included T cells reactive to a p53 mutation in an autologous manner for the treatment of patients with metastatic epithelial cancers (n=12). Except for the two patients who exhibited an objective response (RECIST), most of the patients did not respond to the therapy, possibly due to low frequencies of anti-mutant p53 cells in the infusion product, exhausted phenotype, and/or poor persistence (table 2). To overcome these barriers to TIL treatment, we retrovirally transduced autologous peripheral blood T cells to express an allogeneic anti-mutant p53 TCR. We engineered the HLA-A*02:01-restricted anti-p53 R175H TCR into patient 4349’s lymphocytes (transduction efficiency of 64%) and saw less expression of exhaustion markers relative to the TIL infusion products (table 2). This patient with metastatic breast cancer was refractory to the six prior chemotherapy regimens. After the transfer of 5.3e10 cells, the patient experienced an objective partial response, showing regression by 55% of skin and mediastinal lesions for 7 months. The persistence of the infused T cells was higher than the other patients who received the TIL treatment (table 2).

Conclusions The library of anti-mutant p53 TCRs we have generated can potentially be used to treat ~6% of all cancer patients. We are pursuing the adoptive transfer of TILs against mutant p53 naturally occurring in the tumor or TCR-engineered cells using ‘off-the-shelf’ receptors against mutant p53.

Ethics Approval This study was approved by the Institutional Review Board (IRB) of the NCI, and the approval numbers are as follows:Protocol 10-C-0166 (TIL treatment); Protocol 18-C-0049 (allogeneic TCR engineered T cell therapy)

REFERENCE

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0152

Abstract 152 Table 1 Anti-mutant p53 TCR library
1 N=51,782 solid tumors (http://p53.fr/)
2 Phenotype frequency (http://www.allelefrequencies.net/)

Abstract 152 Table 2 Patients who received mutant p53-reactive cell products
1 TCRB sequencing (Adaptive Biotechnology)
2 Flow cytometry against the murine TCR β constant region
NA not available, NR no response, PR partial response, PD progressive disease, SD stable disease, TX treatment
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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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 institution’s IRB.

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1. Borrello I and Noonan KA. Marrow-Infiltrating Lymphocytes - Role in Biology and 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. Conventional treatment combines several approaches including surgery, chemotherapy, and radiation. However, the prognosis for glioblastoma remains unfavorable, with only 5% of patients surviving more than 5 years post-diagnosis. 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...