POSTER #1517

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Variability in Population Characteristics Among HIV+ ART-Naïve Patients Initiating on Single Tablet Regimens

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BACKGROUND

- Numerous analyses have suggested that patients initiating antiretroviral therapy (ART) on a single tablet regimen (STR) are more adherent, more likely to achieve viral suppression and less likely to be hospitalized.[1-3]
- The number of STR's available has increased notably since 2011.[4,5] A recent study found that three-quarters of all treatment-naïve patients are now initiating on an STR but few studies have assessed the characteristics of naïve patients initiating STR by formulation.[2]

OBJECTIVE:

To evaluate the demographic and clinical characteristics of patients initiating four widely used STRs: efavirenz (EFV)/emtricitabine (FTC)/ tenofovir (TDF); rilpivirine (RPV)/ FTC/ TDF; elvitegravir (EVG)/ cobicistat (c)/ FTC/TDF; and dolutegravir (DTG)/ abacavir (ABC)/ lamivudine (3TC).

METHODS

- The Observational Pharmaco-Epidemiology Research & Analysis (OPERA) database comprises electronic health records from 79 US community-based outpatient HIV or multispecialty clinics in 15 states. The data represent ~70,000 HIV-positive patients (i.e. 7% of the HIV+ patients linked to care in the US). OPERA is the largest US HIV database with data refreshed daily.
- Data from HIV+, ART-naïve adolescent and adults was extracted provided they had baseline labs (HIV-1 RNA viral load (VL), CD4) ≤ 90 days prior to initiating an STR (index) during the case selection window (1/1/2007 to 3/31/2015) and ≥ 1 visit in the 12 months pre-index. Patients with HIV-2, <3 ART agents, or VL≤1,000 copies/ML were excluded.
- Patients were followed from index to the first of the following censoring criteria: regimen change, death, loss to follow-up, or study end (3/31/2016).
- Demographic and clinical characteristics were compared between STR formulations using Pearson Chi-square and Wilcoxon Rank-sum tests.
- Sensitivity analysis was performed to assess the sensitivity of observed differences to time frame using a subset of patients who initiated therapy from 1/1/2012-5/31/2015 when at least 3 STR were available (data not shown).

RESULTS

A total of 5,542 naive patients met study eligibility

- 2,613 patients (47%) initiated with EFV/FTC/TDF; 1,587 (29%) with EVG/ c/ FTC/TDF; 1,139 (21%) with RPV/ FTC/ TDF; and 203 (4%) with DTG/ABC/3TC
- 34% initiated ART when there were ≤2 STR on the market while 66% of the sample initiated ART when there were between 3 and 4 STR's available
- Median (IQR) follow-up varied from a low of 13.8 (12.4, 15.5) in patients initiating on DTG/ABC/3TC, the last STR introduced (2013) to a high of 20.7 (9.3, 41.8) in patients initiating on EFV/FTC/TDF, the first STR introduced (2007). While differences in follow-up were statistically significant, they were also confounded by disparities in the STR launch dates
- Most patients were male (88%), 26-49 years old (65%), from the southern and western US (86%), and Ryan White/ADAP (51%) and/or commercially insured (29%). Thirty-nine percent were African American and 26% were Hispanic. The risk of infection for 61% of patients was MSM. There were significant differences in demographics, risk of infection and payer type by formulation (Table 1).
- Baseline VL and CD4 differed significantly by formulation. Patients initiating DTG/ABC/3TC were more likely to initiate with CD4 count ≤50 cells/μL while patients initiating RPV/FTC/TDF were more likely to present early and least likely to initiate with VL ≥100,000 copies/mL. (Figures 1,2) Patients initiating with EFV/FTC/TDF were more likely to have experienced an AIDS defining event at baseline.

Table 1: Selected Patient Characteristics at Baseline

	Initiated ART with…..				
Baseline Characteristic	**EFV/FTC/TDF N= 2613**	**RPV/FTC/TDF N= 1139**	**EVG/c/FTC/TDF N= 1587**	**DTG/ABC/3TC N= 203**	**P-value**
Male	2354 (90.1%)	931 (81.8%)	1409 (88.8%)	181 (89.2%)	**<0.0001**
Age, Median (IQR)	34.4 (27.1, 43.4)	30.8 (25.3, 41.1)	32.0 (25.5, 42.4)	31.4 (25.5, 41.7)	**<0.0001**
13-25 Years Old	547 (20.9%)	321 (28.2%)	438 (27.6%)	62 (30.5%)	
26-49 Years Old	1794 (68.7%)	713 (62.6%)	983 (61.9%)	117 (57.6%)	
50+ Years Old	272 (10.4%)	105 (9.2%)	166 (10.5%)	24 (11.8%)	**<0.0001**
Race, African American	864 (33.1%)	549 (48.2%)	676 (42.6%)	79 (38.9%)	**<0.0001**
Ethnicity, Hispanic	678 (25.9%)	290 (25.5%)	430 (27.1%)	63 (31.0%)	0.3299
Risk of Infection, MSM	1704 (65.2%)	638 (56.0%)	935 (58.9%)	99 (48.8%)	**<0.0001**
Geographic Region					**<0.0001**
South	1127 (43.4%)	528 (46.4%)	917 (57.9%)	91 (44.8%)	
West	1294 (49.7%)	311 (27.4%)	441 (27.9%)	70 (34.5%)	
Other US Census	184 (7.0%)	298 (26.2%)	225 (14.2%)	42 (20.7%)	
Payer Type*					
ADAP/Ryan White	1393 (53.3%)	558 (49.0%)	774 (48.8%)	100 (49.3%)	**0.0127**
Commercial	671 (25.7%)	336 (29.5%)	523 (34.5%)	70 (34.5%)	**<0.0001**
Medicaid	295 (11.3%)	132 (11.6%)	178 (11.2%)	39 (19.2%)	**0.0077**
Medicare	80 (3.1%)	36 (3.2%)	44 (2.8%)	4 (2.0%)	0.8191
None	386 (14.8%)	163 (14.3%)	189 (11.9%)	8 (3.9%)	**<0.0001**

*Represents the payer of record nearest ART initiation. Patients may have multiple payers, totals may exceed 100%

EFV/FTC/TDF=efavirenz/ emtricitabine/tenofovir disoproxil fumarate; RPV/ FTC/ TDF= rilpivirine/emtricitabine/ tenofovir disoproxil fumarate; EVG/ c/ FTC/TDF=elvitegravir/, cobicistat/emtricitabine/tenofovir disoproxil fumarate; DTG/ABC/3TC= dolutegravir/abacavir/ lamivudine; IQR=interquartile range; MSM=men who have sex with men

Figure 1. Distribution of Baseline VL by Formulation

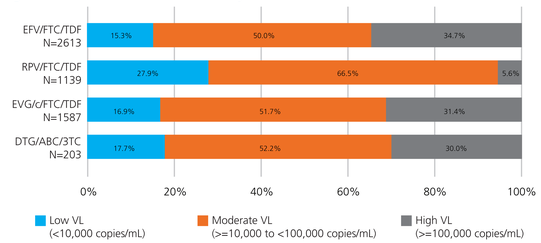


Figure 2. Distribution of Baseline CD4 by Formulation

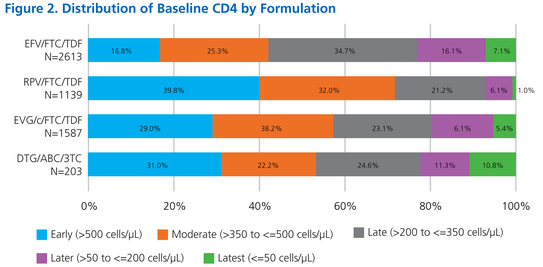
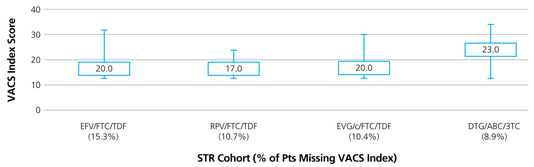


Figure 3. Median (IQR) VACS Index Score, by Formulation



The Veterans Aging Cohort Study (VACS) Index sums pre-assigned points for age, CD4 count, HIV-1 RNA levels, and indices of organ system dysfunction and HIV/HCV co-infection. It was developed in veterans and has been validated in other patient populations, including HIV. It predicts all-cause mortality, cause-specific mortality, and other outcomes.[7]

- Despite the generally young age of the sample, 42.6% of initiators had at least one documented comorbidity. The most frequent comorbidities documented were substance abuse (13.3%), mental health disorders (12.1%) hyperlipidemia (9.5%), liver disease (7.6%), diabetes (2.9%), cardiovascular disease (2.1%) and cancer (1.3%). Twenty-six percent of the study sample had a history of syphilis.
- Patients initiating on EFV/FTC/TDF had significantly higher rates of comorbidity overall as well as of cancer, hyperlipidemia, liver disease and substance abuse specifically. (Table 2)
- Median (IQR) pill burden for both HIV and non-HIV specific medications was 2.0 (1.0, 3.0). The median (IQR) number of non-HIV drug classes patients were taking at index was 1.0 (0.0, 2.0).
- Based on baseline clinical characteristics, median (IQR) VACS mortality index was highest among DTG/ABC/3TC initiators at 23(13, 35) and lowest among patients initiating RPV/FTC/TDF at 17 (13, 23) patients. The impact of a 5-point change in the VACS index on 5-year mortality has been estimated at 30%.6 Higher VACS score in the DTG/ABC/3TC group may be due to the higher proportion of patients ≥50 years old, and those with CD4 counts ≤50 cells/mm3 at the time of initiation. (Figure 3)

Table 2: Selected Baseline Comorbidities

	Initiated ART with…..				
Baseline Comorbidities	**EFV/FTC/TDF N= 2613**	**RPV/FTC/TDF N= 1139**	**EVG/c/FTC/TDF N= 1587**	**DTG/ABC/3TC N= 203**	**P-value**
Any Comorbidity	1,176 (45.0%)	491 (43.1%)	626 (39.4%)	68 (33.5%)	**0.0002**
Invasive Cancer	51 (2.0%)	7 (0.6%)	14 (0.9%)	1 (0.5%)	**0.0015**
Mental Health Disorders	320 (12.2%)	144 (12.6%)	185 (11.7%)	22 (10.8%)	0.81
Anxiety Disorders	145 (5.5%)	70 (6.1%)	117 (7.4%)	13 (6.4%)	0.1301
Bipolar or Manic Disorders	49 (1.9%)	40 (3.5%)	40 (2.5%)	5 (2.5%)	**0.0288**
Major Depressive Disorder	143 (5.5%)	44 (3.9%)	45 (2.8%)	4 (2.0%)	**0.0001**
Schizophrenic Disorder	10 (0.4%)	5 (0.4%)	12 (0.8%)	0	0.3368
Dementia	0	1 (0.1%)	1 (0.1%)	1 (0.5%)	**0.0392**
Hyperlipidermia	257 (9.8%)	110 (9.7%)	154 (9.7%)	7 (3.4%)	**0.0284**
Liver Diseases	249 (9.5%)	70 (6.1%)	97 (6.1%)	7 (3.4%)	**<.0001**
Viral Hepatitis B	95 (3.6%)	28 (2.5%)	31 (2.0%)	1 (0.5%)	**0.0012**
Viral Hepatitis C	148 (5.7%)	39 (3.4%)	63 (4.0%)	5 (2.5%)	**0.0035**
Substance Abuse	383 (14.7%)	147 (12.9%)	183 (11.5%)	25 (12.3%)	**0.0321**
Non-HIV Pill Burden (median, IQR)	1.0 (0.0, 2.0)	0.1 (0.0, 2.0)	0.4 (0.0, 2.0)	1.0 (0.0, 2.0)	**<0.0001**

- While many of the differences observed between the cohorts remained after restricting the study population to patients who initiated an STR from 2012 to 2015, there were notable exceptions; specifically, differences in age, ethnicity and select comorbidities no longer reached levels of statistical significance or, if still significant, suggested a different finding (data not shown).

DISCUSSION

- Patients receiving DTG/ABC/3TC were more likely to be aged 50 or older, to have CD4 count ≤50 cells/μL and a significantly higher VACS scores at the time of HIV treatment initiation. They were not otherwise more notably comorbid.
- Patients receiving EFV/FTC/TDF were more likely to have VL≥100,000 copies/mL, to have had an ADE prior to initiation and to be otherwise more comorbid, most notably to have a history of cancer, hyperlipidemia, liver disease and substance abuse prior to initiation.
- Patients receiving RPV/ FTC/ TDF were more likely to present early and least likely to initiate with VL≥100,000 copies/mL. They were also more likely to be female and African American.
- Patients receiving EVG/ c/ FTC/TDF were otherwise unremarkable in terms of their demographic and clinical characteristics as compared to the other STR initiators.
- These therapy-specific characteristics were observed to change when the population was limited to recent years as a result of changing treatment guidelines and evolution of the epidemic.

KEY FINDINGS:

- There were significant differences among STR initiators in demographics, route of infection, length of follow-up and baseline VL, CD4, VACS Index, non-HIV pill burden, and comorbidity. If prognostic factors are channeling patients into specific therapies, selection bias may confound outcome evaluation and require the use of advanced statistical methods
- Differences were sensitive to study time frame. This may suggest that any existing selection bias is evolving as new STR agents are introduced.

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