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Equivalent Constant Concentration Summarizes Pharmacokinetics in HIV and HCV PK/PD Modeling

Abstract

Introduction

• Equivalent Constant Concentration (ECC) is based on equal average exposure but does not require equal drug intake.
• This constant (a fixed subject) is steady-state drug concentration.
• ECC can be incorporated easily.

Methods

• Three steady-state concentrations for each subject is a simulated population was used in a simple linear model to calculate time-varying viral inhibition.

Results

48-Week Simulations: ECC vs. Full PK

Calculation: Two different methods were used to calculate average concentration and average inhibition.

Case

PK and ECC

1. PK/Inhibitor weekly, weekly, month, and monthly:

   - Triamterene: 100 mg/day
   - Enalapril: 1.25 mg/day
   - Metformin: 250 mg/day
   - Statin: 10 mg/day

   Viral load less than 10 IU/mL at 48 weeks.

2. ECC weekly, monthly:

   - Weekly: 500 mg/day
   - Monthly: 1500 mg/day

   Viral load < 10 IU/mL at 48 weeks.

Discussion

• Average viral inhibition and the corresponding concentration, called ECC, simplify integrative antiviral PK/PD modeling. While the tests here used parameter values appropriate for HCV, comparisons of simulated viral load using ECC vs. full PK with HCV parameters show similar agreement (see Requirement 1). In ECC modeling, ECC allows full between the virus and CYP3A4 metabolites, can be used to improve efficacy but by increasing CYP and by increasing the fraction ECC/CAG efficiency of the Emax function, e.g., average inhibition, is less than the function at the expectation, e.g., CAG, PK-enhancing drugs like ritonavir, which flatten as well as boost concentration profiles, as a well as base concentration profiles that are known.

References