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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)

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Background

Ivonescimab significantly improved PFS over pembrolizumab as first-line therapy for advanced NSCLC in PD-L1 TPS ≥1%. In HARMONi-6, we compared ivonescimab plus chemotherapy versus (vs.) tislelizumab plus chemotherapy in squamous NSCLC regardless of PD-L1 expression (NCT05840016).

Methods

Eligible patients with untreated stage IIIB-IV squamous NSCLC were randomized (1:1) to ivonescimab 20 mg/kg Q3W or tislelizumab 200 mg Q3W, plus paclitaxel (175 mg/m2) and carboplatin (AUC 5) for 4 cycles, followed by ivonescimab or tislelizumab monotherapy as maintenance treatment. Randomization was stratified by disease stage (IIIB/IIIC vs. IV) and PD-L1 TPS (≥1% vs. <1%). The primary endpoint was PFS assessed by independent radiographic review committee (IRRC) per RECIST v1.1. OS is the key secondary endpoint. This is the first planned analysis on PFS with an efficacy boundary of one-sided P=0.0094.

Results

532 patients were randomized: 266 to each arm. At baseline, 63.2% of patients had central tumours, 8.8% had tumour cavitation, and 17.5% had major blood vessel encasement. Baseline characteristics were well balanced between the two arms. The ivonescimab-chemotherapy combination demonstrated a statistically significant improvement in PFS compared with tislelizumab-chemotherapy (HR 0.60, 95% CI 0.46–0.78; p<0.0001). The median PFS is 11.1 months vs. 6.9 months for ivonescimab and tislelizumab groups, respectively, as assessed by IRRC. Consistent benefit was observed across key subgroups. In patients with PD-L1 TPS <1%, the median PFS was 9.9 vs. 5.7 months with an HR of 0.55 (95% CI 0.37-0.82); in patients with PD-L1 TPS ≥1%, the median PFS was 12.6 vs. 8.6 months with an HR of 0.66 (95% CI 0.46-0.95). Safety analyses revealed treatment-related SAE in 32.3% vs. 30.2%, and grade≥3 hemorrhagic events occurred in 1.9% vs. 0.8%, for ivonescimab and tislelizumab groups, respectively.

Conclusions

This phase III trial result suggests first-line ivonescimab-chemotherapy may be a new standard of care for advanced/metastatic squamous NSCLC.

Clinical trial identification

NCT05840016.

Legal entity responsible for the study

Akeso Biopharma, Inc.

Funding

Akeso Biopharma, Inc.

Disclosure

S. Lu: Financial Interests, Personal and Institutional, Research Funding: AstraZeneca, Hutchison , BMS, Heng Rui, BeiGene , Hansoh; Financial Interests, Personal and Institutional, Speaker, Consultant, Advisor: AstraZeneca; Financial Interests, Personal and Institutional, Invited Speaker: Roche, Hansoh, Hengrui ; Financial Interests, Personal and Institutional, Advisory Role: Pfizer, Hutchison, ZaiLab , Yuhan Corporation, Menarini , InventisBio Co. Ltd., Shanghai Fosun Pharmaceutical (Group) Co., Ltd., Simcere Zaiming Pharmaceutical Co., Ltd.; Financial Interests, Personal and Institutional, Member of Board of Directors: Innovent Biologics, INC. Y. Xia: Financial Interests, Personal and Institutional, Other, employee: Akeso Biopharma. All other authors have declared no conflicts of interest.