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Biktarvy® (BIC/FTC/TAF) Use in Black Americans

This document presents available data regarding Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in participants who identify as African American or Black.

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Summary

Clinical Data

In the BRAAVE study, which enrolled virologically suppressed (HIV-1 RNA <50 c/mL) participants who self-identified as African American or Black, switching to BIC/FTC/TAF was noninferior to continuing the baseline regimen of 2 NRTIs plus a third agent at the Week 24 primary endpoint.[1] High rates of virologic suppression were maintained after switching to BIC/FTC/TAF through the Week 48 secondary endpoint and Week 72 of the extension phase, regardless of pre-existing resistance.[2-6] The AEs reported through Week 24 were comparable between participants who switched to BIC/FTC/TAF and those who continued their baseline regimen.[2] Through Week 72, AEs leading to discontinuation were reported in 2.4% of all participants (12 of 493) who switched to BIC/FTC/TAF.[4]

A post-hoc pooled analysis of two Phase 3 studies in treatment-naïve PWH assessed the efficacy and safety of first-line therapy with BIC/FTC/TAF in Black participants over a 5-year period. Virologic suppression rates with BIC/FTC/TAF were high in Black and non-Black participants through Week 240 and no treatment-emergent resistance to BIC/FTC/TAF was reported in either group. Through Week 240, rates of discontinuation due to AEs were low in both groups. The proportion of Black participants who experienced study drug-related AEs was smaller than non-Black participants (20% vs 32%, respectively).[7]

Clinical Studies: Use in Black American PWH

BRAAVE 2020

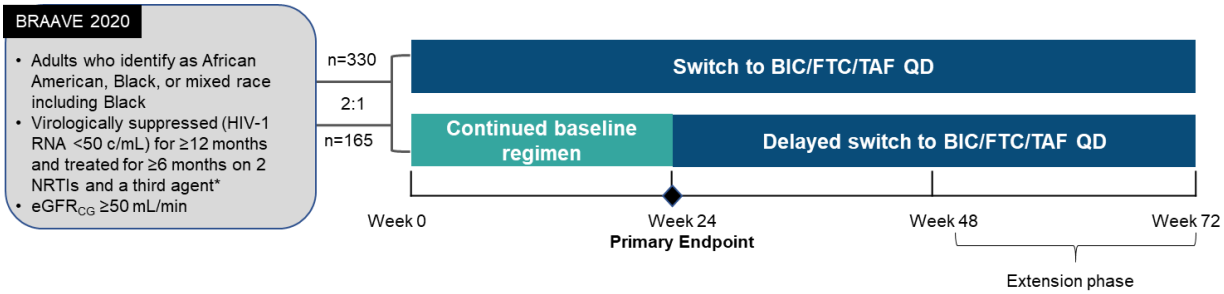
Study Design and Demographics

BRAAVE 2020 was a phase 3b, randomized, open-label, active-controlled study, which evaluated the efficacy and safety of switching to BIC/FTC/TAF or continuing with the baseline regimen of 2 NRTIs plus a third agent in virologically suppressed (HIV-1 RNA

<50 c/mL) PWH who self-identified as African American, Black, or mixed race that included Black (Figure 1). Participants with resistance to NNRTIs or PIs and those with select NRTI resistance substitutions (except for K65R/E/N, T69 insertions, or ≥3 TAMs) were included; participants with primary INSTI resistance were excluded.[1] Participants with pre-existing exclusionary resistance detected after enrollment were permitted to continue in the study. Resistance testing was performed for any participant with HIV-1 RNA ≥200 c/mL at Week 24, 48, 72, last visit, or at the visit following confirmed virologic failure (2 consecutive HIV-1 RNA ≥50 c/mL), with no resuppression of HIV-1 RNA to <50 c/mL while on study drug.[6]

The primary efficacy endpoint was the proportion of participants with HIV-1 RNA ≥50 c/mL at Week 24 by FDA Snapshot Analysis. Secondary efficacy endpoints included the proportion of participants with HIV-1 RNA ≥50 c/mL at Week 48, the proportion of participants with HIV-1 RNA <50 c/mL at Weeks 24 and 48, and the change from baseline in CD4 count at Weeks 24 and 48.[1]

Figure 1. BRAAVE 2020: Study Design[1,2]



*The allowed third agents included any INSTI except BIC, any PI, maraviroc, or any NNRTI except etravirine.

Table 1. BRAAVE 2020: Baseline Demographics and Disease Characteristics[1,8]

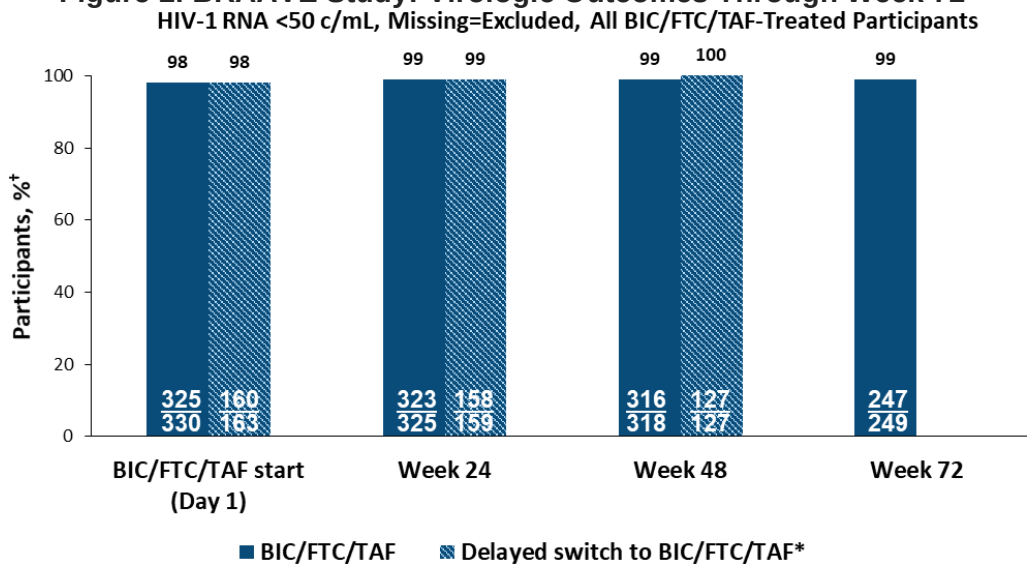
Key Demographics and Characteristics	BIC/FTC/TAF (n=330)	Continued Baseline Regimen (n=165)
Age, median (range), years	49 (18–79)	49 (19–70)
Female sex at birth, %	31	33
HBV coinfection, n	15	3
Body weight, median (Q1, Q3), kg	88 (79, 103)	89 (76, 104)
CD4 count, median (Q1, Q3), cells/μL	747 (570, 922)	758 (494, 969)
$eGFR_{CG}$, median (Q1, Q3), mL/min	110 (88, 132)	107 (86, 132)
Baseline NRTI backbone		
FTC/TAF, %	68	65
FTC/TDF, %	17	21
ABC/3TC, %	13	15
Baseline third agent		
EVG/c, %	38	35
DTG, %	20	24
RPV, %	19	16
EFV, %	10	13
DRV/c or DRV/r, %	5	7
Other, %	8	5

Abbreviations: 3TC=lamivudine; DRV/c=darunavir boosted with cobicistat; DRV/r=darunavir boosted with ritonavir; DTG=dolutegravir; EFV=efavirenz; EVG/c=elvitegravir boosted with cobicistat.

Efficacy Results Through Week 72

Switching to BIC/FTC/TAF was noninferior to continuing the baseline regimen of 2 NRTIs plus a third agent by FDA Snapshot Analysis at the Week 24 primary endpoint. At Week 24, 2/328 (0.6%) participants who switched to BIC/FTC/TAF and 3/165 (1.8%) participants who continued the baseline regimen had HIV-1 RNA ≥50 c/mL (difference, -1.2%; 95% CI: -4.8% to 0.9%). Two participants in the BIC/FTC/TAF group were found to have baseline INSTI resistance and excluded from the primary analyses for this protocol violation. At Week 48, 3 participants initially randomized to BIC/FTC/TAF had HIV-1 RNA ≥50 c/mL. Among the 163 participants who switched from their baseline regimen to BIC/FTC/TAF at Week 24, none had HIV-1 RNA ≥50 c/mL at Week 48. High rates of virologic suppression were maintained through Week 72 in BIC/FTC/TAF and delayed-switch groups (Figure 2).[1]

Figure 2. BRAAVE Study: Virologic Outcomes Through Week 72[5]



*Delayed-switch-to-BIC/FTC/TAF participants were switched at study Week 24, which corresponds to Day 1 in hatched bars.

†Denominator for percentage is number of BIC/FTC/TAF-treated participants with no missing HIV-1 RNA value at any visit.

No significant difference was observed in the mean change in CD4 count levels from baseline to Week 24 between participants who switched to BIC/FTC/TAF (+13 cells/µL) and those who continued their baseline regimen (1 cells/µL; *P*=0.56). The mean change in CD4 count levels from baseline to Week 48 in the BIC/FTC/TAF and delayed-switch groups was +7 cells/µL and -8 cells/µL, respectively.[9]

Safety Results Through Week 72

The AEs reported through Week 24 were comparable between participants who switched to BIC/FTC/TAF and those who continued their baseline regimen (Table 2).[1,2] AEs that led to study discontinuation were reported in 7 participants who switched to BIC/FTC/TAF and in none of the participants who continued with the baseline regimen through Week 24.[1] In a cumulative analysis of safety for all 493 participants who received BIC/FTC/TAF through Week 72, 12 participants discontinued due to AEs overall.[4]

Table 2. BRAAVE Study: Summary of Safety Results through Week 72[1,4]

Safety Outcomes	Week 24		Through Week 72
	BIC/FTC/TAF (n=330)	Continued Baseline Regimen (n=165)	All BIC/FTC/TAF* (n=493)
AEs (all grades)	≥3% of participants in either group		≥5% of participants
Upper respiratory tract infection, %	6	4	9
Cough, %	3	4	–
Diarrhea, %	3	3	–
Arthralgia, %	3	1	5
Headache, %	3	<1	6
Bronchitis, %	2	4	–
Syphilis, %	–	–	6
Nasopharyngitis, %	–	–	5
Hypertension, %	–	–	5
Pain in extremity, %	–	–	6
Grade 3 or 4 AE, %	5	5	–
Serious AE, %	4	4	–
Treatment-related AE, %	11	–	–
Laboratory abnormalities (Grade 3 or 4)	≥2% of participants in either group		≥2% of participants
Glycosuria,† %	3	<1	5
Nonfasting hyperglycemia,† %	2	1	4
Fasting LDL increased, %	–	–	3
Urine RBC‡ (hematuria: quantitative or dipstick), %	–	–	3
AEs that led to discontinuation of study drug, n	7	0	12

*All participants treated with BIC/FTC/TAF including those in the delayed-switch group.
†Reported in the setting of hyperglycemia
‡Reported in women during menses.

Median change from baseline in fasting lipid parameters were numerically similar between participants taking BIC/FTC/TAF through Week 72 and those with delayed switch to BIC/FTC/TAF at Week 48 (Table 3). Through Week 72, lipid-lowering agents were started in 6% of participants who initially switched to BIC/FTC/TAF and in 4% of participants in the delayed-switch group.[4]

Table 3. BRAAVE 2020: Changes in Fasting Lipid Parameters through Week 72[1,4]

	BIC/FTC/TAF Week 72 (N=330)		Delayed Switch to BIC/FTC/TAF Week 48 (N=163)	
	Baseline Values	Median Change from Baseline	Baseline Values	Median Change from Baseline
TC, mg/dL	181	-3	169	+1
LDL, mg/dL	111	-9	102	-4
HDL, mg/dL	54	-3	53	-2
Triglycerides, mg/dL	98	-3	95	-3
TC:HDL ratio	3.3	+0.1	3.1	+0.1

The median weight change from baseline to Week 24 was similar between participants who switched to BIC/FTC/TAF (+0.9 kg) and those who continued their baseline regimen (+0.2 kg; *P*=0.09).[1] In participants who initially switched to BIC/FTC/TAF, median weight change from baseline through Week 72 was +1.7 kg in participants assigned female at birth and +1.9 kg for participants assigned male at birth.[4] Through Week 72, greater increases in body weight were observed in participants who were randomized to switch to BIC/FTC/TAF at Week 0 from a baseline regimen containing TDF (+4.6 kg; *P*=0.012) and ABC (+2.8 kg; *P*=0.07) than in those with baseline regimens that contained TAF (+1.3 kg).[4]

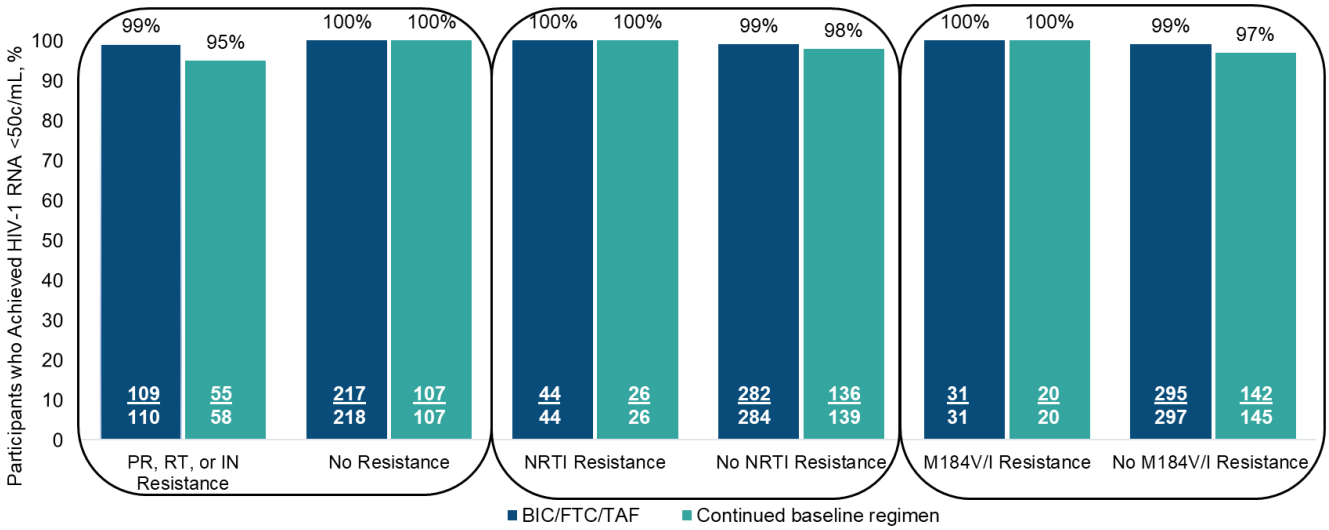
Resistance Analysis Results Through Week 24[10]

At least one pre-existing primary resistance substitution was detected in 34% (170/495) of all participants (Table 4). High rates of virologic suppression (HIV-1 RNA <50 c/mL by LOCF analysis) were maintained in those who switched to BIC/FTC/TAF, regardless of pre-existing resistance (Figure 3). There was no treatment-emergent resistance in either group.

Table 4. BRAAVE 2020: Participants with Pre-Existing Primary Resistance[10]

Resistance Category	BIC/FTC/TAF (n=330)	Continued Baseline Regimen (n=165)
No primary resistance, % (n)	66 (218)	65 (107)
Any primary resistance, % (n)	34 (112)	35 (58)
NNRTI resistance, % (n)	21 (70)	19 (32)
PI resistance, % (n)	11 (36)	15 (25)
NRTI resistance, % (n)	13 (44)	16 (26)
INSTI resistance, % (n)	2 (8)	2 (3)

Figure 3. BRAAVE 2020: Virologic Suppression at Week 24 According to Baseline Resistance[10]*



*The last available HIV-1 RNA during treatment through Week 24 was used in the LOCF analysis. Two participants with INSTI resistance detected by historical genotype were excluded from efficacy analyses.

Resistance Analysis Results Through Week 72[6]

Of the 489 participants who received BIC/FTC/TAF through Week 72, cumulative baseline genotypic data was available for 468 participants (Table 5). Through Week 72, virologic

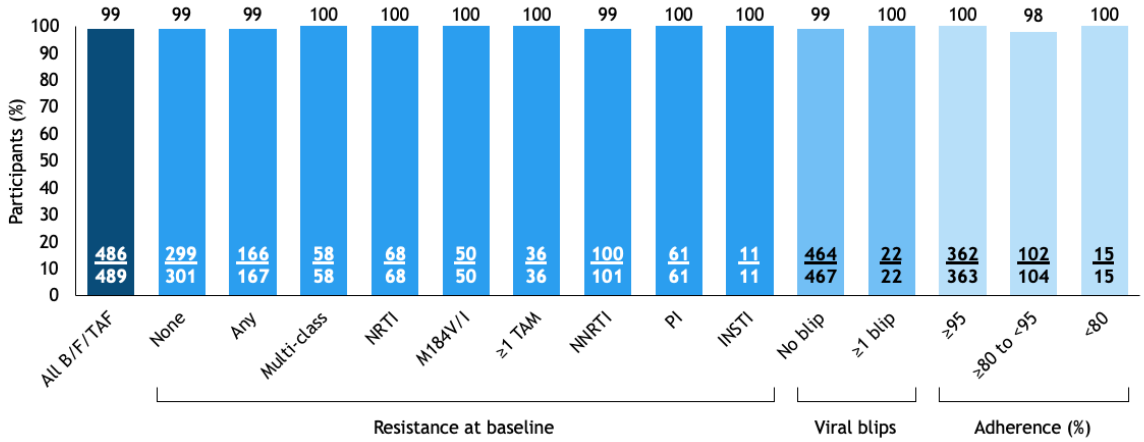
suppression rates ranged from 99% to 100% across groups with varying baseline resistance, viral blips, or suboptimal adherence (Figure 4). No treatment-emergent resistance was detected through Week 72.

Table 5. BRAAVE 2020: Participants with Pre-Existing Resistance Substitutions[6]

Resistance Category	Cumulative Baseline Genotype (n=468)
NRTI resistance, % (n)	15 (68)
K65R, % (n)	1 (4)
M184V/I, % (n)	11(50)
Any TAM, % (n)	8 (36)
1–2 TAMs, % (n)	6 (27)
≥3 TAMs, % (n)	2 (9)
NNRTI resistance, % (n)	22 (101)
K103N/S, % (n)	11 (52)
RPV associated†, % (n)	9 (41)
PI resistance, % (n)	13 (61)
ATV- or DRV-associated‡, % (n)	2 (11)
Primary INSTI resistance, % (n)	2 (11)
T66A, % (n)	<1 (1)
E92G, % (n)	1 (3)
Y143C/H, % (n)	1 (4)
Q148H/K/R, % (n)	1 (3)
Secondary INSTI resistance, % (n)	50 (227)
M50I, % (n)	24 (107)
T97A, % (n)	2 (11)
S119P/R/T, % (n)	22(101)
E157K/Q, % (n)	9 (42)

Abbreviation: ATV=atazanavir.
†RPV associated substitutions are L100I, K101E/P, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188L, H221Y, F227C, and M230I/L in reverse transcriptase.
‡ATV- or DRV-associated substitutions are I47V, I50L/V, I54M/L, L76V, I84V, and N88S in protease.

Figure 4. BRAAVE 2020: HIV-1 RNA <50 c/mL up to Week 72 by Subgroup[6]



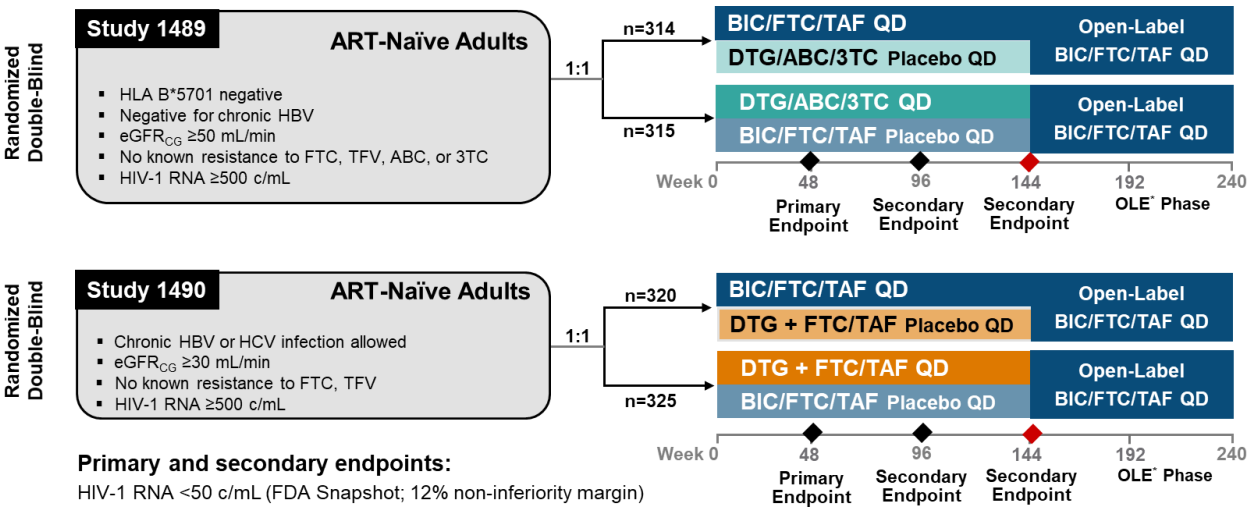
Note: Participants with pre-existing resistance detected post-randomization were permitted to continue in the study and were included in the efficacy analysis.

Pooled Analysis of ART-naïve Black PWH

Study Designs and Demographics

Data from two randomized, double-blind, active-controlled, noninferiority phase 3 studies in ART-naïve participants that evaluated the efficacy and safety of BIC/FTC/TAF with DTG - containing regimens were pooled in a post-hoc analysis to compare results through Week 144 and Week 240 in Black participants (Figure 5).[7]

Figure 5. Studies 1489 and 1490: Study Designs[7]



Abbreviation: HLA=human leukocyte antigen.

Table 6. Studies 1489 and 1490: Baseline Demographics and Disease Characteristics[7]

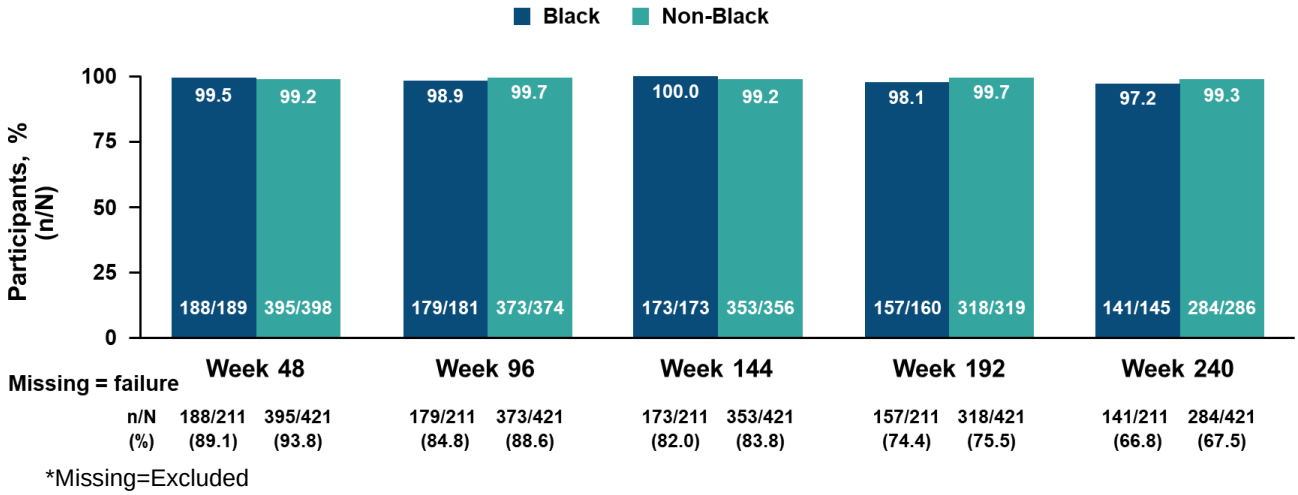
Key Demographics and Characteristics	Black (n=211)	Non-Black (n=421)
Age, median (Q1, Q3), years	30 (25, 41)	34 (27, 44)
Male sex at birth, %	84	91
HIV-1-RNA, log_{10} c/mL, median (Q1,Q3)	4.42 (3.91, 4.93)	4.42 (4.06, 4.88)
HIV-1 RNA >100,000 c/mL, n (%)	42 (20)	76 (18)
CD4 count, cells/µL, median (Q1,Q3)	405 (264, 534)	459 (310, 598)
CD4 count <200 cells/µL, n (%)	37 (18)	42 (10)
Body weight kg Median, (Q1,Q3), n†	80.7 (70.3, 92.5), 211	75.3 (67.1, 85.3), 421

*Includes American Indian or Alaska Native, Asian, Native Hawaiian or Pacific Islander and other.
†Black vs Non-Black median body weight was significantly higher at BL (*P*=0.0003).

Efficacy Results Through Week 240

Virologic suppression rates with BIC/FTC/TAF were high in Black and non-Black participants (Figure 6). CD4 cell count increased from baseline through Week 240 among both Black and non-Black PWH (mean change from baseline: +375 and +319 cells/µL, respectively; *P*=0.0307). No treatment emergent resistance to BIC/FTC/TAF was reported through Week 240.

Figure 6. Studies 1489 and 1490: Rates of VS Through Week 240: HIV-1 RNA <50c/mL[7]*



*Missing=Excluded

The median BIC/FTC/TAF adherence rates through Week 240, in both Black and non-Black groups was high: 96% and 98% respectively. Black participants were more likely to have low adherence (<85%) vs non-Black participants (11% vs 5% participants; *P*=0.0074); 100% of participants from both groups with low adherence (10/10 and 9/9 participants, respectively) had HIV-1 RNA <50 c/mL at Week 240.

Safety Results Through Week 240[7]

The incidence of study-drug related AEs was significantly lower in Black vs non-Black participants (Table 7). AEs occurring in ≥5% of participants in either group included diarrhea (3% vs 5%), nausea (3% vs 5%) and headache (2% vs 6%).

Table 7: Studies 1489 and 1490: Safety Results Through Week 240[7]

Safety Parameters, n (%)	Black (n=211)	Non-Black (n=421)
Any AE	198 (94)	404 (96)
Study drug-related AE	43 (20)	134 (32)
Any Grade 3 or 4 AE	47 (22)	83 (20)
Study drug-related Grade 3 or 4 AE	3 (1)	6 (1)
Discontinuation due to AE	6 (3)[a]	4 (1)[b]

[a] Cardiac arrest, abdominal distension, dyspepsia, tension headache, depressed mood, depression, insomnia, and sleep disorder (n = 1 each); participants could have ≥ 1 event
[b] Cardiac arrest, COVID-19, and drug toxicity (n=1 each).

At Week 240, changes from baseline in eGFR and TC:HDL were similar between Black and non-Black participants. Although the median body weight was higher at baseline in Black participants, the differences in weight change at Week 240 was not statistically significant between Black and non-Black participants.

Treatment-emergent diabetes and hypertension rates were similar between Black vs non-Black participants through Week 240, excluding participants with a medical history of diabetes/hypertension.

References

1. Hagins D, Kumar P, Saag M, et al. Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide in Black Americans With HIV-1: A Randomized Phase 3b, Multicenter, Open-Label Study. *J Acquir Immune Defic Syndr.* 2021;88(1):86-95.
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3. Andreatta K, D'Antoni ML, Chang S, et al. Preexisting Resistance and Week 48 Virologic Outcomes after Switching to B/F/TAF in African American Adults With HIV [Presentation]. Paper presented at: IDWeek Virtual; 21-25 October, 2020.
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5. Andreatta K, D'Antoni ML, Chang S, et al. High Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide in African-American Adults With HIV Including Those with Preexisting Resistance, Viral Blips, and Suboptimal Adherence [Poster 629]. Paper presented at: IDWeek Virtual; 29 Sept-03 Oct, 2021.
6. Andreatta K, D'Antoni ML, Chang S, et al. High efficacy of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in Black adults in the United States, including those with pre-existing HIV resistance and suboptimal adherence. *J Med Virol.* 2024;96(10):e29899.
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9. Hagins D, Kumar P, Saag M, et al. Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide in Black Americans With HIV-1: A Randomized Phase 3b, Multicenter, Open-Label Study [Supplemental Material: Appendix]. *JAIDS.* 2021.
10. Andreatta K, D'Antoni ML, Chang S, et al. Preexisting Resistance and B/F/TAF Switch Efficacy in African Americans [Poster 509]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 08-11 March, 2020; Boston, MA.

Abbreviations

ABC=abacavir
AE=adverse event
ART=antiretroviral therapy
BIC=bictegravir
BRAAVE=BIC/FTC/TAF Regimen for African Americans with HIV and Treatment Experience
c/mL=copies per milliliter
COVID-19=coronavirus disease 2019
DRV=darunavir
$eGFR_{CG}$=eGFR calculated by the Cockcroft-Gault equation
FTC=emtricitabine
INSTI=integrase strand transfer inhibitor
LOCF=last observation carried forward
NNRTI=nonnucleoside reverse transcriptase inhibitor
NRTI=nucleoside reverse transcriptase inhibitor
PI=protease inhibitor
RPV=rilpivirine
TAF=tenofovir alafenamide
TAM=thymidine analog mutation
TC=total cholesterol
TDF=tenofovir disoproxil fumarate

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.

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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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