GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Study 4030

This document is in response to your request for information regarding Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) and results from the phase 3 Study 4030 in virologically suppressed people with HIV (PWH).

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

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

Study 4030 in Virologically Suppressed PWH

Study Design and Demographics

Study 4030 was a phase 3, randomized, double-blind, multicenter, active-controlled study that evaluated the efficacy of BIC/FTC/TAF (n=284) vs DTG + FTC/TAF (n=281) in virologically suppressed PWH, including those with known baseline resistance mutations. Eligible participants were adults currently receiving treatment with DTG + FTC/TAF or DTG + FTC/TDF, with HIV-1 RNA <50 c/mL for ≥3 months if NRTI-R was not known or suspected or ≥6 months if NRTI-R was known or suspected, with no documented INSTI-R or confirmed virologic failure during treatment with an INSTI-containing regimen, and with $eGFR_{CG}$ ≥30 mL/min. Known or suspected resistance to NRTIs, PIs, and/or NNRTIs was permitted. 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 prespecified noninferiority margin of 4%. Participants were randomly assigned in a 1:1 ratio to switch to BIC/FTC/TAF or DTG + FTC/TAF; randomization was stratified according to NRTI-R category at screening based on historical genotype.[1] Baseline demographics and characteristics are presented in Table 1.

Table 1. Study 4030: Baseline Demographics and Disease Characteristics[1]

Key Demographics and Characteristics		BIC/FTC/TAF (n=284)	DTG + FTC/TAF (n=281)
Age, median (range), years		51 (22–79)	50 (20–79)
Female, n (%)		39 (14)	41 (15)
Race, n (%)	White	200 (71)	199 (72)
	Black	68 (24)	61 (22)
	Other	9 (3)	13 (5)
	Asian	3 (1)	3 (1)
	Native Hawaiian/Pacific Islander	2 (1)	1 (<1)
Ethnicity, n (%)	Hispanic or Latino	61 (22)	49 (18)
HIV-1 RNA, n (%)	<50 c/mL	276 (97)	275 (98)
	≥50 c/mL	8 (3)	6 (2)

Key Demographics and Characteristics	BIC/FTC/TAF (n=284)	DTG + FTC/TAF (n=281)
CD4 count, median (IQR), cells/µL	659 (486–885)	642 (462–791)

Abbreviation: CD4=clusters of differentiation-4.

Historical genotypes were collected at screening, and retrospective proviral DNA genotyping was attempted on baseline samples, if available. Overall, baseline genotypic data were available for 83% of participants (470/565; Table 2).[2]

Table 2. Study 4030: Baseline Genotypic Analysis[2]

Category	NRTI RAMs	Participants, n (%)			
		At Randomization[a]	Final[a]	BIC/FTC/TAF (n=284)	DTG + FTC/TAF (n=281)
1[b]	K65R/E/N or ≥3 TAMs	15 (3)	30 (5)	16 (6)	14 (5)
2[c]	Other NRTI resistance	63 (11)	108 (19)	55 (19)	53 (19)
3[d]	No NRTI mutation	487 (86)	427 (76)	213 (75)	214 (76)

[a]Twenty participants were stratified to Categories 1 or 2 based on investigator-suspected NRTI-R that was not confirmed by genotyping.
[b]Resistance Category 1: high-level NRTI resistance, defined as K65R/E/N or ≥3 TAMs, including M41L or L210W, or T69 insertions.
[c]Resistance Category 2: any other pattern of NRTI resistance, including M184V/I, K70E/G/M/Q/S/T, L74V/I, V75A/S/M/T, Y115F, T69D, Q151M, M41L, D67N, K70R, L210W, T215F/Y, or K219E/N/Q/R.

Efficacy Results

Switching to BIC/FTC/TAF demonstrated noninferior efficacy (HIV-1 RNA ≥50 c/mL) according to FDA Snapshot analysis compared with staying on DTG + FTC/TAF at Week 48 (0.4% [1/284] vs 1.1% [3/281]; difference, -0.7%; 95% CI: -2.8% to 1%). At Week 48, 93.3% of participants (265/284) receiving BIC/FTC/TAF and 91.1% of participants (256/281) receiving DTG + FTC/TAF had HIV-1 RNA <50 c/mL according to FDA Snapshot analysis (difference, 2.2%; 95% CI: -2.3% to 6.8%).[1]

Preexisting resistance analyses

Rates of virologic suppression were high (89–100%) regardless of preexisting resistance (Table 3).[2]

Table 3. Study 4030: Week 48 Virologic Outcomes by Class of Preexisting Resistance (FDA Snapshot Analysis and LOCF)[2]

Resistance Category	HIV-1 RNA <50 c/mL at Week 48, n/N (%)		
	BIC/FTC/TAF (n=284)	DTG + FTC/TAF (n=281)	Treatment Differences, % (95% CI)
FDA Snapshot analysis			
Overall	265/284 (93.3)	256/281 (91.1)	2.2 (-2.3 to 6.8)
1: K65R/E/N or ≥3 TAMs[a]	15/16 (94)	14/14 (100)	-6.3 (-30.7 to 19.4)
2: Other NRTI resistance[b]	51/55 (93)	51/53 (96)	-3.5 (-14.2 to 6.9)
3: No NRTI mutations	199/213 (93)	191/214 (89)	4.2 (-1.3 to 9.9)
LOCF method[c]			
Overall	282/283 (99.6)	276/279 (98.9)	-
1: K65R/E/N or ≥3 TAMs[a]	16/16 (100)	14/14 (100)	
2: Other NRTI resistance[b]	55/55 (100)	53/53 (100)	
3: No NRTI mutation	211/212 (99)	209/212 (98)	

Resistance Category	HIV-1 RNA <50 c/mL at Week 48, n/N (%)		
	BIC/FTC/TAF (n=284)	DTG + FTC/TAF (n=281)	Treatment Differences, % (95% CI)
M184V/I	47/47 (100)	34/34 (100)	
NRTI-R	63/63 (100)	55/55 (100)	
NNRTI-R	60/61 (98)	57/57 (100)	
PI-R	15/15 (100)	23/23 (100)	
INSTI-R	15/15 (100)	5/5 (100)	

Abbreviations: LOCF=last observation carried forward; NNRTI-R=non-nucleos(t)ide reverse transcriptase inhibitor resistance; PI-R=protease inhibitor resistance.
[b]Resistance Category 1: high-level NRTI resistance, defined as K65R/E/N or ≥3 TAMs, including M41L or L210W, or T69 insertions.
[b]Resistance Category 2: any other pattern of NRTI resistance, including M184V/I, K70E/G/M/Q/S/T, L74V/I, V75A/S/M/T, Y115F, T69D, Q151M, M41L, D67N, K70R, L210W, T215F/Y, or K219E/N/Q/R.
[c]LOCF analysis did not include 1 participant in the BIC/FTC/TAF group and 2 participants in the DTG + FTC/TAF group who had no on-treatment post baseline data.

A multivariate logistic regression model was used in participants (n=470) with baseline historical and/or proviral DNA genotype data to assess predictors of baseline NRTI-R and M184V/I mutation (Table 4).[2]

Table 4. Study 4030: Multivariate Logistic Regression Model of Predictors of Preexisting NRTI-R or M184V/I Mutation[2]

Variable	Any NRTI Mutation Present		M184V/I Present	
	OR (95% CI)	*P*-Value	OR (95% CI)	*P*-Value
Time since ART start (per year)	1.1 (1.1–1.2)	<0.0001	1.1 (1.1–1.2)	<0.0001
Prior PI-containing regimen	2 (1.2–3.5)	0.0116	2.2 (1.1–4.3)	0.0189
Black race vs non-Black race	2.1 (1.2–3.6)	0.0106	2.5 (1.4–4.6)	0.0026
History of PI resistance	3 (1.3–6.9)	0.0123	2.6 (1.1–6)	0.0295
History of NNRTI resistance	2.4 (1.4–4)	0.0014	2.7 (1.5–4.7)	0.0007

Abbreviations: ART=antiretroviral therapy; OR=odds ratio.

Viral blip analysis[2]

Viral blips were defined as incidences of HIV-1 RNA ≥50 c/mL after HIV-1 RNA <50 c/mL and followed by a return to HIV-1 RNA <50 c/mL. Overall, viral blips occurred in 0.5% of participants in the BIC/FTC/TAF group and in 0.4% of participants in the DTG + FTC/TAF group. Through Week 48, 15 participants (2.7%; BIC/FTC/TAF, n=8; DTG + FTC/TAF, n=7) experienced ≥1 viral blip; 1 participant in the BIC/FTC/TAF group had baseline Category 1 NRTI resistance (3 TAMs and M184I), 1 participant in the DTG + FTC/TAF group had baseline Category 2 resistance (M184V), and 13 participants had baseline Category 3 resistance (no NRTI resistance). One participant in the BIC/FTC/TAF group without baseline NRTI-R experienced 2 blips.

Treatment-emergent resistance analysis[2]

Phenotypic and genotypic resistance testing for integrase, protease, and reverse transcriptase were performed for any participant who met the following criteria for the resistance analysis population: confirmed viral rebound of HIV-1 RNA ≥50 c/mL with a follow-up HIV-1 RNA ≥200 c/mL through Week 48, had HIV-1 RNA ≥200 c/mL at Week 48 or their last study visit, or without a follow-up viral load assessment at the last visit, and did not resuppress while on study drug. Three participants (1%), all from the DTG + FTC/TAF group and with no baseline NRTI-R, met the criteria for resistance analysis; 2 participants had

confirmed virologic failure, and 1 participant had HIV-RNA ≥200 c/mL at the Week 48 visit. No treatment-emergent genotypic or phenotypic resistance to study drugs was detected.

Safety Results[1]

Both treatments were well tolerated, and most AEs were mild or moderate in severity. The most commonly reported AEs (incidence, ≥10%) in the BIC/FTC/TAF group and DTG + FTC/TAF group were nasopharyngitis (11% and 10%, respectively), diarrhea (8% and 10%), and upper respiratory tract infection (7% and 11%). Drug-related AEs that occurred in ≥2% of participants in either group were diarrhea (1% and 2%, respectively) and headache (1% and 2%). Six participants (2%) in each arm discontinued the study because of AEs. One participant in the BIC/FTC/TAF group died of cardiopulmonary arrest, which the study investigator assessed as not being related to study drug, and 1 participant in the DTG + FTC/TAF group died of suspected myocardial infarction, which the study investigator assessed as related to the study drug.

References

1. Sax PE, Rockstroh JK, Luetkemeyer AF, et al. Switching to bictegravir, emtricitabine, and tenofovir alafenamide in virologically suppressed adults with Human Immunodeficiency Virus. *Clin Infect Dis.* 2020:1-9.
2. Acosta RK, Willkom M, Andreatta K, et al. Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) from Dolutegravir (DTG)+F/TAF or DTG+F/Tenofovir Disoproxil Fumarate (TDF) in the Presence of Pre-Existing NRTI Resistance. *J Acquir Immune Defic Syndr.* 2020;85(3):363-371. https://www.ncbi.nlm.nih.gov/pubmed/32701823

Abbreviations

AE=adverse event
BIC=bictegravir
CG=Cockcroft-Gault
DTG=dolutegravir
FTC=emtricitabine
INSTI=integrase strand transfer inhibitor
INSTI-R=integrase strand transfer inhibitor resistance
NRTI=nucleos(t)ide reverse transcriptase inhibitor
NRTI-R=nucleos(t)ide reverse transcriptase inhibitor resistance
NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor
PI=protease inhibitor
PWH=people with HIV
TAF=tenofovir alafenamide
TAM=thymidine analog mutation

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

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

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

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@gilead.com.