Congress Information:

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Abstract:

Keywords: esophageal squamous cell carcinoma, anti-PD-L1 antibody, sugemalimab

Title: GEMSTONE-304: a phase 3 study of sugemalimab plus chemotherapy versus chemotherapy as first-line treatment of patients with unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC)

Background:

Although anti-programmed death 1 (PD-1) antibody plus chemotherapy has recently been approved for first-line (1L) ESCC, anti-programmed death-ligand 1 (PD-L1) antibody may offer another combination option in this setting. Sugemalimab (Suge), an anti-PD-L1 monoclonal antibody, plus fluorouracil and cisplatin (FP) regimen demonstrated preliminary anti-tumor activity in a phase 1b cohort of patients (pts) with advanced ESCC. We present the results from a randomized, double-blinded phase 3 study of Suge or placebo (Pbo) plus FP as 1L treatment of pts with advanced ESCC.

Methods:

Eligible pts were randomized (2:1) into Suge + FP or Pbo + FP arms, stratified by PD-L1 expression status, ECOG PS, and distant metastasis. Pts received intravenous Suge 1200 mg or Pbo every 3 weeks (Q3W) for up to 24 months (m), plus FP regimen (fluorouracil: 800 mg/m^2/day on d1-4; cisplatin: 80 mg/m^2 on d1) Q3W for up to 6 cycles. The primary endpoints were progression-free survival (PFS) as assessed by blinded independent central review (BICR) per RECIST v1.1 and overall survival (OS) in the intent-to-treat (ITT) set. Key secondary endpoints included PFS as assessed by investigator, objective response rate (ORR), duration of response (DoR), and safety. Data cutoff date for final PFS and interim OS was 07 Oct 2022.

Results:

540 pts were randomized to receive Suge + FP (n=358) and Pbo + FP (n=182). The median age was 63.0 years, 87.4% of pts were male, and 78.9% of pts had ECOG PS 1. With a median follow-up of 15.2 m, BICR-assessed PFS prolongation was statistically significant with Suge + FP versus Pbo + FP (median PFS: 6.2 m vs 5.4 m; hazard ratio [HR], 0.67 [95% CI, 0.54−0.82], P=0.0002). Overall survival was also superior with Suge + FP (median OS: 15.3 m vs 11.5 m; HR, 0.70 [95% CI, 0.55−0.90], P=0.0076). Benefits of PFS and OS were generally observed across all pre-specified subgroups including different PD-L1 expression levels. Suge + FP also showed a significantly higher BICR-assessed ORR (60.1% vs 45.2%) and more durable response (median DOR: 6.0 m vs 4.5 m). Grade≥3 treatment-related adverse events (TRAEs) (51.3% vs 48.4%), serious TRAEs (21.5% vs 13.2%), treatment discontinuation due to treatment-emergent AEs (13.3% vs 10.4%), and TRAEs leading to death (1.7% vs 0.5%)

were comparable between Suge + FP and Pbo + FP arms.

Conclusions:

Suge plus FP demonstrated statistically significant and clinically meaningful prolongation of PFS and OS, and improvement of ORR compared with Pbo plus FP. The safety profile was manageable with no new safety signals detected. These results support the use of Suge plus FP as 1L treatment for unresectable locally advanced, recurrent or metastatic ESCC.