CPSA Shanghai 2019

Session: In vitro to In vivo translation and PBPK modeling (1:30 -3:00pm, 4/12/2019)

1. Translational Aspects of Drug Discovery

Matthew R. Wright, Director, Department of Drug Metabolism and Pharmacokinetics, Genentech

The process of drug discovery requires the extrapolation of data generated in one condition into different settings. Some representative examples would include the use of in vitro data to predict in vivo performance; the use of non-clinical data to predict human disposition and the application of data derived from normal, healthy humans to predict behavior in disease. Collectively these examples reflect areas of translational sciences which require different approaches than the deconvolution of data generated within a particular system or experiment. The development and increasing accessibility of systems based approaches, PBPK and quantitative systems pharmacology; provide visible and clear demonstration of the significance of translation in drug discovery. Despite these advances, the success rate of drug development has remained relatively consistent which may suggest that continued evaluation of translational science is warranted.

2. Utilities of Physiologically-based Pharmacokinetic Modeling in Pediatric Drug Development

Ming Zheng, Ph.D., Director, Quantitative Clinical Pharmacology, Bristol-Myers Squibb Co.,

Allometrically based PK prediction is considered adequate for children of 2 years or older. For children younger than 2 years, there can be profound maturation of drug metabolic enzymes and transporters from birth. PBPK models can incorporate enzyme and transporter ontogenies thus be very useful to inform drug development in young children. This presentation will review the state of science, applications and challenges of PBPK modeling and simulation in pediatric drug development and regulatory submissions, and provide an example of PBPK application in the particularly challenging neonate population. The presentation will also review the ontogeny of drug metabolic enzymes and transporters during child development and how such data been incorporated in PBPK models.Ming Zheng

3. Towards Prospective Pharmacokinetic Prediction of Organic Anion Transporting Polypeptide (OATP) Substrates

Jialin Mao, Senior Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech

Abstract: It is known that a scaling factor is typically required when the in vitro uptake data are utilized to predict the pharmacokinetic of OATP substrates. It demonstrates a hurdle for the prospective prediction of the new chemical entity as an OATP substrate. Investigation of the plated human hepatocytes and human embryonic kidney (HEK) 293 cells transfected with OATP1B1 and OATP1B3 in

the presence and absence of 100% human plasma were explored, and the physiologically based pharmacokinetic modelling approach provided an opportunity to understand the in vitro and in vivo extrapolation.