Efavirenz-metabolizing polymorphisms, viral suppression, and depression in HIV-infected individuals initiating antiretroviral therapy in southwestern Uganda

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group). Serial PK for plasma CAB concentrations were collected through 168 hours post dose and unbound CAB concentrations determined at 2 and 24 hours post dose. Non-compartmental PK analysis was performed; geometric least squares (GLS) mean ratios and 90% confidence intervals (CI) were generated.

**Results.** Sixteen subjects completed study; 12 (75%) male, mean age 54 years (range: 35–69), mean BMI 28 kg/m² (range: 24–35), and mean CLR 22 ml/min/1.73m² (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, GLS mean ratios (90% CI) of CAB for AUC(0-T) were 1.48 (1.11, 1.92) 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%).

**Disclosures.** R. Parasrampuria; GlaxoSmithKline: Employee and Shareholder, Salary; S. Ford, PAREXEL International: Employee, Salary; Y. Lou, PAREXEL International: Employee, Salary; C. Fu, PAREXEL International: Employee, Salary; K. Basuki, GlaxoSmithKline: Employee and Shareholder, Salary; A. Tenorio, ViViT Healthcare: Employee and Shareholder, Salary; C. Trezza, ViViT Healthcare: Employee and Shareholder, Salary; W. Spreen, ViViT Healthcare: Employee and Shareholder, Salary; P. Patel, ViViT Healthcare: Employee and Shareholder, Salary.

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

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**Background.** Fostemsavir (FTR) is a prodrug of temsavir (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 (HI) and subjects with hepatic impairment (HI), defined by Child-Pugh (CP) score: mild (CPA), moderate (CPB), or severe (CPC). HI Severity was matched for age, body weight, and sex. Subjects received a single oral dose of FTR 600 mg fasted and serial PK samples for TMR were collected up to 96 hours post-dose. Unbound TMR at 1 and 3 hours post-dose was determined. Total and unbound PK parameters were derived by noncompartmental methods. Geometric mean ratios (GMR) and 90% confidence intervals (CI) for HI vs. HS were derived using linear mixed-effects model. Subjects were monitored for adverse events (AE).

**Results.** 18 subjects with HI (N = 6/CP group) and 12 HS received FTR and completed the study. Total and unbound TMR exposures increased with increasing HI severity (see Table). Total and unbound TMR CL/F decreased with increasing HI severity. Mean % protein binding of TMR was 81.0% in HS and 79.9%, 81.9%, and 76.5% in CPA, CPB, and CPC HI, respectively, and was independent of TMR concentration. There were no deaths, serious AEs, or discontinuations during the treatment period.

**Table: TMR PK in HI and HS**

| TMR PK in HI vs HS [GMR(90% CI)] | Cmax | AUICD-T | CPA | 1.03 (1.01–1.05) | 1.18 (1.06–1.31) | CPB | 1.48 (1.10–1.97) | 1.58 (1.08–2.29) | CPC | 1.72 (1.29–2.30) | 1.74 (1.20–2.54) | Unbound TMR | Cmax | AUICD-T | CPA | 1.46 (1.05–2.04) | 1.29 (0.83–2.00) | CPB | 1.42 (1.02–1.87) | 1.53 (0.98–2.34) | CPC | 2.15 (1.15–3.93) | 2.18 (1.41–3.39) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HI Severity | CPA | CPB | CPC | CL/F (L/hours) | 6.18 (3.0) | 5.17 (6.0) | 38.1 (43) | 35.8 (33) | CL/F (L/hours) | 339 (42) | 259 (58) | 218 (54) | 157 (31) |

**Conclusion.** TMR exposures increase with increasing severity of HI. The increase in 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.

**Disclosures.** H. Sevinsky, ViViT Healthcare: Employee; S. Magee, GlaxoSmithKline: Employee and Shareholder, Salary; P. Ackerman, ViViT Healthcare/GSK: Employee and Shareholder, Salary and Stock; R. Adamczyk, Bristol-Myers Squibb: Employee, Salary; J. Karkas, Bristol Myers Squibb: Employee and Shareholder, Salary; S. Lubin, Bristol-Myers Squibb: Employee, Salary; P. Ravindran, Bristol-Myers Squibb: Employee, Salary; C. Jarnos, ViViT Healthcare: Employee, Salary; T. Eley, Bristol-Myers Squibb: Former Employee during study conduct, Salary; K. Moore, ViViT Healthcare: Employee, Salary.
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 (8%) 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 ≥8 weeks; 25 of 28 (89%) at 3–4 months, 34 of 54 (63%) at 6–8 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.

1395. Patient Experience and Views on Antiretroviral Treatment—Findings from the Positive Perspectives Survey
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Background. While advances in treatment have dramatically improved the life-expectancy of people living with HIV (PLHIV), a number of unmet needs remain. We conducted an international survey of PLHIV to explore their level of satisfaction with current treatment and potential areas of improvement for ARVs.

Methods. Qualitative in-depth interviews were performed with PLHIV to identify key hypotheses. A steering group developed the survey questions which was fielded online from November 2016 to April 2017 in 17 countries across Europe, Africa, and Australia. A mixed sampling/recruitment approach was used to ensure a broad cross-section of PLHIV. Respondents were screened for eligibility prior to receiving access to the online survey.

Results. Overall 1085 PLHIV completed the survey with 40% of respondents from North America. The demographic breakdown was 25% women, 34% ≥50 years, 49% diagnosed >10 years ago, 76 % with co-morbidities. 40% had a college degree or higher, 33% were in full-time employment and 62% lived in a large city. Majority 86 (99%) of patients were integrase experienced, including 6 (6.9%) with baseline integrase resistance. The majority 86 (99%) of patients were treatment experienced and 60 (69%) had been treated with >3 antiretroviral drug classes. 57 (66%) were integrase experienced, including 6 (8%) 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 ≥8 weeks; 25 of 28 (89%) at 3–4 months, 34 of 54 (63%) at 6–8 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 switching 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.

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 therapy 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 (8%) 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 ≥8 weeks; 25 of 28 (89%) at 3–4 months, 34 of 54 (63%) at 6–8 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 switching 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.

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