Safety/tolerability and preliminary antitumor activity of sitravatinib plus tislelizumab in patients with advanced platinum-resistant ovarian cancer (PROC)

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Objective:

Combining a PD-1 inhibitor and an agent with immune modulatory properties may enhance antitumor activity. Sitravatinib, a spectrum-selective tyrosine kinase inhibitor, reduces the number of myeloid-derived suppressor and regulatory T cells while increasing the ratio of M1/M2-polarized macrophages, which may overcome an immunosuppressive tumor microenvironment and augment antitumor responses. Tislelizumab, an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages and abrogate antibody-dependent phagocytosis, has shown clinical activity in patients (pts) with advanced solid tumors. This multicohort, Phase 1b study assessed safety/tolerability and antitumor activity of sitravatinib + tislelizumab in advanced solid tumors (NCT03666143). We report results from the PROC cohort.

Methods:

Anti-PD-(L)1 antibody-naïve pts with histologically confirmed, advanced PROC were enrolled. Pts received sitravatinib 120 mg PO QD and tislelizumab 200 mg IV Q3W. Primary endpoint was safety/tolerability. Secondary endpoints were investigator-assessed objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS) per RECIST v1.1, and overall survival (OS). Ventana SP263 assay was used for PD-L1 IHC.

Results:

As of Oct 13, 2020, 60 PROC pts were enrolled. 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≥3occurredin97%/68%ofpts;TEAEsledtositravatinibdosereductionin50%ofpts. Hypertension(18%)andabdominalpain(12%)werethemostcommonlyreportedGrade≥3TEAEs. There were 2 fatal AEs (malignant GI obstruction, dyspnea), which were deemed unrelated to treatment. Confirmed ORR was 26.4%(95%CI,15.3–40.3),with14ptsachievingpartialresponse;DCRwas77.4%(95%CI,63.8–87.7).Median duration of response was 4.7mo(95%CI,2.8–notestimable).MedianPFSwas4.1mo(95%CI,4.0–5.1); preliminary medianOSwas12.9mo(95%CI,6.3–17.2). There was no clear association between PD-L1 expression and clinical response; plasma VEGF and serum CXCL10 increased after treatment.

Conclusion:

Sitravatinib + tislelizumab was tolerable and showed preliminary antitumor activity in pts with advanced PROC. Further investigation is warranted.