

# PHA 5127 Dose Optimization I

## Case Study III

- 1) 5 mg Dexamethasone were administered to a 40-year old (75 kg) patient through an IV bolus injection. The clearance and volume of distribution of dexamethasone are 3.7 mL/min/kg and 0.82 L/kg, respectively. Assume one-compartment body model and first-order elimination.

Calculate  $k_e$ , half-life ( $t_{1/2}$ ), and  $AUC_{\infty}$

- 2) A new analysis technique has enabled you to measure the drug concentration before and after the blood passes the liver. The plasma concentrations before and after the liver was passed were 6.5 and 2.4 mg/mL, respectively.

Calculate the hepatic clearance (assume a liver blood flow of 1450 mL/min)

- 3) TRUE (T) or FALSE (F)

A change in the clearance will affect the volume of distribution

**T     F**

Clearance and volume of distribution are dependent on each other

**T     F**

If, for a given drug,  $Q_H \gg \gg f_u * CL_{int}$ , the drug is considered to be a high extraction drug

**T     F**

Enzyme induction always affects the hepatic clearance

**T     F**

Plasma protein binding is dependent on liver blood flow

**T     F**

Enzyme induction affects the hepatic clearance of low extraction drug

**T     F**

Drugs with a high volume of distribution are always low extraction drugs

**T     F**

- 4) Define enzyme induction and enzyme inhibition and their potential consequences on pharmacotherapy

- 5) **Assume an intrinsic clearance of i) 40000 L/min and ii) 0.04 L/min. The plasma protein binding and liver blood flow are 60% and 80 L/min, respectively, for both situations.**
- a) Calculate the hepatic clearance for both situations
  - b) Predict the effect of a change in i) plasma protein binding and ii) liver blood flow for both situations.