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

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Aims: Sitravatinib, a spectrum-selective tyrosine kinase inhibitor targeting TAM receptors (Tyro3/Axl/MerTK) and VEGFR2, demonstrated antitumour and immune modulatory activity. Tislelizumab, an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages and abrogate antibody-dependent phagocytosis, showed clinical activity in advanced solid tumours. We report results from the PROC cohort of an ongoing multicohort phase 1b study (BGB-900-103; NCT03666143) assessing safety/tolerability and preliminary antitumour activity of sitravatinib+tislelizumab.

Methods: Anti-PD-(L)1 antibody–naïve patients with histologically confirmed advanced PROC (disease progression <6 months after last platinum treatment), but not platinum-refractory disease, were eligible. Patients received oral sitravatinib 120 mg QD plus intravenous tislelizumab 200 mg Q3W. The primary endpoint was safety/tolerability; key secondary and exploratory endpoints included objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS). PD-L1 (Ventana SP263) and plasma VEGF/serum CXCL10 assessments were retrospective.

Results: As of October 13, 2020, 60 PROC patients (median age, 64 years; median of four prior regimens) were enrolled; 13 (22%) remained on treatment. Median follow-up was 6.0 months. Treatment-emergent adverse events (TEAEs) of any grade/grade ≥3 occurred in 97%/68% of patients; TEAEs led to sitravatinib dose reduction in 50% of patients. Hypertension (18%) and abdominal pain (12%) were the most common grade ≥3 TEAEs. Four fatal AEs were deemed unrelated to treatment. Among 53 evaluable patients, ORR was 26% (95% CI, 15.3-40.3; partial response, n=14); DCR was 77% (95% CI, 63.8-87.7). Median duration of response was 4.7 months (95% CI, 2.83-NE). 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 months (95% CI, 4.0-5.1); preliminary median OS was 12.9 months (95% CI, 6.3-17.2).

Conclusions: Sitravatinib plus tislelizumab was manageable with preliminary antitumour activity in patients with advanced PROC; further investigation is warranted.