Tislelizumab in Combination With Chemotherapy as Treatment for Chinese Patients With Esophageal Squamous Cell Carcinoma (ESCC)

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Background Tislelizumab, an investigational humanized IgG4 monoclonal antibody with high affinity and specificity for PD-1, was engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Previous data showed tislelizumab, as a single agent and in combination with chemotherapy, was generally well tolerated and had antitumor activity in patients (pts) with advanced solid tumors. This phase 2 study (NCT03469557) assessed the safety/tolerability of tislelizumab plus chemotherapy as first-line therapy in pts with gastric cancer and ESCC; results of the ESCC cohort are presented.

Methods Patients with inoperable, locally advanced or metastatic ESCC were treated with tislelizumab (200 mg IV Q3W), cisplatin (80 mg/m² IV Q3W for up to six cycles), and fluorouracil (800 mg/m²/d, Days 1-5 IV Q3W for up to six cycles). Antitumor response was assessed using RECIST v1.1, survival was estimated with Kaplan-Meier methodology, and safety/tolerability was assessed by monitoring adverse events (AEs).

Results As of 31 March 2019, 15 pts (median age, 61 yr; male, 14) were enrolled. Seven of 15 pts had confirmed PR (ORR = 47%; 95% CI: 21.3-73.4), five achieved SD. No pts had PD; three pts were missing a post-baseline radiographic assessment. At data cut-off, median PFS was 10.4 mo (95% CI: 5.6-15.1). Despite a median follow-up of 13.0 mo (95% CI: 12.3-14.0), median OS had not been reached. Anemia (n=12), decreased appetite (n=11), and nausea (n=9) were the most common AEs related to either tislelizumab or chemotherapy. Treatment-emergent AEs of grade ≥3 severity occurring in ≥2 pts regardless of attribution were vomiting and dysphagia (n=4 each), hyponatremia (n=3) as well as anemia, leukopenia, fatigue, lung infection, and decreased weight (n=2 each). One pt experienced a fatal AE (hepatic dysfunction), which was attributed to treatment by the investigator but may have been confounded by progressive disease and underlying hepatitis.

Conclusion Tislelizumab combined with chemotherapy was generally well tolerated and demonstrated antitumor activity in pts with advanced ESCC.