FC-COMPETENT FULLY HUMAN ANTI-TIGIT BLOCKING MONOCLONAL ANTIBODIES DEMONSTRATED POTENT ANTI-TUMOR EFFICACY IN PRECLINICAL MODELS

Weiqiu Lan, Baihong Liu, Yang Chen, Xin Zhang, Jing Zhang, W Frank An, Chaoshue Guo*, Yi Yang, Biocytogen Pharmaceuticals (Beijing) Co., Ltd, Beijing, China

Background T cell immunoreceptor with Ig and ITIM domain (TIGIT) is a high-affinity inhibitory receptor that competes with CD226 for binding to CD155. TIGIT inhibits the activity of both T and NK cells, thereby dampening the immune response against cancer. Anti-TIGIT therapeutic monoclonal antibodies (mAbs) have shown clinical benefit when combined with PD-(L)1 inhibitors. Currently, there are many clinical trials underway to investigate the efficacy and safety of anti-TIGIT therapies. The results from these ongoing trials have shown that TIGIT is a promising target for cancer immunotherapy. In this study, we evaluated three fully human anti-TIGIT mAbs generated from our fully human antibody RenMab™ mice.

Methods Blocking activity of three anti-TIGIT mAbs against the TIGIT/CD155 interaction was assessed using flow cytometry. The affinity to human and cynomolgus TIGIT was measured by surface plasmon resonance (SPR). Stability of the antibody candidates was tested at 40°C for 7 days and at pH 3.5 for 6 hours, respectively. To evaluate the efficacy of anti-TIGIT antibodies in vivo, mAbs were injected into TIGIT humanized mice implanted with MC38 syngeneic tumors.

Results We identified anti-TIGIT mAbs with high affinity to both human and cynomolgus TIGIT. These mAbs were able to block the interaction of CD155 and TIGIT in vitro. Our antibody molecules exhibit desirable physicochemical properties, as we found that the purity remains above 95% after accelerated degradation and low pH treatment. Furthermore, our anti-TIGIT mAbs exhibited potent anti-tumor activity compared to Tiragolumab analog in TIGIT humanized mice with MC38 syngeneic tumors.

Conclusions We successfully generated anti-TIGIT mAbs that demonstrate superior anti-tumor efficacy compared to benchmark in a syngeneic mouse model. These antibodies show promising potential for further development into a novel anti-TIGIT immunotherapy.

REFERENCES

Ethics Approval All animal studies were reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) of Biocytogen Beijing Co., Ltd.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0479