1394 PRECLINICAL CHARACTERIZATION OF BIODEGRADABLE INJECTABLE ANTIGEN PRESENTING NANOPARTICLES AIM INJ FOR IN VIVO TREATMENT OF SOLID TUMORS

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Background NexImmune's artificial immune modulation (AIM™) technology is designed to direct T cell function and drive a T cell-mediated response. AIM antigen-specific immunotherapies rely on a nanoparticle-based artificial antigen presenting cell (aAPC) platform. The off-the-shelf injectable nanoparticles (INJ) are developed using biodegradable PLGA-PEG or PLA-PEG core materials and designed to mimic the function of natural APCs. AIM INJ nanoparticles present (i) an antigen-specific recognition signal delivered by an MHC molecule loaded with an antigenic peptide (Signal 1), and (ii) a co-stimulatory signal (anti-CD28, Signal 2) to induce expansion of the T cells activated through Signal 1.

Methods AIM INJ nanoparticles were synthesized by nanoprecipitation method on the Ignite NanoAssemblr™ microfluidic system. Murine AIM INJ nanoparticles were formulated by conjugating murine protein Signal 1 and 2, and then loading with tumor-specific peptides. Physicochemical characterization, stability, and in vitro functional tests were performed to assess antigen-specific $CD8^+$ T cell proliferation, expansion, and cytokine production upon nanoparticle exposure. In vivo biodistribution and efficacy studies were performed in B16-F10 melanoma model by s.c. injection of AIM INJ nanoparticles. Biodistribution studies were conducted using ^{89}Zr radiolabeled nanoparticles. For the efficacy study, on day 7 after nanoparticle injection, tumor tissues were harvested and stimulated ex vivo to measure the expression of CD107a and cytokines IFN-γ, TNF-α, IL-2 by the tumor infiltrating lymphocytes (TILs).

Results PLGA-PEG based AIM INJ nanoparticles, with ~100nm diameter, PDI < 0.2, and close-to-neutral surface charge, have round morphology and were stable in liquid formulation over 6-months. The peptide-loaded murine AIM INJ nanoparticles activated $CD8^+$ T cells in antigen-specific manner by promoting cell proliferation, expansion, and poly-functionality. The biodistribution studies showed a significantly higher amount of AIM INJ nanoparticle accumulation in the tumor (24 hours) and draining lymph node (96 hours) compared to naked nanoparticles (no proteins/peptides). In an in vivo treatment study, we demonstrated that the peptide-loaded AIM INJ nanoparticles induced significant amounts of poly-functional $CD8^+$ TILs in a B16-F10 melanoma model. In addition, we will present data from ongoing studies using different sizes and formulations of AIM INJ nanoparticles.

Conclusions We demonstrated that biodegradable AIM INJ nanoparticles can activate and expand multiple antigen-specific $CD8^+$ T cells in vitro and in vivo to induce anti-tumor activity. These studies along with other in vivo pre-clinical characterization will be used to support multiple INDs and advance AIM INJ into Phase 1 studies for various solid tumors.

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