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Advanced Pharmacometrics PK/PD Modeling Course Using Phoenix NLME Agenda

DAY 1

Terminology

- Variable
- Dependent variable
- Independent variable
- Parameter
- Model
- Linear and Non-linear model
- Structural model

Population variability
Mixed effects modeling

- Fixed effect parameter
  - Covariate Analysis
- Random effect parameters
  - Between Subject variability
- Between occasion variability
  - Implementation in Phoenix NLME
- Built-in
  - Examples
- Graphical
  - Examples
- Phoenix modeling language (PML)
  - Language through built in and graphical
  - Language through “edit as textual “mode only
  - Dobefore, doafter,while, double
  - Sequence statement
  - while(1), while(condition)
  - If statement
  - Simulate statement
  - Random number generators
- How does the program thinks
  - Program stopping, when, why and implications

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DAY 2

Population Pharmacokinetics and Pharmacodynamics

- Pharmacometric Modeling
  - Maximum likelihood approach
  - Objective function value
  - Optimization procedure
  - Log-likelihood ratio
  - Maximum a posteriori / Posthoc estimates
  - Implementation in Phoenix NLME
- Population Simulation
  - Clinical trial designs
- Special simulation and fitting tools available in pml
  - Steady State and ADDL: New Generic format
  - Simulations
    - ✓ simulate, unif(), norm()
  - Fitting
    - ✓ lpois,lnegbin

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DAY 3

Paper based modeling and Simulation exercises

- Lelanidomide Population PK
  - Normal likelihood
  - Use of "edit as textual" based on built in and graphical template
  - Pk responses
- Population PKPD modeling of eltrombopag in subjects with advanced solid tumors with chemotherapy-induced thrombocytopenia
  - Normal likelihood
  - Transit compartments
  - PK/PD responses
- Population PK/PD of homocysteine in the presence of Methotrexate
  - Normal Likelihood
  - PK/PD/covariate analysis
- Population pharmacokinetics and exposure toxicity analysis of Vatalanib in patients with myelodysplastic syndromes
  - Normal Lilkelihood
  - Standard Population PK analysis
- Volume Kinetics for Infusion Fluids
  - Normal Likelihood
  - Extension of drug mass balance to fluid mass balance
- Population Pharmacokinetic/Pharmacodynamic Model of Clozapine for Characterizing the Relationship Between Accumulated Exposure and PANSS Scores in Patients With Schizophrenia
  - Normal Likelihood
  - PK/PD
  - Use of graphical mode
- Population pharmacokinetic of sorafnebit
  - Normal Likelihood
  - Transit statement
- Target-mediated pharmacokinetic/pharmacodynamic model based meta-analysis and dosing regimen optimization of a long-acting release formulation of exenatide in patients with type 2 diabetes mellitus
  - Normal Likelihood
  - Edit as textual
  - TMDD
- A population pharmacokinetic/pharmacodynamic model of thrombocytopenia characterizing the effect of trastuzumab emtansine (T-DM1) on platelet counts in patients with HER2-positive metastatic breast cancer
  - Normal Likelihood
  - Transit compartments
  - Use of edit as texual mode
- Pharmacometric tools to extrapolate PK from adults to children
  - Normal Likelihood
  - Special PK covariate relationships
  - Use of "edit as tectual

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