ABSTRACT

Data regarding the effect of the *CYP2B6* 18492T→C polymorphism on plasma efavirenz concentrations and 96-week virologic responses in patients coinfected with HIV and tuberculosis (TB) are still unavailable. A total of 139 antiretroviral-naive HIV-infected adults with active TB were prospectively enrolled to receive efavirenz 600 mg-tenofovir 300 mg-lamivudine 300 mg. Eight single nucleotide polymorphisms (SNPs) within *CYP2B6* were genotyped. Seven SNPs, including 64C→T, 499C→G, 516G→T, 785A→G, 1375A→G, 1459C→T, and 21563C→T, were included for *CYP2B6* haplotype determination. The *CYP2B6* 18492T→C polymorphism was studied in 48 patients who carried haplotype *1/*1. At 12 and 24 weeks after antiretroviral therapy, plasma efavirenz concentrations at 12 h after dosing were measured. Plasma HIV RNA was monitored every 12 weeks for 96 weeks. Of 48 patients {body weight [mean ± standard deviation (SD)], 56 ± 10 kg}, 77% received a rifampin-containing anti-TB regimen. No drug resistance-associated mutation was detected at baseline. The frequencies of the wild type (18492TT) and the heterozygous (18492TC) and homozygous (18492CC) mutants of the *CYP2B6* 18492T→C polymorphism were 39%, 42%, and 19%, respectively. At 12 weeks, mean (±SD) efavirenz concentrations of patients who carried the 18492TT, 18492TC, and 18492CC mutants were 2.8 ± 1.6, 1.7 ± 0.9, and 1.4 ± 0.5 mg/liter, respectively ($P = 0.005$). At 24 weeks, the efavirenz concentrations of the corresponding groups were 2.4 ± 0.8, 1.7 ± 0.8, and 1.2 ± 0.4 mg/liter, respectively ($P = 0.003$). A low efavirenz concentration was independently associated with 18492T→C ($\beta = -0.937$, $P = 0.004$) and high body weight ($\beta = -0.032$, $P = 0.046$). At 96 weeks, 19%, 17%, and 28% of patients carrying the 18492TT, 18492TC, and 18492CC mutants, respectively, had plasma HIV RNA levels of >40 copies/ml and developed efavirenz-associated mutations ($P = 0.254$). In summary, the *CYP2B6* 18492T→C polymorphism compromises efavirenz concentrations in patients who carry *CYP2B6* haplotype *1/*1 and are coinfected with HIV and tuberculosis.