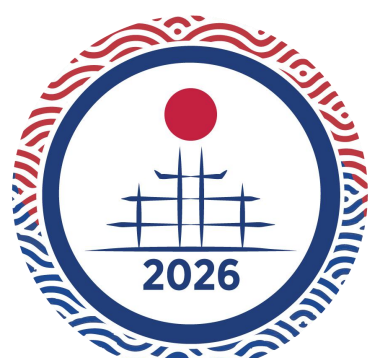


P2.382: HACTION: A Phase III Randomized Trial of Aumolertinib Plus Chemotherapy vs. Monotherapy in EGFR-Mutant Advanced NSCLC with High-Risk Factors

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IASLC 2026 World
Conference on Lung Cancer

SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

BACKGROUND

Epidermal growth factor receptor (EGFR) mutation is one of the most common driver alterations in non-small cell lung cancer (NSCLC). Third_x0002_generation EGFR-TKIs such as aumolertinib are established as first-line standard therapy for EGFR-mutant (19del/L858R) advanced NSCLC. However, patients with high-risk factors—such as brain metastases, high tumor burden, tumor suppressor gene co-mutations, or PD-L1 expression—still have a poor prognosis with limited benefit from TKI monotherapy, representing a significant unmet clinical need. While the AENEAS2 study has provided high-level evidence for the application of aumolertinib plus chemotherapy as first-line therapy in the overall population, high-level evidence specifically validating this combination therapy in this high-risk subgroup remains lacking. This phase III trial aims to address this critical unmet need.

STUDY DESIGN

This prospective, multicenter, open-label, randomized controlled phase III study is conducted across approximately 13 sites in China. Eligible patients are 18-75 years old with stage IIB-IV EGFR-mutant (19del/L858R) NSCLC and harbor at least one high-risk factor: 1) brain metastases; 2) high tumor burden (≥ 2 metastatic sites, pleural/pericardial metastasis, or N3/multiple-station N2 disease); 3) tumor suppressor gene co-mutations (TP53, RB1, APC, PTEN, BRCA1/2, CHEK2, ATM, etc.); or 4) PD-L1 tumor proportion score (TPS) $\geq 1\%$. A total of 1,035 patients will be randomized 1:1 to receive either aumolertinib (110 mg QD) plus carboplatin (AUC=5) and pemetrexed (500 mg/m²) for four cycles, followed by aumolertinib plus pemetrexed maintenance (experimental arm), or aumolertinib monotherapy (control arm). The primary endpoint is investigator-assessed progression-free survival (PFS) per RECIST v1.1. Secondary endpoints include objective response rate (ORR), disease control rate (DCR), duration of response (DoR), overall survival (OS), and safety profiles.

