NextDose
A clinical pharmacology collaboration tool

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Next Dose -- A Bridge

Population modeling
Clinic

Busulphan
Age 10 Months Weight 8.8 Kg

Day 1
Day 4

Nominal infusion time

Team Effort
• Clinician
• Pharmacist
• Phlebotomist
• Lab Scientist

"I need some help and guidance in the AUC calculations and dose prediction/adjustment calculations for this drug." Hospital Lab Scientist

Note rising concentrations after nominal end of infusion means there must be an error in either dosing history (e.g. longer infusion than 2 hours) or the way that blood samples were obtained (e.g. contamination from catheter used for infusion).
**Pharmacodynamics**

*Children*


**Target Range**

0.6 to 0.9 mg/L; Target Concentration 0.77 mg/L

Corresponds to Target AUC of 1125 umoL⋅min

**Bayesian Dose Adjustment**

- Well established methodology for TCI based dose prediction
  - Sheiner 1977
  - Applied to busulphan paediatric BMT (Bleyzac 2001, Salinger 2010)
- Flexible
  - Not affected by sampling times (provided they are accurate)
  - Loading dose can be different from maintenance dose
- Output
  - Estimate of patient’s clearance (CL) and dose
  - Any dosing interval (e.g. q6h, daily, continuous infusion)

**AUC Dose Adjustment from Busulfex label (PDL 2006)**


Calculations of AUC:

\[
AUC_{\text{Dose Adjustment}} = \frac{\text{TargetConc} \times \text{CL} \times \text{interval}}{\text{Dose}}
\]

For example, if a patient received a dose of 1 mg/bolus and the

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- Collaboration Tool Recognizing Responsibility
  - Clinicians (age, weight, disease)
  - Pharmacists (formulation, dose, time)
  - Phlebotomists (blood sample time)
  - Laboratory (concentration measurement)

- Extensible
  - Medicines
  - Covariates
  - Security

Demonstration

nextdose.org

Questions

- Practical
  - Number and timing of blood samples for busulphan measurement?

- Clinical
  - Intermittent doses or continuous infusion?

- Theoretical
  - Should doses be adjusted to achieve total treatment target AUC target or target AUC/conc after the first dose(s)?