A Phase 2 study of tislelizumab monotherapy in patients with previously treated, locally advanced, unresectable or metastatic microsatellite instability-high/mismatch repair-deficient solid tumors

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Objective:
Tislelizumab (TIS) is an anti-programmed cell death protein-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis. TIS monotherapy is generally well tolerated and has antitumor activity in patients (pts) with solid tumors, including microsatellite instability-high (MSI-H) or mismatch-repair-deficient (dMMR) tumors. This single-arm, multicenter, Phase 2 study evaluated the efficacy and safety of TIS monotherapy in adult Chinese pts.

Methods:

Eligible pts with previously treated, locally advanced, unresectable/metastatic histologically confirmed MSI-H/dMMR solid tumors were enrolled. Pts received TIS 200 mg IV every 3 weeks until disease progression, unacceptable toxicity, or withdrawal. The primary 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 overall response rate (ORR; RECIST v1.1). Secondary endpoints included duration of response (DoR), disease control rate, and safety.

Results:

Between Sep 2018–Aug 2020, 80 pts were enrolled (median age 53 years; range 19-81 years) and 74 were included in the primary efficacy analysis set. At a median follow-up of 11.78 months, ORR by IRC was 45.9% (n=34/74; 95% CI 34.3, 57.9) in all tumor types (1-sided p<0.0001), including 4 complete responses (CR) and 30 partial responses (PR). Observed ORR by IRC was 39.1% (n=18/46; 95% CI 25.1, 54.6) in colorectal cancer (CRC) pts and 57.1% (n=16/28; 95% CI 37.2, 75.5) in non-CRC pts. Of 74 pts, 53 (71.6%) had disease control and 39 (52.7%) achieved CR, PR, or durable stable disease by IRC ≥24 weeks. Median DoR by IRC has not been reached; no disease progression was reported in the 34 responders, with 33 responders still on treatment (12-month DoR rate=100%). Treatment-emergent adverse events (TEAEs) ≥Grade 3 occurred in 47.5% (n=38/80) pts, of which 21.3% (n=17/80) were lab abnormalities. Immune-mediated TEAEs ≥Grade 3 were 5.0% (n=4/80).

Conclusion:

TIS achieved statistical significance and demonstrated clinically meaningful improvement in ORR in pts with MSI-H or dMMR solid tumors. Treatment effect was consistent and durable across tumor types. TIS was generally well tolerated, with no new safety signals. The data support TIS as a new treatment option in this population.