202 IN VIVO AND IN VITRO CHARACTERIZATION OF AIM ACT, A NOVEL NANOPARTICLE-BASED TECHNOLOGY, EXPANDED MART-1 SPECIFIC T CELLS

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Background NexImmune is developing highly differentiated immunotherapies to target, activate and expand tumor antigen-specific T cells using the proprietary Artificial Immune Modulation (AIM™) nanotechnology platform. The AIM nanoparticle (AIM-np) technology functions as synthetic dendritic cells capable of directing a specific T cell-mediated immune response. By mimicking natural T cell biology, NexImmune's non-genetically engineered cellular therapy product candidates (AIM ACT) are designed to combine the attributes of cellular precision, potency, and persistence with reduced potential for undesired toxicities.

Methods Here we present an example of AIM ACT expanded MART-1 specific T cells and their phenotypic and functional characterization in vitro and in vivo. Leukopaks from healthy donors were used to produce AIM ACT T cell products with our proprietary AIM ACT enrichment and expansion (E+E) manufacturing process and antigen peptide-loaded AIM-nanoparticles.

Results The final MART1 T cell products include up to 62.8% (20.8% in average) MART-1-specific CD8+ T cells as determined by MART1 peptide (ELAGIGILTV)-loaded multimer staining. MART1-specific T cells were tested in flow cytometry-based and live cell imaging-based cytotoxicity assays using HLA-A2 positive MART1 peptide-loaded target cells. The AIM ACT-generated T cells showed potent cytotoxicity to MART1 peptide-loaded target cells in vitro, while unloaded control cells were not killed. In over 30 independent AIM ACT E+E clinical scale runs, the expanded T cells consisted of a combined average of 91.7% T stem cell like, central and effector memory T cells, as determined by CD62L, CD45RA and CD95 staining. These phenotypes have been associated with long term in vivo persistence and anti-tumor efficacy. In a human melanoma PDX model, we confirmed that transfusion of AIM ACT T cells resulted in long term survival in vivo and significant reduction of tumor growth with complete tumor clearance in 6 out of 15 animals.

Conclusions The results demonstrate that AIM ACT MART1 T cells have long term persistence and anti-tumor activity in solid tumors such as melanoma, and that the AIM ACT E+E approach is a reproducible clinical scale manufacturing process for non-genetically engineered antigen-specific T cells. The AIM ACT platform is currently being used for generating T cell products for our current clinical trials, NEXI-001 (NCT04284228) and NEXI-002 (NCT04505813), and our pre-clinical development for HPV-associated malignancies. The findings support initiating Phase I trials of adoptive T cell therapy in solid tumors.

Ethics Approval The study was approved by the Institutional Animal Care and Use Committee (IACUC).

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