GI-102, A NOVEL CD80-IGG4-IL2V3 FUSION PROTEIN
DRIVING LYMPHOCYTE EXPANSION AND ANTI-CANCER
POTENTIAL THROUGH REGULATION OF IMMUNE CELLS
IN THE TUMOR MICROENVIRONMENT

Min Park, Kayoung Shin, Seoho Kim, Haejong Lee, Yuseong Lee*, Jisoo Kim, Eunjin Lee,
Sungman Oh, Kyungwha Lee, Chong Woo Park, Ilhyun Kim, Young Min Oh, Wonjae Lee,
Yaein Amy Shim, Young-Gyu Cho, Young Jun Koh, Kookhwan Kim, Myoung Ho Jang. GI
Innovation Inc., Seoul, Songpa-gu, Republic of Korea

Background Interleukin-2 (IL-2) is a pleiotropic cytokine that
plays pivotal roles in the immune response. It induces the
proliferation of T cells and NK cells and demonstrates therapeu tic anti-tumor activity. CD80 expressed on antigen-presenting
cells provides co-stimulatory signals for T cell activation and
immune responses via CD28 binding. Conversely, CD80 acts as a checkpoint molecule when bound to CTLA-4.
Despite the active and progressive efforts put into the develop ment of immune checkpoint inhibitors for cancer therapy,
notable unmet medical needs continue to persist. To address
these challenges and provide a safe and effective immune-boosting agent, we generated a novel CD80-IgG4-IL2v3 bispecific fusion protein which allows tumor-targeted delivery of IL-2 and robust proliferation of anti-tumor effector cells.

Methods The evaluation of anti-tumor efficacy and tumor-infiltrating lymphocytes (TIL) was conducted using the EMT6 syngenetic tumor model. Analysis of peripheral lymphocyte alterations was carried out in nonhuman primates (NHP). Intra-tissue concentration analysis of GI-102 was performed utilizing the LL/2 syngeneic tumor model.

Results The N-terminal CD80 domain of GI-102 is designed
to target and block CTLA-4, while the C-terminal IL-2v3
domain has no binding affinity to IL-2RA, while maintaining
the affinity towards IL-2RBβ. In the EMT6 syngeneic mouse model, GI-102-treated group showed significantly reduced
tumor volume and percent of tumor growth rate compared
with other groups. The analysis of the TIL revealed that GI-
102 induced a robust expansion of both CD8+ T and NK
cells in tumor microenvironment (TME), relative to vehicle
control and Proleukin®. However, in comparison to Proleu-
kin®, injection of GI-102 did not lead to an expansion of
Tregs population in TME compared. A similar pattern was
observed in peripheral lymphocytes of NHP that were adminis-
tered GI-102 and Proleukin®. Human PBMC treated with
GI-102 were analyzed for cytokine release, and no increase in
inflammatory cytokines associated with cytokine release syn-
drome was observed with GI-102. Following the injecting GI-
102 into mice bearing LL/2 tumors, elevated levels of GI-102
were detected from serum, tumor and lymphoid organs, sug-
gestig the CD80-guided distribution of the molecule towards
area reach in lymphocytes.

Conclusions GI-102 is a novel anti-cancer agent that activates
immune cells and modulates tumor-infiltrating lymphocytes.
This potent IL-2-based bispecific fusion protein has great
potential to deliver effective therapeutic outcomes for a vari-
ous types of cancer. It exhibits low toxicity and does not acti-
vate Treg, further enhancing its therapeutic value as the next-
generation IL-2.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1062