Leveraging Donor-Derived, In-Vitro PBMC Assay to Model B cell Depletion and Test Efficacy of B Cell–Targeted Agents for Non-Hodgkin's Lymphoma Indications

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The success of CD20 B cell targeting therapies like Rituximab has generated interest in developing more effective B cell targeting drug candidates for Non-Hodgkins Lymphoma (NHL) indications. The current landscape of B-NHL treatment involves several B cell targeting therapeutics, including Bispecific antibodies such as Glofitamab and Epcoritamab, and CAR-T treatments that have shown promise in clinical trials. These T-cell redirecting therapies, particularly Bispecifics, can be effective as monotherapies or in combinations with chemotherapy or immunomodulatory agents, with the potential to increase the curative fraction in B-NHLs. However, there is a need for physiologically relevant in-vitro systems to study B cell depletion caused by these therapies and evaluate their efficacy prior to in-vivo studies to aid in preclinical assessment and translational evaluation.

This poster presents an optimizable, donor-derived peripheral blood mononuclear cells (PBMC) assay designed to test and quantify B cell depletion in response to drug compounds in an in-vitro setting. The assay utilizes freshly isolated donor PBMCs to retain the circulating immune compartment, where Primary B cells act as targets, while NK or T cell populations are employed as effectors depending on the therapeutic agent. Rituximab, a CD20 targeting monoclonal antibody, is utilized as a proof-of-concept drug treatment. The assay aims to study B cell depletion in response to drug treatments in a more physiological manner by retaining the donor's effector and target cell ratio. In order to gain insights into underlying immune responses, flow cytometry is utilized to perform immunophenotyping of B cell, NK cell, and T cell populations in the assay samples. To enable comprehensive detection of B cells and minimize competition with Rituximab, the frequency of CD22+ B cells is measured to quantify B cell depletion in drug-treated samples compared to untreated samples.

This assay has the potential to provide early insights into the mechanisms of action of B cell targeting drug candidates in patient derived cells. Additionally, it allows for the investigation of correlations between NK and T cell-mediated B cell depletion in patient populations. By utilizing this in-vitro PBMC assay, we can obtain preliminary dose-response results, screen potential drug candidates, and quantify drug efficacy in a more efficient and physiologically relevant manner.