Initial Regimen Duration in Female Patients Taking Integrase Strand Transfer Inhibitors (INSTIs) in the OPERA Observational Database

Felix Carpio[1], Cassidy Henegar[2], Jennifer Fusco[2], Evelyn Byrd Quinlivan[3], Vani Vannappagari[4], Michael Aboud[5], Kimberly Smith[4], Gregory Fusco[2]

[1]AltaMed Health Care Service, Los Angeles, CA; [2]Epividian, Inc., Durham, NC; [3]AIDS Healthcare Foundation, Atlanta, GA;
[4]ViiV Healthcare, Inc., Research Triangle Park, NC; [5]ViiV Healthcare, Inc., Brentford, Middlesex, UK

BACKGROUND

- Women experience unique complexities with antiretroviral therapy (ART).[1,2] These circumstances may interfere with chosen treatment strategies, as well as short- and long-term adherence.
- INSTIs are potent, generally well-tolerated, and may offer improved dosing frequency and pill burden for patients with complex circumstances, including women.[3]
- Differences in treatment effectiveness and durability between drugs in the INSTI ART class, which include dolutegravir (DTG), raltegravir (RAL), and elvitegravir (EVG), have not been evaluated specifically among female HIV+ patients.

OBJECTIVE:

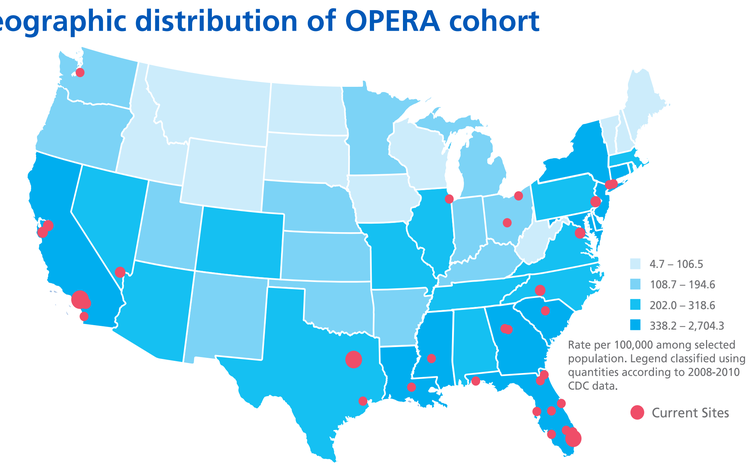
To describe and compare twelve-month regimen durability among HIV-infected women initiating DTG, RAL, or EVG.

METHODS

Study Population

- Selected from the OPERA database, which includes electronic health record data from patients in care at 79 clinics in 15 US states (Figure 1).

Figure 1. Geographic distribution of OPERA cohort



- HIV+ women initiating their first INSTI-containing regimen after first active visit in the OPERA database and between August 12, 2013 (DTG approval) and November 30, 2015
- Viral load required within 120 days prior to INSTI start date.

Study Design and Analysis

- Each patient was observed from INSTI start date until discontinuation of the initial INSTI, loss to follow-up, death, or study end (November 30, 2016), whichever date came first.
- Kaplan-Meier methods and multivariable Cox proportional hazard models were used to estimate the association between specific INSTI exposure and discontinuation within the first 12 months of taking the drug.
- All analyses were conducted separately for treatment-naïve and treatment-experienced women at the INSTI start date.

RESULTS

- Of the 11,817 HIV+ women in the OPERA database at data freeze, 537 treatment-naïve and 878 treatment-experienced women initiated an INSTI-based regimen within the study period.

Table 1. Baseline demographic and clinical characteristics by INSTI for treatment-naïve HIV+ women

	Treatment-Naive				
Characteristic n(%) or median(IQR)	**DTG n=208**	**RAL n=69**	**p-value DTG vs. RAL**	**EVG n=260**	**p-value DTG vs. EVG**
Age (years)	40 (31, 49)	44 (38, 51)	**0.03**	39 (30, 47)	0.27
African American	133 (63.9)	45 (65.2)	0.85	185 (71.2)	0.30
Log10 Viral Load	4.8 (4.3, 5.2)	4.5 (3.7, 5.2)	**0.03**	4.6 (3.9, 5.1)	**<0.01**
CD4 cells/ µL	240 (53, 434)	226 (81, 408)	0.85	292 (96, 467)	**0.03**
Comorbid condition[1]	120 (57.7)	41 (59.4)	0.80	122 (46.9)	**0.02**
Hx substance abuse	28 (13.5)	8 (11.6)	0.69	32 (12.3)	0.72

[1] Diagnoses of an autoimmune disease, cardiovascular disease, invasive cancer, endocrine disorder, mental health condition, liver disease, bone disorder, peripheral neuropathy, renal disease, or hypertension.

Table 2. Baseline demographic and clinical characteristics by INSTI for treatment-experienced HIV+ women

	Treatment-Experienced				
Characteristic n(%) or median(IQR)	**DTG n=504**	**RAL n=116**	**p-value DTG vs. RAL**	**EVG n=258**	**p-value DTG vs. EVG**
Age (years)	48 (38, 54)	49 (42, 56)	0.49	43 (34, 41)	**<0.01**
African American	342 (67.9)	60 (51.7)	**<0.01**	169 (65.5)	0.51
Log10 Viral Load	1.5 (1.3, 3.9)	1.7 (1.3, 4.1)	0.33	1.5 (1.3, 3.7)	0.88
CD4 cells/ µL	532 (261, 803)	469 (216, 749)	0.24	576 (290, 823)	0.30
Comorbid condition[1]	428 (84.9)	90 (77.6)	0.06	186 (72.1)	**<0.01**
Hx substance abuse	86 (17.1)	10 (8.6)	**0.02**	44 (17.1)	0.99

[1] Diagnoses of an autoimmune disease, cardiovascular disease, invasive cancer, endocrine disorder, mental health condition, liver disease, bone disorder, peripheral neuropathy, renal disease, or hypertension.

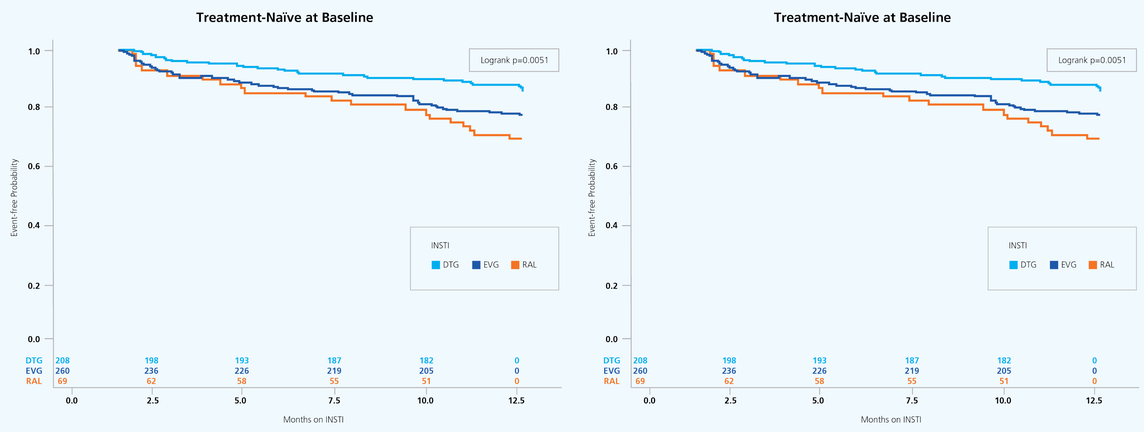
- By the time they initiated an INSTI, treatment-experienced women starting DTG had been on ART longer (median 38 months) than patients starting RAL (22 months; p<0.01) or EVG (26 months; p<0.01).
- Multivariable Cox regression (Table 3) and Kaplan-Meier estimates (Figure 2) indicate longer times to discontinuation within the first year of exposure for women taking DTG compared to women taking RAL or EVG.

Table 3. Multivariable estimates of time to discontinuation of initial INSTI within the first 12 months on treatment

	Treatment-Naive		Treatment-Experienced	
	Discontinuation Events n(%)	**Adjusted[1] HR (95% CI)**	**Discontinuation Events n(%)**	**Adjusted[2] HR (95% CI)**
DTG	38 (18.3)	1.	108 (21.4)	1.
RAL	27 (39.1)	2.46 (1.49, 4.05)	42 (36.2)	2.17 (1.51, 3.12)
EVG	68 (26.2)	1.59 (1.07, 2.38)	71 (27.5)	1.39 (1.02, 1.88)

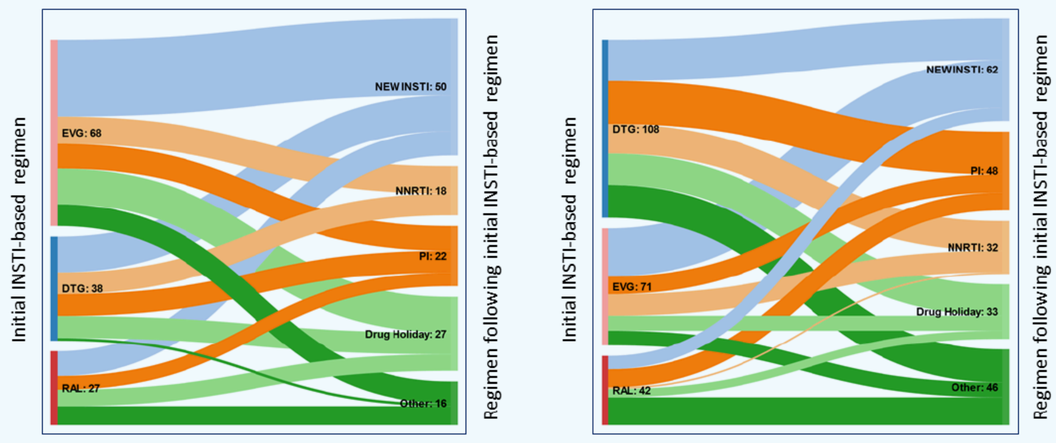
[1] Adjusted for age at INSTI initiation, race, baseline viral load
[2] Adjusted for age at INSTI initiation, race, baseline viral load, and number of ART classes previously experienced

Figure 2. Kaplan-Meier estimates of time to discontinuation of first INSTI-based regimens in the first twelve months of exposure



- For treatment-naïve and treatment-experienced women discontinuing their initial INSTI within 12 months of initiation, the most common regimens following discontinuation contained a different INSTI (Figure 3). Drug holidays of more than 45 days were also common in both treatment groups.

Figure 3. Switch to post-initial INSTI regimen among a) treatment-naïve and b) treatment-experienced women discontinuing first INSTI-based regimen



- Discontinuations following lab abnormalities or reported intolerances/toxicities did not differ significantly between INSTIs in either treatment group.
- Virologic failure (VL >200 copies/mL) occurred prior to just 12% of discontinuations in the first year among treatment-naïve women and 10% among treatment-experienced women, without differences across INSTIs.

CONCLUSIONS:

- In a large cohort of HIV+ women in care in the US, women taking DTG were the least likely to discontinue in the first year of treatment with an initial INSTI compared to women taking RAL or EVG, regardless of prior ART exposure at baseline.
- Among women who discontinued their initial INSTI-based regimen, switching to another INSTI and treatment interruptions were common, while virologic failure prior to discontinuation was not. Patients may be discontinuing effective INSTI-based regimens due to access issues.

REFERENCES

1. Addo MM, Altfeld M. Sex-based differences in HIV type 1 pathogenesis. J Infect Dis 2014; 209 (Suppl 3): S86-92.
2. Short WR, Anderson JR. Caring for women with HIV: Unique needs and challenges. Cleveland Clin J Med 2014; 81(11):691-701.
3. Park TE, Mohamed A, Kalabalik J, Sharma R. Review of integrase strand transfer inhibitors for the treatment of human immunodeficiency virus infection. Expert Rev Anti Infect Ther 2015; 13(10): 1195-212.

ACKNOWLEDGEMENTS

This research wouldn't be possible without the participation of HIV caregivers and their patients. Additionally, we are grateful for the following contributions: Robin Beckerman (SAS programming), Rodney Mood (site selection and support), Ted Ising (database architecture and support), and Bernie Stooks (database support).

Support: This research was funded by ViiV Healthcare

ViiV Healthcare

Epividian®