CASE STUDY

Using PBPK to Extrapolate Animal Tissue Concentrations to Humans

Background and Problem

An approved small molecule therapeutic has shown efficacy in numerous target organs of interest in clinical trials. The client wished to show that this efficacy was explained by high drug penetration into these tissues.

Our Solution

Mouse biodistribution data was collected. A physiological-based pharmacokinetic (PBPK) model was built using the physicochemical data of the drug compound and the pharmacokinetics information in mice, which was then extrapolated to humans by optimizing absorption and clearance to human plasma data. The PBPK model was used to predict human tissue concentrations in various organs.

Outcome

The PBPK model showed that at the therapeutic dose, drug concentration exceeds the in vitro EC50 in numerous target organs of interest. In addition, the model suggested tissue binding and eventual dissociation from the target, which was consistent with the proposed mechanism of action for this drug.

Physiologically Based Pharmacokinetic Modeling

PBPK modeling can be utilized in multiple stages of drug development. New guidance from regulatory agencies has highlighted key areas for the use of PBPK models, showing their ever-growing acceptance. Allucent scientists can help you untangle the complex data requirements of PBPK models, and bring these powerful modeling tools to bear on complex problems facing drug development.

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