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ABSTRACT

Data on the pharmacogenetic markers of *CYP2B6* and biological factors associated with hepatotoxicity in HIV-infected patients receiving an efavirenz-based antiretroviral therapy (ART) regimen are very limited. A total of 134 HIV-infected Thai adults were prospectively enrolled to receive a once-daily regimen of efavirenz 600 mg/tenofovir/lamivudine. Seven single nucleotide polymorphisms (SNPs) within *CYP2B6* were genotyped using real-time PCR. At 12 weeks after ART, plasma efavirenz concentrations at 12 h after dosing were measured. The mean ± standard deviation patient age was 37 ± 8 years, and 77.6% were male. The median (IQR) CD4 count was 43 cells/mm^3 (17–105 cells/mm^3). Eighteen patients (13.4%) had positive anti-HCV and 5 patients (3.7%) had positive HBsAg. The frequencies of heterozygous/homozygous mutants of each SNP were 64C>T (11%), 499C>G (0%), 516G>T (55%), 785A>G (63%), 1375A>G (0%), 1459C>T (3%) and 21563C>T (62%). The three most frequent haplotypes identified included *1/*6 (40.3%), *1/*1 (34.3%) and *6/*6 (8.2%). The median (IQR) plasma efavirenz concentration was 2.3 mg/L (1.4–3.7 mg/L). At 24 weeks, median (IQR) serum ALP was 98 mg/dL (73–133 mg/dL) and direct bilirubin was 0.11 mg/dL (0.10–0.19 mg/dL). The proportion of grade 1 and grade 2 elevated serum ALP was 12.7% and 1.5%, respectively. By multivariate analysis, factors associated with high ALP, total bilirubin and direct bilirubin included *CYP2B6* haplotype *6/*6, high serum ALP at Week 0 and positive anti-HCV (all $P < 0.05$). In summary, HIV-infected patients with the pharmacogenetic marker '*CYP2B6* haplotype *6/*6' may have increased susceptibility to hepatotoxicity with efavirenz-based ART.