

POSTER PRESENTATION

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CD8⁺ T cell responses in metastatic melanoma patients receiving an adenovirally antigen engineered dendritic cell vaccine +/- IFN- α

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Dendritic cells (DC), the primary antigen presenting cells and stimulators of naïve immune cells, are uniquely positioned to promote anti-tumor immunity. We developed a DC vaccine which expresses three full length melanoma antigens tyrosinase, MART-1, and MAGE-A6 engineered with an Ad type 5 adenovirus “AdVTMM2” which can activate CD8⁺ and CD4⁺ T cells as well as natural killer (NK) cells. A clinical trial testing this vaccine as well as the potential effects of IFN- α administration post-vaccination has enrolled 36 patients to date (NCT01366144). Peripheral blood banked at baseline, post-DC vaccination, and after either observation or one month of high dose IFN- α was tested for anti-tumor immunity. Here, we present initial immune response testing of the 12 HLA-A2⁺ patients who were able to be assessed for circulating CD8⁺ T cell frequencies by HLA-A2-peptide dextramers. Patient PBMCs were analyzed by MHC dextramer binding assay to determine 1) the frequency of CD8⁺ cells specific to vaccine encoded antigens in the subset of HLA-A2⁺ patients and 2) potential determinant spreading to antigens not in the vaccine, 3) frequency and co-expression of the checkpoint inhibitor molecules CTLA-4, PD-1, and TIM-3 on CD8⁺ T cells, and 4) to characterize three NK cell subpopulations. On the CD8⁺ T cells, PD-1 was the checkpoint molecule most commonly expressed, while CTLA-4 was minimally expressed. TIM-3 was the checkpoint molecule most commonly expressed on all three subpopulations of NK cells. We observed that most patients developed vaccine-encoded antigen-specific responses, and a subset demonstrated determinant spreading to non-vaccine encoded antigens gp100 and/or NY-ESO-1. Expression of checkpoint

molecules changed on both T and NK cells through the treatment periods, and the function (by IFN γ ELISPOT) was also assessed. This study will aid in the design of more effective dendritic cell vaccines and adjuvants for metastatic melanoma patients.

Trial registration

ClinicalTrials.gov identifier NCT01366144.

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