Correlates of efavirenz exposure in chilean patients affected with human immunodeficiency virus reveals a novel association with a polymorphism in the constitutive androstane receptor

Cortes, Claudia P.

Siccardi, Marco

Chaikan, Ammara

Owen, Andrew

Zhang, Guijun

Porte, Charles J L La

OBJECTIVE: To explore the effect of demographics and single-nucleotide polymorphisms in cytochrome P450 (CYP) 2B6, 2A6, UDP-glucuronosyltransferase (UGT) 2B7, and the constitutive androstane receptor (CAR) genes on efavirenz pharmacokinetics in a Chilean cohort affected with human immunodeficiency virus. METHODS: Timed plasma samples obtained throughout the dosing interval were analyzed for efavirenz concentrations with liquid chromatography/tandem mass spectrometry. DNA from whole-blood samples was used for genetic analysis. Data were analyzed using a Mann-Whitney statistical test; furthermore, a Pearson or Spearman correlation was used. A multivariate analysis was then conducted using multiple linear regression by best subset analysis. RESULTS: Overall 219 patients were included, 208 patients had measurable efavirenz levels and available genetic samples. The overall median (interquartile range) of efavirenz concentration was 2.6 (2.1-3.7) mcg/mL. In multivariate regression analysis,