synteract®
BRINGING CLINICAL TRIALS TO LIFE

Application of Population Pharmacokinetics in Drug Development

Population pharmacokinetics (PopPK) uses mathematical and statistical models to estimate PK parameter values and the associated variability of a drug using data from all individuals across different studies. The variability in the PK will typically increase as the number of individuals and studies increase. This variability may be attributed to intrinsic factors (weight, gender, genetics, race, ethnicity, etc.) or extrinsic factors (concomitant medication, diet, drug formulation, etc.).

PopPK utilizes a modeling methodology known as "Non-linear mixed effect modeling." This modeling approach enables the drug developer to quantify the variability in the PK parameters, identify the intrinsic or extrinsic factors (also known as covariates) that contribute to the variability in the exposure; and understand the magnitude by which these covariates contribute to the variability in the exposure. Unlike traditional PK modeling and non-compartmental approaches, which rely on rich plasma samples, PopPK modeling has the inherent advantage of using sparse samples, which makes it suited for analysis of the sparse data from Phase III trials or for rare and orphan drugs. PopPK plays a pivotal role in the design and analysis of pediatric studies as these studies require minimal number of PK samples for various ethical, practical, and recruitment reasons.

PopPK plays a key role across all phases of clinical development. At the preclinical stage, PopPK modeling provides guidance for First-in-Human dose for the early phase of clinical trials. During mid- and later-stage clinical development, PopPK helps in predicting optimal dosing and sampling schemes, PK/PD relationships, and the effect of applicable covariates on dose exposure.

Regulatory Position

The Food and Drug Administration (FDA) and the European Medicines Agency (EMA) acknowledge the importance of PopPK modeling in regulatory decision making. FDA utilizes PK modeling and simulation extensively to review data as a part of regulatory process and to make informed decisions. According to Dr. Scott Gottlieb, Commissioner of Food and Drug Administration (2017-2019), "Almost 100% of all NDAs for new molecular entities have components of modeling and simulation."

Pop PK Services

The Synteract Pharmacometrics team can provide the following PopPK services:

- Critical assessment and expert advice of programs and protocols
- PopPK model development using validated technologies (Phoenix NLME and/or NONMEM).

- Identification of covariates associated with inter-individual variability in drug exposure.
- Model-based study design and dose optimization/recommendations for testing in clinical trials.
- Preclinical PK modeling and FIH predictions.
- Prediction of drug exposure-response and dosing recommendations in specific patient populations (e.g., patients with renal or hepatic impairment).
- Dose extrapolation from adults to pediatrics
- Determining optimum PK sampling

Contact Us today to learn how our team can facilitate your next drug development program.