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/m^2 (range: 24–35), and mean CLcr 22 mL/minute (range: 17–29) and 121 mL/minute (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) for AUC(0-¥), Cmax, C24, CL/F, and t1/2 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 plasma 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. Bakshi**, GlaxoSmithKline: Employee and Shareholder, Salary; **A. Tenorio**, ViiV Healthcare: Employee and Shareholder, Salary; **C. Trezza**, ViiV Healthcare: Employee and Shareholder, Salary; **W. Spreen**, ViiV Healthcare: Employee and Shareholder, Salary; **P. Patel**, ViiV Healthcare: Employee and Shareholder, Salary

1390. Pharmacokinetics of Temsavir, 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 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 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 models. Subjects were monitored for adverse events (AEs).

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 CLT/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)]				
Total TMR	Cmax		AUC(0-T)	
CPA	1.34 (1.00–1.79)		1.18 (0.81–1.72)	
CPB	1.48 (1.11–1.97)		1.58 (1.08–2.29)	
CPC	1.72 (1.29–2.30)		1.74 (1.20–2.54)	
Unbound TMR	Cmaxu		AUC(0-T)u	
CPA	1.46 (1.05–2.04)		1.29 (0.83–2.00)	
CPB	1.42 (1.02–1.97)		1.51 (0.98–2.34)	
CPC	2.15 (1.55–3.00)		2.18 (1.41–3.39)	
TMR CLT/F in HS and HI [geometric mean (%CV)]				
HI Severity	HS	CPA	CPB	CPC
CLT/F (L/hours)	61.8 (30)	51.7 (60)	38.1 (43)	35.8 (33)
CLT/Fu (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**, ViiV Healthcare: Employee, Salary; **M. Magee**, GlaxoSmithKline: Employee and Shareholder, Salary; **P. Ackerman**, ViiV 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. Llamoso**, ViiV Healthcare: Employee, Salary; **T. Eley**, Bristol-Myers Squibb: Former Employee during study conduct, Salary; **K. Moore**, ViiV Healthcare: Employee, Salary

1391. Efavirenz-metabolizing polymorphisms, viral suppression, and depression in HIV-infected individuals initiating antiretroviral therapy in southwestern Uganda

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Background. Single-nucleotide polymorphisms (SNPs) in *CYP2B6* have previously been associated with a 10-fold range in trough plasma efavirenz concentrations, but associations between these SNPs and efavirenz (EFV)-mediated viral suppression and tolerability remain unclear.

Methods. We evaluated three SNPs in *CYP2B6* (rs3745274, rs28399499, and rs4803419, Illumina OmniExpress) among HIV-infected Ugandans observed in a cohort study every 3–4 months from 2005–2015. Genotypes from these SNPs were used to group participants into previously described pharmacokinetic strata: extensive (EXT), intermediate (INT), and slow metabolizers (Figure 1). The primary outcomes were viral suppression, defined by an undetectable viral load in the first measurement a minimum of three months after ART initiation, and incident depression in the first two years, defined by a mean score >1.75 on the Hopkins Symptom Checklist. We fitted standard and generalized estimating equations (GEE) logistic regression models for viral suppression and depression, respectively. Models were adjusted for clinical and demographic covariates that reached a significance of $P <$ 0.25 in unadjusted models.

Results. Among 103 participants with genotyping, there were no differences in pre-ART viral load or depression by metabolism strata ($P > 0.5$). Minor allele frequencies for rs3745274, rs28399499, and rs4803419 were 33%, 7%, and 4%, respectively. Approximately 79%, 78%, and 94% of participants were suppressed at their first viral load measurement in the extensive, intermediate, and slow metabolizer strata, respectively (Figure 2; $P = 0.35$). In adjusted models, metabolism strata were not associated with viral suppression (AOR_{INT} 0.81, 95% CI 0.26–2.56; AOR_{SLOW} 3.92, 95% CI 0.39–39.40) or with depression (AOR_{INT} 1.95, 95% CI 0.75–5.09; AOR_{SLOW} 0.72, 95% CI 0.17–3.02; Table).

Conclusion. We did not identify an association between efavirenz-metabolizing polymorphisms and viral suppression or depression in a cohort of HIV-infected individuals initiating ART in southwestern Uganda. Future work should reassess these relationships with larger samples and longer-term outcomes and explore additional polymorphisms that may be associated with efavirenz metabolism in this population.

Figure 1.

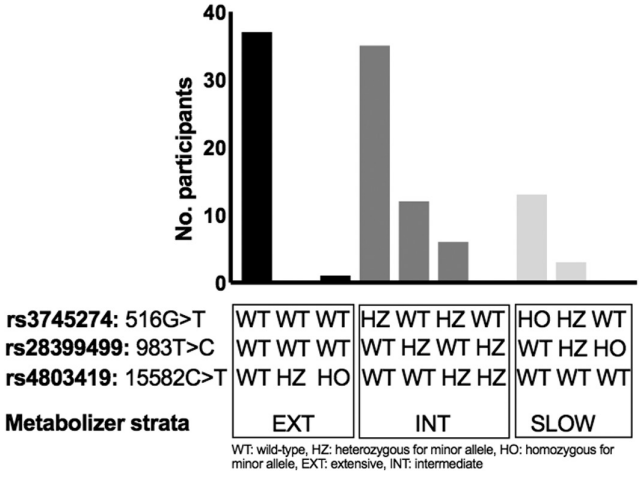

Figure 2.

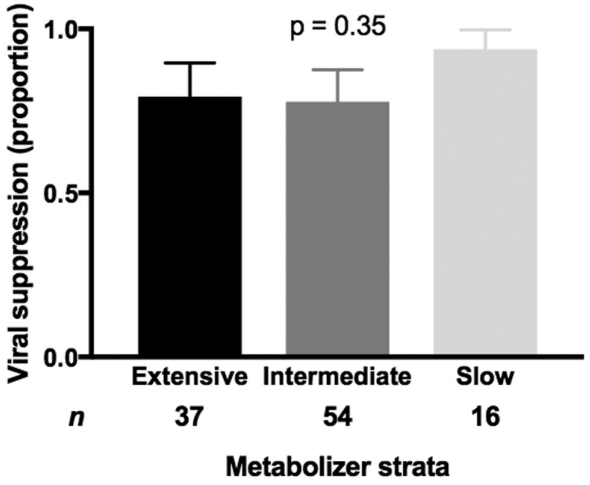

Table. Generalized estimating equations logistic regression models for depression

Variable	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Demographics				
Age				
≤ 30	REF	--		
31-40	1.47 (0.52-4.14)	0.47		
41-50	1.25 (0.37-4.23)	0.72		
> 50	1.87 (0.47-7.40)	0.37		
Female	1.73 (0.70-4.28)	0.23	0.75 (0.31-1.83)	0.52
Married	1.12 (0.52-2.42)	0.77		
Secondary education	0.63 (0.24-1.64)	0.34		
Asset index				
1st quint.	REF	--		
2nd quint.	1.06 (0.38-2.93)	0.43		
3rd quint.	0.60 (0.18-2.01)	0.41		
4th quint.	0.93 (0.31-2.81)	0.90		
5th quint.	0.71 (0.23-2.20)	0.55		
Year of enrollment				
2005-07	REF	--	REF	--
2008-10	2.09 (0.69-6.31)	0.19	1.91 (0.71-5.17)	0.20
2011-13	1.14 (0.43-2.99)	0.80	4.74 (1.83-12.27)	0.001
Clinical measures				
CD4+ count	1.03 (0.87-1.22)	0.75		
Viral load suppressed	0.59 (0.32-1.08)	0.088	0.59 (0.28-1.24)	0.17
ART duration	0.99 (0.99-1.00)	0.24	1.00 (0.99-1.01)	0.80
TB co-infection	1.57 (0.56-4.39)	0.39		
Baseline depression	8.47 (3.24-22.11)	< 0.001	7.99 (3.28-19.44)	< 0.001
Baseline suicidal ideation	3.28 (1.18-9.14)	0.023	1.86 (0.65-5.34)	0.25
Psychosocial measures				
Physical health summary score				
1st quart.	REF	--	REF	--
2nd quart.	0.23 (0.11-0.51)	< 0.001	0.22 (0.08-0.59)	0.003
3rd quart.	0.18 (0.07-0.44)	< 0.001	0.20 (0.07-0.55)	0.002
4th quart.	0.07 (0.01-0.33)	< 0.001	0.11 (0.03-0.42)	0.001
Heavy drinking	0.29 (0.04-2.18)	0.23	0.29 (0.04-2.32)	0.24
Metabolism strata				
Extensive	**REF**	**--**	**REF**	**--**
Intermediate	**2.58 (0.93-7.18)**	**0.069**	**1.95 (0.75-5.09)**	**0.17**
Slow	**0.93 (0.19-4.51)**	**0.98**	**0.72 (0.17-3.02)**	**0.65**

Notes: Asset index was calculated with the method described by Filmer and Pritchett. The Physical Health Summary score was taken from the MOS-HIV. Heavy drinking was based on the 3-item heavy consumption subset of the AUDIT-C screen. Viral load suppression was defined by an undetectable viral load; limit of detection ranged from 400 to 40 copies/mL as the study progressed.

Disclosures. **P. Hunt**, Merck: Consultant, Consulting fee; Gilead: Consultant, Consulting fee; Viiv: Consultant, Consulting fee

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 darunvair (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 (6.9%) 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 6–8 weeks, 25 of 28 (89%) at 3–4 months, 35 of 41 (85%) at 5–6 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.

1393. 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 9 countries across North America, Europe 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 (98%) were currently taking ARVs with 53% taking a Single Tablet Regimen (STR). 87% of those diagnosed within last 2 years had started treatment within 6 months of diagnosis, compared with 40% of those diagnosed > 10 years ago. Of those on treatment, 87% were satisfied with their current ARV regimen. 33% had changed treatment in the last 12 months with the main reasons for switching being reducing severity or frequency of side effects (43%) and reducing the pill burden (31%). 73% of those on treatment were worried about the long-term effects of ARVs. Reducing these long-term effects (25%) and the potential availability of longer lasting treatments (21%) were identified as the 2 most important potential improvements to current regimens. 62% were open to changing to an ARV regimen with fewer drugs as long as their HIV remained suppressed. Demographics and results for the North American cohort were generally similar to the overall global results.

Conclusion. In this international survey, the majority of PLHIV were satisfied with their current regimen, with reducing long-term adverse effects of ARVs and a longer lasting treatment identified as the most important potential improvements.

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