96-week update: Change in weight and BMI associated with switching to bictegravir/emtricitabine/tenofovir alafenamide vs. a dolutegravir-based regimen among virologically suppressed adults living with HIV

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BACKGROUND

- Increased weight and BMI have been observed among people living with HIV (PLWH) initiating second generation integrase strand transfer inhibitors (INSTIs)[1,2]
- Previously, we demonstrated that switching to a bictegravir (BIC) vs. dolutegravir (DTG) based regimen (DBR) among virologically suppressed PLWH was associated with lower annualized weight gain of a similar magnitude post-switch compared to pre-switch at Week 48 (-0.59 kg/year vs. -0.13 kg/year respectively, p=0.45)[3]
- At Week 48, PLWH switched to DTG/rilpivirine (RPV) experienced the lowest annualized weight gain post-switch (-4.19 kg/year, 95% confidence interval (CI) [-7.43, -1.14]) whereas those switching to DTG/lamivudine (3TC) experienced the highest annualized weight gain post-switch (2.92 kg/year, 95% CI [1.04, 4.65])[3]
- Here, we report updated changes in weight and BMI among those switching to a BIC vs. DBR through 96 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/ emtricitabine (F)/ tenofovir alafenamide (TAF) vs. a DBR at the Orlando Immunology Center (OIC) through 144 weeks, here we report 96-week results
- Eligible participants included all PLWH switched to BIC/F/TAF, F/TAF plus DTG, DTG/abacavir (ABC)/ 3TC, DTG/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

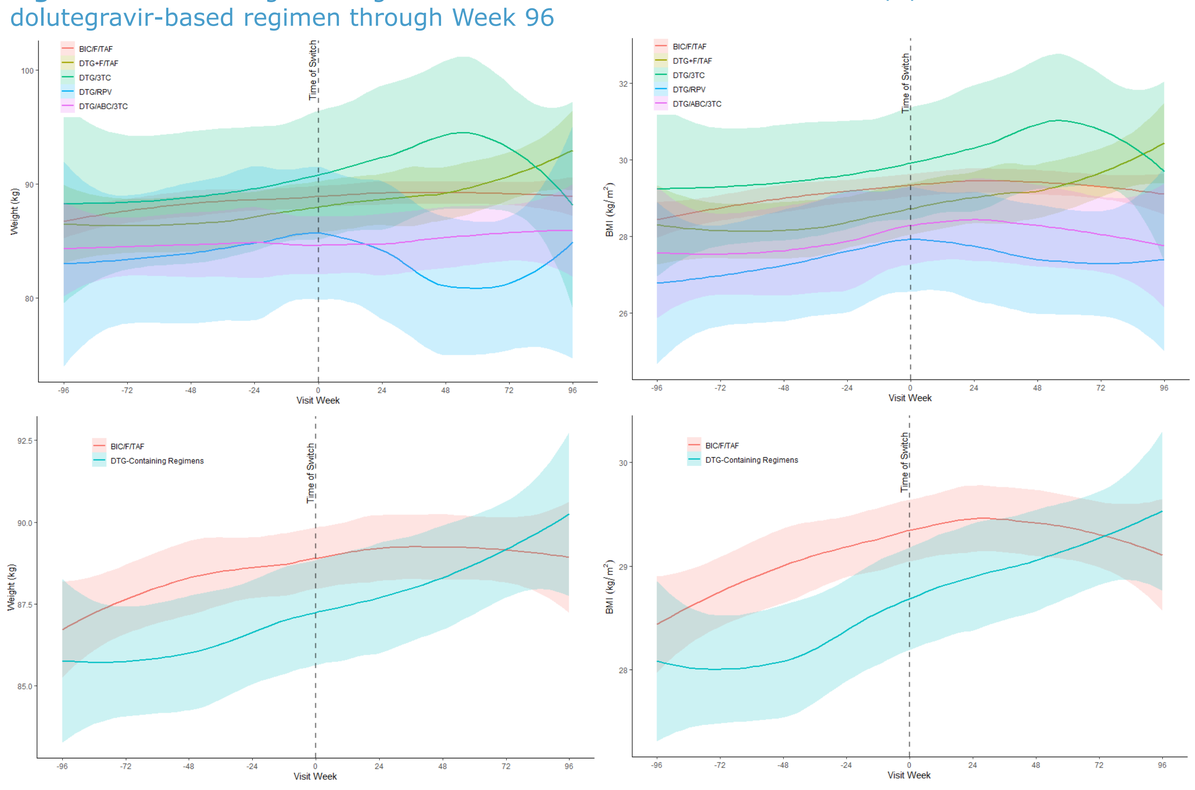
RESULTS

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
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, 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)
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, 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; 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

Figure 1. Mean change in weight and BMI before and after switch to BIC/F/TAF vs. a dolutegravir-based regimen through Week 96



At Week 96, switching to BIC/F/TAF vs. a DBR were both associated with lower annualized weight gain post-switch compared to pre-switch (-0.75 kg/year vs. -0.37 kg/year respectively, p=0.34), with similar results 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 96 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)	1.11 (0.84, 1.37)*	1.09 (0.78, 1.41)*	1.16 (0.68, 1.65)*	1.29 (0.41, 2.18)*	0.61 (-0.09, 1.31)	1.15 (-0.41, 2.72)	1.09 (0.12, 2.05)*
Post-switch Kg/year (95% CI)	0.47 (0.19, 0.76)*	0.35 (0, 0.69)	0.79 (0.3, 1.29)*	1.31 (0.42, 2.21)*	0.59 (-0.13, 1.33)	-1.53 (-3.22, 0.1)	1.75 (0.82, 2.68)*
Pre-post difference Kg/year (95% CI)	-0.63 (-0.98, -0.29)*	-0.75 (-1.17, -0.33)*	-0.37 (-0.99, 0.24)	0.02 (-1.09, 1.15)	-0.01 (-0.94, 0.93)	-2.68 (-4.61, -0.73)*	0.66 (-0.6, 1.92)

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

Switching to DTG/3TC continued to be associated with highest annualized weight gain post-switch compared to pre-switch whereas switching to DTG/RPV continued to be associated with the lowest annualized weight gain post-switch compared to pre-switch at Week 96

Table 3. Change in cardiometabolic factors among patients switching to BIC/F/TAF vs. a dolutegravir-based regimen from baseline to Week 96

	BIC/F/TAF N (%)	DTG+F/TAF N (%)	DTG/ABC/3TC N (%)	DTG/RPV N (%)	DTG/3TC N (%)	P-value
New HTN Diagnosis	1/351 (0.3)	2/77 (3)	6/31 (20)	0/26 (0)	2/17 (12)	**<0.001**
New DM2 Diagnosis	4/527 (1)	1/111 (1)	1/41 (2)	0/34 (0)	1/26 (4)	0.24
New Obesity Diagnosis	10/474 (2)	0/107 (0)	1/37 (3)	2/35 (6)	0/25 (0)	0.17
New NAFLD Diagnosis	4/579 (1)	0/121 (0)	2/44 (5)	1/41 (2)	2/32 (6)	**0.008**
New HLD Diagnosis	4/232 (2)	1/69 (1)	2/21 (10)	3/8 (40)	1/11 (9)	**<0.001**
Started HTN medications	8/351 (2)	2/76 (3)	4/45 (9)	0/42 (0)	0/15 (0)	0.14
Discontinued HTN medications	8/612 (1)	0/130 (0)	0/45 (0)	0/42 (0)	1/34 (3)	0.44
Started DM2 Medications	3/538 (0.6)	3/120 (3)	0/45 (0)	2/42 (5)	1/28 (4)	**0.02**
Discontinued DM2 medications	3/611 (0.5)	0/131 (0)	0/45 (0)	0/42 (0)	0/34 (0)	0.99
Started Vit E for NAFLD	1/599 (0.2)	0/128 (0)	0/45 (0)	0/42 (0)	0/30 (0)	0.99
Discontinued Vit E for NAFLD	0/611 (0)	0/131 (0)	0/45 (0)	0/42 (0)	0/34 (0)	0.99
Started HLD medications	9/337 (3)	2/86 (2)	5/45 (11)	2/41 (5)	0/17 (0)	0.08
Discontinued HLD medications	9/609 (2)	1/131 (0.8)	0/45 (0)	4/41 (10)	0/34 (0)	**0.03**
Referral to OIC wellness clinic	6/609 (2)	2/131 (2)	1/45 (2)	1/42 (2)	3/33 (10)	0.06
Started weight loss medications	33/536 (6)	7/118 (6)	0/39 (0)	1/38 (3)	1/26 (4)	0.61

Significant P-values have been bolded for ease of interpretation
Variability in denominator due to missing data
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 small but significant differences in the number newly diagnosed with hypertension, fatty liver disease, and hyperlipidemia and those starting diabetes medications and discontinuing lipid lowering therapy at Week 96

RESULTS cont'd

Table 4. Factors associated with mean annualized 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	1.42 (0.99, 1.84)*	0.62 (0.15, 1.08)*	-0.80 (-1.39, -0.20) *
≥50 years	0.85 (0.52, 1.18)*	0.38 (0.03, 0.73 *	-0.47 (-0.87, -0.07) *
Sex			
Male	1.10 (0.83, 1.37) *	0.62 (0.33, 0.91) *	-0.48 (-0.85, -0.12) *
Female	1.15 (0.31, 1.98) *	-0.46 (-1.41, 0.47)	-1.60 (-2.62, -0.62) *
Race/Ethnicity			
Caucasian	1.08 (0.73, 1.43) *	0.42 (0.05, 0.79) *	-0.66 (-1.13, -0.19) *
Black	1.37 (0.71, 2.03) *	0.21 (-0.5, 0.93)	-1.15 (-1.98, -0.33) *
Hispanic/Latino	0.88 (0.42, 1.34) *	0.97 (0.46, 1.48) *	0.09 (-0.54, 0.72)
Other	1.10 (-0.45, 2.54)	0.87 (-0.46, 2.78)	-0.23 (-1.74, 1.8)
Baseline BMI			
<18.5 kg/m²	-0.81 (-1.91, 0.32)	1.99 (0.64, 3.39) *	2.80 (0.72, 4.88) *
18.6-24.9 kg/m²	0.51 (0.13, 0.88) *	0.81 (0.41, 1.21) *	0.30 (-0.19, 0.80)
25-29.9 kg/m²	0.71 (0.34, 1.09) *	0.80 (0.41, 1.20) *	0.09 (-0.39, 0.56)
≥30 kg/m²	2.01 (1.44, 2.58) *	-0.14 (-0.75, 0.46)	-2.15 (-2.89, -1.42) *
Nadir CD4+ T-cell count			
<200 cells/mm3	1.24 (0.77, 1.72) *	1.17 (0.67, 1.68) *	-0.07 (-0.73, 0.58)
≥200 cells/mm3	1.03 (0.72, 1.35) *	0.05 (-0.29, 0.38)	-0.99 (-1.38, -0.59) *
Baseline CD4+ T-cell count			
<200 cells/mm³	2.8 (0.89, 4.59) *	-0.49 (-2.4, 2.03)	-3.28 (-5.82, 0.02)
≥200 cells/mm³	1.07 (0.8, 1.33) *	0.50 (0.21, 0.78) *	-0.57 (-0.92, -0.22) *
Duration of HIV infection			
0-5 years	2.25 (1.42, 3.09) *	-0.04 (-0.96, 0.87)	-2.29 (-3.37, -1.22) *
6-10 years	1.24 (0.74, 1.73) *	1.04 (0.51, 1.56) *	-0.20 (-0.92, 0.51)
>10 years	0.80 (0.47, 1.12) *	0.33 (-0.02, 0.68)	-0.46 (-0.88, -0.05) *
Pre-switch Anchor Drug			
NNRTI	0.91 (0.45, 1.36) *	1.25 (0.76, 1.74) *	0.34 (-0.28, 0.97)
PI	1.89 (1.05, 2.74) *	-0.41 (-1.31, 0.49)	-2.30 (-3.48, -1.13) *
INSTI	1.01 (0.68, 1.35) *	0.39 (0.04, 0.75) *	-0.62 (-1.05, -0.19) *
Pre-switch NRTI			
TAF	1.22 (0.88, 1.57) *	0.16 (-0.22, 0.53)	-1.07 (-1.53, -0.61) *
TDF	1.11 (0.63, 1.59) *	1.03 (0.53, 1.55) *	-0.08 (-0.71, 0.55)
ABC	0.35 (-0.36, 1.06)	0.85 (0.13, 1.56) *	0.49 (-0.38, 1.36)
Baseline Smoker			
Yes	1.53 (0.73, 2.32) *	0.33 (-0.5, 1.17)	-1.20 (-2.14, -0.25) *
No	1.02 (0.74, 1.29) *	0.51 (0.22, 0.8) *	-0.51 (-0.88, -0.14) *
Baseline Psychiatric Comorbidities			
Yes	1.09 (0.66, 1.53) *	0.23 (-0.24, 0.69)	-0.87 (-1.41, -0.33) *
No	1.12 (0.79, 1.44) *	0.66 (0.31, 1.01) *	-0.46 (-0.91, -0.01) *
Use of medications associated with weight gain			
Yes	0.99 (0.38, 1.59) *	-0.02 (-0.66, 0.63)	-1.00 (-1.74, -0.27) *
No	1.15 (0.86, 1.44) *	0.63 (0.32, 0.94) *	-0.52 (-0.91, -0.13) *
Use of medications associated with weight loss			
Yes	1.12 (0.23, 2) *	-1.17 (-2.11, -0.21) *	-2.28 (-3.38, -1.18) *
No	1.10 (0.83, 1.38) *	0.67 (0.38, 0.96) *	-0.44 (-0.80, -0.07) *
Referral to OIC wellness clinic			
Yes	-4.99 (-17.48, 7.78)	-8.91 (-21.99, 3.51)	-3.91 (-16.75, 11.44)
No	1.14 (0.88, 1.40) *	0.51 (0.23, 0.79) *	-0.63 (-0.97, -0.28) *
Self-report of physical activity			
Yes	-0.57 (-2.33, 1.20)	-0.74 (-2.59, 1.08)	-0.17 (-2.08, 1.77)
No	1.15 (0.88, 1.41) *	0.51 (0.22, 0.79) *	-0.64 (-0.99, -0.29) *
Self-report of dieting			
Yes	-1.27 (-4.29, 1.70)	-0.43 (-3.39, 2.61)	0.84 (-2.33, 4.26)
No	1.13 (0.87, 1.39) *	0.51 (0.23, 0.79) *	-0.62 (-0.96, -0.28) *

*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

Baseline BMI<18.5 kg/m² was the only evaluated factor associated with significantly higher annualized weight gain post-switch, whereas multiple factors were associated with significantly lower annualized weight gain post-switch, but among them referral to the internal wellness clinic and baseline CD4⁺ T-cell count<200 cells/mm³ were associated with the lowest annualized weight gain post-switch

CONCLUSIONS

- At Week 96, switching to a BIC vs. DBR continued to be associated with lower annualized weight gain of a similar magnitude post-switch
- DTG/RPV and BIC/F/TAF switches were the only groups with significantly lower annualized weight gain post-switch compared to pre-switch trajectories at Week 96
- Though many factors were associated with lower annualized weight gain post-switch, referral to the OIC wellness clinic continued to be associated with the greatest amount of weight loss post-switch compared to pre-switch at Week 96
- These findings continue to support the favorable metabolic profile of second-generation INSTIs. For those struggling with weight gain, referral to services that provide counseling on nutrition, exercise and pharmacotherapy for weight loss may be a valuable intervention

References
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