1390. Pharmacokinetics of Tamsivir, the Active Moiety of the Prodrug Fostemsavir, in Subjects with Hepatic Impairment

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Background. Fostemsavir (FTR) is a prodrug of tamsivir (TMR), a first-in-class attachment inhibitor that binds directly to HIV-1 gp120, preventing initial viral attachment and entry into host CD4+ T cells. TMR is primarily metabolized via hydrolytic and oxidative pathways; impaired hepatic function may alter TMR pharmacokinetics (PK).

Methods. AI438053 (NCT02467335) was an open-label, nonrandomized study in healthy subjects (HS) and subjects with hepatic impairment (HI), defined by Child-Pugh (CP) score: mild (CPA), moderate (CPB), or severe (CPC). HS were matched for CL/F, T1/2, and unbound TMR exposures in patients with mild or moderate HI is not expected to alter the safety profile of FTR. The risk/benefit of higher TMR exposures in severe HI is under evaluation.

Results. Sixteen subjects completed study; 12 (75%) male, mean age 54 years (range = 28–71), mean BI = 24 kg/m² (range = 18.5–28), and mean Clcr = 22 mL/min (range: 17–29) and 121 mL/min (range: 95–162) for renal impaired and healthy subjects, respectively. CAB PK parameters were similar between severe renal impairment and healthy subjects. Based on preliminary PK, CLs mean ratios (90% CI) for AUC(0-¥), Cmax, CPB and CPC were 0.97 (0.835, 1.14), 1.01 (0.865, 1.17), 1.02 (0.868, 1.20), 1.03 (0.881, 1.20) and 0.93 (0.831, 1.04), respectively. Although highly protein bound, the unbound fraction was higher in subjects with severe renal impairment with GLS mean ratio (90% CI) of 1.31 (0.843, 2.03) at 2 hours and 1.51 (1.19, 1.92) at 24 hours post dose. One renal impairment subject developed grade 3 lipase elevation considered drug-related by investigator, otherwise all reported adverse events (AE) were Grade 1 in severity with no serious AEs reported.

Conclusion. Plasma CAB exposures in subjects with severe renal impairment were similar to healthy subjects; therefore, no dose adjustment of CAB is required in renal impairment. Although no data are available, CAB PK is not expected to be affected in subjects undergoing dialysis given CAB’s non-renal clearance and high protein binding (≥99%).
1392. Darunavir and Dolutegravir Combination Therapy in ART experienced HIV-infected Patients: A Preliminary Report
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Background. Patients with HIV may require change in therapy for simplification, salvage, or to avoid side effects. There is limited data on the use of dolutegravir (DTG) and ritonavir- or cobicistat-boosted darunavir (DRV) combination therapy alone or with additional active agents in patients with HIV. The objectives of this study were to describe the current use and indications of DTG/DRV combination and to evaluate its effectiveness on viral load suppression (VLS).

Methods. A retrospective chart review of HIV-infected patients, 18 years or older, seen at our clinic between August 2013 and December 2015 who were on DRV/DTG combination alone or with additional active agents was conducted. Demographic, clinical, and laboratory information was collected. Descriptive statistics were used for data analysis.

Results. Eighty-seven patients were included in the study: 64 (74%) on DRV/DTG alone and 23 (26%) on DRV/DTG plus additional agents. Mean age was 49.3 (18–79); 29 (33.3%) were female; and 77 (89%) were black. Coronary artery disease (CAD) or CAD equivalent was present in 27 (31%), chronic kidney disease in 24 (28%), and chronic hepatitis B infection in 3 (3%) patients. The majority 86 (99%) of patients were treatment experienced; 60 (69%) had been treated with 3 or more antiretroviral drug classes; 57 (66%) were integrase experienced, including 6 (6%) with baseline integrase resistance. Baseline HIV viral load was >200 copies/mL in 41 (47%) and CD4 count was <200 in 29 (33%) patients. Reason for switch was reported as salvage in 42 patients (48%) simplification in 33 patients (38%), renal impairment in 11 patients (13%), and other in 6 patients (7%). VLS was achieved or maintained in 40 of 46 patients (87%) who presented for follow up at 4–8 weeks, 25 of 28 (89%) at 3–4 months, 20 of 25 (80%) at 6–7 months, and 55 of 61 (90%) at 7–12 months after starting therapy. Six patients were later switched off of DRV/DTG to another combination, of whom only two required switch due to intolerance ( rash in 1 and large pill size in 1).

Conclusion. Our preliminary results suggest that darunavir/dolutegravir combination is a viable switch option in HIV patients with the majority of patients achieving or maintaining VLS at 1 year of follow up and only 2 patients required a regimen change due to intolerance.

Disclosures. All authors: No reported disclosures.