Biktarvy® (BIC/FTC/TAF) Comparison With DTG/3TC

This document is in response to your request for information regarding Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) compared with dolutegravir/lamivudine (DTG/3TC) in people with HIV (PWH).

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Summary

Clinical Studies: BIC/FTC/TAF vs DTG/3TC

Six prospective clinical studies evaluated outcomes in PWH who were VS or ARV naive and were treated with BIC/FTC/FTC or DTG/3TC.[1-7]

- In three studies that reported virological outcomes, rates of VF were similar or noninferior between treatment groups.[2-5]
- Five studies reported weight-related outcomes.[1-6] In three studies, there was no significant difference between the BIC/FTC/TAF and DTG/3TC groups in the change in weight from baseline to Week 48 or 96.[3-5] In one study, through 144 weeks of treatment, BIC/FTC/TAF and DTG/3TC were both associated with a lower annualized weight gain than pre-switch rates (P<0.05 in the BIC/FTC/TAF arm).[1] In two studies, increases in weight or trunk fat mass were significantly greater in the BIC/FTC/TAF group than in the DTG/3TC group (P<0.05).[2,6]
- In three studies that reported outcomes related to metabolic and laboratory parameters, changes from baseline to Week 48 or 96 were not significantly different between groups.[3,5,6]
- In the DEBATE study, VS PWH who switched to BIC/FTC/TAF experienced increases in CD4+ T-cells and classical monocytes, whereas those who switched to DTG/3TC had increases in CD4+ cell subtypes, CD8+ T-cells with markers of exhaustion, and nonclassical monocytes.[7]

Real-World Studies: BIC/FTC/TAF vs DTG/3TC

In an analysis of VS PWH who switched to BIC/FTC/TAF or DTG/3TC, VF occurred infrequently (2% vs 3%, respectively), and the risk of regimen DC was greater with DTG/3TC than with BIC/FTC/TAF (19% vs 17%, respectively).[8]

In a retrospective cohort study conducted among PWH who initiated BIC/FTC/TAF or DTG/3TC, ARV-naive patients had no significant between-group differences in absolute weight change or the proportion of patients with >10% weight increase; however, there was a significant difference among VS patients in absolute weight gain (BIC/FTC/TAF, +2.4 kg;

DTG/3TC, +1 kg; *P*<0.001) and >10% weight increase (BIC/FTC/TAF, 13.8%; DTG/3TC, 7%; *P*<0.001).[9]

In a retrospective analysis, the IRs of treatment DC after switching were similar between the BIC/FTC/TAF and DTG/3TC groups, and the risk of DC was not significantly different between groups. Similar percentages of patients achieved virological suppression.[10]

In a prospective cohort study in ARV-naive PWH who received BIC/FTC/TAF or DTG/3TC, there were no significant differences between groups in weight, BMI, lipid measures, or HSI scores at Week 96.[11]

In a retrospective cohort study, both BIC/FTC/TAF and DTG/3TC decreased expression of inflammatory markers at Month 24.[12]

In a retrospective analysis that evaluated time to treatment DC in VS PWH who switched to BIC/FTC/TAF or DTG + 3TC, there was no significant difference between the two groups in the estimated probability of maintaining the study regimen after 24 weeks.[13]

Clinical Studies: BIC/FTC/TAF vs DTG/3TC

Prospective, Longitudinal Cohort Study in VS PWH[1]

A prospective, single-center, longitudinal cohort study was conducted using data from electronic medical records of VS PWH who switched to BIC/FTC/TAF (n=673) or a DTG-based regimen, including DTG/3TC (n=36), to compare pre- and post-switch changes in weight, BMI, and cardiometabolic parameters through 144 weeks of treatment. Key inclusion criteria were the availability of two consecutive (≥3 months apart) baseline measures of VL <50 c/mL pre-switch, ≥4 clinic visits with weight/BMI measures within 2 years of switch, and ≥2 clinic visits with weight/BMI measures within 1 year post-switch. Trajectories of pre- and post-switch weight and BMI changes were estimated using linear spline models.

At Week 144, BIC/FTC/TAF was associated with a significantly lower (*P*<0.05) annualized weight gain post-switch compared with pre-switch trajectories.

Table 1. Adjusted Annualized Mean Weight Change Pre- and Post-Switch to BIC/FTC/TAF or DTG/3TC (Rolle et al)[1]

Kg/Year (95% CI)	BIC/FTC/TAF (n=673)	DTG/3TC (n=36)
Pre-switch	1.12 (0.81–1.43)	1.35 (0.38–2.31)
Post-switch	0.23 (-0.04 to +0.51)	1.08 (0.31–1.85)
Difference	-0.88 (-1.24 to -0.53)	-0.27 (-1.32 to +0.79)

From baseline to Week 144, participants who switched to DTG-based regimens had significantly higher rates of newly diagnosed HTN (*P*=0.001), NAFLD (*P*=0.001), and hyperlipidemia (*P*=0.044) than participants who switched to BIC/FTC/TAF. In the BIC/FTC/TAF and DTG/3TC groups, new diagnoses of HTN occurred in 20/387 (5%) and 4/17 (24%), respectively; NAFLD in 8/637 (1%) and 4/34 (12%); and hyperlipidemia in 16/252 (6%) and 1/10 (10%). There were no significant differences between groups in the number of participants who were newly diagnosed with type 2 DM or obesity; had a change in medication for HTN, type 2 DM, or hyperlipidemia; or initiated weight loss medications.

Open-Label, Multicenter Clinical Trial (PASO-DOBLE)[2]

A phase 4, open-label, multicenter, randomized clinical trial was conducted to assess the efficacy of switching to DTG/3TC (n=277) compared with switching to BIC/FTC/TAF (n=276) in VS (VL <50 c/mL for ≥24 weeks) PWH with no prior VF or known/suspected resistance. Prior regimens included TDF, EFV, or COBI-containing regimens. Randomization was stratified by baseline TAF use and sex at birth. The primary endpoint was the proportion of participants with plasma VL ≥50 c/mL at Week 48 by FDA Snapshot analysis (4% noninferiority margin), and the key secondary endpoint was weight change.

In the ITT-E population at Week 48, switching to DTG/3TC was noninferior to switching to BIC/FTC/TAF, with 0.7% of participants in the BIC/FTC/TAF group and 2.2% of participants in the DTG/3TC group with VL ≥50 c/mL (difference, 1.4%; 95% CI: -0.5 to 3.4). Twenty-six participants (9.4%) in the BIC/FTC/TAF group and 16 (5.8%) in the DTG/3TC group had viral blips by Week 48 (*P*=0.106), and 1 participant in the BIC/FTC/TAF group had CVF (VL ≥50 c/mL with a second consecutive VL ≥200 c/mL) through Week 48 with no treatment-emergent resistance.

The mean change in weight from baseline through Week 48 (adjusted for baseline value, sex, ± TAF in previous ART, age, and ethnicity) was +1.81 kg in the BIC/FTC/TAF group and +0.89 kg in the DTG/3TC group (mean adjusted difference, +0.92 kg; 95% CI: 0.17–1.66; *P*=0.016). A total of 52 participants (20%) in the DTG/3TC group and 75 participants (29.9%) in the BIC/FTC/TAF group had >5% weight gain at Week 48 (adjusted OR, 1.81; 95% CI: 1.19–2.76; *P*=0.006). In a subanalysis of pre-switch NRTI use among participants with >5% weight gain, there was a numerically larger proportion of participants with weight gain on BIC/FTC/TAF vs DTG/3TC when switching from ABC or TDF; however, a statistical analysis was not presented.

DRAEs were reported in 27 participants (9.8%) in the BIC/FTC/TAF group and in 19 (6.9%) in the DTG/3TC group (*P*=0.213); Grade 3 to 4 AEs were reported in 10 participants (3.6%) and 3 participants (1.1%), respectively (*P*=0.049).

Open-Label Study (DYAD)

A phase 4, randomized, open-label study evaluated the efficacy and safety of switching to DTG/3TC (n=149) compared with staying on BIC/FTC/TAF (n=73) in VS PWH with no history of VF and no documented or suspected major INSTI or NRTI resistance. Eligible participants had undetectable VL for ≥3 months and had been receiving BIC/FTC/TAF for ≥3 months. The primary endpoint was the percentage of participants with VL ≥50 c/mL at Week 48 by FDA Snapshot analysis (6% noninferiority margin) in the ITT-E population.[3]

After study completion, 63 participants in the BIC/FTC/TAF group and 124 participants in the DTG/3TC group continued into the open-label extension phase. At Week 96, 2% of participants (3/149) in the DTG/3TC group and 1% (1/73) in the BIC/FTC/TAF group had a VL ≥50 c/mL (adjusted treatment difference, 0.6%; 95% CI: -4.6% to 5.5%). From Week 48 to Week 96, 1 additional participant in the DTG/3TC group had CVF; no treatment-emergent resistance was detected.[4]

The mean change from baseline in eGFR in the BIC/FTC/TAF and DTG/3TC groups was +0.87 mL/min/1.73 m^2 and -3.37 mL/min/1.73 m^2 (*P*=0.03), respectively, at Week 48 and +1 mL/min/1.73m^2 and -4.5 mL/min/1.73m^2 (*P*<0.05) at Week 96. No significant differences were observed between groups in mean changes from baseline in Cr levels, lipid parameters (TC, LDL, HDL, TG, or TC:HDL ratio), weight, or BMI at either time point.[3,4] From baseline to Week 96, DRAEs were reported in 42 participants (28%) in the DTG/3TC

group and in 4 participants (5%) in the BIC/FTC/TAF group. DRAEs led to study withdrawal in 11 participants (7%) in the DTG/3TC group; no participants in the BIC/FTC/TAF group discontinued due to a DRAE.[4]

PROs through Week 48[14]

PROs among participants in DYAD were assessed for treatment satisfaction (HIVTSQ/c), HIV/ART-related symptoms (HIV-SI), and willingness to switch ART (among participants who switched to DTG/3TC) at baseline, Week 24, and Week 48. ANCOVA models compared changes in HIV-SI and HIVTSQ/c scores from baseline between treatment groups, adjusting for age, gender, race or ethnicity, duration of HIV diagnosis and ARV use, prior duration of BIC/FTC/TAF, and baseline scores. Compared with the BIC/FTC/TAF group, the DTG/3TC group reported numerically larger improvements in the total HIV-SI symptom score at Weeks 24 and 48, but these differences were not statistically significant. Based on the HIV-SI symptom scores, headache and diarrhea were more frequently reported as bothersome with DTG/3TC vs BIC/FTC/TAF at Weeks 24 (headache, 16% vs 6%, respectively; *P*=0.04) and 48 (diarrhea, 10% vs 0%, respectively; *P*=0.01); there were no other significant differences through Week 48. In addition, there were no significant differences between treatment groups in the HIVTSQ/c total score or for any individual treatment satisfaction score item through Week 48. The most frequently reported reasons for switching to DTG/3TC therapy included an interest in research of new HIV therapies (85%), physician request to participate in the study (60%), and concerns about long-term effects of the current regimen (23%).

Open-Label Switch Study (INSTINCT)[5]

The randomized, open-label, multicenter INSTINCT trial evaluated the effect of switching from DTG/3TC to BIC/FTC/TAF (n=70) vs staying on DTG/3TC (n=71) on metabolic parameters and systemic inflammation (eg, levels of IL-6). Eligible participants were VS PWH (VL <50 c/mL) on stable ART with DTG/3TC for ≥48 weeks. Efficacy at Week 96 and changes from baseline to Week 96 in IL-6, metabolic and renal parameters, CD4 and CD8 cell counts, and CD4/CD8 ratio were evaluated. In the BIC/FTC/TAF and DTG/3TC groups, baseline demographics were as follows: mean age was 45.6 and 44.7 years, respectively; 15.7% and 11.3% were female; 72.9% and 83.1% were Caucasian; and mean duration of virologic suppression was 6.8 and 6.2 years.

No significant differences between groups were observed in changes in IL-6 levels from baseline to Week 96, with a median fold change of 1.2 for the BIC/FTC/TAF group and 2 for the DTG/3TC group (*P*=0.106). At Week 96, the rates of VF were similar between groups: BIC/FTC/TAF, 1.6%; DTG/3TC, 1.6% (difference in risk of VL >50 c/mL, 0.01% [95% CI: -0.07 to 0.04]); 90.6% and 93.7% of participants in the BIC/FTC/TAF and DTG/3TC groups, respectively, had a VL <50 c/mL and 7.8% and 4.8% did not have virologic data . Changes from baseline to Week 96 were similar between groups for body weight (mean change, 1.22 [95% CI: 0.31–2.13] kg), TC:HDL ratio, TG, $eGFR_{CKD\text{-}EPI}$, and glucose. The trajectories of changes from baseline to Week 96 in CD4 and CD8 cells and CD4/CD8 ratio were similar between groups. No safety data were reported.

Single-Center Study[6]

A single-center, randomized, open-label, controlled trial compared metabolic outcomes between PWH who switched to or stayed on BIC/FTC/TAF (n=43) and those who switched to DTG/3TC (n=87). Week 48 secondary outcomes included weight, BMI, waist

circumference, lipids, insulin resistance, dual-energy X-ray absorptiometry scan, and FibroScan.

At baseline, there were significant differences between groups in weight (*P*=0.013), waist circumference (*P*=0.006), and BMI (*P*=0.024). Virologic suppression was maintained through Week 48, with no differences between groups. Analyses using linear mixed models adjusted for baseline BMI demonstrated significant differences between groups in mean changes from baseline to Week 48 in several parameters (Table 2), and changes in lean body mass, TC, LDL, TG, glucose, insulin, HOMA-IR, liver fibrosis, and FibroScan results were not significantly different between groups. From baseline to Week 48, greater treatment-mediated changes in trunk fat were seen in participants with a BMI >30 kg/m^2 (BIC/FTC/TAF, +1.4 kg; DTG/3TC, -1.1 kg) than in participants with a BMI <30 kg/m^2 (BIC/FTC/TAF, +0.6 kg; DTG/3TC, +0.2 kg). Safety data were not reported.

Table 2. Metabolic Parameters With Significant Between-Group Differences From Baseline to Week 48 (Degroote et al)[6]

Parameter	BIC/FTC/TAF (n=43)	DTG/3TC (n=87)	*P*-Value
ALT, U/L	+4.55	-0.73	0.04
HDL, mg/L	-2.84	-0.043	0.043
Lean trunk mass, g	-474	+112	0.032
Trunk fat mass, g	+719	+41	0.043
Fat, %	+1.32	-0.04	0.003

Prospective, Open-Label Switch Study (DEBATE)[7]

The randomized, open-label, prospective DEBATE study compared immunological outcomes between PWH who switched from their ARV regimen to BIC/FTC/TAF (n=33) or DTG/3TC (n=33). Eligible participants were taking a triple-drug ARV regimen and had undetectable HIV VL for >12 months. Blood samples were collected at baseline and at 6 and 12 months.

Although the absolute numbers of T cells and monocytes were similar between groups at 12 months, there were differences between the groups in the changes in a number of cell subtypes. Classical monocytes (CD14++CD16-) increased in participants in the BIC/FTC/TAF group from baseline to 6 months (*P*=0.009; between groups at 6 months, *P*=0.0028). From baseline to 12 months, activated CD4+ T cells significantly increased among participants in the BIC/FTC/TAF group (*P*=0.0367). Participants who switched to DTG/3TC had significantly greater increases from baseline to 12 months in additional subtypes of CD4+ T cells (terminally differentiated T [*P*=0.0007] and exhausted cells [*P*=0.0004]), transitional memory lymphocytes (*P*<0.0001) and T memory stem cells (*P*=0.0019), nonclassical monocytes (CD14+CD16++; *P*=0.0195), and CD8+ markers of exhaustion (*P*=0.0426; between groups at 12 months, *P*=0.026) than participants in the BIC/FTC/TAF group. No significant changes from baseline in CD19+ B cells were observed in either group.

Real-World Studies: BIC/FTC/TAF vs DTG/3TC

OPERA Longitudinal Cohort Analysis in the US[8]

An analysis was performed in VS (VL <200 c/mL) PWH who were enrolled in the longitudinal OPERA cohort and switched to BIC/FTC/TAF (unweighted, n=3512; weighted, n=3527) or

DTG/3TC (unweighted, n=2327; weighted, n=2213) between August 2020 and June 2022. Outcomes included treatment DC (defined as any ART change or a treatment gap >45 days) and CVF (defined as 2 consecutive VLs ≥200 c/mL or ≥1 VL 200 c/mL and treatment DC).

In the unweighted population, after a median (IQR) follow-up of 16 (11–22) months in the BIC/FTC/TAF group and 15 (10–21) months in the DTG/3TC group, there were no significant differences in VF between groups at VL thresholds of ≥200 c/mL (main analysis) and ≥50 c/mL (sensitivity analysis; Table 3).

Table 3. OPERA IPTW Cohort: Risk of VF With VL ≥200 c/mL and VL ≥50 c/mL[8]

Treatment Group	VF Threshold	VF, n (%)	VF Criteria	IR (95% CI) per 100 PY	aHR[a] (95% CI)
BIC/FTC/TAF	VL ≥200 c/mL	84 (2)	2 × VL ≥200 c/mL: 71% 1 × VL ≥200 c/mL + DC: 29%	1.7 (1.4–2.2)	0.84 (0.59–1.18)
DTG/3TC		59 (3)	2 × VL ≥200 c/mL: 56% 1 × VL ≥200 c/mL + DC: 44%	2.1 (1.6–2.7)	
BIC/FTC/TAF	VL ≥50 c/mL	310 (9)	2 × VL ≥50 c/mL: 81% 1 × VL ≥50 c/mL + DC: 19%	6.7 (6–7.4)	1.04 (0.86–1.26)
DTG/3TC		179 (8)	2 × VL ≥50 c/mL: 67% 1 × VL ≥50 c/mL + DC: 33%	6.4 (5.5–7.4)	

[a]Adjusted for Black race, payer, CD4 cell count, and eGFR level.

Treatment with DTG/3TC was associated with a greater risk of regimen DC than treatment with BIC/FTC/TAF (Table 4). Reasons for treatment-related DCs in the BIC/FTC/TAF and DTG/3TC groups were as follows: last VL ≥200 c/mL, 3% vs 5%; adverse diagnosis or side effect, 3% vs 4%; lab abnormality, ≤1% for each. DC of DTG/3TC occurred significantly earlier than DC of BIC/FTC/TAF, and more patients switched to long-acting ART from prior DTG/3TC than from BIC/FTC/TAF.

Table 4. OPERA IPTW Cohort: Risk of ARV DC[8]

Treatment Group	DCs, n (%)	IR (95% CI) per 100 PY	aHR[a] (95% CI)
BIC/FTC/TAF	599 (17)	12.4 (11.4–13.4)	0.83 (0.73–0.94)
DTG/3TC	425 (19)	14.8 (13.4–16.3)	

[a]Adjusted for Black race, payer, CD4 cell count, and eGFR level.

Retrospective Cohort Study (DRAGON)[9]

A retrospective, multicenter, observational cohort study was conducted to assess factors associated with weight gain after switching to BIC/FTC/TAF or DTG/3TC (each, n=1227) among ARV-naive (BIC/FTC/TAF, n=283; DTG/3TC, n=98) or treatment-experienced and VS (BIC/FTC/TAF, n=944; DTG/3TC, n=1129) PWH of Asian origin. The primary endpoints were the absolute weight change and the proportion of patients with >10% weight increase. Secondary endpoints included the proportion of patients with VL <50 c/mL and <200 c/mL by FDA Snapshot analysis at Week 48. At baseline, there was no significant difference between groups in mean weight (P=0.07).

From baseline to Week 48, there were no significant differences between groups in absolute weight change or in the proportion of patients with >10% weight increase among ARV-naive patients; however, there were significant differences between groups among VS patients (Table 5). A total of 168 patients (6.8%) had a ≥10% weight increase. Per a logistic regression analysis, risk factors associated with ≥10% weight increase were the following: ARV-naive status, baseline CD4 count >500 cells/mcL, TDF or TAF use prior to switching to

BIC/FTC/TAF, previous EFV use, and previous boosted protease inhibitor use (each, *P*≤0.01).

Table 5. DRAGON Study: Mean Absolute Weight Change and the Proportion of Patients With >10% Weight Increase From Baseline to Week 48[9]

	Weight Change	BIC/FTC/TAF	DTG/3TC	Difference (95% CI); *P*-Value
ARV-naive	Absolute,[a] kg	+3.2	+3.8	0.6 (-1.5 to +2.7); NS
	>10% increase, %	18.6	23.9	NS
VS	Absolute,[b] kg	+2.4	+1	-1.4 (-2 to -0.8); *P*<0.001
	>10% increase, %	13.8	7	*P*<0.001

Abbreviation: NS=nonsignificant.
[a]BIC/FTC/TAF, n=221; DTG/3TC, n=46.
[b]BIC/FTC/TAF, n=558; DTG/3TC, n=559.
Note: CIs were not reported for the proportion of patients with >10% weight increase.

At Week 48, DTG/3TC was noninferior to BIC/FTC/TAF in achieving or maintaining virological suppression (Table 6).

Table 6. DRAGON Study: Effectiveness of BIC/FTC/TAF and DTG/3TC at Week 48[9]

	Week 48 VL, c/mL	BIC/FTC/TAF, %	DTG/3TC, %	Adjusted Difference[a] (95% CI)
ARV-naive	<50	92.6	87.8	-4.8 (-11.96 to +2.4)
	<200	97.9	98	0.1 (-3.1 to +3.3)
VS	<50	98	96.5	-1.5 (-2.9 to -0.1)
	<200	99.3	98.1	-1.2 (-2.2 to -0.2)

[a]The noninferiority margin for the adjusted difference was -12% for ARV-naive patients with VL <50 c/mL and -5% in VS patients with VL <200 c/mL.

Retrospective, Real-World Study in Spain[10]

A retrospective, single-center study conducted between April 2019 and November 2022 in PWH who were VS (VL <50 c/mL) for ≥6 months before study inclusion and were switched to BIC/FTC/TAF (n=332) or DTG/3TC (n=358) was performed to compare rates of treatment DC and safety and efficacy outcomes.

The IRs of treatment DC after switching were similar between the BIC/FTC/TAF and DTG/3TC groups, and the risk of DC was not significantly different between groups (Table 7). Reasons for treatment DC in the BIC/FTC/TAF and DTG/3TC groups included loss to follow-up (10.5% vs 5%), AEs (2.1% vs 1.9%), death (2.1% vs 1.1%), and drug-drug interaction (0.6% vs 0). AEs that resulted in treatment DC in the BIC/FTC/TAF group were weight gain (n=4), dyslipidemia (n=2), and arthralgia (n=1); AEs that resulted in treatment DC in the DTG/3TC group were anxiety and/or insomnia (n=3), subjective lipoatrophy (n=1), cavum cancer and difficulty swallowing the pill (n=1), abdominal pain (n=1), and weight gain (n=1). No differences in weight gain were observed between groups.

Table 7. Retrospective Study in Spain: Risk of Treatment DC[10]

Treatment Group	DCs, n (%)	IR (95% CI) per 100 PY	HR (95% CI)	aHR[a] (95% CI)
BIC/FTC/TAF (n=332)	51 (15.4)	6.25 (4.7–7.89)	1.28 (0.81–2.02); *P*=0.297	1.2 (0.71–2) *P*=0.494
DTG/3TC (n=358)	31 (8.7)	4.44 (3.5–5.3)		

[a]Adjusted for a number of factors, including age, gender, place of birth, risk behaviors for acquisition of HIV, and comorbidities, via a Cox regression analysis.

In the BIC/FTC/TAF and DTG/3TC groups, similar percentages of patients had virological suppression (VL <50 c/mL; 96.1% vs 96.4%), low-level viremia (VL 51–500 c/mL; 3% vs

2.5%), and VF (VL >200 c/mL; 0.9% vs 1.1%). All cases of VF were associated with poor adherence. No resistance mutations were observed among the BIC/FTC/TAF-treated patients with VF, and all continued the same treatment.

Multicenter, Prospective Cohort Study in ARV-Naive PWH[11]

A study was conducted using data from CoRIS, a prospective multicenter cohort, to evaluate changes in weight and laboratory markers and the incidence of metabolism-related clinical events (ie, DM, HTN, and use of lipid-lowering drugs) in ARV-naive participants who received BIC/FTC/TAF or DTG/3TC for 96 weeks (N=680). Participants were PS matched by age, sex, race, baseline VL, CD4 nadir count, transmission group, use of weight-modifying treatments (eg, antidiabetics, psychotropics, or steroids), and tobacco use.

At 96 weeks, there were no significant differences between groups in weight, BMI, lipid measures, or HSI scores (Table 8).

Table 8. Mean Change From Baseline to Week 96 in Weight and Lipids (Garcia-Ruiz de Morales et al)[11]

Parameter, Mean (95% CI)	BIC/FTC/TAF (n=340)	DTG/3TC (n=340)	*P*-Value
Weight, kg	1.37 (0.93–1.82)	1.48 (0.9–2.07)	0.774
BMI, kg/m^2	0.62 (0.41–0.82)	0.5 (0.28–0.73)	0.472
TC, mg/dL	11.6 (8.4–14.8)	9.6 (6.4–12.8)	0.377
HDL, mg/dL	3.7 (2.7–4.6)	3.6 (2.5–4.6)	0.907
LDL, mg/dL	6.4 (3.7–9.1)	5.4 (2–8.7)	0.649
TG, mg/dL	8 (-0.4 to +16.4)	3.3 (-5.2 to +11.8)	0.438
Cholesterol ratio	-0.08 (-0.21 to +0.05)	-0.06 (-0.17 to +0.04)	0.823
HSI	0.18 (-0.25 to +0.6)	0.17 (-0.27 to +0.62)	0.992

There were no significant differences between groups in the incidence of metabolic events through 96 weeks of treatment (Table 9).

Table 9. Incidence of Metabolic Events at 96 Weeks of Treatment (Garcia-Ruiz de Morales et al)[11]

Parameter, n (%)	BIC/FTC/TAF (n=340)	DTG/3TC (n=340)	OR (95% CI)	*P*-Value
Dyslipidemia	35 (10.3)	38 (11.2)	1.1 (0.67–1.78)	0.71
NAFLD	23 (6.8)	21 (6.2)	0.91 (0.49–1.67)	0.755
Overweight	22 (6.5)	28 (8.2)	1.3 (0.73–2.32)	0.379
HTN	11 (3.2)	12 (3.5)	1.09 (0.48–2.52)	0.832
Obesity	3 (0.88)	6 (1.8)	2.02 (0.5–8.14)	0.324
DM	1 (0.3)	2 (0.6)	2.01 (0.18–22.23)	0.571

Retrospective Cohort Study: Inflammatory Signatures[12]

An analysis of the effects of BIC/FTC/TAF vs DTG/3TC on inflammatory signatures in ARV-naive participants within the CoRIS cohort was conducted. Eligible participants (eg, those with plasma samples from before ART initiation and after 24±6 months) were PS matched (1:1), with age, sex, baseline CD4/CD8 ratio, and baseline VL as covariates. After PS-matching (174 participants were PS matched) and sample quality control, data were analyzed for 148 participants. At baseline, 11 proteins were overexpressed among participants in the BIC/FTC/TAF group vs the DTG/3TC group. After 2 years of treatment, the signals noted at baseline in the BIC/FTC/TAF group were undetectable, and in both

groups, the expression of some inflammatory proteins, including those associated with pathogen response (ie, CXCL9, CXCL11, and CD6), was reduced.

Retrospective, Real-World Study in Italy[13]

A retrospective analysis of VS PWH who were switched to BIC/FTC/TAF (n=126) or DTG + 3TC (n=350) was performed to evaluate time to treatment DC at an Italian medical center. At Week 24, there were 15 treatment DCs in the DTG + 3TC group (rate: 8.8 per 100 PY of follow-up): gastrointestinal toxicity (n=5), neuropsychiatric events (n=3), other toxicity (n=4), and other/unknown reasons (n=3). There were 6 treatment DCs in the BIC/FTC/TAF group (rate: 12.5 per 100 PY of follow-up): gastrointestinal toxicity (n=2), neuropsychiatric events (n=2), and other/unknown reasons (n=2). There was no significant difference between the two groups in the estimated probability of maintaining the study regimen after 24 weeks.

There was a significant decrease in LDL cholesterol after 24 weeks in the BIC/FTC/TAF group (median change: -13 mg/dL; P=0.026), whereas patients in the DTG + 3TC group experienced a significant decrease in TG (-14 mg/dL; P<0.001) and a significant increase in HDL cholesterol (+3 mg/dL; P=0.031). No cases of VF (≥2 consecutive VLs >50 c/mL) were observed in either group.

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Abbreviations

3TC=lamivudine
ABC=abacavir
AE=adverse event
aHR=adjusted hazard ratio
ART=antiretroviral therapy
ARV=antiretroviral
BIC=bictegravir
c/mL=copies per mL
CD=clusters of differentiation
CVF=confirmed virologic failure
CKD-EPI=Chronic Kidney Disease Epidemiology Collaboration
COBI=cobicistat
DC=discontinuation
DM=diabetes mellitus
DRAE=drug-related adverse event
DRV/c=darunavir/cobicistat
DTG=dolutegravir
EFV=efavirenz
FTC=emtricitabine
HIV-SI=HIV Symptom Index Distress Module
HIVTSQ/c=HIV Treatment Satisfaction Questionnaire/ Change Version
HOMA-IR=Homeostatic Model Assessment for Insulin Resistance
HSI=hepatic steatosis index
HTN=hypertension
IL-6=interleukin-6
INSTI=integrase strand transfer inhibitor
IPTW=inverse probability of treatment weighting
IR=incidence rate
ITT-E=intent-to-treat exposed
NAFLD=nonalcoholic fatty liver disease
NRTI=nucleos(t)ide reverse transcriptase inhibitor
OPERA=Observational Pharmaco-Epidemiology Research and Analysis
OR=odds ratio
PS=propensity score
PWH=people with HIV
PY=patient-years
TAF=tenofovir alafenamide
TAM=thymidine analog mutation
TC=total cholesterol
TDF=tenofovir disoproxil fumarate
TG=triglycerides
VF=virologic failure
VL=viral load
VS=virologically suppressed

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