IDENTIFICATION AND CHARACTERIZATION OF AN ALLOGENEIC INKT-CAR TARGETING BCMA

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Background Chimeric antigen receptor (CAR) T cell therapy has shown outstanding benefit in hematological malignancies with three autologous CAR-T therapies commercially available and several in clinical development. The use of autologous T cells to manufacture CAR therapies has several disadvantages including production time, cost, lengthy time to treatment and dependence on patient T cell functionality. An allogeneic off the shelf CAR product can overcome these issues. We use invariant natural killer T (iNKT) cells as basis for our allogeneic cell therapy platform. Invariant NKT cells are innate-like lymphocytes that bridge innate and adaptive immune response to promote anti-cancer immunity. iNKT cells share characteristics of T cells and Natural Killer (NK) cells, expressing both an invariant T Cell Receptor (iTCR) and canonical NK receptors. They can be activated by recognition of lipid antigens through the iTCR, pro-inflammatory cytokines and recognition of stress ligands. Moreover, iNKT do not cause Graft versus Host Disease making them an ideal platform for allogeneic CAR cell therapy. Here we describe a novel allogeneic iNKT-CAR product targeting BCMA designed to promote effective anti-cancer immunity

Methods Our proprietary CARDIS™ platform is a 2-stage discovery process where screening of highly diverse scFv libraries via phage display is followed by selection of potent CARs using mammalian display platform. Using this high throughput approach, we can interrogate large cell-based CAR libraries for specific binding and activation simultaneously, as well as eliminate tonic signaling at an early stage. This novel platform enabled rapid identification of a candidate CAR (agent-F6) for the targeting of BCMA. Anti-cancer efficacy of stably expressed BCMA CAR in expanded iNKT cells has been tested

Results Agent-F6 expressed at high levels in iNKT cells. Functional characterization demonstrated potent cytotoxic activity of agent-F6 expressing iNKT cells against human hematologic tumor cell lines expressing BCMA in vitro. Activated agent-F6 iNKT cells display a pro-inflammatory phenotype when challenged with tumor cell lines. Furthermore, using a multiple myeloma in vivo xenograft model, infusion of agent-F6 iNKT cells showed comparable tumor control to a clinical-stage BCMA CAR reference.

Conclusions MiNK therapeutics is developing the next generation allogeneic CAR-iNKT therapies by using 1) a CAR discovery platform that allows more rapid and efficient identification of antigen-specific and biologically potent CAR candidates and 2) an iNKT cell platform naturally lacking alloreactivity that allows rapid engineering and expansion of an off-the-shelf CAR product.

Ethics Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards

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