RATIONALE 302: Randomized, Phase 3 study of tislelizumab vs chemotherapy as second-line treatment for advanced unresectable/metastatic esophageal squamous cell carcinoma

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Background:

Tislelizumab (tisle) showed activity in patients (pts) with solid tumors, including esophageal squamous cell carcinoma (ESCC).

Methods:

Global Phase 3 study NCT03430843 enrolled adults with advanced/metastatic ESCC who progressed after prior systemic therapy. Pts were randomized (1:1) to receive tisle 200 mg intravenously every 3 weeks or Investigator Choice Chemotherapy (ICC) paclitaxel, docetaxel, or irinotecan until progression or unacceptable toxicity and stratified for ICC, region, and ECOG PS. The primary endpoint was overall survival (OS) in all patients. The key secondary endpoint was OS in the programmed cell death-ligand 1

(PD-L1) ≥ 10% by visual combined positive score (vCPS)-population. Other secondary endpoints included (by RECIST v1.1) progression-free survival, overall response rate (ORR), duration of response (DoR), and safety.

Results:

Overall, 512 pts (median age: 62 years) from 132 sites in 10 countries in Asia (404 pts [79%]), Europe and North America (108 pts [21%]) were randomized to tisle (n=256) or ICC (n=256). Of these, 157 pts (tisle [n=89], ICC [n=68]) were PDL1 ≥10%. In Spain, 24 patients (tisle [n=14], ICC [n=10]) were enrolled at 8 sites. The study met its primary endpoint: tisle significantly improved OS vs ICC (median OS: 8.6 vs 6.3 m; HR 0.70, 95% CI 0.57-0.85, p=0.0001). Significant OS improvement was seen also in PD-L1≥10% population (median OS: 10.3 vs 6.8 m; HR 0.54, 95% CI: 0.36-0.79, p=0.0006). Survival benefit was consistent across pre-defined subgroups. Tisle had a higher ORR (20.3% vs 9.8%) and response duration (median DoR: 7.1 vs 4.0 m; HR 0.42, 95% CI 0.23-0.75). Fewer pts had ≥Grade 3 (46% vs 68%) treatment-emergent and ≥Grade 3 treatment related AEs with tisle (19% vs 56%).

Conclusion:

Tisle demonstrated statistically significant and clinically meaningful improvement in OS vs ICC in pts with advanced/metastatic ESCC after first-line systemic therapy. Tisle showed a higher and longer response with tolerable safety profile.