Randomized, Phase 3 study of second-line tislelizumab vs chemotherapy in advanced or metastatic esophageal squamous cell carcinoma, RATIONALE 302: Asia subgroup

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Background:

In the global Phase 3 study RATIONALE 302 (NCT03430843), tislelizumab (TIS) demonstrated statistically and clinically significant improvement in overall survival (OS) vs chemotherapy (chemo) (median OS 8.6 vs 6.3 months; HR 0.70; 95% CI 0.57, 0.85; p=0.0001) in patients with advanced or metastatic esophageal squamous cell carcinoma (ESCC). Here, we report data from the Asia subgroup.

Methods:

Eligible patients who had disease progression after first-line systemic therapy were randomized 1:1 to receive TIS 200 mg intravenously once every three weeks or chemo (paclitaxel, docetaxel, or irinotecan) until disease progression, intolerable toxicity, or withdrawal. The primary endpoint was OS in all randomized patients (Intent-to-treat population). The key secondary endpoint was OS in patients with PD-L1 Tumor Area Positivity Score* ≥ 10%; other secondary endpoints included progression-free survival (PFS), objective response rate (ORR), duration of response (DoR), health-related quality of life, and safety.

Results:

Of the 512 randomized patients, 404 (79%) were enrolled from China, Taiwan, Japan, and Korea and constituted the Asia subgroup (n=201 TIS, n=203 chemo). At data cut-off (December 1, 2020), median follow-up was 6.9 months in the Asia subgroup. Median OS was 8.5 months with TIS vs 6.3 months with chemo (HR 0.73; 95% CI 0.59, 0.90). Median PFS was 1.5 months with TIS vs 1.7 months with chemo (HR 0.81; 95% CI 0.64, 1.02). TIS resulted in a higher ORR (20.4% [95% CI 15.1, 26.6] vs 9.4% [95% CI 5.7, 14.2]) and longer median DoR (7.4 vs 4.0 months; HR 0.42; 95% CI 0.21, 0.84) vs chemo. In the safety analysis set (n=201 TIS, n=191 chemo), patients treated with TIS had fewer treatment-related adverse events (TRAEs) (74.1% vs 95.3%), fewer ≥ Grade 3 TRAEs (19.4% vs 57.1%), fewer serious TRAEs (15.4% vs 20.9%), and a similar incidence of TRAEs leading to death (2.5% vs 2.6%) vs chemo.

Conclusions:

In the Asia subgroup, TIS improved OS and tumor response vs chemo as second-line treatment in patients with advanced or metastatic ESCC and showed a well-tolerated safety profile. These findings were consistent with published results in the overall population.

*The TAP score methodology has been previously referred to as visually-estimated combined positive score (vCPS) and was previously presented at the American Society of Clinical Oncology 2021, June 4–8, 2021, ESMO World Gastrointestinal Congress 2021, June 30–July 3, 2021, and The Chinese Society of Clinical Oncology 2021, September 25–29, 2021