KEYNOTE-B59: DOSE ESCALATION OF A PHASE 1/2 FIRST-IN-HUMAN, OPEN-LABEL STUDY OF GI-101, A NOVEL IMMUNOCYTOKINE COMBINING CD80-IL2V, IN COMBINATION WITH PEMBROLIZUMAB IN ADVANCED SOLID TUMORS

1Byung Chul Cho*, 1Jae Lyun Lee, 2Sang Joon Shin, 3Byoung Yong Shim, 4Hyo Jin Lee, 5Jung-Yun Lee, 6John Powderly, 7Cho Yeon Lee, 8Julia Cohen, 9Nari Yoo, 10Myung Hwan Kim, 11Kyoung Hyun Kim, 12Dong Kim, 13Myung Ho Jang. 1Yonsei Cancer Center and Severance Hospital, Seoul, Republic of Korea; 2Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; 3St. Vincent’s Hospital, College of Medicine, The Catholic University of Korea, Suwon, Republic of Korea; 4Chungnam National University Hospital, Daejeon, Republic of Korea; 5Department of Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, Republic of Korea; 6Carolina BioOncology Institute, Huntersville, NC, USA; 7Korea University Anam Hospital, Seoul, Republic of Korea; 8Merck and Co., Inc., Rahway, NJ, USA; 9GI Innovation, Inc, Seoul, Republic of Korea; 10Severance Biomedical Science Institute, Yonsei University College of Medicine, Seoul, Republic of Korea; 11Korea University College of Medicine, Seoul, Republic of Korea; 12Brain Korea 21 PLUS Project for Medical Science, Yonsei University College of Medicine, Seoul, Republic of Korea

Background GI-101 (CD80-IL2v) is a novel immunocytokine, designed to direct IL-2v to tumor and immune cells. IL-2v of GI-101 is engineered to maximize the expansion of cytotoxic T and NK cells but not Treg cells, and CD80 further inhibits Treg cell function. GI-101 demonstrated single agent activity in an anti-PD-L1 experienced patient (ORR 5.9%) in heavily-treated population.1 Here we report clinical outcomes from dose escalation of Part B of the study.

Methods Keynote-B59 is an ongoing, phase 1/2 study of GI-101 monotherapy and in combination with various agents in patients (pts) with advanced solid tumors. In dose escalation of Part B, pts received intravenous GI-101 (0.002–0.15 mg/kg) and pembrolizumab (200 mg) on day 1 of each 21-day cycle. The primary objective is to assess safety, tolerability and maximum tolerated dose (MTD) and/or combination RP2D (cRP2D).

Results As of 20 Apr 2023, 25 pts with any solid tumors who failed on standard of care received GI-101 plus pembrolizumab. The median number of prior therapies were 3 (1–9), and 64% were previously treated with immune checkpoint blockade (ICI) therapy. Treatment-related adverse events occurred in 23 pts (92%), with the most common events (≥ 20%) being pyrexia (48%), AST/AST increased (28%, 24%). One case of dose-limiting toxicity was observed; MTD was not reached. 0.15 mg/kg GI-101 Q3W was established as the cRP2D based on the desirable expansion of peripheral immune cells and anti-cancer activities. Objective responses were observed in 4 of 24 evaluable pts (ORR 16.7%) regardless of prior anti-PD(L)1 therapy; 2 confirmed PR in pts with NSCLC and clear cell RCC (ccRCC), both failed on previous anti-PD(L)1 therapy, and 2 unconfirmed PR in pts with metastatic carcinoma of unknown origin (MUCOC) and ccRCC. The ORR in pts who failed on previous ICI therapy was 13.3% while that of ICI-naïve population was 22.2%. Overall disease control rate was 66.7% including 4 pts of SD > 6 months. Pts who had objective response showed significantly higher level of central memory T and CD8+ T cell expansion in peripheral blood. In a patient achieved PR, significant infiltration of CD8+ T and NK cells were observed in tumor microenvironment with minimal impact on Treg cells.

Conclusions GI-101 was well tolerated when combined with pembrolizumab in pts with advanced solid tumors. GI-101 plus pembrolizumab demonstrated anti-tumor activity in a heavily pre-treated patient population, with prior anti-PD(L)1 therapies. The dose expansion phase of the study is currently ongoing.

Trial Registration Clinical trial identification: NCT04977453

REFERENCE

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