Safety/Tolerability and Preliminary Antitumor Activity of Sitravatinib Plus Tislelizumab in Patients With Advanced Platinum-Resistant Ovarian Cancer (PROC)

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Background: Combining a PD-1 inhibitor and an agent with immune modulatory and antitumor properties may enhance antitumor activity of either agent. Sitravatinib, a spectrum-selective TKI targeting TAM receptors (Tyro3/Axl/MerTK) and VEGFR2, reduces the number of myeloid-derived suppressor cells and regulatory T cells while increasing the ratio of M1/M2-polarized macrophages, which may overcome an immunosuppressive tumor microenvironment and augment antitumor immune responses. Tislelizumab, an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages and abrogate antibody-dependent phagocytosis, has shown single-agent clinical activity in patients (pts) with advanced solid tumors. This open-label, multicohort, phase 1b study assessed safety/tolerability and preliminary antitumor activity of sitravatinib + tislelizumab in advanced solid tumors (BGB-900-103; NCT03666143). We report results from the PROC cohort.
Methods: Anti-PD-(L)1 antibody–naïve pts with histologically confirmed, advanced PROC (disease progression <6 mo after last platinum treatment) were enrolled. While platinum-resistant pts were included, pts with platinum-refractory disease were excluded. Patients received sitravatinib 120 mg PO QD and tislelizumab 200 mg IV Q3W. Primary endpoint was safety/tolerability of sitravatinib + tislelizumab. Key secondary endpoints were investigator-assessed objective response rate (ORR), disease control rate (DCR), and progression-free survival (PFS) per RECIST v1.1; overall survival (OS) was also assessed. PD-L1 IHC assay (Ventana SP263) and assessment of plasma VEGF/serum CXCL10were retrospective.
Results: As of Oct 13, 2020, 60 PROC pts were enrolled; 13 (22%) remained on treatment. Median age was 64 yrs (range 26-80); pts received a median of 4 (range 1-11) prior regimens. Median follow-up was 6.0 mo (range 0.2-23.4). Treatment-emergent adverse events (TEAEs) of any grade/grade ≥3 occurred in 97%/68% of pts; TEAEs led to sitravatinib dose reduction in 50% of pts. Nausea (33%), hypertension (18%), and abdominal pain (12%) were the most commonly reported grade ≥3 TEAEs. The 2 fatal AEs (malignant GI obstruction, dyspnea) were deemed unrelated to treatment. Confirmed ORR was 26.4%

(95% CI, 15.3-40.3), with 14 pts achieving partial response; DCR was 77.4% (95% CI, 63.8-87.7). Median duration of response was 4.7 mo (95% CI, 2.8-not estimable). There was no clear association between PD-L1 expression and clinical response; plasma VEGF and serum CXCL10 increased after treatment (*P*<0.0001 for both). Median PFS was 4.1 mo (95% CI, 4.0-5.1); preliminary median OS was 12.9 mo (95% CI, 6.3-17.2).
Conclusions: Sitravatinib + tislelizumab was tolerable and showed preliminary antitumor activity in pts with advanced PROC. Further investigation of sitravatinib + tislelizumab in OC is warranted.