Impact of Lopinavir Limit of Quantification (LOQ)-Censored Data Replacement on Population Pharmacokinetic (PK) Plasma and Saliva Modeling in HIV-Infected Children

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Introduction

- Low measured drug concentrations are usually censored on the basis of a limit of quantification (LOQ)
- There is no standard definition of LOQ; typically it is chosen during assay development/validation on the basis of percent coefficients of variation (CV%) that are generally equal to or below 20% [1] and are also below the accepted therapeutic range of drug concentration should one exist
- Censored data present a problem during construction of pharmacokinetic/pharmacodynamic population models by compromising detection of peripheral compartments. Censoring also may confound attempts to quantify adherence or dose optimization.
- Numerous methods have been proposed to replace LOQ-censored drug concentrations. [2]
- We quantified the effect of three common methods plus replacement with random values on a PK model of lopinavir (LPV) in plasma and saliva in HIV-infected children.

Results

- 10/173 (5%) plasma and 44/173 (25%) saliva samples <LOQ (15.6% overall)
- All four methods resulted in similar parameter estimates and predicted vs. observed LPV concentrations in plasma, less so in saliva.
- The population parameter estimates from the Random method were 2.8 x 10³, 3.8 x 10¹, and 5.2 x 10⁵ times as likely as the 0.5, 0 and Omit methods, respectively.
- Since model likelihood is strongly dependent on method of LOQ replacement, LOQ censoring should be abolished in favor of concentration and SD reporting for all concentrations, even 0.

References