CERTARA

PBPK Modeling and Simulation for Biologics

Mechanistic modeling isn't just for small molecules anymore

Biological medicines ("biologics" or "large molecule drugs") are a rapidly growing segment of the pharmaceutical industry's pipeline. And their pharmacokinetic (PK) properties are quite distinct from that of small molecules.

Certara's Simcyp Simulator—a sophisticated physiologically-based pharmacokinetic (PBPK) modeling and simulation platform—can predict the pharmacokinetics of small molecule *and* biological medicines using laboratory-derived data. It links *in vitro* data to *in vivo* ADME (absorption, distribution, metabolism, and excretion) and pharmacokinetic/pharmacodynamic (PK/PD) outcomes to help explore potential clinical complexities prior to human studies and support decision-making in drug development.

The Simcyp whole body simulation methodology can predict the pharmacokinetics and pharmacodynamics of small molecule, antibody drug conjugates, and biological medicines using laboratory-derived data. The simulator includes a unique set of genetic, physiological and epidemiological databases that facilitate the simulation of virtual populations of differing demographies and ethnicities.

Advancing the understanding of therapeutic antibodies

Monoclonal antibodies (mAbs) are large Y-shaped proteins that are produced by immune cells to defend the body against pathogens. A hallmark of antibodies is their ability to specifically bind to epitopes, or the parts of the antigen that the immune system recognizes, on their molecular targets. This property has been harnessed by drug companies to develop treatments for certain cancers and autoimmune diseases. More than 40 mAbs and derivatives have been approved for a variety of therapeutic applications and about 500 more are currently in different stages of development.

The Simcyp Simulator can simulate mAb PK in humans using a mechanistic minimal PBPK model wherein the body is divided into three compartments: plasma, tissue, and lymph with the tissue compartment being further sub-divided into vascular, endothelial, and interstitial spaces. The model can account for the levels of both endogenous IgG and exogenous therapeutic mAbs in each compartment and sub-compartment.

Supporting mechanism-driven studies of ADCs

The Simcyp Simulator also offers a PBPK model for antibody drug conjugates (ADCs). ADCs are a new class of targeted biologic therapies for oncology. They combine the ability of monoclonal antibodies to target cancer cells with the tumor cell killing ability of chemotherapy drugs. This new, scientifically complex therapeutic approach can have a breakthrough impact on the oncology market. According to the report "Global Antibody Drug Conjugate Market Outlook 2020," the ADC market is anticipated to reach around $12.7 billion by 2020. This Simcyp Simulator model enables mechanism-driven studies of ADCs and drug-drug interactions (DDIs).

Enabling smarter biologics drug development for pediatrics

PBPK is now considered a key component of pediatric drug development, especially for infants and neonates. Simcyp Pediatric—a module within the Simcyp Simulator—allows modeling PK in neonates, infants and children. The Simcyp Simulator's pediatric biologics module also allows user-defined IgG catabolic and systemic clearance ontogeny profiles for large molecules. This provides valuable information relevant to first-time dosing decisions and the design of pediatric clinical studies.

Developing safer, more effective biological medicines

Used by most of the top 40 global pharmaceutical companies (including all of the top 10), together with the US FDA, other key regulatory agencies, and leading academic institutions, the Simcyp Simulator assists in dose selection and informing product labeling. Certara has built on its existing PBPK expertise to develop models that allow analyzing the impact of both small and large molecule drugs on the body.

Why use PBPK for biologics?

Integrating PBPK into your drug program can yield multiple benefits. By using a mechanistic approach like PBPK, you gain the ability to account for the mechanisms responsible for biologic drug disposition. Likewise, this approach can help bridge from pre-clinical to clinical studies to prospectively simulate the likely outcome of dosing. Finally, there are often critical physiological differences between healthy volunteers and patients that can impact drug PK. PBPK models can account for altered physiology in disease states—changes in renal/hepatic function, changes in plasma protein levels, etc—and assess their impact on pharmacokinetics.

Characterizing biologic drugs' PK in a more mechanistic manner will help bring safer, more efficacious treatments to market.

About Certara

Certara is a leading provider of decision support technology and consulting services for optimizing drug development and improving health outcomes. Certara's solutions, which span the drug development and patient care lifecycle, help increase the probability of regulatory and commercial success by using the most scientifically advanced modeling and simulation technologies and regulatory strategies. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions and key regulatory agencies.

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