Change in weight and BMI associated with switching to bictegravir/emtricitabine/tenofovir alafenamide vs. a dolutegravir-based regimen among a prospective longitudinal cohort of virologically suppressed adults living with HIV

Charlotte-Paige Rolle MD MPH[1,2], Jeffrey Garrett APRN[1], Devonnae Sterling BS[3], Brandon Cohen[3], Parth Chandan[3], Daniela Castro[3], Vu Nguyen MS[1], Kiran Patel[4], Edwin DeJesus[1,5]

Orlando Immunology Center[1], Department of Global Health, Emory University Rollins School of Public Health[2], University of Central Florida[3], Gilead Sciences[4], University of Central Florida College of Medicine[5]

Abstract ID #XX

Charlotte-Paige Rolle, MD, MPH
Director of Research Operations
Orlando Immunology Center
1707 N. Mills Avenue, Orlando, FL 32803
E-mail: crolle@oicorlando.com

BACKGROUND:

- Increased weight and BMI have been observed among treatment-naïve-and-experienced people living with HIV (PLWH) initiating bictegravir (BIC) and dolutegravir (DTG)[1,2]
- However, studies have not established a clear relationship between this weight gain and adverse cardiometabolic outcomes[1,2,3]
- Given that 2- and 3-drug DTG and BIC-based regimens are first-line antiretroviral options for treatment-experienced PLWH, we assessed change in weight, BMI and cardiometabolic parameters from a prospective longitudinal cohort of virologically suppressed PLWH switched to BIC/emtricitabine (F)/tenofovir alafenamide (TAF) vs. a DTG-based regimen (DBR) through the first 48 weeks compared to 2 years prior to switch

METHODS:

- Prospective longitudinal study to compare pre-and-post switch change in weight, BMI and cardiometabolic parameters among virologically suppressed adults switched to BIC/F/TAF vs. a DBR at the Orlando Immunology Center (OIC) through 144 weeks, here we report 48-week results
- Eligible participants included all PLWH switched to BIC/F/TAF, F/TAF plus DTG, DTG/abacavir (ABC)/ lamivudine (3TC), DTG/ rilpivirine (RPV) or DTG/3TC as a complete regimen between February 7th, 2018, and July 31st, 2020

Key inclusion criteria included:

- Availability of two consecutive baseline HIV-1 RNA values <50 copies/mL (at least three months apart) in the year prior to switch
- Attendance at ≥4 clinic visits with corresponding weight/BMI values in the 2 years prior to switch
- Attendance at ≥ 2 clinic visits with corresponding weight/BMI values in the year following switch

- PLWH were excluded if they were pregnant, had unstable thyroid disease or baseline Grade 3 or 4 laboratory abnormalities
- Demographics, lab values, clinical parameters and data on weight, BMI, and cardiometabolic factors are collected from the EMR 2 years prior to switch through 144 weeks post-switch
- Linear spline models were fit to estimate and compare the trajectories of weight and BMI changes observed pre-and-post-switch. Adjusted piecewise linear mixed-effects models were fit to examine factors associated with weight and BMI change pre-and-post-switch

RESULTS:

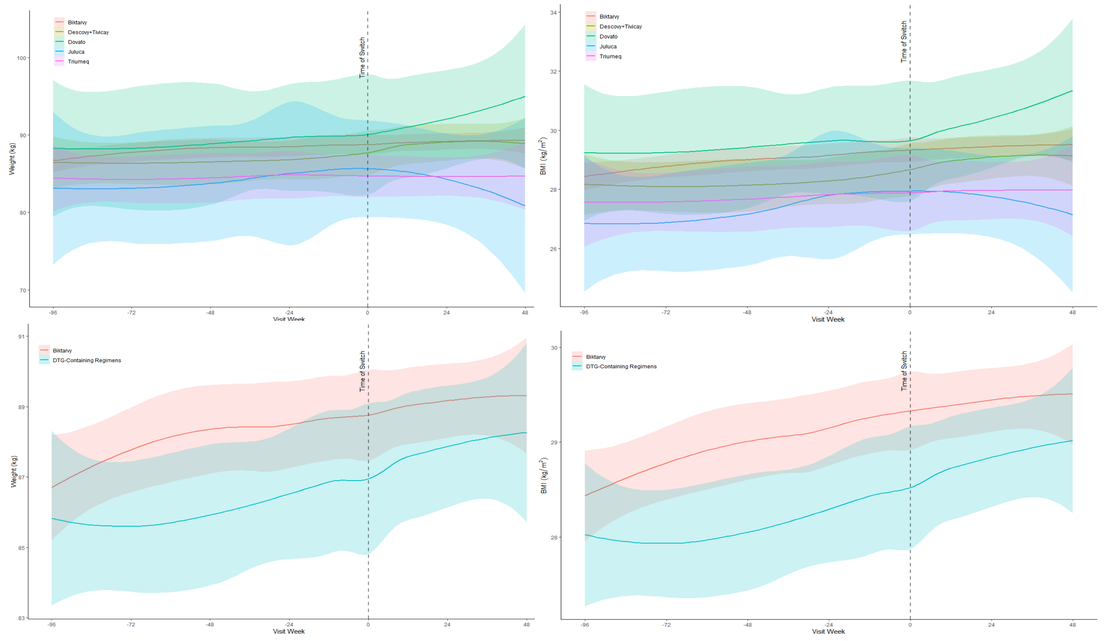
Table 1. Baseline demographic and clinical characteristics

Characteristic	N=956
Median Age (range)	53 (21, 83)
Sex	
Male, n (%)	809 (85)
Female, n (%)	147 (15)
Race	
Caucasian, n (%)	686 (72)
Black, n (%)	166 (17)
Asian, n (%)	2 (0.2)
Other, n (%)	102 (10.8)
Ethnicity	
Hispanic/Latino, n (%)	162 (17)
Not Hispanic/Latino, n (%)	794 (83)
BMI, median (range)	27.9 (14.3, 66.5)
Weight, median (range), kg	85 (43.9, 185.2)
BIC/F/TAF switches	**673**
Regimen prior to switch	
Dual NRTI+NNRTI, n (%)	148 (22)
Dual NRTI+PI, n (n%)	69 (10)
Dual NRTI+INSTI, n (%)	401 (60)
Other, n (n%)	55 (8)
NRTI prior to switch	
TAF, n (%)	472 (70)
TDF, n (%)	135 (20)
ABC, n (%)	19 (3)
Anchor drug prior to switch	
DTG, n (%)	103 (16)
RAL or EVG/c, n (%)	298 (44)
DRV or ATV, n (%)	70 (10)
EFV, n (%)	89 (13)
RPV, n (%)	37 (5)
DBR switches	**283**
DTG+F/TAF	148 (52)
DTG/ABC/3TC	51 (18)
DTG/RPV	48 (17)
DTG/3TC	36 (13)
Regimen prior to switch	
Dual NRTI+NNRTI, n (%)	43 (15)
Dual NRTI+PI, n (n%)	42 (15)
Dual NRTI+INSTI, n (%)	147 (52)
Other, n (n%)	51 (18)
NRTI prior to switch	
TAF, n (%)	64 (23)
TDF, n (%)	116 (41)
ABC, n (%)	45 (16)
Anchor drug prior to switch	
DTG, n (%)	91 (32)
RAL or EVG/c, n (%)	50 (18)
DRV or ATV, n (%)	39 (14)
EFV, n (%)	17 (6)
RPV, n (%)	21 (7)

Abbreviations. BMI, Body Mass Index; ART, antiretroviral therapy; BIC/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; ABC, abacavir; DTG, dolutegravir; RAL, raltegravir; EVG, elvitegravir; c, cobicistat; DRV, darunavir; ATV, atazanavir; EFV, efavirenz; RPV, rilpivirine; DDI, drug-drug interaction; DBR, dolutegravir-based regimen; F, emtricitabine; 3TC, lamivudine

RESULTS cont'd:

Figure 1. Mean change in weight and BMI before and after switch to BIC/F/TAF vs. a dolutegravir-based regimen through Week 48



At Week 48, switching to BIC/F/TAF vs. a DBR were both associated with lower annualized weight gain post-switch (-0.59 kg/year vs. -0.13 kg/year respectively, p=0.45), with similar trends observed for changes in BMI.

Table 2. Adjusted annualized mean weight change pre-/-post switch to BIC/F/TAF vs. a dolutegravir-based regimen through 48 weeks

	All N=956	BIC/F/TAF N=673	DBRs (grouped) N=283	DTG+F/TAF N=148	DTG/ABC/3TC N=51	DTG/RPV N=48	DTG/3TC N=36
Pre-Switch Kg/year (95% CI)	1.09 (0.82, 1.37)*	1.08 (0.75, 1.41)*	1.13 (0.64, 1.62)*	1.23 (0.36, 2.10)*	0.69 (0.03, 1.36)*	1.54 (-0.27, 3.33)	0.92 (-0.31, 2.17)
Post-Switch Kg/year (95% CI)	0.63 (0.18, 1.08)*	0.49 (-0.05, 1.04)	1.00 (0.20, 1.81)*	1.58 (0.26, 2.91)*	0.13 (-1.15, 1.41)	-4.19 (-7.43, -1.14)*	2.92 (1.04, 4.65)*
Pre-Post Difference Kg/year (95% CI)	-0.46 (-0.98, 0.06)	-0.59 (-1.21, 0.03)	-0.13 (-1.08, 0.82)	0.35 (-1.22, 1.93)	-0.56 (-2.14, 1.02)	-5.74 (-9.40, -2.20)*	2.00 -.02, 3.84)

*denotes significant P-value <0.05
Abbreviations. BIC/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DBR, dolutegravir-based regimen; DTG, dolutegravir; ABC, abacavir; 3TC, lamivudine; RPV, rilpivirine; CI, confidence interval

Patients switched to BIC/F/TAF had lower annualized weight gain post-switch compared to all DBRs except for those switched to DTG/RPV. Among those switched to DBRs, the highest annualized weight gain post-switch was observed among those switched to DTG/3TC (+2.00 kg/year, 95% confidence interval (CI): -0.02, 3.84) whereas the lowest annualized weight gain post-switch was observed among those switched to DTG/RPV (-5.74 kg/year, 95% CI: -9.4, -2.2).

Table 3. Change in cardiometabolic factors among patients switching to BIC/F/TAF vs. a dolutegravir-based regimen from baseline to Week 48

	BIC/F/TAF N (%)	DTG+F/TAF N (%)	DTG/ABC/3TC N (%)	DTG/RPV N (%)	DTG/3TC N (%)	P-value
New HTN Diagnosis	4 (0.007)	2 (0.02)	1 (0.03)	0 (0)	0 (0)	0.55
New DM2 Diagnosis	4 (0.007)	1 (0.008)	0 (0)	0 (0)	0 (0)	0.99
New Obesity Diagnosis	9 (0.02)	3 (0.02)	0 (0)	1 (0.03)	0 (0)	0.77
New NAFLD Diagnosis	1 (0.002)	0 (0)	0 (0)	0 (0)	1 (0.03)	0.14
New HLD Diagnosis	2 (0.005)	0 (0)	0 (0)	0 (0)	0 (0)	0.99
Started HTN medications	18 (0.05)	7 (0.08)	0 (0)	3 (0.06)	0 (0)	0.25
Discontinued HTN medications	11 (0.02)	4 0.03)	0 (0)	0 (0)	0 (0)	0.68
Started DM2 Medications	12 (0.02)	3 (0.02)	0 (0)	1 (0.02)	1 (0.03)	0.74
Discontinued DM2 medications	2 (0.003)	2 (0.01)	0 (0)	0 (0)	0 (0)	0.47
Started Vit E for NAFLD	3 (0.005)	0 (0)	0 (0)	0 (0)	0 (0)	0.99
Discontinued Vit E for NAFLD	1 (0.002)	0 (0)	0 (0)	0 (0)	0 (0)	0.99
Started HLD medications	16 (0.04)	6 (0.06)	3 (0.06)	2 (0.04)	1 (0.05)	0.82
Discontinued HLD medications	11 (0.02)	6 (0.04)	0 (0)	1 (0.02)	0 (0)	0.3
Referral to OIC wellness clinic	12 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0.51
Started weight loss medications	26 (0.04)	8 (0.06)	0 (0)	0 (0)	2 (0.07)	0.20

Significant P-values have been bolded for ease of interpretation.
Abbreviations. BIC/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DTG, dolutegravir; ABC, abacavir; 3TC, lamivudine; RPV, rilpivirine; HTN, hypertension; DM2, Type 2 diabetes; NAFLD, nonalcoholic fatty liver disease; HLD, hyperlipidemia; Vit E, vitamin E; OIC, Orlando Immunology Center

There were no significant differences in new onset cardiometabolic disease, medications started or discontinued for cardiometabolic disease, referrals to the OIC wellness clinic and the proportion starting weight loss medications by treatment group at Week 48

RESULTS cont'd:

Table 4. Factors associated with mean annualized mean weight change following switch to BIC/F/TAF vs. a dolutegravir-based regimen

Characteristic	Pre-Switch Kg/year 95%CI	Post-Switch Kg/year 95%CI	Pre-Post Difference Kg/year 95%CI
Age			
<50 years	1.44 (1.01, 1.86)*	0.61 (-0.13, 1.36)	-0.82 (-1.70, 0.06)
≥50 years	0.81 (0.45, 1.16)*	0.65 (0.09, 1.20)*	-0.16 (-0.78, 0.46)
Sex			
Male	1.05 (0.77, 1.33)*	1.06 (0.59, 1.53)*	0.01 (-0.54, 0.57)
Female	1.32 (0.47, 2.16)*	-1.52 (-2.84, -0.21)*	2.84 (1.44, 4.24)*
Race/Ethnicity			
Caucasian	1.07 (0.71, 1.43)*	0.69 (0.10, 1.28)*	-0.39 (-1.07, 0.30)
Black	1.38 (0.72, 2.05)*	-0.02 (-1.18, 1.12)	-1.41 (-2.76, -0.07)*
Hispanic/Latino	0.83 (0.29, 1.37)*	1.04 (0.18, 1.89)*	0.21 (-0.74, 1.16)
Other	1.29 (-0.11, 2.72)	0.17 (-1.83, 2.07)	-1.12 (-3.26, 0.93)
Baseline BMI			
<18.5 kg/m²	-0.84 (-1.86, 0.18)	2.24 (-0.23, 4.73)	3.09 (0.01, 6.17)*
18.8-24.9 kg/m²	0.42 (0.02, 0.83)*	1.30 (0.63, 1.98)*	0.88 (0.10, 1.66)*
25-29.9 kg/m²	0.64 (0.26, 1.02)*	1.26 (0.63, 1.89)*	0.62 (-0.10, 1.34)
≥30 kg/m²	2.11 (1.54, 2.68)*	-0.58 (-1.53, 0.36)	-2.70 (-3.78, -1.61)*
Nadir CD4⁺ T-cell count			
<200 cells/mm³	1.25 (0.76, 1.75)*	1.18 (0.38, 1.99)*	-0.07 (-1.00, 0.86)
≥200 cells/mm³	1.00 (0.68, 1.32)*	0.29 (-0.25, 0.83)	-0.71(-1.33, -0.09)*
Baseline CD4⁺ T-cell count			
<200 cells/mm³	3.08 (0.79, 5.38)*	-1.23 (-4.31, 1.82)	-4.31 (-7.38, -1.24)*
≥200 cells/mm³	1.05 (0.77, 1.32)*	0.67 (0.22, 1.13)*	-0.37 (-0.90, 0.16)
Duration of HIV infection			
0-5 years	2.33 (1.47, 3.20)*	-0.41 (-1.90, 1.08)	-2.75 (-4.45, -1.05)*
6-10 years	1.17 (0.70, 1.64)*	1.48 (0.62, 2.34)*	0.31 (-0.74, 1.37)
>10 years	0.78 (0.43, 1.12)*	0.48 (-0.07, 1.04)	-0.29 (-0.92, 0.33)
Pre-Switch Anchor Drug			
NNRTI	0.75 (0.33, 1.16)*	2.15 (1.38, 2.92)*	1.40 (0.46, 2.34)*
PI	1.90 (1.10, 2.71)*	-0.50 (-1.90, 0.90)	-2.40 (-4.11, -0.70)
INSTI	1.05 (0.69, 1.41)*	0.34 (-0.24, 0.91)	-0.71 (-1.36, -0.07)
Pre-Switch NRTI			
TAF	1.25 (0.89, 1.62)*	0.13 (-0.48, 0.74)	-1.12 (-1.82, -0.42)
TDF	0.97 (0.50, 1.44)*	1.71 (0.95, 2.46)*	0.74 (-0.14, 1.61)
ABC	0.36 (-0.34, 1.06)	0.57 (-0.62, 1.76)	0.21 (-1.22, 1.64)
Baseline Smoker			
Yes	1.51 (0.62, 2.39)*	0.62 (-0.68, 1.91)	-0.88 (-2.29, 0.51)
No	1.01 (0.73, 1.28)*	0.63 (0.15, 1.10)*	-0.38 (-0.94, 0.18)
Baseline Psychiatric Comorbidities			
Yes	1.00 (0.54, 1.46)*	0.47 (-0.26, 1.20)	-0.53 (-1.34, 0.29)
No	1.17 (0.83, 1.50)*	0.75 (0.17, 1.32)*	-0.42 (-1.09, 0.26)
Use of medications associated with weight gain	0.98 (0.32, 1.65)*	-0.83 (-1.89, 0.24)	-1.81 (-2.99, -0.62)*
Yes	1.13 (0.84, 1.42)*	1.11 (0.63, 1.60)*	-0.01 (-0.58, 0.56)
No			
Use of medications associated with weight loss	0.85 (-0.06, 1.76)	-1.12 (-2.60, 0.35)	-1.97 (-3.64, -0.30)*
Yes	1.12 (0.84, 1.41)*	0.82 (0.35, 1.30)*	-0.30 (-0.85, 0.25)
No			
Referral to OIC wellness clinic	-3.36 (-15.04, 8.21)	-16.87 (-30.9, -2.36)*	-13.51 (-30.79, 3.89)
Yes	1.11 (0.85, 1.38)*	0.73 (0.29, 1.18)*	-0.38 (-0.89, 0.14)
No			
Self-report of physical activity	-0.31 (-2.24, 1.63)	-2.11 (-5.03, 0.80)	-1.80 (-5.17, 1.52)
Yes	1.12 (0.84, 1.39)*	0.76 (0.31, 1.21)*	-0.36 (-0.88, 0.16)
No			
Self-report of dieting	-0.66 (-3.87, 2.54)	-3.57 (-8.35, 1.16)	-2.91 (-8.56, 2.69)
Yes	1.10 (0.83, 1.37)*	0.79 (0.35, 1.23)*	-0.31 (-0.82, 0.2)
No			

*denotes a significant P-value <0.05
Abbreviations. BMI, Body Mass Index; BIC/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DBR, dolutegravir-based regimen; DTG, dolutegravir; ABC, abacavir; 3TC, lamivudine; RPV, rilpivirine; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; NRTI; nucleoside reverse transcriptase inhibitor; TAF, tenofovir alafenamide; TDF tenofovir disoproxil fumarate;; OIC, Orlando Immunology Center; CI, confidence interval

Female sex, lower baseline BMI, and switching from an NNRTI were significantly associated with higher annualized weight gain post-switch. However, compared to switching from INSTIs, switching from efavirenz (EFV) was associated with significantly higher annualized weight gain post-switch (+3.11 kg/year, p<0.001), whereas switching from rilpivirine (RPV) was associated with significantly lower weight gain (-2.17 kg/year, p=0.022). Black race, baseline BMI≥30 kg/m², nadir CD4⁺ T-cell count≥200 cells/mm³, baseline CD4⁺ T-cell count<200 cells/mm³, shorter duration of HIV infection, and use of medications associated with both weight gain and weight loss were all associated with significantly lower annualized weight gain post-switch

CONCLUSIONS:

- In this real-world cohort, switching to a BIC vs. DBR were both associated with lower annualized weight gain post-switch that was not significantly different at Week 48
- DTG/RPV switches were the only group that experienced significantly lower annualized weight change post-switch, whereas DTG/3TC switches had the highest annualized weight gain post-switch but this was not significantly different compared to pre-switch weight gain
- There were no significant changes in any of the cardiometabolic parameters studied between treatment groups at Week 48
- Switching from NNRTIs was associated with higher annualized weight gain post-switch however, switching specifically from EFV was associated with higher weight gain whereas switching from RPV was associated with lower weight gain post-switch
- These data overall support the favorable metabolic profile of second-generation INSTIs which is important given that these are guideline-preferred options for most PLWH, including those who are ageing and facing an increasing number of medical comorbidities

References
[1]Sax et al. Clin Infect Dis. 2020 Sep 12;71(6):1379-1389
[2]Lake at al. Clin Infect Dis. 2020 Dec 3;71(8):e471-e477.
[3]Erlandson et al. Clin Infect Dis. 2021 Oct 20;73(8):1440-1451

This work was supported by a research grant from Gilead Sciences, IN-US-380-5785 (PI: Rolle)