1139 EFFICACY OF INJECTABLE ANTIGEN PRESENTING NANOPARTICLES (AIM INJ), IN SOLID TUMOR MODELS

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Background NexImmune's Artificial Immune Modulation (AIM) nanoparticle (NP) platform (AIM INJ) is an injectable multi-antigen specific off-the-shelf immunotherapy designed to directly modulate T cell responses in vivo. It consists of a PLA-PEG NP conjugated with two proteins, a dimeric IgG MHC-class I fusion protein loaded with a tumor peptide and an anti-CD28 antibody for co-stimulation. Multiple batches of NPs, loaded with a single peptide, are mixed to create a multi-antigen specific NP product. AIM INJ NP expanded T cells are antigen-specific, polyfunctional and consist of memory phenotypes associated with anti-tumor activity and immunologic memory.

Methods We performed adoptive transfer of OVA-TCR transgenic OT-1 cells into C57BL/6 mice followed by S.C. injection of OVA peptide-loaded NPs. NPs between 35 and 90 nm in size and two doses were tested. To further evaluate the efficacy in a solid tumor model, C57BL/6 mice were implanted with B16F10-OVA tumor cells. On day 6, 1.5 million OT-1 T cells were adoptively transferred into the tumor-bearing mice. Control NPs or OVA-NPs were injected S.C. on days 7, 14 and 21 after tumor injection and tumor volume was monitored.

Results We demonstrated the ability of AIM INJ NPs to activate and expand antigen-specific T cells in vivo. NPs of all sizes induced expansion of OT-1 T cells while non-specific control NPs did not. In B16F10-OVA tumor model, treatment of mice with OVA-NPs significantly delayed tumor growth and increased survival as compared to mice treated with control NPs. OVA-NPs treated mice had significantly higher amounts of OVA specific tumor infiltrating lymphocytes and higher percentage of functional OT-1 T cells in spleen as demonstrated in ex vivo killing assays. Additional data from an ongoing B16F10 mouse melanoma model with AIM INJ NPs targeting the endogenous melanoma antigen gp100 will be presented.

Conclusions AIM INJ NPs can activate, expand antigen-specific $CD8^+$ T cells and elicit anti-tumor activity in vivo. The combination of antigen-peptide targets loaded on the AIM INJ NP can be changed to address different tumors. These studies along with other in vivo pre-clinical studies including further evaluation of a dose regimen and route of administration will be used to support our INDs for using AIM INJ in Phase 1 studies for solid tumors. AIM INJ potentially addresses gaps in immunotherapies by driving multiple tumor antigen-specific T cells into the tumor, establishing T cell memory for durability and using an off-the-shelf modality supporting easier access and scalability.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1139