Restoring Innate and Adaptive Immune Repertoire in Multiple Myeloma for Therapeutic Application

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BACKGROUND

Despite advances and improvements in survival, majority of multiple myeloma (MM) patients ultimately relapse. Extensive analysis on the properties of tumor cells has provided interesting insights into disease biology allowing for the identification of novel targets and development of new therapies. However, microenvironmental influences, especially the immune microenvironment, are key to drive the disease and impact outcome. In addition to humoral immunodeficiencies, the immunosuppressive microenvironment observed in MM includes a dysfunction in the adaptive immune system with an increase in immunosuppressive cells (Treg or myeloid derived supressor cells). This is accompanied by a significant impairment of innate immunity, specifically a progressive decline in natural killer (NK) cells function (low expression of activating receptors and high expression of certain inhibitory receptors). These factors allow tumor immune escape and ultimately myeloma cell growth.

NKTR-255 is a polymer-conjugated human IL-15 that retains binding affinity to the alpha subunit of IL-15R but induces a reduced clearance to thereby provide a sustained pharmacodynamic response. Our aim in this study was to evaluate the role of NKTR-255 to overcome some of the immune dysfunction observed in MM.

OBJECTIVES

1. NKTR-255 enhances ex vivo expansion of memory CD8+ T cell subsets from PBMC of MM patients
2. NKTR-255 induces growth of NKT cells in MM patients
3. NKTR-255 expands MM NK cells
4. Activation of NK cells derived from MM patients by NKTR-255

MATERIALS & METHODS

We have evaluated the impact of NKTR-255 and IL-15 on effective immune cell populations from peripheral blood of healthy donors (HD) and MM patients at different stages of disease. NK cells were isolated by negative cell populations from peripheral blood of healthy donors (HD) and MM patients at different stages of disease. NKTR-255 was prepared using TESA Technologies and used at concentrations range from 0.1 to 1000 ng/mL.

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