Updated analysis from a Phase 2 study of tislelizumab (TIS) monotherapy in patients (pts) with previously treated, locally advanced, unresectable/metastatic microsatellite instability-high (MSI-H)/mismatch repair-deficient (dMMR) solid tumors

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Abstract

Background: TIS is an anti-programmed cell death protein-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis. Primary results from this single-arm, multicenter, open-label, Phase 2 study evaluating TIS in pts with MSI-H/dMMR solid tumors, showed a clinically meaningful improvement in the objective response rate (ORR) for this patient population. Here we report results from the updated analysis (NCT03736889).

Methods: Eligible adult pts with previously treated, locally advanced, unresectable/metastatic histologically confirmed MSI-H/dMMR solid tumors with ≥1 measurable lesion (RECIST v1.1) and an Eastern Cooperative Oncology Group performance status of ≤1 were enrolled. Pts received TIS 200 mg intravenously every 3 weeks until disease progression, unacceptable toxicity, or withdrawal. The efficacy analysis set were all pts who received any dose of TIS with measurable disease per independent review committee (IRC) at baseline. The primary endpoint was IRC-assessed ORR (RECIST v1.1). Secondary endpoints included duration of response (DoR), time to response (TTR), disease control rate (DCR), progression-free survival (PFS) (all IRC-assessed [RECIST v1.1]), overall survival (OS), and safety. Programmed-death ligand-1 (PD-L1) immunohistochemistry assay (Ventana SP263) was applied retrospectively.

Results: Between Sep 2018–Jul 2021, 80 pts were enrolled (median age 53 years; range 19–81 years) and 75 were included in the efficacy analysis set. In this updated efficacy analysis set, at a median follow-up of 15.2 months, ORR_{IRC} was 46.7% (n=35; 95% CI 35.1, 58.6) in all tumor types (1-sided p<0.0001), including 5 complete responses (CR) and 30 partial responses (PR). ORR_{IRC} was 39.1% (n=18; 95% CI 25.1, 54.6) in colorectal cancer

(CRC) pts (N=46), 55.6% (n=5; 95% CI 21.2, 86.3) in G/GEJC pts (N=9), and 60.0% (n=12; 95% CI 36.1, 80.9) in other pts (N=20). Of the pts who responded (n=35), one patient had disease progression. Median DoR was not reached, median TTR_{IRC} was 11.9 weeks (range 8.4–98.9) and DCR was 72.0% (95% CI 60.4, 81.8). Median PFS_{IRC} was not reached (95% CI 7.5, not estimable [NE]). Median OS (safety analysis set) was not reached (95% CI 28.7, NE). No clear association was observed between PD-L1 expression and clinical efficacy. Treatment-emergent adverse events (TEAEs) ≥Grade 3 occurred in 48.8% (n=39) of pts. The most common ≥ Grade 3 TEAE was anemia, 10.0% (n=8). Immune-mediated TEAEs ≥ Grade 3 were 8.8% (n=7).

Conclusions:

With a longer follow up time, TIS demonstrated clinically meaningful improvement in ORR in pts with MSI-H or dMMR solid tumors. TIS was generally well tolerated, with no new safety signals. These data support TIS as a new treatment option for this patient population.