Background Immunotherapy with Immune checkpoint inhibitors (ICIs) has revolutionized cancer treatment over the last decade. Despite the phenomenal success of ICIs, the clinical response is confined to a small subset of patients. Conventional biomarkers such as PDL1 expression and Tumor Mutational Burden (TMB) rely on invasive biopsies and remain inadequate in predicting clinical benefits for patients. Therefore, there is an urgent need to develop better noninvasive biomarkers to predict the response to ICIs and to identify patients for whom these therapies are both safe and effective. A novel blood-based functional assay, peripheral T cell cytotoxicity (PeriCyto), has previously been shown to accurately predict the clinical response for advanced non-small cell lung cancer (NSCLC) in Japanese patients.1 2 The present study aimed to assess clinical feasibility of PeriCyto in predicting the response to ICIs in a US patient cohort.

Methods Prospective samples (n=13) were obtained from patients with diverse solid tumors prior to treatment with ICIs either as monotherapy or in combination with chemotherapy/targeted therapy. Peripheral Blood Mononuclear Cells (PBMCs) isolated from whole blood were cocultured with U251 cells in the presence of an EphA2/CD3 Bispecific T cell Engager antibody (BiTE). After 48hrs, peripheral T cell cytotoxicity was measured using the 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium assay (MTS) assay. PBMCs from a healthy donor with an established cytotoxicity score served as an internal positive control for the assay.

Results The study evaluated the positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of PeriCyto in 13 patients with diverse set of cancers. As previously published1 2 the assay was able to accurately predict the clinical response in the subgroup of patients with advanced NSCLC (4/4). Combining data from patients with all cancer types, the PPV was ~70% and NPV was determined to be 100% (n=13). The assay identified all patients who subsequently responded to ICIs (sensitivity 100%), whereas specificity was 50%. The latter was driven by incorrect prediction of positive treatment response in tumor types traditionally known to be immunologically ‘cold’, raising the possibility that these non-responding histologies may reflect tumor types wherein peripheral T cells are activatable but remain absent or suppressed in the TME.

Conclusions Overall, these early pilot findings indicate that PeriCyto can help to identify patients who may benefit from ICIs. Limitations include small sample size and single site design. Future efforts will focus on expansion of this patient cohort and extending followup to further assess PeriCyto predictive value.

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REFERENCES