Safety, tolerability, and preliminary antitumor activity of sitravatinib plus tislelizumab (TIS) in patients (pts) with unresectable locally advanced or metastatic gastric cancer/gastroesophageal junction cancer (GC/GEJC)

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Background:

Sitravatinib is a selective tyrosine kinase inhibitor targeting TAM and VEGFR2 that reduces the number of myeloid-derived suppressor and regulatory T cells and increases the ratio of M1/M2-polarized macrophages. This may help to overcome an immunosuppressive tumor microenvironment and augment antitumor responses. TIS, an anti-programmed cell death protein-1 (PD-1) antibody designed to minimize binding to FcγR on macrophages and abrogate antibody-dependent phagocytosis, has shown activity in pts with multiple advanced solid tumors. This multicohort, Phase 1/2 study assessed the safety/tolerability and efficacy of sitravatinib alone or with TIS (BGB-900-104; NCT03941873). We report results from the Phase 2 GC/GEJC cohort receiving sitravatinib plus TIS.

Methods:

Eligible pts were aged ≥ 18 years, had inoperable locally advanced or metastatic GC/GEJC, had failed or were ineligible for current standard of care, must not have received prior immunotherapy, had an ECOG PS of 0–1, and ≥1 measurable lesion (RECIST v1.1). Pts received sitravatinib 120 mg orally once daily and TIS 200 mg intravenously every three weeks. The primary endpoint was objective response rate (ORR) (RECIST v1.1; by investigator). Secondary endpoints included duration of response (DoR), disease control rate (DCR), progression-free survival (PFS) (all per RECIST v1.1; by investigator), and safety and tolerability. Exploratory endpoints included overall survival (OS).

Results:

As of July 12, 2021, 24 pts were treated. Median age was 62.5 years (range: 44–74), 83.3% of pts were male, and 62.5% of pts had received ≥ 2 prior lines of systemic therapy. Median study follow-up was 5.2 months (range: 1.0–8.0); 5 pts (20.8%) remained on treatment. Confirmed ORR was 12.5% in 3 pts (95% CI: 2.7–32.4), all of whom achieved partial responses. Median DoR was not estimable (95% CI: 3.5 months–NE), DCR was 66.7% (95% CI: 44.7–84.4), and median PFS was 3.4 months (95% CI: 2.0–NE). Median OS was not estimable (95% CI: 4.7 months–NE); the landmark OS rate at 6 months was 71.3% (95% CI: 46.1–86.3). Treatment-emergent adverse events (TEAEs) of any Grade/Grade ≥ 3 were reported in 95.8%/50.0% of pts. Serious TEAEs were observed in 45.8% of pts (n=11). The most common Grade ≥ 3 TEAEs included hypertension, upper abdominal pain, and respiratory failure (all n=2; 8.3%). In total, 3 pts (12.5%) experienced ≥ 1 TEAE leading to discontinuation of sitravatinib, and 2 pts (8.3%) experienced ≥ 1 TEAE leading to discontinuation of TIS. Dose reductions of sitravatinib due to TEAEs occurred in 6 pts (25.0%).

Conclusions:

The combination of sitravatinib plus TIS showed preliminary antitumor activity, and a manageable safety profile, in pts with pre-treated, advanced GC/GEJC. Further investigation in this pt population is warranted.