Perioperative Pharmacodynamic Effects of Ociperlimab in Combination With Tislelizumab in Patients With Advanced Solid Tumors: AdvanTIG-105 Phase 1 Dose-Escalation Study

Wei Tan,†2 Yang Shi,‡2 Han Yan,‡ Zhirong Shen,3 Nageshwar Budha,3 Ahsan Rizwan,3 Ruigi Huang,3 Hao Zheng,3 Rang Gao,3 Sophia Frantzas,†4 Steven Kao,†4 Tarek Meniawy,†4 Yun Zhang†4

Shanghai (Shanghai) Co., Ltd., Shanghai, China; ‘Beigene (Beijing) Co., Ltd., Beijing, China; ‘Beigene (USA) Co., Ltd., San Mateo, CA, USA; ‘Monash Health, Melbourne, Australia; ‘Monash University, Melbourne, Australia; ‘China O’Brien Life House, Sydney, Australia.

†Lincoln Clinical Research and University of Western Australia, Nedlands, Western Australia, Australia. *Primary author. †Presenting author. ‡Corresponding author.

Pharmacodynamic assessments in the AdvanTIG-105 dose-escalation study demonstrated reduced total Treg frequency at higher doses and downregulation of TIGIT on Treg, CD4+, and CD8+ T cells in peripheral blood following multiple ociperlimab doses. Total CD4+ and CD8+ T-cell frequencies were unaffected within the first cycle of ociperlimab and tislelizumab dosing.

Induced cytokine release of IL12/23p40, CCL4, and CXCL10 at C1D8 and IFNγ and TNFα at C2D1 suggested enhanced proinflammatory effects of myeloid cells and enhanced immune response upon ociperlimab monotherapy and in combination with tislelizumab.

The pharmacodynamic observations support the potential mechanism of action of ociperlimab as an Fc-competing anti-TIGIT monoclonal antibody.

BACKGROUND

• T cell immunoregulator with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain (TIGIT) is a co-inhibitory, immune checkpoint receptor that is upregulated on T cells and natural killer cells in multiple solid tumors, which can inhibit antitumor immune responses

• Ociperlimab (BGBA1217) is a novel, humanized monoclonal antibody that binds to TIGIT with high affinity and specificity, and has demonstrated competent binding with C1q and αFv receptors while inducing antibody-dependent cell cytotoxicity

• AdvanTIG-105 is a phase 1 study of ociperlimab in combination with tislelizumab, an anti-PD-1 antibody, in patients with advanced solid tumors. The safety, pharmacokinetics, and preliminary antitumor activity results in the AdvanTIG-105 dose-escalation study were reported at ASCO 2021. The preliminary efficacy of a P-D-L1-positive non-small cell lung cancer cohort in the dose-expansion study was presented at WCLC 2022

METHODS

Study Design and Patients

A phase 1 dose-escalation study was conducted in 32 patients with advanced, metastatic, unresectable solid tumors for which standard therapy was ineffective, intolerable, or unacceptable. (ClinicalTrials.gov: NCT04074782; Figure 1)

Pharmacodynamic Assessments

Peripheral blood samples were collected at specified timepoints and analyzed by flow cytometry to monitor changes in total and TIGIT-expressing immune cell subsets including Treg, CD4+, and CD8+ T cells, before and after treatment. Data from 450-, 900-, and 1800-mg cohorts were analyzed for trend changes in total Treg, Treg+ Treg+, and CD8+ T cells after dosing

Plasma samples were tested using Multi-Scalar Discovery V-gene panels to assess the cytokines/chemokine release upon treatment

*Results comparing cytokine induction at C2D1 and C1D1 with baseline were descriptive

RESULTS

Conclusions

• Total Treg frequency decreased over time following a higher dose (900 mg and 1800 mg), but not at a lower dose (450 mg) of ociperlimab (Figure 2)

• No differences in total CD4+ and CD8+ T-cell populations were found across doses

• TIGIT downregulation was observed on blood Treg, CD4+, and CD8+ T cells at C1D8 after ociperlimab monotherapy with multiple doses (Figure 3)

• The reduced TIGIT expression was sustained within the first two cycles of treatment

• IFNγ and TNFα release in plasma was significantly increased at C2D1 but not at C1D8

• The enhanced IFNγ and TNFα release indicate induced expression function of immune cells after ociperlimab/tislelizumab combination treatment (Figure 5)

• Proinflammatory cytokines/chemokines, IL12/23p40, CCL4, and CXCL10, primarily derived from myeloid cells, were enhanced at C1D8 after ociperlimab treatment and in C2D1 after combination with tislelizumab (Figure 4)

• Here we report the pharmacodynamic biomarker data derived from human peripheral blood in the AdvanTIG-105 dose-escalation study

Figure 2. Treg Frequency Was Reduced Following Dosage Treatment at Higher Doses

Figure 3. TIGIT Was Downregulated in Blood Treg, CD4+, and CD8+ T Cells After Dosing

Figure 4. Proinflammatory Cytokines/Chemokines Were Induced at C1D8 After Ociperlimab Treatment

Figure 5. Enhanced IFNγ/TNFα Release Was Observed at C2D1 After Ociperlimab/Tislelizumab Treatment