BMS Clinical Pharmacology and Pharmacometric Networking Event at ASCPT

ASCPT Micro-Learning

Tunde Bello, Bindu Murthy, Li Zhu, Anna Kondic, Neelima Thanneer, and Brian Schmidt

Wednesday July 12th 2023
Clinical Pharmacology, Pharmacometrics, Disposition & Bioanalysis

Li Zhu
Executive Director
Head of Clinical Pharmacology
HOCT

Neelima Thanneer
Executive Director
Head of Data Science & Clinical Pharmacology Analysis & Reporting

Ann Kondic
Executive Director
Head of Pharmacometrics

Brian Schmidt
Executive Director
Head of Mechanistic Modeling (QSP &PBPK)

Akintunde (Tunde) Bello
Senior Vice President
Head of CPPDB

Sandra McVicar
Executive Associate II

Bindu Murthy
Executive Director
Head of Clinical Pharmacology ICVNS

Vibha Jawa
Executive Director
Biotherapeutic Bioanalysis

Li Zhu
Executive Director
Head of Clinical Pharmacology HOCT

Jim Shen
Executive Director Head of Regulated Bioanalysis (BA) Operations

Akintunde (Tunde) Bello
Senior Vice President
Head of CPPDB

Vibha Jawa
Executive Director
Biotherapeutic Bioanalysis

Matthew Hoffman
Senior Director Development Biotransformation

Sandra McVicar
Executive Associate II
CPP Groups & Functions

Clinical Pharmacology (ICVN & HOCT)
Bindu Murthy & Li Zhu
- Support early/late-stage dev programs
- Design & execute clin pharm strategy

Pharmacometrics (PMx)
Anna Kondic
- Perform/oversee Pmx analyses for submissions
- Oversee PMx modeling infrastructure and best practices

Clin Pharm Analysis & Reporting & Data Science
Neelima Thanneer
- NCA for clinical trials & regulatory submissions
- Clin pharm sections to protocols and CSR’s
- Programmers Integrate clinical trial & PK data for pop PK & PK/PD analyses

Mechanistic Modeling (QSP & PBPK)
Brian Schmidt
- Perform modeling activities to support early & late-stage programs
Introduction & Overview of ICVN

July 2023

Bindu Murthy, PharmD, MS
ASCPT Microlearning Event
ICVN Portfolio Consists of 3 Therapeutic Area Pillars Targeting a Broad Range of Novel Mechanisms & Modalities to Treat Disease with High Unmet Medical Need

ICVN Clinical Pharmacology & Pharmacometrics

- Immunology
  - Dermatology
  - Rheumatology
  - Irritable Bowel Disease
  - Pulmonary

- Cardiovascular
  - Arterial Thrombosis & Embolism
  - Heart Failure
  - Cardiomyopathies

- Neurosciences
  - Multiple Sclerosis
  - Alzheimers
  - Neurodegenerative Diseases

Novel Mechanisms
Join the ICVN Clinical Pharmacology & Pharmacometrics Community at Bristol Myers Squibb

Meet the Leadership Team

- Bindu Murthy
  Executive Director, Head of ICVN

- Jacqueline Davis
  Executive Associate

- Urvil Aras
  Senior Director, Head of Immunology

- Sandra Merall
  Senior Director, Head of Cardiovascular

- Daniel Tatolian
  Senior Director, Head of Neurosciences

Mission: Design fit-for-purpose Clinical Pharmacology plan & Execute through a combination of innovative clinical studies & Quantitative Analysis Approaches to inform drug development decisions

Meet the Passionate Scientists
To improve patient care by providing quantitative clinical pharmacology and drug development expertise to innovate breakthrough therapeutics that will help cancer patients.

**Our Deliverables**

- **Phase I/II:** Integrated PK, PK/PD and QSP modeling to support MoA and POC Go/No-Go decisions
- **Phase III:** Comprehensive E-R analyses enable optimal dose selection and pivotal study design
- **Filing:** Robust clin pharm package to support favorable benefit/risk assessment at the filing and during life cycle management

**Our Pipeline and Drug Platforms**

- **Oncology Solid Tumors and Hematology**
  - 14 Marketed Medicines
  - 36+ Clinical Stage Programs

- **Drug Platforms**
  - Antibody Drug Conjugates
  - Biologics
  - Cell Therapy
  - Small Molecule
  - Protein Homeostasis
  - Millimolecules
ALNUCTAMAB, A BCMA × CD3 T-CELL ENGAGER FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA (Poster #P883)

GPRC5D-TARGETED CAR T-CELL THERAPY FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA (Poster #S193)
What is Pharmacometrics (PMx) What is Model-Informed Drug Development (MIDD)?

- **PMx** is modeling & simulation applied to the characterization of pharmacokinetics, exposure-response (safety, efficacy, and biomarker), and disease progression

- **MIDD** is the use of model-based analyses to inform drug development and regulatory decisions by:
  - Bridging data gaps
  - Avoid or reduce scope of clinical studies

Learn & Confirm Paradigm of MIDD
VISION

Be a recognized leader and champion of Model Informed Drug Development methods and applications to address data gaps and enhance efficiency of drug development

MISSION

* Partner strategically with CP on the characterization of PK and E-R relationship, quantifying impact of patient-specific factors
* Collaborate with IT and other BMS functions to aid in the development and adoption of new methodologies to streamline drug development with emphasis on key questions to CPP
Data Science & Clinical Pharmacology Analysis and Reporting (DS/CPAR)

**Mission:** *Build a high-quality foundation for quantitative analysis to better characterize drugs and bring them to patients.*

**Data Science:**
- Integrate clinical and pharmacokinetic data to prepare analysis datasets for pharmacometric and non-compartmental analyses across all TAs for internal decisions and regulatory filings
- Follow rigorous, systematic processes to account for deficiencies in source data consistently across studies to enable modeling activities

**CPAR:**
- Responsible for study-level PK analysis and reporting and ensure it is standardized across protocols and programs
- Participate in continuous improvement initiatives related to optimizing PK data flow, PK analysis, reporting and outsourcing

**External Focus:**
- Developed programming standards and designed automation tools to create harmonization in pharmacometric datasets across the pharmaceutical industry

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<th>CPAR Tasks (PK sections)</th>
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QSP & PBPK department: mechanistic modeling to advance drug discovery and development

Mechanistic modeling

Application of mathematical models describing a biological system to predict outcomes

Physiologically Based Pharmacokinetics (PBPK)
Modeling of what body does to the drug

Quantitative Systems Pharmacology (QSP)
Modeling of what the drug does to the body

Mission

• Provide scientific, decision-enabling modeling and analysis derived from mechanistic data to support research & development

• Establish staged and long-term innovation in computational methods, modeling, and data utilization

Bristol Myers Squibb™
Mechanistic modeling can help with a variety of questions

- **Target**: is a disease sensitive to targets of interest?
- **Properties**: are drug properties appropriate (PK, binding, safety, tissue delivery)?
- **Translational strategy**: what are mechanistic drivers and biomarkers, and what does a good target population look like?
- **Dose range for first-in-human and proof-of-mechanism**: can I remove unnecessary low dose levels, assess efficacious dose range, and identify maximum dose?
- **Dose for phase 2 and proof-of-concept**: update with PK data, assess trial design, evaluate combinations, model patient groups, and assess biomarkers
- **Confirmatory and understanding for phase 3**: improve prediction accuracy for new trial design, suggest new patient populations, and justify/confirm optimal results
- **Post Market**: new indications, new combinations, and more convenient dosing regimens

**Challenges across stage**

- Research
- Development
- Post Market

**Decision Gates**

- Targets
- Properties
- Doses, translational strategy, combination, indications

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Mechanistic modeling strategies are applied fit-for-purpose to enhance discovery, translational, and development programs.