PRELIMINARY RESULTS OF GII-101-P101 (KEYNOTE-B59): GI-101 (CD80-IGG4 FC-IL2V) AS A SINGLE AGENT AND IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED AND/OR METASTATIC SOLID TUMORS

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Background GI-101 is a novel bispecific fusion protein containing CD80 and interleukin-2 variant, designed to boost immune cell proliferation including cytotoxic T and NK cells without increasing Treg cell. A first-in-human study was performed to evaluate safety and efficacy of GI-101 as a monotherapy and in combination with pembrolizumab.

Methods Patients (pts) with advanced/metastatic solid tumors that have progressed on standard of care (SOC), or for whom no SOC exists, or SOC was deemed not appropriate, received escalating doses of GI-101 monotherapy or GI-101 in combination with 200 mg pembrolizumab intravenously every 3 weeks. The primary objective was to assess safety, tolerability and maximum tolerated dose and/or RP2D utilizing a conventional 3+3 design.

Results 25 pts received GI-101 monotherapy (n=16) or in combination with pembrolizumab (n=9) between Aug 2021 and July 2022. The median number of prior systemic therapies was 3 [1–6] and 64% of pts were previously treated with immunotherapy. No dose-limiting toxicities up to 0.15 mg/kg were reported with planned dose level of 0.002–0.6 mg/kg.

Treatment-related adverse events (TRAEs) occurred in 11 (69%) and 5 (56%) pts in the single and combination cohorts, respectively. Three pts experienced Grade 3+ TRAEs (19%) with GI-101 monotherapy and no Grade 3+ TRAEs were reported with combination. Anti-tumor activities were seen both in single agent and in combination. One confirmed partial response (PR), among 16 pts, in metastatic urothelial carcinoma with a time to progression of 121 days was observed with GI-101 monotherapy. The patient previously experienced immunotherapy with best response of progressive disease. Additionally, two ongoing pts were observed PRs in combination cohorts among nine pts [one confirmed PR in non-small cell lung cancer (NSCLC) and 1 unconfirmed PR in metastasis of unknown origin]. The NSCLC patient had acquired resistance to previous immunotherapies with best response of PR and stable disease (SD), respectively. In single and combination cohorts of diverse tumor types, five and three pts had SDs. Median duration of treatment was 61 (15–171+) days. Systemic exposure to GI-101 increased with dose-escalation with half-life of 7.5–10.1 hours, resulting in a dose-dependent increase in NK and CD8+ T cells, without significant impact on Treg cells in peripheral blood.

Conclusions GI-101 was well tolerated as monotherapy and in combination with pembrolizumab in pts with previously treated, advanced solid tumors. Preliminary anti-tumor activity was seen both in monotherapy and in combination with pembrolizumab. The dose-escalation is currently ongoing to identify RP2D.

Trial Registration Clinical trial identification: NCT04977453