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Characterization of neoepitope (neoE)-specific T cells from peripheral blood for adoptive neoTCR-T cell therapy for patients with breast cancer (bc) or ovarian cancer (oc).

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Abstract 331: Characterization of neoepitope (neoE)-specific T cells from peripheral blood for adoptive neoTCR-T cell therapy for patients with breast cancer (bc) or ovarian cancer (oc)

Abstract

Introduction: Broad application of neoTCR-T cell therapy involves isolation of mutation-targeted CD8 T cells from the blood of patients with different tumor types. An ultra-sensitive process streamlined for high-throughput capture of neoE-specific T cells from blood is leveraged for producing a fully personalized adoptive T cell therapy for trial participants with BC or OC (NCT03970382).

Methods: Expressed mutations were identified by comparative sequencing of blood cells and tumor tissue. HLA typing was performed with OpiType. Proprietary algorithms were used to predict and prioritize tumor-exclusive neoE-HLA candidates. A library of barcoded HLA-mutational neoantigen complexes was used to interrogate PBMCs from each patient using imPACT Isolation Technology® (Dalmas et al., 2020). NeoTCRs cloned from captured antigen-experienced CD8 T cells were precision genome engineered into healthy donor T cells for functional characterization, including secretion of cytokines and effector molecules (Jacoby et al., 2019; Sennino et al., 2019). Based on pre-specified prioritization criteria, up to 3 actionable neoTCRs were selected for manufacturing the products for each individual.

Results: Six patients (2 BC/4 OC) successfully underwent neoTCR product selection. The median age was 59.5 years (range 38-69). Patients received a median of 5.5 prior regimens for metastatic disease (range 4-9). Median tumor mutational burden (TMB) was 2.7 (range 0.9-13.4). HLA-neoantigen libraries contained a median of 91 snares (range 29-262) and represented 6/6 HLA alleles in 4 patients and 5/6 in the remaining 2. A median of 8.5 distinct neoE-specific T cells (range 5-15) were isolated per patient. Following functional characterization 13 neoTCRs met selection criteria: three patients with 3 TCRs, one with 2 TCRs, and two had a single TCR. The median predicted neoE:HLA affinity of the selected TCRs was 77 nM (range 6.3 - 5866) and the median IFN-g EC50 was 4 ng/mL (range 1-431).

Conclusion: Relevant antigen-experienced, tumor mutation-targeted CD8 T cells were isolated from the blood of heavily pre-treated BC and OC patients with low TMB (<10 mutations/Mb). Correlations between TCR characteristics and clinical and biomarker data are planned. This approach holds potential for broad use in women with BC or OC.

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