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JUPITER-06: A randomized, double-blind, phase III study of toripalimab versus placebo in combination with first-line chemotherapy for treatment naive advanced or metastatic esophageal squamous cell carcinoma (ESCC)

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Background

Platinum-based chemotherapy is the standard first-line treatment for advanced or metastatic ESCC. Toripalimab, a humanized monoclonal antibody against PD-1, showed promising efficacy results as first-line treatment for ESCC in combination with paclitaxel plus cisplatin (TP) in a phase Ib trial. Here, we report the results of JUPITER-06 (NCT03829969), a randomized, double-blind phase III trial of toripalimab in combination with TP for advanced or metastatic ESCC.

Methods

Patients with treatment-naïve, advanced or metastatic ESCC were randomized (1:1) to receive 240 mg toripalimab or placebo in combination with TP Q3W up to 6 cycles, followed by toripalimab or placebo maintenance. Stratification factors were ECOG performance score and prior radiotherapy. The primary endpoints were progression-free survival (PFS) by a blinded independent central review (BICR) per RECIST v1.1 and overall survival (OS).

Results

A total of 514 ESCC patients were randomized; 257 in each arm. At a prespecified interim analysis on March 22, 2021, with median follow-up of 7.4 and 7.3 months in the two arms, there was a significant improvement in OS for toripalimab over placebo (HR=0.58 [95% CI: 0.43-0.78], P=0.00037) with median OS of 17.0 vs. 11.0 months. One-year OS rates were 66.0% vs. 43.7%. A significant improvement in PFS by BICR was also detected for toripalimab over placebo (HR=0.58 [95% CI: 0.46-0.74], P<0.00001). The OS and PFS benefits were observed across key subgroups, including all PD-L1 expression subgroups. The incidence of Grade ≥3 adverse events (AEs) (73.2% vs 70.0%) and fatal AEs (8.2% vs 8.2%) were similar between the two arms; however, AEs leading to discontinuation of toripalimab/placebo (11.7% vs 6.2%); immune-related AEs (irAEs) (37.0% vs. 26.5%) and Grade ≥3 irAEs (6.6% vs. 1.6%) were more frequent in the toripalimab arm.

Conclusions

The addition of toripalimab to standard first-line chemotherapy in patients with ESCC showed superior PFS and OS over chemotherapy alone with a manageable safety profile. These results support the use of toripalimab with TP chemotherapy as a new first-line treatment for advanced or metastatic ESCC.

Legal entity responsible for the study

Shanghai Junshi Biosciences and Coherus Biosciences.

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Disclosure

R. Xu: Financial Interests, Personal, Advisory Role: Bristol-Myers Squibb; Financial Interests, Personal, Advisory Role: Merk Serono; Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Advisory Role: Astellas; Financial Interests, Personal, Advisory Role: AstraZeneca. All other authors have declared no conflicts of interest.

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