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-2Rβ 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 in vivo. 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.

Acknowledgements The authors would like to thank all the patients who are participating in this study. The study is sponsored by GI Innovation, Inc.

Trial Registration NCT04977453

REFERENCE

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.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.470