Safety, tolerability, and preliminary antitumor activity of sitravatinib plus tislelizumab (TIS) in patients (pts) with unresectable locally advanced or metastatic hepatocellular carcinoma (HCC)

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Background:

Sitravatinib is a selective tyrosine kinase inhibitor 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, has shown activity in 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 HCC cohort receiving sitravatinib plus TIS.

Methods:

Eligible pts were aged ≥ 18 years, had unresectable locally advanced or metastatic HCC, had received 1 or 2 prior lines of systemic treatment, had an ECOG PS of 0–1, ≥ 1 measurable lesion (per RECIST v1.1), and had Barcelona Clinic Liver Cancer (BCLC) stage B or C disease. Pts with anti-PD-1/PD-L1 antibody-naïve HCC must have failed or been ineligible for current standard of care. 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 [INV]). Secondary endpoints included duration of response (DoR), disease control rate (DCR), progression-free survival (PFS) (all per RECIST v1.1; by INV), and safety and tolerability. Exploratory endpoints included overall survival (OS).

Results:

As of July 12, 2021, 43 pts were treated (21 pts were anti-PD-1/PD-L1 antibody naïve and 22 pts were refractory/resistant [R/R]) and 10 pts (23.3%) remained on treatment. The median age of pts was 55 years (range: 29–71), 88.4% were male, and 74.4% had BCLC Stage C disease at study entry. With a median study follow-up of 8.6 months (mo) (range: 0.7–10.6), confirmed ORR was 10.0% (4 pts) (95% CI: 2.8–23.7); all 4 pts achieved partial responses. Median DoR and PFS were 5.4 mo (95% CI: 4.1–5.7) and 4.8 mo (95% CI: 3.2–6.9), respectively. DCR was 85.0% (95% CI: 70.2–94.3). Median OS was not estimable (95% CI: 8.6 mo–NE); the landmark OS rate at 9 mo was 71.4% (95% CI: 47.2–86.0) and 52.7% (95% CI: 23.2–75.5) in pts with anti-PD-1/PD-L1 antibody-naïve HCC and R/R HCC, respectively. Treatment-emergent adverse events (TEAEs) of any Grade/Grade ≥ 3 were reported in 97.7%/48.8% of pts. Serious TEAEs were observed in 27.9% of pts (n=12). The most common Grade ≥ 3 TEAE was palmar-plantar erythrodysesthesia (n=4; 9.3%). Pts experienced ≥ 1 TEAE that led to discontinuation of sitravatinib (n=4; 9.3%) and TIS (n=4; 9.3%). Dose reductions of sitravatinib due to TEAEs occurred in 15 pts (34.9%).

Conclusions:

Sitravatinib plus TIS was tolerable and showed preliminary antitumor activity in pre-treated, advanced HCC. Further investigation in this pt population is warranted.