A PHASE I/II STUDY TO EVALUATE THE SAFETY, TOLERABILITY AND PRELIMINARY EFFICACY OF GLS-012 MONOTHERAPY AND IN COMBINATION WITH ZIMBERELIMAB IN PATIENTS WITH ADVANCED MELANOMA (TRIUMPH-01)

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Background Lymphocyte-activated gene 3 (LAG-3) is an immune checkpoint receptor protein that negatively regulates T-cell activation. The objective of this study (ClinicalTrials.gov identifier: NCT05909436) was to evaluate the safety, tolerability, and preliminary efficacy of GLS-012, a LAG-3-blocking antibody, monotherapy and in combination with zimberelimab (anti-PD-1 mAb) in patients with advanced melanoma after progression on standard treatment.

Methods The dose escalation stage of this study has a traditional 3 + 3 dose escalation design with planned cohorts of fixed-dose GLS-012 with 40, 80, 240, 480, 800 mg Q3W and followed by a dose escalation of combination therapy with less than and equal to the recommended phase 2 dose (RP2D) of GLS-012 and a fixed-dose zimberelimab with 360 mg Q3W. DLT observation period was 21 days after the first dose. The primary endpoints were the number of patients with a dose-limiting toxicity (DLT) and maximum tolerated dose (MTD) in the dose escalation stage. In dose expansion stage, patients received intravenous 240mg GLS-012 Q3W as monotherapy, and were assigned to receive RP2D GLS-012 combined with a fixed-dose 360 mg zimberelimab Q3W as combination therapy. The primary endpoint was safety in the dose expansion stage.

Results As of May 18th, 2023, 17 patients with advanced melanoma after progression on standard treatment (median age: 55 yr [range: 33–75]; ECOG PS: 0 [n = 12], 1 [n = 5]) were enrolled for GLS-012 monotherapy dose escalation and dose expansion. The median number of medications was 4 (range: 1–9). All the 13 patients in the dose escalation cohorts have completed the first cycle of treatment (DLT observation period). No DLT was observed, and MTD was not reached. The most common treatment-related adverse event (TRAE) was decreased white blood cell count which happened in 2 patients. No Grade ≥3 TRAE was observed. By the investigator-assessment per RECIST 1.1, in 14 evaluable patients, stable disease (SD) was observed with 8 patients. Conclusions GLS-012 has acceptable toxicity and shows preliminary antitumor activity in patients with advanced melanoma after progression on standard treatment.

Trial Registration ClinicalTrials.gov identifier: NCT05909436

Ethics Approval The study (Triumph-01) was approved by the ethics committee of Beijing Cancer Hospital (approval number: 2022YW114). All participants provided signed informed consent before any study procedure.

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