Physiologically Based Pharmacokinetic (PBPK) Modeling to support dosing recommendations for patients with renal Impairment—Are we there yet?

2017 ASCPT Workshop
Friday March 17 1:15-2:45 PM

Chairs: Ying Ou, Amgen & Robin O'Connor–Semmes, PAREXEL

Network and Community: Development, Regulatory and Outcome (DRO), Regulatory Science; Quantitative Pharmacology (QP), Pharmacometrics & Pharmacokinetics
A Brief History of PBPK Models

- **1937**: One of the earliest PK models was a “PBPK Model”.
  - Teorell, et al., Arch Intern Pharmacodyn

- **1971**: Whole-body PBPK model was first described.
  - Dedrick and Bischoff et al. Methotrexate PK. J. Pharm Sci.

- **1977**: The disposition of polychlorinated biphenyls - used in toxicology environmental risk assessment.
  - Andersen et al, CPT.

- **1999**: Workshop on PBPK in drug development and regulatory science. Rowland, Peck et al. AAPS J

- **2002**: Increasing availability of commercial Platforms (Simcyp, GastroPlus, PKSim)

- **2010**: EMA and FDA released its draft PBPK guidance

- **2012**: WHO 2010 PBPK guidance

- **2016**: FDA 2012 use of PBPK in DDI guidance

Research and publications from pharmaceutical scientists
To provide an update on the current state of a timely topic - potential use of PBPK for dosing recommendation for patients with renal impairment.

- There have been multiple examples of drug labeling for drug-drug interaction (DDI) informed by PBPK, however the use of PBPK to support drug labeling for renal impairment dose recommendation is limited.

- Dedicated renal impairment studies can be challenging to conduct due to patient access difficulties (e.g., patients with severe renal impairment and ESRD patients not on dialysis).
Workshop Agenda

Introduction:
◦ Objective of workshop and a brief PBPK history

Speaker 1: Dr. Steve Hall: PBPK Modeling to support dosing recommendations for patients with renal Impairment–Effects on non-renal clearance

Speaker 2: Dr. Ping Zhao: The readiness and specific paths of using PBPK support dosing recommendation in patients with renal impairment

Speaker 3: Dr. Kathy Giacomini: Towards quantitative prediction of the effect of renal impairment: filling the gap for drug transporters

Each speaker will have ~ 25 minutes (including Q&A) for the presentation

Additional Q&A session (5 to 10 minutes) toward the end of the workshop