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Sintilimab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced or metastatic esophageal squamous cell cancer: First results of the phase III ORIENT-15 study

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Background

ORIENT-15 is a global, randomized, double-blind study to evaluate the efficacy and safety of sintilimab + chemo (S+C) vs chemo (C) as first-line (1L) treatment in patients (pts) with unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC).

Methods

Eligible pts were randomized 1:1 to sintilimab/placebo 200 mg Q3W for up to 24 months +chemo (TP: paclitaxel 175 mg/m^2 Q3W + cisplatin 75 mg/m^2 Q3W or CF: cisplatin 75 mg/m^2 Q3W+5-FU 800 mg/m^2 on d1-5 Q3W). Randomization was stratified by ECOG PS (0 vs 1), liver metastasis (presence vs absence), chemo regimen (TP vs CF). Treatment continued until progression, unacceptable toxicity or withdrawal. No crossover was permitted. The primary end points were OS in the pts with PD-L1 combined positive score (CPS) ≥10 and all pts. The secondary endpoints were PFS and ORR (RECIST v1.1; by investigator) in the pts with PD-L1 CPS ≥10 and all pts. Data cutoff for interim analysis was Apr 9, 2021.

Results

At data cutoff, 659 pts (86% male, 97% Chinese, 87% metastatic) were randomized (327 S+C, 332 C). Median follow-up was 11.4 months. Sintilimab + chemo vs chemo was superior for OS in all pts (median 16.7 vs 12.5 mo, HR 0.628, 95% CI 0.508-0.777, P < 0.0001) and CPS ≥10 pts (median 17.2 vs 13.6 mo, HR 0.638, 95% CI 0.480-0.848, P =0.0018). PFS was superior with S+C vs C in all pts (median 7.2 vs 5.7 mo, HR 0.558, 95% CI 0.461-0.676, P <0.0001) and CPS ≥10 pts (median 8.3 vs 6.4 mo, HR 0.580, 95% CI 0.449-0.749, P <0.0001). ORR was 75.5 vs 56.9% in all pts, with median DOR of 8.3 vs 5.6 mo. ORR was 78.7 vs 57.5% in CPS ≥10 pts, with median DOR of 8.5 vs 5.5 mo. Of pts receiving at least one drug dose, treatment-related adverse events (TRAEs) rates were 98.2% vs 98.2%. Grade ≥3 TRAEs rates were 59.9% vs 54.5%. Discontinuation rates from TRAEs were 20.8% vs 12.3%. Death rates from TRAEs were 2.8% vs 1.8%.

Conclusions

OS, PFS and ORR are all significantly improved in S+C vs C, with a manageable safety profile in the pts with PD-L1 CPS ≥10 and all pts. Especially the HR of OS is less than 0.7 in all pts. The results demonstrate that the combination of sintilimab and chemo can be considered as a new 1L treatment in patients with advanced or metastatic ESCC.

Clinical trial identification

NCT03748134.

Legal entity responsible for the study

Innovent Biologics, Inc., China.

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Disclosure

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