Title

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

Authors

Jeffrey C. Goh,[1]* Jermaine Coward,[1] Bo Gao,[2] Ines Pires da Silva,[3] Mark Voskoboynik,[4] Daphne Day,[5] Amy Body,[5] Hui K. Gan,[6] Xin Li,[7]Jingchao Sun,[8] Cong Fei,[9] Liu Yang,[7] Michael Millward[10]

Affiliations

1. *Medical Oncology, Icon Cancer Centre, Brisbane, QLD, Australia;*
2. *Medical Oncology, Blacktown Cancer and Haematology Centre, Blacktown, NSW, Australia;*
3. *Cancer Centre, Blacktown and Westmead Hospitals, Sydney, NSW, Australia;*
4. *Medical Oncology, Nucleus Network, Melbourne, VIC, Australia and Central Clinical School, Monash University, Melbourne, VIC, Australia;*
5. *Medical Oncology, Monash Health and Monash University, Melbourne, VIC, Australia;*
6. *Department of Oncology, Austin Health, Heidelberg, VIC, Australia;*
7. *Clinical Development, BeiGene (Beijing) Co., Ltd., Beijing, China;*
8. *Global Statistics and Data Science, BeiGene (Beijing) Co., Ltd., Beijing, China;*
9. *Clinical Biomarker, BeiGene (Beijing) Co., Ltd., Beijing, China,*
10. *Cancer Trials, Linear Clinical Research & University of Western Australia, Nedlands, WA, Australia*

Abstract

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-PD-1 antibody engineered to minimize binding to FcγR on macrophages and abrogate antibody-dependent phagocytosis, has shown activity in patients (pts) with advanced solid tumors. This multicohort, Phase 1b study assessed the safety/tolerability and antitumor activity of sitravatinib + TIS in advanced solid tumors (NCT03666143). We report results from the PROC cohort.

Methods:

Pts who were anti-PD-(L)1 antibody-naïve with histologically confirmed, advanced PROC were enrolled. Pts received sitravatinib 120 mg daily and TIS 200 mg intravenously every three weeks. The primary endpoint was safety/tolerability. Secondary endpoints included investigator-assessed objective response rate (ORR), disease control rate (DCR), and progression-free survival (PFS) per RECIST v1.1.

Results:

By March 29, 2021, 63 pts were enrolled (n=59, efficacy evaluable). Median age was 66 yrs (range 26–80); pts received a median of 4 (range 1–11) prior regimens. Median follow-up was 8.9 mo (range 0.6–28.9). Treatment-emergent adverse events (TEAEs) of any Grade/ ≥ Grade 3 occurred in 100.0%/75.0% of pts; TEAEs led to sitravatinib dose reduction in 55.6% of pts. Hypertension (17.5%) and fatigue (9.5%) were the most commonly reported ≥ Grade 3 TEAEs. There were 5 fatal TEAEs, which were unrelated to treatment. Confirmed ORR was 28.8% (95% CI 17.8–42.1), with 17 pts achieving partial response; DCR was 79.7% (95% CI 67.2–89.0). Median duration of response was 5.6 mo (95% CI 2.8–22.3). Median PFS was 4.1 mo (95% CI 3.5–5.1). No association was observed between PD-L1 (by Ventana SP263) and clinical efficacy. Post-treatment change of plasma VEGF, VEGFR2, and serum IP-10 was seen.

Conclusions:

The combination of sitravatinib + TIS was tolerable and showed preliminary antitumor activity in pts with advanced PROC. Further investigation is warranted.