

Phase 1b/2 Trial of BGB-A445 (OX40 Agonist) With or Without Tislelizumab in Urothelial Carcinoma, Renal Cell Carcinoma, and Melanoma

1980P

Bin Lian,¹ Qingyun Zhang,² Shuang Zhang,³ Xiubao Ren,⁴ Yu Chen,⁵ Jiasheng Bian,⁶ Jiayuan Zhang,⁷ Rui Liu,⁸ Fan Bai,⁷ Chuanliang Cui,¹ Jun Guo¹

¹Department of Melanoma and Sarcoma, Peking University Cancer Hospital & Institute, Beijing, China; ²Cancer Hospital of Guangxi Medical University, Guangxi, China; ³West China Hospital, Sichuan, China; ⁴Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; ⁵Fujian Cancer Hospital, Fuzhou, China; ⁶Shandong Cancer Hospital and Institute, Jinan, China; ⁷BeOne Medicines, Ltd, Shanghai, China; ⁸BeOne Medicines, Ltd, Beijing, China

CONCLUSIONS

- BGB-A445 was generally well tolerated as monotherapy and in combination with tislelizumab
- Although antitumor activity was limited with BGB-A445 monotherapy, antitumor activity was observed with BGB-A445 plus tislelizumab combination therapy, including among patients who switched from BGB-A445 monotherapy
- Immune cell biomarker findings indicated the potential functional activity of BGB-A445, consistent with its mechanism of action

INTRODUCTION

- OX40 is a costimulatory receptor expressed on intratumoral T cells that has been shown to enhance antigen-stimulated T-cell responses and prevent tumor-induced immune tolerance in preclinical models^{1,2}
- In mouse tumor models, OX40 agonism depleted intratumoral Tregs, which correlated with tumor regression³
- BGB-A445 is a humanized immunoglobulin G (IgG) 1 monoclonal antibody agonist of OX40
- Here, we report the final results of the phase 1b/2 trial (NCT05661955) evaluating BGB-A445 alone and in combination with tislelizumab in advanced urothelial carcinoma (UC), renal cell carcinoma (RCC), and melanoma

METHODS

- This open-label, multicenter, parallel-assignment trial enrolled patients with UC (cohorts A, B, G), RCC (cohorts C, D), or melanoma (cohorts E, F, H, I) (**Figure 1**)
- Patients received intravenous BGB-A445 alone or BGB-A445 plus tislelizumab on day 1 of each 21-day cycle
- Treatment continued until disease progression, intolerable toxicity, or completion of 2 years of study treatment
- Patients assigned to BGB-A445 monotherapy who experienced disease progression were given the option to switch to a combination of BGB-A445 plus tislelizumab
- Safety/tolerability profile was assessed among patients assigned to their initial cohort (Period 1) and separately among patients who switched from monotherapy to combination therapy (Period 2)
 - Treatment-emergent adverse events (TEAEs) were classified by MedDRA v27.0 and graded per CTCAE v5.0
- Antitumor activity was assessed per RECIST v1.1 and reported in terms of confirmed responses
- Multiplex immunohistochemistry using seven cell markers (CD3, CD4, CD8, Foxp3, OX40, Ki67, PanCK) was performed to assess the pharmacodynamic effect of BGB-A445 monotherapy, with paired baseline and cycle 3 day 1 tumor samples available from six patients in cohort E

Figure 1. Study Design

