A PHASE 1/2, OPEN-LABEL, DOSE ESCALATION AND EXPANSION STUDY OF GI-101 AS A SINGLE AGENT AND IN COMBINATION WITH A PEMBROLIZUMAB, LENVATINIB OR LOCAL RT IN ADVANCED SOLID TUMORS (KEYNOTE-B59)

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Background GI-101 is a novel bispecific fusion protein containing CD80 and interleukin-2 (IL-2) variant, designed to exhibit high affinity to cytotoxic T-lymphocyte-associated protein 4 (CTLA4) and preferential binding to IL-2R β subunit. In various animal models, GI-101 exerted strong anti-tumor efficacy, accompanied by robust stimulation of CD8+ T and NK cell proliferation without a significant increase in regulatory T cells. GI-101 also elicited synergistic anti-tumor efficacy when used in combination with pembrolizumab (anti-PD1 agents), lenvatinib (tyrosine kinase inhibitor) and radiation in vivo.¹ Given the complementary mechanisms of action of GI-101 via blocking CTLA4 with IL-2 activity to enhance the proliferation and activation of effector T and NK cells, it was hypothesized that GI-101 as a single agent or in combination with other immunotherapies, VEGF inhibitors or RT may exert anti-tumor activity in cancers with high unmet needs.

Methods KEYNOTE-B59 (NCT04977453) is an ongoing phase 1/2 study composed of 4 parts. This study is planned to enroll approximately 374 patients across the indications. Patients assigned to Part A and B receive either GI-101 monotherapy (Part A) or GI-101 + 200 mg of pembrolizumab (Part B) via IV infusion on every 3 weeks (q3w). In Part C, patients will receive GI-101 q3w in combination with lenvatinib (oral, once daily). In Part D, patients will be given GI-101 q3w in combination with local tumor irradiation. Each part is initiated with dose-escalation/optimization phases which will enroll patients with advanced solid tumors, except Part D that enrolls advanced melanoma and sarcoma only. This phase utilizes conventional 3+3 design to determine the maximum tolerated dose and recommended phase 2 dose (RP2D) of GI-101 as a monotherapy and in combination. Once RP2D is determined, patients will be enrolled in dose-expansion phases of each part that includes specific tumor types, such as solid cancers failed on standard of care, treatment-naïve unselected or CPI-treated solid tumors. Patients with advanced solid tumors and recovered from prior therapy will be enrolled. This study will assess safety, tolerability, dose-limiting toxicities, MTD, RP2D, preliminary anti-tumor activity, and pharmacokinetics/pharmacodynamics of GI-101 as a single agent and in combination.

Results This study is currently enrolling patients with advanced or metastatic solid tumors.

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Trial Registration NCT04977453

REFERENCE

1. Pyo KH, Synn CB, Koh YJ, et al. Comprehensive preclinical study on GI-101, a novel CD80-IgG4-IL2 variant protein, as a therapeutic antibody candidate with bispecific immuno-oncology target. *Cancer Res* 2021;**81**(13_Suppl).

Ethics Approval This study was approved by Severance hospital institutions' Ethics Review Board (IRB); approval number 4-2021-0185, Asan Medical center's IRB; approval number 2021-0669.

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