GLOBAL GATORS SYMPOSIUM

BILBAO SPAIN

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Bio

I joined Gilead Sciences, Inc.in 2022, bringing 15 years of experience between academia, Pharmacometrics consulting and the pharmaceutical industry. I received my BS and MS in Computer Engineering and Science at the University of the Basque Country (Spain). I received my Ph.D. degree in Computer Science from the same university. During my Ph.D., I did an internship at the Center for Biomedical Informatics at Harvard Medical School (Boston, MA). My post-doctoral research was developed at University of Navarra, School of Pharmacy (Spain) and Indiana University, Division of Clinical Pharmacology, School of Medicine (Indianapolis, IN), being later promoted to assistant professor. In 2014, I started working at the PK/PD & Pharmacometrics Department with Eli Lilly (Indianapolis, IN), using modeling and simulation to inform decision making in all phases of drug development (preclinical and clinical) across a range of therapeutic areas. In 2020, I transitioned to Metrum Research Group where I provided pharmacometrics and clinical pharmacology support to multiple pharmaceutical companies. I have maintained an adjunct position at Indiana University, Division of Clinical Pharmacology, School of Medicine since 2014.

Abstract

Measurement of monoclonal antibody target engagement in vivo is important to understand drug activity and helps to set and characterize safe and efficacious doses in the clinic. When antibodies are directed against cell-surface targets, engagement of the antibody with its target can be assessed by multiple approaches. Direct measurement of antibody binding to the cell-surface target can be achieved by using an appropriate flow cytometry receptor occupancy assay. Alternatively, if the cellular antigen is shed or secreted, measurement of dose dependent soluble target accumulation in serum or plasma over time following dosing of the antibody may be possible. Pharmacokinetics/pharmacodynamics modeling approaches can be used to estimate soluble target engagement based on the drug exposure and corresponding accumulation of total soluble target. Lastly, characterization of target mediated drug disposition and incorporation of PK modeling can allow indirect estimation of cell-surface receptor occupancy. These various approaches to determining target engagement rely on varying underlying assumptions and range in bioanalytical complexity, cost, and other characteristics. Here, we present a direct comparison of receptor occupancy, soluble target accumulation, and characterization of nonlinear PK as approaches to characterize antibody target engagement in vivo. The results of this comparison have implications for selecting doses in subsequent trials, for assessing the safety and activity of the antibody, and for determining which assays are most suitable to carry forward to support further clinical development.