849 NT-I7, A NOVEL LONG-ACTING INTERLEUKIN-7, IMPROVES ENGRAFTMENT OF PATIENT IMMUNE CELLS AND EFFICACY OF ANTI-PD-1 THERAPY IN A PRECLINICAL HUMANIZED MELANOMA MODEL

[1]Yee Peng Phoon*, [1]Kang Kai, [2]Alexandra Wolfarth, [2]Sara Ferrando-Martinez, [2]Byung Ha Lee, [1]Brian Gastman. [1]*Cleveland Clinic, Cleveland, OH, United States*; [2]*NeoImmuneTech, Inc., Rockville, MD, United States*

Background Although immune checkpoint inhibitors (ICIs) have led to significant massive improvements in melanoma survival, half of these patients fail to benefit, necessitating the discovery of novel strategies. There is a pivotal need for the development of preclinical models to evaluate 'next-generation' immunotherapies prior to clinical investigation.

In this study, we developed and optimized our all-autologous humanized melanoma mouse model for the study of NT-I7 (efineptakin alfa), a long-acting recombinant human IL-7. Because NT-I7 has been shown to enhance T cell proliferation and survival in both humans and mice, we hypothesized NT-I7 would both improve the engraftment of patient immune cells and the efficacy of anti-PD-1 therapy in our humanized mouse model.

Methods Both tumor cells and peripheral blood lymphocytes (PBLs) were collected from melanoma patients to establish our autologous humanized melanoma mouse model. Tumor-bearing NSG mice were infused with matched melanoma PBLs prior to receiving 10 mg/kg NT-I7. Optimization of the model was performed and evaluated by measuring engraftment of the patient immune cells via flow cytometry and comparing tumor growth. The optimized autologous melanoma model was then used to test the efficacy of NT-I7 combined with anti-PD-1 therapy.

Results NT-I7 was well tolerated in the preclinical humanized melanoma mouse model. The optimal dosing of NT-I7 was determined to be two subcutaneous injections of 10 mg/kg NT-I7 1-2 weeks apart after infusing unexpanded PBLs. NT-I7 dramatically increased engraftment of patient PBLs in the spleen and infiltration of the tumor, with a majority of T cells being $CD4^+$. NT-I7 also enhanced the anti-tumor response with decreased tumor growth compared to vehicle control. In combination with anti-PD-1, NT-I7 continued to boost immune cell engraftment, with a majority of T cells still being $CD4^+$. While NT-I7 and anti-PD-1 displayed a similar modest anti-tumor effect as monotherapies, combination treatment significantly decreased tumor growth compared to control.

Conclusions Our all-autologous humanized melanoma mouse model allows us to evaluate novel immunotherapies in the context of matched patient immune and tumor cells. NT-I7 dramatically improves engraftment of patient PBLs. When combining NT-I7 and anti-PD-1 therapy, tumor control was significantly improved. In sum, we have developed a platform to feasibly design NT-I7 combination therapies to identify optimal strategies that can be translated into clinical investigations.

Ethics Approval All human tissue was obtained at the Cleveland Clinic under a protocol approved by the institutional review board with written informed consent obtained from each patient. Animal studies were performed in accordance with the guidelines of and approved by the Institutional Animal Care and Use Committee at the Cleveland Clinic.

http://dx.doi.org/10.1136/jitc-2022-SITC2022.0849

J Immunother Cancer: first published as 10.1136/jitc-2022-SITC2022.0849 on 7 November 2022. Downloaded from http://jitc.bmj.com/ on November 28, 2023 by guest. Protected by copyright.