Application of PBPK to Drug Development Decisions

Joga Gobburu PhD FCP MBA
Professor, School of Pharmacy
University of Maryland
Rational Application of PBPK to Drug Development Decisions

Joga Gobburu PhD FCP MBA
Professor, School of Pharmacy
University of Maryland
Potential Areas of PBPK Application

- Drug-Drug Interactions
- Biopharmaceutics
- Bioequivalence
- Special Populations
- Medical Counter Measures

AGENDA
DDI Applications

1. Screening
2. Lead Optimization
3. ADMET
4. Clinical Trials
5. Waivers & Labeling
6. NDA Approved
7. 1 Drug to market

PLAN
DDI Applications

Figure 2. Overview of modeling strategy and workflow.

Figure 5. PBPK model-predicted concentration-time profile of buprenorphine after (a) 32-mg single-dose subcutaneous administration of CAM2038 Q1W formulation with and without interaction with oral administration of ketoconazole 200 mg twice daily, (b) 32-mg single-dose subcutaneous administration of CAM2038 Q1W formulation with and without interaction with oral administration of rifampin 600 mg once daily, (c) 152-mg single-dose subcutaneous administration of CAM2038 Q4W formulation with and without interaction with oral administration of ketoconazole 200 mg twice daily, and (d) 152-mg single-dose subcutaneous administration of CAM2038 Q4W formulation with and without interaction with oral administration of rifampin 600 mg once daily.

Liu T et al. JPS 2018
DDI Applications – Beyond Labeling

Screening → Lead Optimization → ADMET

PLAN

1 Drug to market → NDA Approved

Waivers & Labeling → Clinical Trials
Biopharmaceutics

Food Effect
- Food Effect
- Alcohol Effect

Formulation Changes
- IVIVC
- Dissolution Specs
- Mfg Changes
Bioequivalence

Systemic Effects  Local Effects  Quality Mgmt.
Special Populations

Pregnancy

Fetus

Pediatrics
PBPK has very little to add to Allometry in Predicting Pediatric PK

Allometric Scaling Predicted Pediatrics Clearance over Observed Pediatrics Clearance

Prediction Discrepancy

Drug Index

Liu T et al. JCP 2017
Potential Areas of PBPK Application

- Drug-Drug Interactions
- Biopharmaceutics
- Bioequivalence
- Special Populations
- Medical Counter Measures