Biktarvy® (BIC/FTC/TAF) Use in People With HIV-2

This document is in response to your request for information regarding Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in people with HIV-2.

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

Product Labeling[1]

Indications and Usage

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 ARV treatment history and not virologically suppressed, with no known or suspected substitutions associated with resistance to the integrase strand inhibitor class, FTC, or TFV, 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 TFV.

Microbiology

Antiviral activity in cell culture

The triple combination of BIC, FTC, and TAF was not antagonistic with respect to antiviral activity in cell culture.

BIC*:* BIC displayed antiviral activity in activated PBMCs against clinical isolates of HIV-1 representing groups M, N, and O, including subtypes A, B, C, D, E, F, and G, with a median EC_{50} value of 0.55 nM (range <0.05 to 1.71 nM). The EC_{50} value against a single HIV-2 isolate was 1.1 nM.

FTC*:* In PBMCs acutely infected with HIV-1 subtypes A, B, C, D, E, F, and G, the median EC_{50} value for FTC was 9.5 nM (range 1–30 nM) and against HIV-2 was 7 nM.

TAF: TAF displayed antiviral activity in cell culture against all HIV-1 groups (M, N, O), including subtypes A, B, C, D, E, F, and G (EC_{50} values ranged from 0.1–12 nM) and strain-specific activity against HIV-2 (EC_{50} values ranged from 0.9–2.6 nM).

Real-World Data on BIC/FTC/TAF Use in People With HIV-2

Retrospective French Study[2]

Study design and demographics

A non-comparative, retrospective study was conducted in France in 2023 to determine the outcomes of people with HIV-2 who were treated with BIC/FTC/TAF (N=24). CD4 cell counts and plasma viral loads were evaluated, and HIV-2 resistance mutations were assessed in RNA/DNA according to plasma viral load and per physician request. BIC, FTC, and TFV plasma C_{24h} levels were determined, and values for BIC C_{24h} were compared with the phenotypic susceptibility threshold (the IC_{90} of BIC) for HIV-2.

Table 1. Baseline Demographics and Disease Characteristics (Joly et al)[2]

Key Demographics and Characteristics		BIC/FTC/TAF (N=24)
Age, median (IQR), years		58 (53–61)
Female, n		14
Born in West Africa, n		22
CDC Classification System for HIV Infection, n	Category A	15
	Category B	4
	Category C	5
Time since HIV-2 diagnosis, median (IQR), years		19 (8–23)
CD4 count, median (IQR), cells/mm^3		580 (380–697)
Nadir, median (IQR), cells/mm^3		319 (174–432)
Zenith plasma viral load	<100 c/mL, n	13
	>100 c/mL, n	11
	Median (IQR), c/mL	597 (513–5670)
Treatment-naïve,[a] n		5
Prior ARV regimens, median (IQR), n		2 (1–3)
ARV regimen prior to switch,[b] n	2 NRTIs + DRV/r	5
	History of failure	3
	2 NRTIs + RAL	10
	History of failure	3
	2 NRTIs + DTG	4
	History of failure	1

Abbreviations: CDC=Centers for Disease Control; DRV/r=darunavir/ritonavir; DTG=dolutegravir; INSTI=integrase strand transfer inhibitor; NRTI=nucleos(t)ide reverse transcriptase inhibitor; RAL=raltegravir.
[a]Three treatment-naïve patients had a detectable viral load (57, 94, and 130 c/mL).
[b]Genotypic resistance testing was available in 5/8 patients, and no INSTI resistance mutations were detected.

Results

The median (IQR) duration of BIC/FTC/TAF treatment was 27.8 (16.4–36.2) months. At the evaluation, all patients had a viral load <40 c/mL, and the median (IQR) CD4 cell count was 615 (472–787) cells/mm^3 (compared with CD4 count at BIC/FTC/TAF initiation, *P*=0.29). The mean CD4 count change from baseline was 54±248 cell/mm^3 in the overall population and 106±166 cell/mm^3 among ARV-naïve patients.

In the pharmacokinetic assessment of the 20 evaluable patients, BIC C_{24h} was ≥20-fold the IC_{90} value of BIC on HIV-2 strains.

One patient discontinued BIC/FTC/TAF secondary to an increase in weight. Other safety data were not provided.

In Vitro Data With Components of BIC/FTC/TAF

In vitro data on the individual components of BIC/FTC/TAF show potent inhibition of HIV-2 and select wild-type mutations.[3-7]

References

1. Enclosed, Gilead Sciences Inc. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Joly V, Ferre VM, Cresta M, et al. Immuno-virological and Clinical Follow-up of HIV-2 Patients Receiving BIC/FTC/TAF [Poster 539]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); February 19-22, 2023; Seattle, WA.
3. Le Hingrat Q, Collin G, Damond F, et al. In vitro analysis of the replicative capacity and phenotypic susceptibility to integrase inhibitors of HIV-2 mutants with integrase insertions. *J Antimicrob Chemother.* 2022;77(2):409-412.
4. Smith RA, Raugi DN, Wu VH, et al. Comparison of the Antiviral Activity of Bictegravir against HIV-1 and HIV-2 Isolates and Integrase Inhibitor-Resistant HIV-2 Mutants. *Antimicrob Agents Chemother.* 2019;63(5):e00014-00019. https://www.ncbi.nlm.nih.gov/pubmed/30803972
5. Bartolo I, Borrego P, Gomes P, et al. In vitro evaluation of novel reverse transcriptase inhibitors TAF (tenofovir alafenamide) and OBP-601 (2,3-didehydro-3-deoxy-4-ethynylthymidine) against multi-drug resistant primary isolates of HIV-2. *Antiviral Res.* 2019;161:85-89.
6. Callebaut C, Stepan G, Tian Y, Miller MD. In Vitro Virology Profile of Tenofovir Alafenamide, a Novel Oral Prodrug of Tenofovir with Improved Antiviral Activity Compared to That of Tenofovir Disoproxil Fumarate. *Antimicrob Agents Chemother.* 2015;59(10):5909-5916. http://www.ncbi.nlm.nih.gov/pubmed/26149992
7. Andreatta K, Miller MD, White KL. HIV-2 Antiviral Potency and Selection of Drug Resistance Mutations by the Integrase Strand Transfer Inhibitor Elvitegravir and NRTIs Emtricitabine and Tenofovir In Vitro. *J Acquir Immune Defic Syndr.* 2013;62(4):367–374.

Abbreviations

ARV=antiretroviral
BIC=bictegravir
C_{24h}=plasma concentration 24 hours postdose
CD4=cluster of differentiation 4
EC_{50}=half maximal effective concentration
FTC=emtricitabine
IC_{90}=90% inhibitory concentration
PBMC=peripheral blood mononuclear cell
TAF=tenofovir alafenamide
TFV=tenofovir

Product Label

For the full indication, important safety information, and boxed warning, 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

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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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