Efficacy and Safety Data From a Phase 1/2 Trial of Tislelizumab in Chinese Patients With Non-Small Cell Lung Cancer (NSCLC)

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Background PD-(L)1 inhibitors have provided new treatment approaches for patients with NSCLC; however, resistance to PD-(L)1 inhibitors or low PD-L1 expression may limit clinical benefit. Tislelizumab, a monoclonal antibody with high affinity and specificity for PD-1, was recently approved in China for the treatment of previously treated classical Hodgkin lymphoma. Tislelizumab was engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Preliminary reports from this study (NCT04068519) showed that tislelizumab monotherapy was generally well tolerated and demonstrated antitumor activity in Chinese patients with advanced solid tumors. We now present data from patients with NSCLC.

Method This multi-arm, open-label, nonrandomized phase 1/2 study evaluated safety/tolerability, antitumor activity, and survival in patients with histologically/cytologically confirmed advanced solid tumors treated with tislelizumab. Eligible patients progressed on, or were intolerant to, their last standard antitumor treatment and were anti-PD-(L)1 therapy treatment-naïve. Patients received intravenous tislelizumab 200 mg every 3 weeks until loss of clinical benefit or unacceptable toxicity. Patients were considered PD-L1-positive if ≥10% of their tumor cells had PD-L1 membrane staining at any intensity using the VENTANA PD-L1 (SP263) assay. Antitumor response was assessed by RECIST v1.1, overall survival (OS) was estimated by Kaplan-Meier analysis, and safety/tolerability was examined by monitoring adverse events (AEs).

Results As of 01 December 2018, 56 patients with NSCLC (nonsquamous, n=31 [55%]; squamous, n=25 [45%]) were enrolled. Forty patients (71%) were male, 53 (95%) had metastatic disease, and 23 (41%) had never smoked; one patient each had an *EGFR* mutation or *ALK* rearrangement. Patients were heavily pretreated, with 16 patients (29%) receiving ≥3 lines of prior systemic therapy. The most common treatment-related AEs (TRAEs) were increased AST (n=14; 25%), increased ALT (n=13; 23%), and rash (n=8; 14%). Increased AST (n=3; 5%) and increased ALT (n=2; 4%) were the only grade ≥3 TRAEs occurring in ≥2 patients. Immune-related AEs (irAE) were reported in 12 patients (21%) and were generally of low severity, including 1 patient with grade 2 pneumonitis; 4 patients (7%) experienced a grade ≥3 irAE. The objective response rate (ORR) was 18% (95% CI: 8.9, 30.4), with an ORR of 17% (95% CI: 4.7, 37.4) and 19% (95% CI: 7.5, 37.5) in patients who were PD-L1-positive (n=24) and PD-L1-negative (n=31), respectively. With a median follow-up of 14.6 months (95% CI: 12.0, 15.6), median OS was not reached in patients with NSCLC. Updated data with a follow-up of ≥2 years will be presented, including OS.

Conclusion Tislelizumab was generally well tolerated and demonstrated antitumor activity in NSCLC patients regardless of PD-L1 expression status. Tislelizumab is being evaluated as a single agent or with chemotherapy in phase 3 studies in NSCLC patients (NCT03358875, NCT03594747, and NCT03663205).