 2025. Chicago, IL, USA. Oral presentation 8506. doi:10.1200/JCO.2025.43.16_suppl.8506

7. Lu S, Wang J, Yang N, et al. Savolitinib combined with osimertinib versus chemotherapy in EGFR-mutant (EGFRm) and MET-amplification (METamp) advanced NSCLC after disease progression on EGFR tyrosine kinase inhibitor (TKI): Results from a randomized phase 3 SACHI study. Presented at: 2025 ASCO Annual Meeting; 30 May–3 June 2025. Chicago, IL, USA. Oral presentation LBA8505. doi:10.1200/JCO.2025.43.17_suppl.LBA8505