Results Here we present the successful induction of 4–5 $CD8^+$ and 4–7 $CD4^+$ T-cell responses per patient, generated using peripheral blood mononuclear cells from multiple melanoma patients during these successful process engineering runs. We then extensively characterized these T-cell responses and demonstrate that these responses are functional, specific and have cytolytic capacity. Moreover, the induced T cells can recognize autologous tumor.

Conclusions NEO-STIM is a novel platform that generates *ex vivo* T-cell responses to high-quality neoantigen targets. NEO-PTC-01, the neoantigen-specific T cell product generated from this process, is a potent adoptive cell therapy targeting multiple immunogenic neoantigens in patients with metastatic melanoma.

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154 MARROW-INFILTRATING LYMPHOCYTES (MILS): A NOVEL ADOPTIVE IMMUNOTHERAPY FOR HEMATOLOGICAL AND SOLID TUMORS

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Background Marrow infiltrating lymphocytes ($MILs^{TM}$) are the product of activating and expanding bone marrow T cells.[1] The bone marrow is a specialized niche in the immune system enriched for antigen-experienced, memory T cells. In patients with multiple myeloma and other hematological malignancies that relapse post-transplant, MILs have been shown to contain tumor antigen-specific T cells and adoptive cell therapy (ACT) using MILs has demonstrated antitumor activity.[2 3] The bone marrow has been shown to harbor tumor-antigen specific T cells in patients with melanoma,[4 5] glioblastoma,[6] breast,[7] non-small-cell lung[8] and pancreatic cancers.[9] Here, we sought to determine if tumor-specific MILs could be expanded from the bone marrow of patients with a range of different solid tumors.

Methods Bone marrow and blood samples were collected from patients with advanced and metastatic cancers. To date, samples have been collected from a minimum of four patients with non-small cell lung cancer (NSCLC), prostate cancer, head and neck cancer, glioblastoma, and breast cancer. Samples from patients with multiple myeloma were used as a reference control. Utilizing a 10-day proprietary process, MILs and peripheral blood lymphocytes (PBLs) were activated and expanded from patient bone marrow and blood samples, respectively. T cell lineage-specific markers (CD3, CD4 and CD8) were characterized by flow cytometry pre- and post-expansion.Tumor-specific T cells were quantitated in expanded MILs and PBLs using a previously described cytokine-secretion assay [2]. Briefly, autologous antigen-presenting cells (APCs) were pulsed with lysates from allogeneic cancer cell lines and co-cultured with activated MILs or PBLs. APCs pulsed with irrelevant mis-matched cancer cell line lysates or media alone were used as negative controls. Tumor-specific T cells were defined as the IFNgamma-producing population by flow cytometry.

Results MILs were successfully expanded from all patient bone marrow samples tested, regardless of tumor type. Cytokine-producing tumor-specific CD4+ and CD8+ T cells were detected in each of the expanded MILs. In contrast, tumor-specific T cells were not detected in any of the matched activated and expanded PBLs.

Conclusions MILs have been successfully grown for all solid tumor types evaluated, including NSCLC, prostate, head and neck, glioblastoma and breast cancer. Clinical studies have been completed in patients with multiple myeloma and other hematological cancers. [2 3] A phase IIa trial to evaluate MILs in combination with a checkpoint inhibitor is underway in patients with anti-PD1/PDL1-refractory NSCLC (ClinicalTrials.gov Identifier: NCT04069936). The preclinical data presented herein demonstrate that expanding MILs is feasible. MILs-based therapies hold therapeutic promise across a wide range of tumor indications.

Ethics Approval This study was approved by each participating instituion's IRB.

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155 IPSC-DERIVED NK CELLS MEDIATE ROBUST ANTI-TUMOR ACTIVITY AGAINST GLIOBLASTOMA

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Background Gliomas represent the most common brain tumors within the central nervous system, with glioblastoma being the most aggressive type.[1] Conventional treatment combines several approaches including surgery, chemotherapy, and radiation.[2] However, the prognosis for glioblastoma remains unfavorable, with only 5% of patients surviving more than 5 years post-diagnosis.[3] Thus, new treatment approaches are urgently needed. Natural killer (NK) cells directly lyse malignantly transformed or virally infected cells and secrete inflammatory cytokines that polarize cytotoxic immunity. Allogeneic