Abstract

Rituximab is a monoclonal antibody (mAb) among the top 10 best-selling drugs, with global sales estimated to exceed $7B in 2015. Rituximab is indicated to treat conditions including chronic lymphocytic leukemia (CLL), B-cell non-Hodgkin's lymphoma, and various autoimmune disorders. Population pharmacokinetic studies have revealed considerable differences in the final levels of rituximab found in the blood after a course of therapy, and these levels correlate with therapeutic outcomes. With current dosing regimens, a substantial fraction of the patients may not be receiving an efficacious dose. During clinical development, laboratory-based tests are used to monitor rituximab levels in patients, but these tests are not available to physicians after approval. Currently, there are no point-of-care (POC) tests available to monitor the levels of rituximab in patients. The goal of this project is to develop low cost POC devices that provide a quantitative measure of rituximab levels in blood. These tests will help physicians personalize the dosing of patients and identify early rituximab treatment failures resulting from low drug levels. Our core enabling technology platform is based on mimetope peptides, termed Veritopes^{TM}, that mimic the cognate ligand of a given mAb and specifically bind at the antigen binding site. Veritopes^{TM} are cheap, robust, and simple to integrate into lateral flow immunoassay (LFA) that then enables inexpensive POC testing. In preliminary studies, we demonstrated the feasibility of Veritope^{TM}-based LFA for the qualitative detection of rituximab, trastuzumab, and bevacizumab levels in biologic fluids as well as the potential to develop quantitative tests. In this Phase II project, we will complete the development of a CLIA-waivable rituximab monitoring test that can be performed at the POC from a single drop of blood. We will integrate the LFA strips into single-use, disposable digital LFA reader devices that can provide quantitative analysis of the test strips. These devices will be validated in a clinical trial in partnership with UCSD Moores Cancer Center using blood samples from patients treated with rituximab. The data generated during this Phase II study will be incorporated in our technical data package to submit to FDA for clearance of our device, which will be the first FDA cleared device for biologic drug monitoring at the POC.

This innovative product will fulfill of an unmet clinical need for a rapid, cost effective, and accurate dose monitoring assay. Precision dosing through data-driven, personalized regimens will improve treatment outcomes and maximize the efficient use of this and other monoclonal antibody therapeutics.