Single-Agent Tislelizumab, an Anti-PD-1 Antibody: Results From a Phase 1 Expansion Cohort in NSCLC Patients

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Background Tislelizumab is an investigational monoclonal antibody with high affinity and specificity for PD-1. Tislelizumab 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 reports from this first-in-human study (NCT02407990), and other early phase studies, suggested tislelizumab was generally well tolerated and had antitumor activity in patients with advanced solid tumors.

Methods Patients in nine dose-expansion cohorts received tislelizumab administered at a dose of 5 mg/kg Q3W, including a NSCLC cohort. Adverse events (AEs) were assessed per NCI-CTCAE 4.03 and tumor assessments were performed Q9W (RECIST v1.1). PD-L1 was retrospectively assessed with the VENTANA PD-L1 (SP263) assay; PD-L1-positive (PD-L1$^+$) NSCLC was defined as ≥25% tumor cells expressing PD-L1 by immunohistochemistry.

Results A total of 49 patients with NSCLC (median age 62 years [39–78]) received tislelizumab. Twenty-three patients were Caucasian and 21 were Asian; 34 patients were current/former smokers. Forty-four patients had received prior systemic chemotherapy (1 line, n=24; 2 lines, n=10; ≥3 lines, n=10). As of 27 Oct 2018, median study follow-up was 11.2 months (0.5–27.7) and 46 patients were evaluable for response. Confirmed partial responses (PRs; n=6) and stable disease (n=23) were observed. The objective response rate was 13% (95% CI: 4.9–26.3) and the disease control rate was 63% (95% CI: 47.6, 76.8). Of the 37 patients with PD-L1 evaluable samples, PRs were seen in three of 16 patients (19%) with PD-L1$^+$ NSCLC and two of 21 patients (10%) with PD-L1$^-$ NSCLC. Across all patients, median overall survival (OS) was 11.5 months (95% CI: 9.3, not reached [NR]). Median OS was 15.1 months (95% CI: 4.2, NR) for patients with PD-L1$^+$ NSCLC and 11.2 months (95% CI: 6.1, NR) for patients with PD-L1$^-$ NSCLC. Hypothyroidism was the most commonly reported treatment-related AE (TRAE; n=6), followed by hyperthyroidism, fatigue, and pneumonitis (n=5 each). Eight grade ≥3 TRAEs were reported in six patients: pneumonitis (n=3), autoimmune colitis, vomiting, elevated ALT, elevated AST, and macular rash (n=1 each). A single treatment-related death due to pneumonitis occurred in a patient with compromised pulmonary capacity at baseline.

Conclusions Tislelizumab was generally well tolerated and demonstrated antitumor activity in NSCLC patients. Tislelizumab is being evaluated as a single agent or with chemotherapy in phase 3 studies in NSCLC patients (NCT03358875, NCT03594747, and NCT03663205).