516 Tenofovir DF 150 mg Once Daily in HIV-Infected Adults With Moderate Renal Impairment

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Background: Renal impairment significantly alters tenofovir pharmacokinetics. The recommended tenofovir disoproxil fumarate (TDF) dose is 300 mg every 48 hours for adults with moderate renal function impairment (creatinine clearance 30-49 mL/min). New dosage strengths and formations of TDF may permit once daily dosing for these patients. We compared the pharmacokinetics of TDF 300 mg every 48 hours with 150 mg once daily in HIV-infected adults with moderate renal function impairment receiving lopinavir/ritonavir (LPV/r)-based antiretroviral therapy.

Methodology: Phase I, non-randomized, open-label pharmacokinetic study (ClinicalTrials.gov Identifier: NCT01671982). Consenting HIV-positive adults with a confirmed creatinine clearance 30 to <50 mL/min receiving TDF 300 mg every 48 hours as part of LPV/r-based HAART and an HIV-1 RNA viral load (VL) <50 copies/mL were enrolled. HBs-antigen positive adults were excluded. Intensive steady-state 48-hour blood sampling for PK assessment was performed at enrolment; blood samples were collected (pre-dose) and then at 0.5, 1.0, 1.5, 2.0, 4.0, 6.0, 8.0, 12, 24, 36, 48 hours post-dose. Immediately afterwards, the tenofovir dose was changed to 150 mg once daily. Intensive 24-hour blood sampling was repeated 2 weeks later; blood samples were drawn pre-dose, and at 0.5, 1.0, 1.5, 2.0, 4.0, 6.0, 8.0, 12, 24 hours post-dose. Subjects returned to the standard TDF dose after the PK sampling. Tenofovir plasma concentrations were determined using a HPLC assay and tenofovir pharmacokinetic parameters were calculated using noncompartmental analysis.

Results: Twenty HIV-infected adults (40% female) were enrolled. Median (range) age was 53 years (39-82), weight 49.5 kg (37.8-75.1), serum creatinine (SCr) 1.3 mg/dL (0.9-2.1), creatinine clearance (CrCL) 42.0 mL/min (31.7-49.7) and CD4 count 596 cell/mm3 (113-1063). Eighteen subjects had evaluable PK data available. With TDF 300 mg every 48 hours, the TDF AUC0-48h, Cmax and C48h were 9.61 (6.06-18.92) µg.hr/mL, 0.68 (0.44-1.31) µg/L and 0.07 (0.03-0.11), respectively. With TDF 150 mg every 24 hours, the TDF AUC0-24h, Cmax and C24h were 4.80 (2.61-9.29) µg.hr/mL, 0.42 (0.24-0.73) µg/L and 0.10 (0.05-0.20), respectively. The TDF geometric mean ratio (GMR) of AUC0-48h for every 24- versus every 48 hours dosing was 1.00 (90% CI 0.92-1.09). Tenofovir Cmax was significant lower ($p<0.01$) and Clast (i.e. C48h vs. C24h) significantly higher ($p<0.01$) with daily TDF dosing. All subjects remained virologically suppressed and no drug-related adverse events were reported.

Conclusions: Switching TDF 300 mg every 48 hours to 150 mg every 24 hours provided equivalent tenofovir exposure in patients with moderate renal function impairment receiving LPV/r-based antiretroviral therapy.