GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Efficacy and Safety in Virologically Suppressed Adults with HIV-1

This document discusses data from Gilead studies for the use of Biktarvy® (bictegravir/emtricitabine/ tenofovir alafenamide [BIC/FTC/TAF]) in virologically suppressed adults with HIV-1 infection.

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The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi

Summary

Product Labeling[1]

BIC/FTC/TAF is indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥14 kg:

- with no ARV treatment history or
- with an antiretroviral treatment history and not virologically suppressed, with no known or suspected substitutions associated with resistance to the integrase strand inhibitor class, emtricitabine, or tenofovir, or
- to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA <50 c/mL) on a stable ARV regimen with no known or suspected substitutions associated with resistance to BIC or tenofovir.

Gilead Studies

In virologically suppressed adults infected with HIV-1, switching to BIC/FTC/TAF demonstrated high rates of efficacy compared with staying on the following baseline regimens:

- Boosted DRV or ATV + 2 NRTIs through Week 140[2,3]
- DTG + ABC/3TC or DTG/ABC/3TC through Week 168[4,5]
- E/C/F/(TAF or TDF) or ATV+RTV+FTC/TDF at Weeks 48 and 96[6,7]
- DTG + FTC/(TAF or TDF) at Week 48[8]
- 2 NRTIs plus a third agent through Week 72[9]

In a real-world cohort from the BICSTaR study, 97% of TN participants and 95% of TE participants taking BIC/FTC/TAF were virologically suppressed at Month 24 using a missing=excluded analysis.[10]

There was no treatment-emergent resistance in Phase 3 clinicals trials of participants treated with BIC/FTC/TAF.[2,4,6,7,11,12]

BIC/FTC/TAF was well tolerated.[2-4,6,7,11] The most common drug-related AEs for the BIC/FTC/TAF arm in any study included headache, flatulence, and nausea.[2,4,6,7,11]

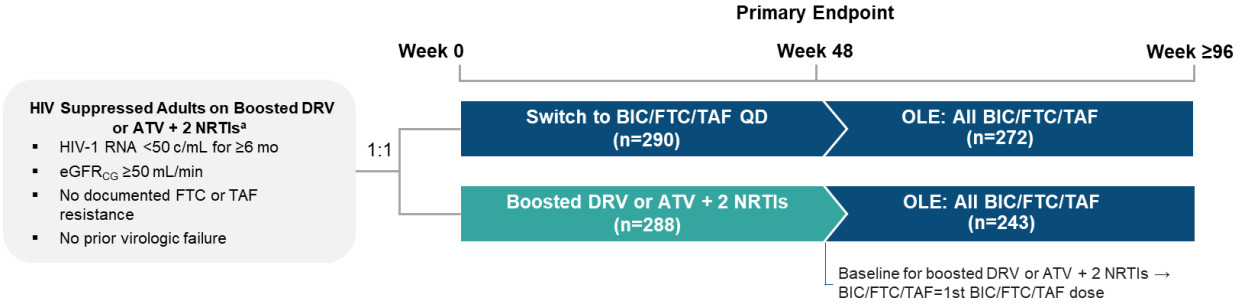
Gilead Studies

Study GS-US-380-1878

Study design and demographics[2]

A phase 3, prospective, randomized, open-label clinical trial that compared switching to BIC/FTC/TAF 50/200/25 mg single tablet regimen (n=290) vs staying on a baseline regimen of boosted DRV or ATV + 2 NRTIs (n=287) in virologically suppressed adults infected with HIV-1 (Figure 1). Key inclusion criteria were HIV-1 RNA <50 c/mL at screening for ≥6 months, $eGFR_{CG}$ ≥50 mL/min, and no documented or suspected resistance to NRTI components of study drugs. The primary endpoint was the proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 by FDA Snapshot analysis with a pre-specified non-inferiority margin of 4%. Secondary endpoint was the proportion of participants with plasma HIV-1 RNA <50 c/mL at Week 48. Baseline demographics and disease characteristics are presented below (Table 1).

Figure 1. Study Design (Study 1878)[3,13]



[a]Suppressed on regimen for ≥6 months; NRTIs included: abacavir/lamivudine (ABC/3TC) or emtricitabine/tenofovir disoproxil fumarate (FTC/TDF), ritonavir or cobicistat boosted.

Table 1. Baseline Demographics and Disease Characteristics (Study 1878)[2]

	BIC/FTC/TAF (n=290)	Boosted DRV or ATV + 2 NRTIs (n=287)
Age, median years (range)	48 (20–74)	47 (21–79)
Male, %	84	82
Race/ethnicity, %		
White	65	66
Black or African descent	27	25
Hispanic/Latino ethnicity	21	16
Median CD4 cell count, cells/µL	617	626
HBV co-infection/HCV co-infection, n	8 / 5	6 / 5
Median $eGFR_{CG}$, mL/min	107	105

	BIC/FTC/TAF (n=290)	Boosted DRV or ATV + 2 NRTIs (n=287)
Screening ARVs by NRTIs and PIs, %		
FTC/TDF / ABC/3TC	84 / 15	84 / 15
DRV / ATV	56 / 43	53 / 46

Results through Week 48

Efficacy[2]

Switching to BIC/FTC/TAF demonstrated non-inferior efficacy (HIV-1 RNA ≥50 c/mL) by the FDA Snapshot analysis vs staying on a baseline regimen of boosted DRV or ATV + 2 NRTIs at the Week 48 (primary endpoint) (2% vs 2%, respectively; difference, 0%; 95% CI: -2.5% to 2.5%; *P*=1.00). Switching to BIC/FTC/TAF also demonstrated non-inferior efficacy vs staying on a baseline regimen of boosted DRV or ATV + 2 NRTIs based on the secondary endpoint of the proportion of participants with HIV-1 RNA <50 c/mL at Week 48 (92% vs 89%, respectively; difference 3.2%; 95% CI: -1.6% to 8.2%; *P*=0.20). Five participants in the BIC/FTC/TAF group had HIV-1 RNA ≥50 c/mL: 2 participants with HIV-1 RNA ≥50 c/mL in the Week 48 window, 1 participant who discontinued treatment before Week 48 due to lack of efficacy, and 2 participants who discontinued treatment before Week 48 due to other reasons (ex: investigator or participant decision, loss to follow-up, non-compliance with study drug, protocol violation, pregnancy, study termination by sponsor) with last available HIV-1 RNA ≥50 c/mL.

The mean change from baseline in CD4+ count at Week 48 was +25 cells/mm^3 in participants who switched to BIC/FTC/TAF and +0 cells/mm^3 in participants who stayed on their baseline regimen of boosted DRV or ATV + 2 NRTIs.

Resistance

Eight participants met the protocol-defined criteria for resistance testing. Of these, ½ participants from the BIC/FTC/TAF arm and 2/6 participants from the boosted PI arm resuppressed to HIV-1 RNA <50 c/mL without a change in regimen.[13] No treatment-emergent resistance was detected in participants taking BIC/FTC/TAF. One participant who remained on their baseline regimen of ABC/3TC + RTV-boosted DRV experienced virologic failure with a treatment-emergent L74V mutation in reverse transcriptase at Week 24.[2] This mutation is associated with reduced susceptibility to ABC.[14]

Safety

Both regimens were well-tolerated. AEs occurring in ≥5% of participants (all grades) in either the BIC/FTC/TAF or boosted DRV or ATV + 2 NRTIs arms, respectively, were: headache (12% vs 4%), diarrhea (8% vs 6%), nasopharyngitis (7% vs 12%), URTI (7% vs 8%), back pain (4% vs 6%), and arthralgia (4% vs 5%). The most common drug-related AEs (≥2%) for BIC/FTC/TAF were headache (5%), flatulence (2%), and nausea (2%).[15] There were no discontinuations of BIC/FTC/TAF due to headache. The initial onset of headache occurred primarily within the first 8 weeks of switching to BIC/FTC/TAF and most were mild (Grade 1) in severity. By Week 48, the prevalence of headache decreased to 2% in the BIC/FTC/TAF arm vs 1% with boosted DRV or ATV + 2 NRTIs.[2]

There were 2 discontinuations due to AEs from BIC/FTC/TAF (rash [1], which was not considered related to study drug, and schizophrenia [1]) and 1 discontinuation in participants who stayed on their baseline regimen (acetabular fracture and acute kidney

injury). Two deaths occurred during the study (1 in each arm) and neither was considered related to study drug.[2]

There were no discontinuations due to renal AEs and no cases of proximal renal tubulopathy or Fanconi syndrome in participants on BIC/FTC/TAF.[15]

Grade 3 or 4 laboratory abnormalities occurring in ≥2% of participants in either BIC/FTC/TAF or boosted DRV or ATV-containing regimen treatment arms, respectively, were LDL elevation (>190 mg/dL): 4% each arm; amylase elevation (>2 × ULN): 2% each arm; glycosuria (4+ on dipstick): 2% vs 1% (all in the setting of hyperglycemia);[15] ALT elevation (>5 × ULN): 2% vs 1%; total bilirubin (>2.5 × ULN): 1% vs 15%; TC (>300 mg/dL): 1% vs 2%; hematuria (>75 RBC/high power field): 2% vs 3%.[15,16]

Median changes from baseline in $eGFR_{CG}$ of -4.3 mL/min vs +0.2 mL/min were observed for participants who received BIC/FTC/TAF vs those who stayed on boosted DRV or ATV + 2 NRTIs, respectively (*P*=0.0005). Participants who switched the NRTI component of their regimen from TDF or ABC to TAF experienced decreases in renal biomarkers, or smaller increases in renal biomarkers vs those who remained on their baseline regimens (Table 2).

Table 2. Median % Changes from Baseline in Quantitative Proteinuria at Week 48 (Study 1878)[15,16]

	Baseline FTC/TDF-Containing Regimen			Baseline ABC/3TC-Containing Regimen		
	BIC/FTC/TAF (n=245)	Boosted DRV or ATV + 2 NRTIs (n=243)	*P*-Value[a]	BIC/FTC/TAF (n=45)	Boosted DRV or ATV + 2 NRTIs (n=44)	*P*-Value[a]
UACR, %	-2.1	+9.9	0.11	+4.2	+1.1	0.77
RBP:Cr, %	-17.7	+34.9	<0.0001	+5.4	+25.8	0.47
ß2M:Cr, %	-40.3	+31.6	<0.0001	-19.5	+7.3	0.21

[a]*P*-values from the 2-sided Wilcoxon rank sum test to compare the 2 treatment groups.

Switching to BIC/FTC/TAF was associated with small, significant decreases in TG and TC:HDL ratio (Table 3). At baseline, 16.2% of BIC/FTC/TAF participants and 15.7% of boosted DRV or ATV + 2 NRTIs participants were taking lipid-lowering agents (*P*=0.91). During the study, 3% of BIC/FTC/TAF and 3% of ATV + 2 NRTIs participants initiated lipid-lowering medications (*P*=0.64).[2]

Table 3. Change from Baseline in Fasting Lipid Parameters at Week 48 (Study 1878)[16]

	BIC/FTC/TAF		Boosted DRV or ATV + 2 NRTIs		*P*-Value[a]
	Baseline Values (n=283)	Median Change from Baseline[b]	Baseline Values (n=277)	Median Change from Baseline[b]	
TC, mg/dL	188	+1	183	+5	0.32
LDL, mg/dL	121	0	118	+3	0.47
HDL, mg/dL	47	+3	46	+1	0.13
TG, mg/dL	122	-6	121	+4	0.002
TC:HDL ratio	4.0	-0.2	3.8	0	0.033

[a]*P*-values from the 2-sided Wilcoxon rank sum test to compare the changes at Week 48 between the two treatment groups.
[b]Week 48 values were not available for all participants.

Extension phase results

The long-term efficacy and safety of BIC/FTC/TAF were evaluated in an OLE.[3,13] Of the 532 participants who completed the 48-week randomized phase, 515 entered the OLE phase. The all BIC/FTC/TAF group consisted of participants who received ≥1 dose of BIC/FTC/TAF; this was measured at the first dose of BIC/FTC/TAF in the OLE for participants who switched at Week 48.[13]

Efficacy

Median (Q1, Q3) duration of BIC/FTC/TAF exposure was 101 (72,120; maximum 181) weeks.[13] High rates (96-100%) of virologic suppression were maintained through 180 weeks in the all BIC/FTC/TAF group in a missing=excluded analysis;100% of participants (n=14) who remained in the study through Week 180 maintained HIV-1 RNA <50 c/mL.[13] CD4 cell counts remained stable throughout the OLE phase at Weeks 96 and 120.[3]

Resistance

No treatment-emergent resistance to BIC/FTC/TAF was detected throughout the randomized or OLE phases, and 98% of BIC/FTC/TAF participants (212/217) with any primary baseline resistance maintained HIV-1 RNA <50 c/mL at the last study visit.[13]

Safety

BIC/FTC/TAF was well tolerated, and no participant discontinued treatment due to renal or bone AEs during the OLE all BIC/FTC/TAF phase. Four AEs occurred that were considered related to BIC/FTC/TAF and led to study discontinuation (diarrhea and vomiting [n=1], rash and pruritis [n=1], insomnia [n=1], suicidal ideation [n=1]). Two additional serious AEs occurred during the OLE phase that were attributed to BIC/FTC/TAF (suicidal ideation in a participant with preexisting bipolar and borderline personality disorder [n=1], and deep vein thrombosis [n=1]).

Table 4. AEs and Grade 3 or 4 Laboratory Abnormalities that Occurred in ≥5% of Participants (Study 1878)[3]

AE and Grade 3 or 4 Laboratory Abnormalities	All BIC/FTC/TAF (N=534)
Nasopharyngitis, %	15
URTI, %	13
Headache, %	12
Diarrhea, %	10
Back pain, %	8
Syphilis, %	7
Lipase, %	7
Cough or influenza, %	6

The median change in $eGFR_{CG}$ 96 weeks after initiation of BIC/FTC/TAF was -3.4 mL/min. A median increase from baseline of 2.2 kg in body weight was observed.

Study GS-US-380-1844[4]

Study design and demographics

A phase 3, randomized, double-blind study evaluated the safety and efficacy of switching to BIC/FTC/TAF (n=282) vs staying on a baseline regimen of DTG + ABC/3TC or DTG/ABC/3TC single tablet regimen (n=281) in virologically suppressed adults infected with HIV-1 (Figure 2). Key inclusion criteria were HIV-1 RNA <50 c/mL at screening for ≥3 months with no history of treatment failure, $eGFR_{CG}$ ≥50 mL/min, and no documented or suspected resistance to study drugs. The primary endpoint was the proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 by the FDA Snapshot analysis with a pre-specified non-inferiority margin of 4%.[4] Secondary endpoints were the proportion of participants with plasma HIV-1 RNA <50 c/mL by the FDA Snapshot analysis, change from baseline in CD4+ count, and change from baseline in hip and spine BMD all at Week 48.[17] Baseline demographics and disease characteristics are presented below (Table 5).[4]

Figure 2. Open Label Extension Study Design (Study 1844)[4]

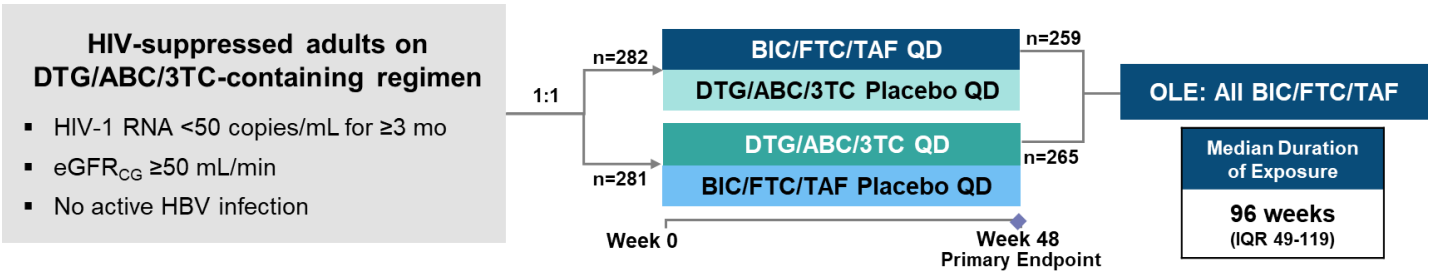


Table 5. Baseline Demographics and Disease Characteristics (Study 1844)[4]

	BIC/FTC/TAF (n=282)	DTG/ABC/3TC (n=281)
Age, median years (range)	47 (21–71)	45 (20–70)
Male, %	88	90
Race/ethnicity, %		
White	73	73
Black or African descent	21	22
Hispanic/Latino ethnicity	16	19
Median CD4 cell count, cells/µL	732	661
Median eGFRCG, mL/min	101	101

Results through Week 48

Efficacy[4]

Switching to BIC/FTC/TAF demonstrated non-inferior efficacy compared to staying on a baseline regimen of DTG/ABC/3TC by FDA Snapshot analysis at Week 48 (primary endpoint) (HIV-1 RNA ≥50 c/mL: 1% vs <1%, respectively; difference, 0.7%; 95% CI: -1.0% to 2.8%; *P*=0.62). Virologic suppression (HIV-1 RNA <50 c/mL) was maintained in 94% of participants switching to BIC/FTC/TAF vs 95% of participants staying on a baseline regimen of DTG/ABC/3TC (difference, -1.4%; 95% CI: -5.5% to 2.6%; *P*=0.59).

Three participants in the BIC/FTC/TAF group had HIV-1 RNA ≥50 c/mL, with 1 participant in each of the following categories: HIV-1 RNA ≥50 c/mL in the Week 48 window; treatment discontinued before Week 48 due to AE or death with last available HIV-1 RNA ≥50 c/mL; and treatment discontinued before Week 48 due to reasons other than lack of efficacy, AEs, or death (ex: investigator or participant decision, loss to follow-up, non-compliance with study drug, protocol violation, pregnancy, study termination by sponsor) with last available HIV-1 RNA ≥50 c/mL.

The mean change from baseline in CD4+ count at Week 48 was -31 cells/mm^3 in participants who switched to BIC/FTC/TAF and +4 cells/mm^3 in participants who stayed on DTG/ABC/3TC.

Resistance[4]

Five participants met protocol-defined criteria for resistance testing (3 BIC/FTC/TAF and 2 DTG/ABC/3TC). No treatment-emergent resistance was detected in participants in either treatment arm. Two participants (one in each arm) with possible intermittent adherence were virologically resuppressed (HIV-1 RNA <50 c/mL) without changing their regimen. Three participants (2 BIC/FTC/TAF and 1 DTG/ABC/3TC) discontinued the study early with HIV-1 RNA >200 c/mL.

Safety[4]

There was a significant difference in the number of all grade drug-related AEs between the two arms: 8% in the BIC/FTC/TAF arm and 16% in the DTG/ABC/3TC arm (*P*=0.006). The difference in incidence of drug-related AEs between the two arms was mainly a result of drug-related gastrointestinal AEs (ie, flatulence, nausea, and diarrhea) and neuropsychiatric (ie, abnormal dreams and insomnia) in the DTG/ABC/3TC arm (Table 6).

Table 6. Most Common Treatment-Related AEs (Study 1844)[4]

	BIC/FTC/TAF (n=282)	DTG/ABC/3TC (n=281)	*P*-Value
Headache, %	2	3	0.80
Diarrhea, %	1	1	0.45
Abnormal dreams, %	<1	2	0.12
Fatigue, %	<1	1	0.37
Flatulence, %	0	2	0.03
Nausea, %	0	2	0.03
Insomnia, %	0	1	0.12

AEs (due to any cause) that occurred in ≥5% of participants in the either the BIC/FTC/TAF or DTG/ABC/3TC arms, respectively, were: URTI (both 10%), nasopharyngitis (7% vs 8%), headache (both 7%), diarrhea (9% vs 5%), arthralgia (7% vs 4%), and insomnia (3% vs 5%). There were 6 discontinuations (2%) due to AEs in participants treated with BIC/FTC/TAF (headache [2], vomiting [1], cerebrovascular accident [1], abnormal dreams [1], and suicidal ideation [1, not considered related to study treatment by investigator]) and 2 discontinuations (1%) due to AEs in participants treated with DTG/ABC/3TC (headache [1], pruritus [1]). There were no discontinuations due to renal AEs and there were no cases of proximal renal tubulopathy or Fanconi syndrome in either arm.

Two deaths occurred during the study (both in the BIC/FTC/TAF arm), but neither were considered to be related to study drug.

Grade 3 or 4 laboratory abnormalities that occurred in ≥2% of participants in either BIC/FTC/TAF or DTG/ABC/3TC treatment arms, respectively, were LDL elevation: 5% each arm; amylase elevation: 2% vs 0%; ALT elevation: 2% vs 0%; CK elevation: 2% each arm; fasting hyperglycemia: 2% vs 1%; and glycosuria: 2% vs 1% (all in setting of hyperglycemia). Grade 3 and 4 ALT abnormalities were not deemed study-drug related, did not disrupt study drug administration, and were associated with the following AEs: acute HCV infection (n=3), acute hepatitis A virus infection (n=1), alcohol abuse (n=1), and non-alcoholic ateatohepatitis (n=1). All amylase elevations were not associated with pancreatitis, and 4/7 cases had normal lipase. There were no cases of rhabdomyolysis.[18]

There were small but statistically significant differences in the median change from baseline in $eGFR_{CG}$ between treatment groups: +1.0 mL/min for BIC/FTC/TAF vs -1.8 mL/min for DTG/ABC/3TC; *P*=0.0002. At Week 48, changes in renal biomarkers between treatment groups were similar (Table 7).

Table 7. Change from Baseline in Quantitative Proteinuria at Week 48 (Study 1844)[19]

	BIC/FTC/TAF (n=282)		DTG/ABC/3TC (n=281)		*P*-Value[a]
	Baseline Ratio	Median % Change from Baseline	Baseline Ratio	Median % Change from Baseline	
UACR, mg/g	5.6	+14.3%	5.4	+8.7%	0.74
RBP:Cr, µg/g	99.2	+19.6%	96.2	+29.1%	0.31
ß2M:Cr, µg/g	75	+20.9%	77.3	+16.5%	0.53

[a]From 2-sided Wilcoxon rank-sum test for % change from baseline at Week 48 for each marker for treatment comparison.

Changes from baseline in BMD were similar and did not differ significantly between treatment arms through Week 48. The mean percent change from baseline to Week 48 for BIC/FTC/TAF vs DTG/ABC/3TC for lumbar spine BMD was 0.69% vs 0.42% (*P*=0.33) and for hip BMD was 0.3% vs 0.16% (*P*=0.47), respectively. Switching to BIC/FTC/TAF was associated with similar changes in fasting lipid parameters compared to remaining on DTG/ABC/3TC except that there was a small, significant decrease in TGs in the BIC/FTC/TAF arm (Table 8). The percent of participants who initiated lipid-lowering medications during the study was BIC/FTC/TAF, 1%; DTG/ABC/3TC, 4% (*P*=0.033).

Table 8. Change from Baseline in Fasting Lipid Parameters at Week 48 (Study 1844)[19]

	BIC/FTC/TAF		DTG/ABC/3TC		*P*-Value[a]
	Baseline Values (n=279)	Median Change from Baseline[b]	Baseline Values (n=274)	Median Change from Baseline[b]	
TC, mg/dL	182	0	186	+2	0.77
LDL, mg/dL	113	+1	118[c]	+2	0.42
HDL, mg/dL	49	-1	48	0	0.13
TG, mg/dL	111	-5	111	+3	0.028
TC:HDL ratio	3.7	0	3.8	0	0.56

[a]*P*-values from 2-sided Wilcoxon rank-sum test.
[b]Week 48 values were not available for all participants.
[c]n=275 for baseline LDL in DTG/ABC/3TC arm.

Patient reported outcomes through Week 48[20,21]

Methods

Patient reported outcomes from the HIV-SI, PSQI, SF-36 PCS/MCS, and WPAI administered at baseline, Week 4, Week 12, and Week 48 further characterized treatment tolerability in studies 1489 and 1844. Treatment differences were assessed using logistic regression models (HIV-SI adjusted for age, sex, race, baseline HIV-SI count, baseline Veterans Aging Cohort Study Index, medical history of serious mental illness, baseline SF36 physical and mental scores, and years since HIV diagnosis; PSQI adjusted for baseline PSQI poor sleep quality and baseline SF-36 MCS). Longitudinal modeling was also performed to show the prevalence of bothersome symptoms and poor sleep quality over time using generalized mixed models that included treatment, time, time-by-treatment interaction, and covariates in the logistic regression model. Treatment differences were characterized by statistically significant differences in prevalence at two or more time points in the adjusted logistic regression model or at one time point in both the adjusted logistic regression and the longitudinal model.

Results

Switching to BIC/FTC/TAF was associated with a significantly lower prevalence of select patient-reported bothersome symptoms and poor sleep quality compared to remaining on DTG/ABC/3TC (Table 9). Hair loss/change at Week 4 was the only symptom that favored DTG/ABC/3TC, but there was no difference in the prevalence of hair loss/change between the 2 treatment arms from Week 4 to Week 48.

No treatment differences were noted between treatment arms using SF-36 PCS/MCS and WPAI tools.

Table 9. Patient Reported Symptoms after Switching to BIC/FTC/TAF vs DTG/ABC/3TC (Study 1844)[20,21]

Patient Reported Outcomes	Results[a]
HIV-SI Bothersome Symptom	
Dizzy/lightheadedness	Favors BIC/FTC/TAF
Sad/down/depressed	Favors BIC/FTC/TAF
Nervous/anxious	Favors BIC/FTC/TAF
Nausea/vomiting	Favors BIC/FTC/TAF
Loss of appetite	Favors BIC/FTC/TAF
Difficulty sleeping	Favors BIC/FTC/TAF
PSQI	
Poor Sleep Quality	Favors BIC/FTC/TAF

[a]Statistically significant (P<0.05) at ≥2 time points in adjusted logistic regression model, or at 1 time point in adjusted logistic regression model and longitudinal model.

Extension phase results[5]

The efficacy and safety of BIC/FTC/TAF through Week 168 were evaluated in an OLE. The all BIC/FTC/TAF group consisted of participants who received ≥1 dose of BIC/FTC/TAF; this was measured at the first dose of BIC/FTC/TAF in the OLE for participants who switched at Week 48.

Efficacy

HIV-1 RNA <50 c/mL was maintained in 99-100% of participants taking BIC/FTC/TAF at all measured time points, using a missing=excluded analysis, through 168 weeks. At Week 168, 14 participants in the BIC/FTC/TAF group were still in the study and 100% had HIV-1 RNA <50 c/mL.

Resistance

No emergent resistance to BIC/FTC/TAF was reported and 99% of BIC/FTC/TAF participants (159/161) with any primary baseline resistance mutation maintained HIV-1 RNA <50 c/mL.

Safety

There were no reports of proximal renal tubulopathy or study discontinuations due to renal AEs. Most fasting lipid levels remained stable in participants who received BIC/FTC/TAF in the randomized and OLE phases. Median LDL levels increased from Week 48 to Week 96 (+2 mg/dL to +12 mg/dL change from baseline, respectively) and 3% of participants began lipid-modifying agents during the study. The median weight change from baseline to Week 120 was +1.8 kg among all BIC/FTC/TAF participants.

Table 10. Safety Outcomes (Study 1844)[4]

	BIC/FTC/TAF (n=547)
Any AE, n (%)	446 (82)
Most common AE (≥5% of participants)	
URTI, %	14
Nasopharyngitis, %	10
Diarrhea, %	10
Arthralgia, %	6
Back pain, %	6
Headache, %	6
Sinusitis, %	6
Bronchitis, %	5
Syphilis, %	5
Any Grade 3 or 4 AE, n (%)	33 (6)
Any treatment-related AE,[a] n (%)	39 (7)
Any serious AE, n (%)	47 (9)
Any AE leading to study discontinuation,[b] n (%)	7 (1)
Death,[c] n (%)	3 (1)

[a]Most treatment-related AEs were Grade 1; headache was the most common (2%).
[b]In the OLE, 1 participant experienced a treatment-related headache that led to discontinuation.
[c]One treatment-emergent death occurred during the OLE (hypertensive cardiovascular disease in participant with medical history of hypertension and hypercholesteremia) and was not considered related to treatment. The other 2 deaths were previously reported (Week 48).

Additional Gilead Studies[7-9,22,23]

Additional Gilead clinical trials were conducted in the following populations of participants infected with HIV-1 who were virologically suppressed and switched to BIC/FTC/TAF: women, adults including those with baseline NRTI-R, and people identifying as African American or Black (Table 11). High rates of virologic suppression were maintained with no new safety signals. A 12 month follow up of participants in a real world cohort also showed high rates of virologic suppression using a missing=excluded analysis and a similar safety profile to what was found in Phase 3 clinical trials.

Table 11. Additional Gilead Studies in Virologically Suppressed Participants Switched to BIC/FTC/TAF[7-10,22]

Trial Number	Comparator Arm	Patient Population	Efficacy Endpoints	Safety Summary
GS-US-380-1961[7]	E/C/F/(TAF or TDF) or ATV + RTV + FTC/TDF	Virologically suppressed adult women (N=470)	Week 48: Switching to BIC/FTC/TAF demonstrated non-inferior efficacy by FDA Snapshot analysis. HIV-1 RNA ≥50 c/mL in BIC/FTC/TAF vs SBR (1.7% vs 1.7%, respectively; difference, 0%; 95% CI: -2.9% to 2.9%)	AEs occurring in ≥5% of participants (all grades) in either the BIC/FTC/TAF or baseline arms at Week 48: nasopharyngitis, urinary tract infection, URTI, headache, and vulvovaginal candidiasis.
GS-US-380-4030[8]	DTG + FTC/TAF or DTG + FTC/TDF	Virologically suppressed adults, including those with known BL resistance mutations (INSTI-R mutations excluded) (N=565)	Week 48: Switching to BIC/FTC/TAF demonstrated non-inferior efficacy by FDA Snapshot analysis. HIV-1 RNA ≥50 c/mL in BIC/FTC/TAF vs SBR (<1% vs 1%, respectively; difference, -0.7%; 95% CI: -2.8% to +1.0%). Rates of virologic suppression were high regardless of pre-existing NRTI-R.	AEs occurring in ≥5% of participants (all grades) in either the BIC/FTC/TAF or baseline arms at Week 48: nasopharyngitis, diarrhea, URTI, headache, arthralgia, influenza, fatigue, insomnia, back pain, bronchitis, cough.
GS-US-380-4580 (BRAAVE 2020)[9,22]	2 NRTIs + third agent[a]	Virologically suppressed adults self-identifying as African American, Black, or mixed race, including Black (N=495)	Week 24: Switching to BIC/FTC/TAF demonstrated non-inferior efficacy by FDA Snapshot analysis. HIV-1 RNA ≥50 c/mL in BIC/FTC/TAF vs SBR (difference, -1.2%; 95% CI: -4.8% to 0.9%).	AEs occurring in ≥5% of participants (all grades) in either the BIC/FTC/TAF or baseline arms at Week 24: URTI.
BICSTaR Study[10]	Single-arm, observational study	Real world cohort of ARV naïve and virologically suppressed participants with HIV (N=838)	Month 24: During treatment with BIC/FTC/TAF, 97% of TN participants (104/107) and 95% of TE participants (497/521) were virologically suppressed (HIV-1 RNA <50 c/mL) using a missing=excluded analysis.	Drug-related AEs occurring in ≥1% of participants receiving BIC/FTC/TAF at 24 months: weight increased, depression, nausea, diarrhea, fatigue.

[a]The allowed third agents included any INSTI except BIC, any PI, maraviroc, or any NNRTI except etravirine.
Abbreviations: SBR=staying on baseline regimen; BL=baseline

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Abbreviations

3TC=lamivudine
ABC=abacavir
AE=adverse event
ARV=antiretroviral
ART=antiretroviral therapy
ATV=atazanavir
ß2M=beta-2-microglobulin
BIC=bictegravir
c/mL=copies/mL
CK=creatinine kinase
DRV=darunavir
DTG=dolutegravir
E/C/F/(TAF or TDF)=elvitegravir/cobicistat/emtricitabine/(tenofovir alafenamide or tenofovir disoproxil fumarate)
eGFRCG=estimated glomerular filtration rate by Cockcroft-Gault
FTC=emtricitabine
HIV-SI=HIV Symptom Index
IN=integrase
INSTI-R=integrase strand transfer inhibitor resistance
MCS=Mental Component Summary
NNRTI=non-nucleoside reverse transcriptase inhibitor
NRTI-R=nucleoside reverse transcriptase inhibitor resistance
OLE=open- label extension
PCS=Physical Component Summary
PI=protease inhibitor
PR=protease
PSQI=Pittsburgh Sleep Quality Index
RBP=retinol-binding protein
RTV=ritonavir
SF-36=36-Item Short Form Health Survey
TAF=tenofovir alafenamide
TC=total cholesterol
TDF=tenofovir disoproxil fumarate
TE=treatment- experienced
TG=triglycerides
TN=treatment-naïve
UACR=urine albumin to creatinine ratio
ULN=upper limit of normal
URTI=upper respiratory tract infection
WPAI=Work Productivity and Activity Impairment

Product Label

For the full indication, important safety information, and Boxed Warning(s), please refer to the Biktarvy US Prescribing Information available at:
www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi

Follow-Up

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