First Report of Efficacy and Safety From a Phase 2 Trial of Tislelizumab, an Anti-PD-1 Antibody, for the Treatment of PD-L1$^+$ Locally Advanced or Metastatic Urothelial Carcinoma (UC) in Asian Patients

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Background Tislelizumab, an investigational anti-PD-1 antibody, 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 showed tislelizumab was generally well tolerated and had antitumor activity in patients (pts) with advanced solid tumors, including UC.

Method This phase 2 clinical trial (CTR20170071) conducted in China and Korea assessed the safety, tolerability, and efficacy of tislelizumab (200 mg Q3W) in pts with PD-L1$^+$ UC previously treated with ≥1 platinum-containing therapy. Prior treatment with a PD-(L)1 inhibitor was not allowed. During screening, archival tissue or fresh biopsy from all pts was sent to a central laboratory for PD-L1 testing via the VENTANA SP263 IHC assay. Patients were considered PD-L1$^+$ if ≥25% of tumor or immune cells had PD-L1 expression. The primary efficacy endpoint was ORR (RECIST v1.1), assessed by an independent review committee (IRC). Secondary efficacy endpoints included DoR, PFS, and OS; AE incidence and severity were secondary safety endpoints.

Results Between 04 Jul 2017 and 28 Feb 2019**,** 113 pts received tislelizumab for a median of 15 wks and were followed up for a median of 8 mo. Urinary bladder (n=51) and renal pelvis (n=31) were common primary tumor sites. Of the 104 evaluable pts, a confirmed objective response was observed in 24 pts (ORR=23%, 95% CI: 15.4, 32.4), including 8 CR and 16 PR per IRC assessment. Median DoR per IRC was not reached at the time of protocol-defined analysis; 19/24 (79%)

responders had ongoing responses at data cutoff. Median PFS and OS were 2.1 and 9.8 mo, respectively. Anemia (27%), decreased appetite (19%), and pyrexia (17%) were the only TRAEs occurring in >15% of pts; anemia (7%) was the only grade 3-4 TRAE occurring in ≥5% pts. Four pts experienced a grade 5 AE attributed to treatment by the investigator (hepatic failure, n=2; respiratory arrest, n=1; renal impairment, n=1).

Conclusion Tislelizumab was generally well tolerated and demonstrated clinical activity in pts with PD-L1^{+} UC.