Clinical Profile of Tislelizumab in Chinese Patients With Microsatellite Instability High (MSI-H) or Mismatch Repair-Deficient (MMRd) Solid Tumors: Preliminary Results From an Indication-Expansion Cohort

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Objective Solid tumors characterized by MSI-H/MMRd, such as colorectal cancer (CRC), are sensitive to PD-1 blockade. Tislelizumab is a humanized IgG4 monoclonal antibody with high affinity/specificity for PD-1. Tislelizumab was specifically engineered to minimize $F_c\gamma R$ binding on macrophages that, based on preclinical evidence, is believed to minimize potentially negative interactions with other immune cells. In the dose-verification part of this phase 1/2 study, tislelizumab was generally well tolerated and the recommended dose of tislelizumab was established as 200 mg IV every three weeks (Q3W).

Methods In the indication-expansion component of this study, the antitumor activity (RECIST v1.1) and safety/tolerability (NCI-CTCAE v4.03) of tislelizumab are being evaluated in Chinese patients (pts) with CRC or other tumors whose MSI-H or MMRd status was tested either by a local or a central laboratory. Enrolled pts receive tislelizumab 200 mg IV Q3W until unacceptable toxicity, consent withdrawal, or no evidence of continued clinical benefit.

Results As of 8 Dec 2017, 11 pts with solid tumors (median age 48 yrs [range: 37–71]) were enrolled. The majority of pts were male (64%) and had received ≥1 line of systemic therapy (91%); primary tumor site for most pts was CRC (n=9, 82%). Central testing confirmed 6 pts had tumors with MSI-H (n=5) or MMRd (n=1). Eleven enrolled pts had a median follow-up duration of 3.4 months (range: 0.33–5.88); 8 pts (73%) remained on treatment. Of the 5 pts with centrally confirmed MSI-H or MMRd that are evaluable for response assessment (n=4, CRC; n=1, primary site unknown), 2 pts with CRC achieved unconfirmed partial response and 3 had stable disease. Two additional evaluable pts with confirmed non-MSI-H/MMRd had disease progression. Overall, anemia, increased ALT, and increased AST (n=3/11 each) were the most common AEs considered related to treatment. No treatment-related grade ≥3 AE was reported.

Conclusions Tislelizumab demonstrated preliminary antitumor activity in patients with MSI-H/MMRd solid tumors. The safety profile of tislelizumab was generally tolerable.