Assisting Pharmacometric Simulation with the Use of Shiny

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Acknowledgement

Sponsors

Metrum Team

- Kyle Baron
- John Mondick
- Bill Knebel
- Marc Gastonguay

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Pharmacometrics

Development and application of pharmaco-statistical models of drug efficacy and safety from preclinical and clinical data to improve drug development knowledge management and decision-making [1]

[1] Lalonde RL, et.al, Model-based drug development, Clin Pharmacol Ther, 2007

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Challenges

- Computation for pharmacometric modeling and simulation can be time-consuming

- Communication
  - Clear communication between pharmacometircs and project team

  - Demonstrate impact of the analysis along with key assumptions for stakeholders

  - Rapid decision making based on current state of knowledge

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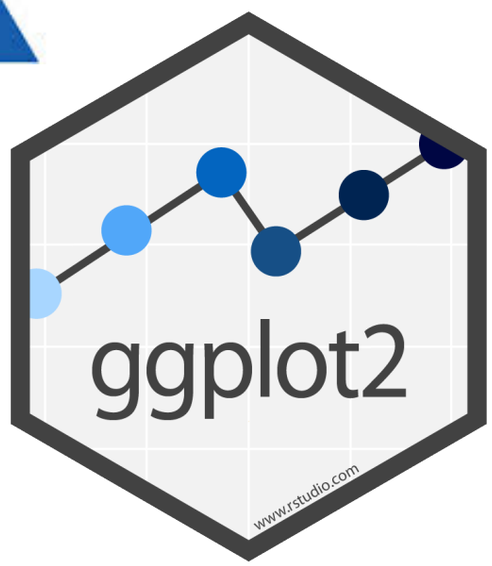

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Shiny

- User-friendly interface
- Interactive presentation
- Real-time computation

Drug XYZ Bioequivalence Trial Simulator | BE Simulation | Simulation Output

Study Design | BE Results | Sensitivity Analysis

Number of study subjects

24

Recruitment of male and female

(•) Random ( ) Fixed

Probability of female [0,1]

0.25

Sampling time points after dosing (hours)

0.5,1,1.5,2,2.083,2.167,2.25,2.33,2.5,2.75,3,3.25,3.5,4,6,10

Formulation effect on

(•) F ( ) Clearance

0.9

Number of trials to be simulated

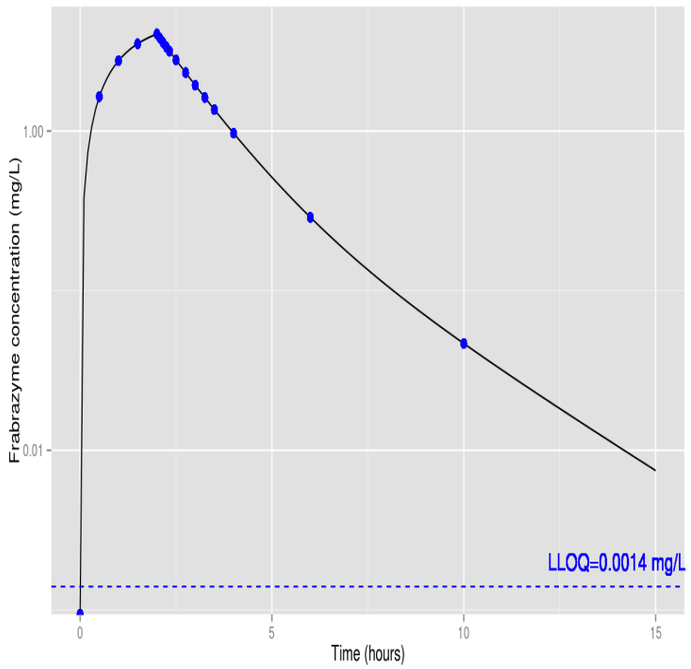
500

Set simulation seed (a positive integer)

1234

Run Simulation

Typical Concentration-Time Profile to assess sampling times



AUC0_last	AUC0_inf	AUClast/AUCinf
11.16	11.26	0.99

Study Design | BE Results | Sensitivity Analysis

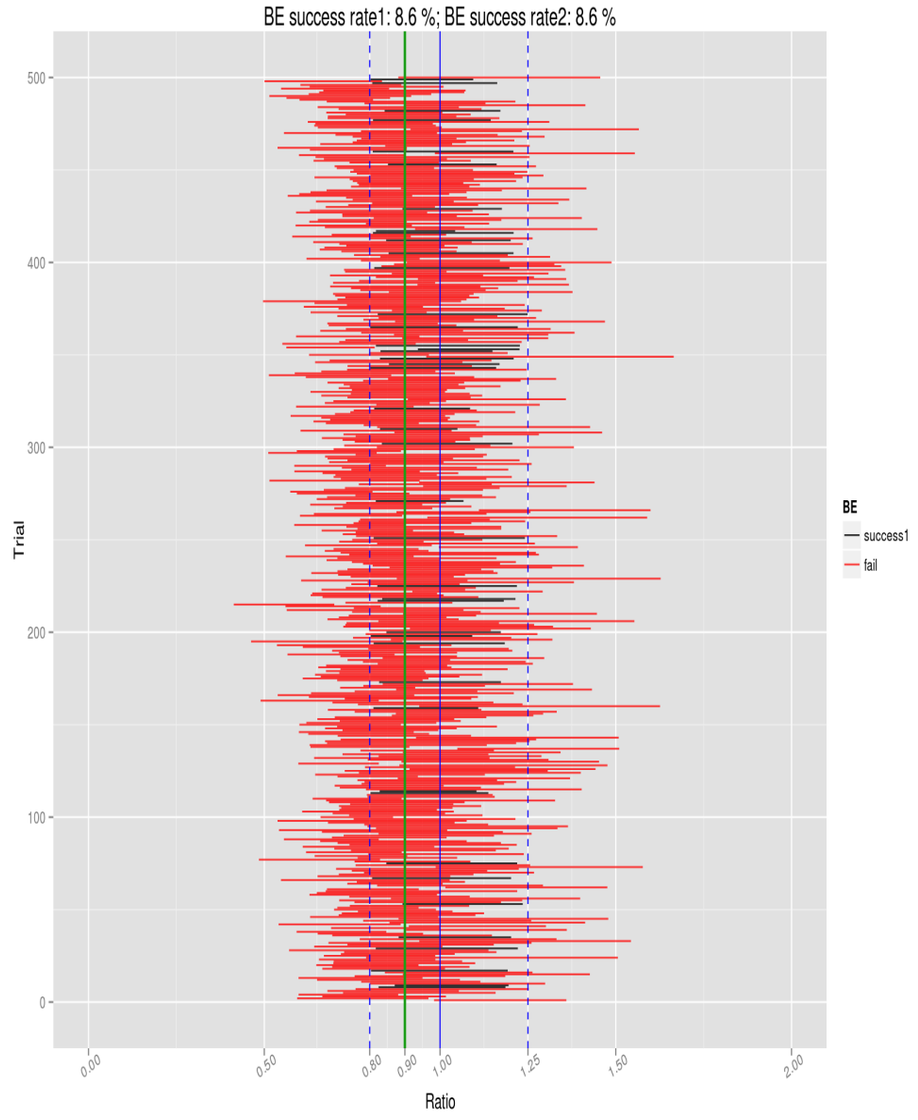
Bioequivalence Criteria

80~125%

Download Study Design and BE results

Success Rate1: percentage of trails where 90% confidence interval of the ratio falls within BE criteria range

Success Rate2: percentage of trials where 90% confidence interval of the ratio falls within BE criteria range AND the point estimate of the ratio falls between 0.8 and 1.25



Each horizontal line represents 90% confidence interval of the estimated ratio of test to reference in AUC; Green solid line: True formulation difference; Blue solid line: reference line; Blue dash line: BE criteria.

Bioequivalence (BE) trial simulation to evaluate the probability of success based on user-defined study deign

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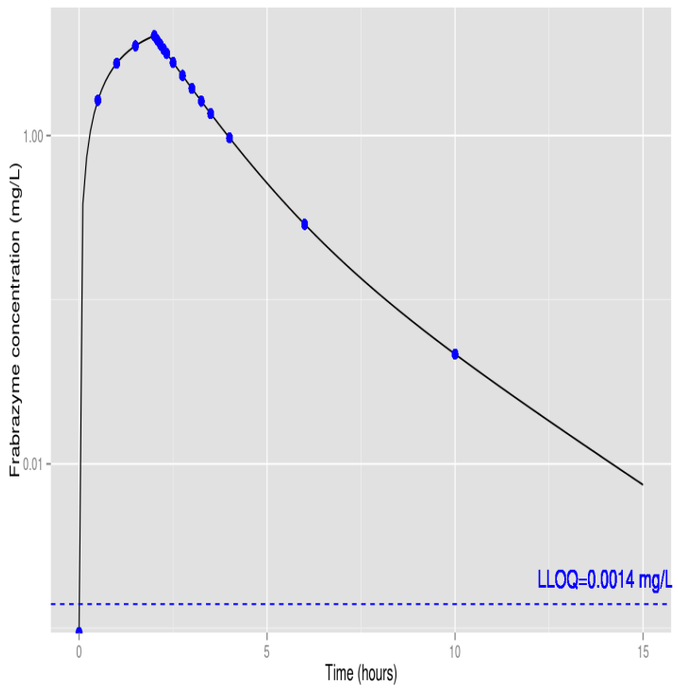

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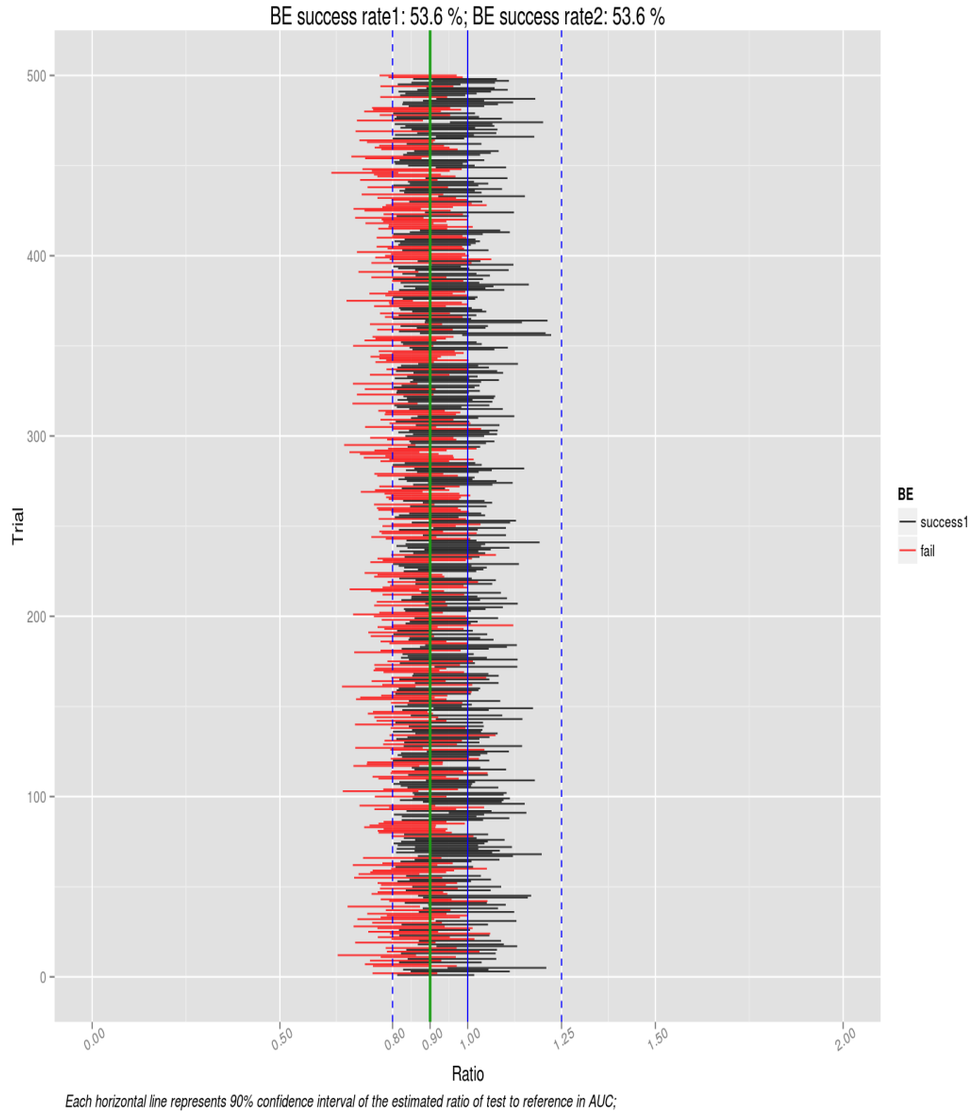

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Drug XYZ simulation to explore the immediate release (IR) formulation and the sustained release (SR) formulation

Dosing Regimen | PK profile | Exposure metrics table | Simulation Output

IR formulation

Dose (mg): 20

SR formulation

Dose (mg): 40

Duration of release (hour): 12

Run Simulation

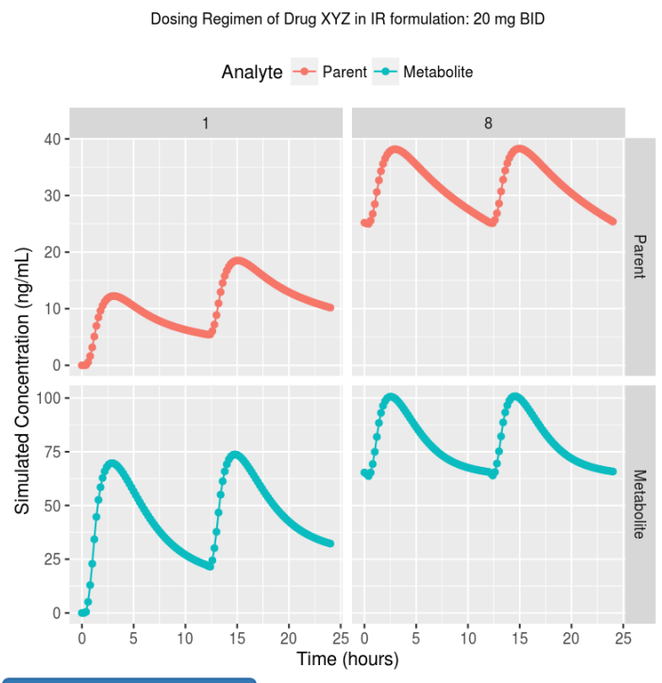
Drug XYZ simulation to explore the immediate release (IR) formulation and the sustained release (SR) formulation

Dosing Regimen | PK profile | Exposure metrics table | Simulation Output

IR formulation

PK profile in days

1 2 3 4 5 6 7 8

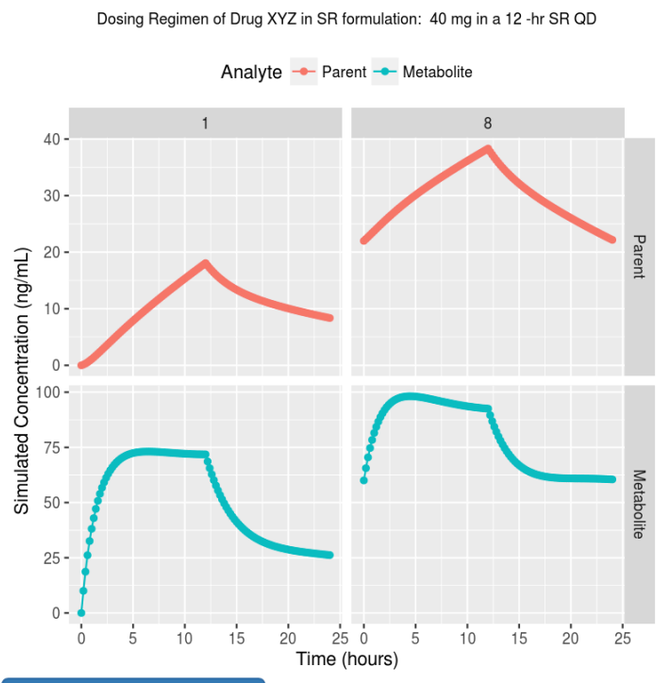


Download IR plot

SR formulation

PK profile in Days

1 2 3 4 5 6 7 8



Download SR plot

Visualize and compare the exposure between sustained release and immediate release formulations

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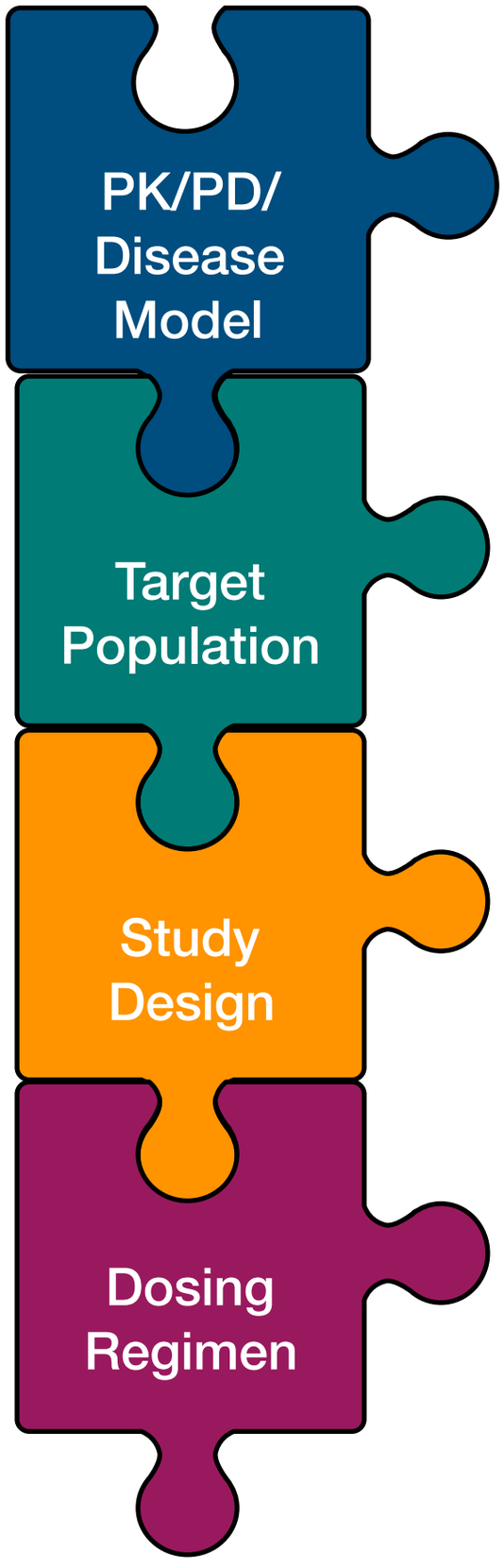

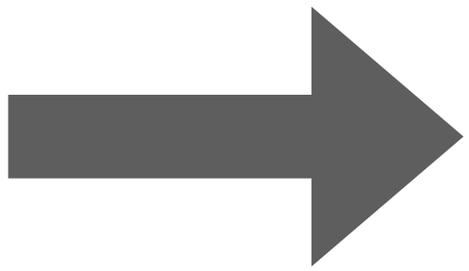

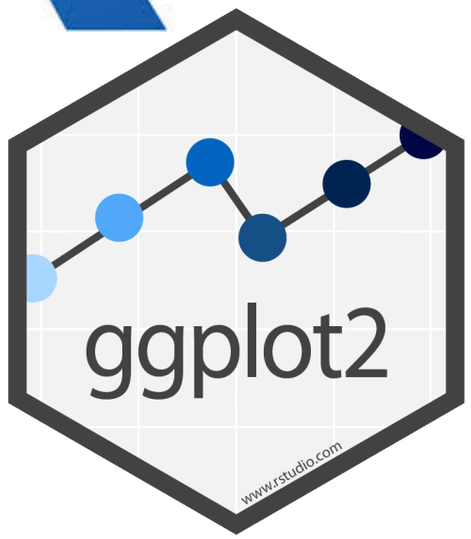

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