DEVELOPMENT OF A FLOW CYTOMETRIC RECEPTOR OCCUPANCY ASSAY FOR CLINICAL ANALYSIS OF IMMUNE CHECKPOINT INHIBITOR THERAPEUTICS

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Background PD-1 (CD279) is an immune checkpoint inhibitor that is expressed on the surface of T cells. Therapies inhibiting PD-1 interactions have become the most popular checkpoint inhibitor utilized in cancer immunotherapies. While treatments with anti-PD-1 can be highly effective, the combination of PD-1 with targeted treatment against other immune checkpoint molecules or costimulatory molecules has largely improved patient outcomes in the clinic. The pharmacokinetics of these treatments, including the retention of therapies to their target molecules, has played a critical role establishing effective dosing and treatment regimens. However, performing these assays can be costly, time intensive to develop, and require specialized equipment and expertise.

Methods Here, Champions Oncology has established a receptor occupancy (RO) assay against PD-1 in a scalable fashion using high dimensional flow cytometry. Flow cytometry is a powerful single cell technique that allows for the interrogation of drug-target cell interactions at the single cell level and has been utilized to evaluate receptor occupancy for several molecules, including PD-1.

Results Champions Oncology has developed a panel that includes a drop-in channel to evaluate both the receptor occupancy of PD-1 and the expression of other key checkpoint markers used in combination therapies. The receptor occupancy assay was evaluated for both assay sensitivity and reproducibility. This assay has been further developed to be scalable and stable up to 48–72 hours on fresh whole blood samples.

Conclusions Collectively, this assay establishes the strength of the drug-target interaction, the sensitivity to which PD-1 interactions can be evaluated, and flexible nature of the custom-designed assay.

Ethics Approval All human biological samples utilized for the research described in this abstract have been procured or collected after an Informed Consent form has been issued according to the current local legislation. All animals studies described in this abstract have been conducted under Champions’ approved IACUC.

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