Gilead Sciences, Inc. is providing this document to you, a US Healthcare Professional, in response to your unsolicited request for medical information.

GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Use in Baseline Resistance: Overview

This document is in response to your request for information regarding the use of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in people with HIV-1 (PWH) with baseline (BL) resistance. This response was developed according to principles of evidence-based medicine and contains data from clinical trials and real-world studies (N≥500).

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.

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 ARV treatment history and not VS, with no known or suspected substitutions associated with resistance to the INSTI class, FTC, or TFV, or
- to replace the current ARV regimen in those who are VS (HIV-1 RNA <50 c/mL) on a stable ARV regimen with no known or suspected substitutions associated with resistance to BIC or TFV.

Clinical Data on the Use of BIC/FTC/TAF in PWH With BL Resistance

Across several clinical studies in ARV-naive and VS participants, treatment with BIC/FTC/TAF resulted in high rates of virologic suppression (98–100%) at varying timepoints, regardless of the presence of BL resistance.[2-5]

Real-World Data on the Use of BIC/FTC/TAF in PWH With BL Resistance

In the Gilead BICSTaR study, rates of virologic suppression at Month 12 were 98% and 97% among VS participants with and without preexisting PRMs, respectively.[6]

A retrospective French cohort study evaluated virologic outcomes with BIC/FTC/TAF in TE PWH according to the presence of PRMs and virologic status. Virologic suppression was higher in patients with no preexisting PRMs than in those with preexisting PRMs (92.8% and 86.4%, respectively; *P*=0.0147). VF occurred at a higher rate in patients with preexisting PRMs than in those without preexisting PRMs (12.9% and 7.2%, respectively; *P*=0.0205).[7]

Clinical Data on the Use of BIC/FTC/TAF in PWH With BL Resistance

ARV-Naive PWH: Initiating BIC/FTC/TAF

Studies 1489 and 1490

An integrated viral resistance analysis of two phase 3 BIC/FTC/TAF clinical trials in ARV-naive participants (Studies 1489 and 1490) was conducted. All participants were screened using HIV-1 genotypic data with PR and RT population sequencing data. Exclusion criteria included FTC or TAF resistance (Studies 1489 and 1490) and ABC or 3TC resistance (Study 1489). Participants with resistance to NRTIs were excluded.[2]

Efficacy results at Week 144[2]

BIC/FTC/TAF demonstrated non-inferior efficacy (ie, HIV-1 RNA <50 c/mL) to DTG/ABC/3TC (Study 1489) and DTG + FTC/TAF (Study 1490) through Week 144. Preexisting drug resistance using a mutation frequency cutoff of ≥15% did not affect efficacy outcomes, as 98% of the pooled study population with transmitted drug resistance substitutions achieved HIV-1 RNA <50 c/mL, compared with 97% of participants without resistance at Week 144 by last observation carried forward analysis.

Safety results at Week 144[8]

The most common all-grade AEs reported in ≥10% of all participants in the BIC/FTC/TAF groups in either study through Week 144 were nausea, diarrhea, URTI, headache, nasopharyngitis, back pain, fatigue, cough, and syphilis. There were 6 AEs that led to study drug discontinuation among participants who were receiving BIC/FTC/TAF (all in Study 1490), and study TRAEs occurred in 30% (Study 1489) and 22% (Study 1490) of participants who were receiving BIC/FTC/TAF.

VS PWH: Switching to BIC/FTC/TAF

Studies 1878 and 1844

An integrated viral resistance analysis of two phase 3 BIC/FTC/TAF clinical studies in VS participants (Studies 1878 and 1844) was conducted. Exclusion criteria included documented resistance to study drugs or a history of VF. Retrospective analyses of HIV-1 proviral DNA from BL samples were attempted for all participants treated with BIC/FTC/TAF and for a limited number of participants in the comparator groups.[3]

Efficacy results at Week 48[3]

At Week 48, 561/570 participants (98%) in the pooled BIC/FTC/TAF group, 280/285 participants (98%) in the PI + 2 NRTIs group, and 280/281 participants (>99%) in the DTG/ABC/3TC group achieved virologic suppression. Virologic failure rates were low and were consistent with the rates in previously published snapshot analyses. A total of 213/217 participants (98%) with any preexisting PRM achieved virologic suppression at Week 48.

Results from the open-label extension phase

In Study 1878, 98% of participants with any preexisting PRM (PR, RT, IN) who received BIC/FTC/TAF maintained HIV-1 RNA <50 c/mL at the last study visit.[9] In Study 1844, 99% of participants with any primary BL resistance mutation who received BIC/FTC/TAF maintained HIV-1 RNA <50 c/mL.[10]

Safety results

In Study 1878, the most common all-grade AEs reported in ≥10% of all participants who received ≥1 dose of BIC/FTC/TAF through a median exposure of 101 weeks were headache, nasopharyngitis, URTI, and diarrhea. AEs that led to discontinuation and were considered study drug related by investigators occurred in 4 participants who received BIC/FTC/TAF.[11] In Study 1844, the most common all-grade AEs reported in ≥10% of all participants who received ≥1 dose of BIC/FTC/TAF through a median exposure of 96 weeks were URTI, nasopharyngitis, and diarrhea. There were 39 TRAEs (mostly Grade 1) in the BIC/FTC/TAF group, and AEs led to discontinuation in 7 participants.[10]

Study 4030

A phase 3, randomized, double-blind, multicenter, active-controlled study evaluated the efficacy of BIC/FTC/TAF (n=284) vs DTG + FTC/TAF (n=281) in PWH who were VS, including those with known BL resistance mutations. Known or suspected resistance to NRTIs, PIs, and NNRTIs was permitted.[12]

Efficacy results at Week 48

Switching to BIC/FTC/TAF demonstrated non-inferior efficacy (HIV-1 RNA ≥50 c/mL) by FDA Snapshot analysis compared with staying on DTG + FTC/TAF at the Week 48 primary endpoint.[12] High rates (98–100%) of virologic suppression were observed in participants with BL resistance in both treatment groups.[4]

Safety results at Week 48[12]

The most frequently reported AEs (≥10%) in either group were nasopharyngitis, diarrhea, and URTI. AEs led to study drug discontinuation in 6 participants (2%) in each arm.

BRAAVE 2020 study

A phase 3, randomized, open-label, active-controlled study evaluated the safety and efficacy of switching to BIC/FTC/TAF (n=330) or continuing a BL regimen of two NRTIs plus a third agent (n=165) in VS PWH who were located in the US and self-identified as Black or African American. Exclusion criteria consisted of primary INSTI or NRTI resistance (K65R/E/N, T69 insertions, or ≥3 TAMs). Resistance to PIs, NNRTIs, and NRTIs (M184V/I, 1–2 TAMs, and other substitutions) was permitted. Participants were randomly assigned in a 2:1 ratio to stay on BL regimen or switch to BIC/FTC/TAF until Week 24, at which point participants randomly assigned to stay on BL regimen were switched to BIC/FTC/TAF until Week 48. After Week 48, all participants were given the option to participate in the extension phase, in which they received BIC/FTC/TAF for an additional 24 weeks. BL resistance was analyzed using historical genotypes and retrospective HIV-1 proviral DNA genotype testing of BL samples. Overall, 36% of participants had ≥1 preexisting PRM substitution at BL (Table 1).[5]

Table 1. BRAAVE 2020: Participants With Preexisting Primary Resistance-Associated Substitutions at BL[5]

Preexisting BL Resistance, n (%)	BL Genotype Available (n=468)
No preexisting PRM substitutions (PR, RT, IN[a])	301 (64)
≥1 preexisting PRM substitution (PR, RT, IN[a])	167 (36)
Single class	109 (23)
Multiclass	58 (12)
Two classes	42 (9)
Three classes	16 (3)

[a]IN imputed as wild type for the 15 participants with PR/RT data only.

Efficacy results through Week 72

Switching to BIC/FTC/TAF was non-inferior to continuing the BL regimen at Week 24 (primary endpoint: HIV-1 RNA ≥50 c/mL at Week 24).[13] High rates of virologic suppression (98–100%) were maintained through Week 72 in the overall population treated with BIC/FTC/TAF, regardless of preexisting resistance, viral blips, or adherence levels. All participants with preexisting multiclass resistance had virologic suppression at their last study visit. In participants with ≥1 preexisting PRM substitution at BL or no preexisting resistance at BL, 99% of participants in both groups had virologic suppression at their last study visit. No treatment-emergent resistance was detected.[5]

Safety results through Week 72

A safety analysis was not conducted in the subgroup of participants with BL resistance. In the overall safety analysis, switching to BIC/FTC/TAF was well tolerated, and AEs were comparable between the two treatment arms at Week 24.[13] All-grade AEs that occurred at Week 72 in ≥5% of participants who received BIC/FTC/TAF at any time (n=493) included URTI, syphilis, headache, pain in extremity, arthralgia, hypertension, and nasopharyngitis. AEs led to 6 study drug discontinuations between BL and Week 24, 3 discontinuations between Weeks 24 and 48, and 3 discontinuations after Week 48.[14]

Real-World Data on the Use of BIC/FTC/TAF in PWH With BL Resistance

BIC/FTC/TAF in PWH With PRMs in the BICSTaR Study[6]

Study design

BICSTaR is an ongoing, multinational, prospective, observational cohort study evaluating the effectivness, safety, and tolerability of BIC/FTC/TAF in PWH in the clinical setting, including 1083 TE PWH. Of the 996 participants who were VS, 105/441 participants (24%) with available genotype data at BL had preexisting PRMs (NRTI, n=66 [15%]; NNRTI, n=56 [13%]; PI, n=28 [6%]; INSTI, n=1 [0.2%]). The 555 VS participants with no available genotype data at BL were considered to not have PRMs. The effectivness and tolerability of 12 months of BIC/FTC/TAF in TE PWH with BL PRMs were assessed.

Effectiveness results at Month 12

Among participants who were VS at BL and had available data at Month 12, 99% of participants (78/79) with preexisting PRMs and 98% of participants (739/758) without preexisting PRMs were VS (M=E analysis). Among participants with viremia at BL, 100% of PWH with preexisting PRMs (9/9) and 85% of PWH without preexisting PRMs (44/52) achieved virologic suppression at Month 12 (M=E analysis). Of the 20 participants with detectable viral load at Month 12, 19 had no preexisting PRMs, and 1 participant with preexisting PRMs experienced an isolated viral blip (HIV-1 RNA, 78 c/mL) before becoming resuppressed by the next visit.

Safety results at Month 12

Through Month 12, 17 participants (16%) with any preexisting PRMs and 98 participants (11%) without preexisting PRMs discontinued BIC/FTC/TAF due to AEs (n=12 [11%] and n=59 [7%], respectively), TRAEs (n=9 [9%] and n=47 [5%]), and lack of effectivness (n=1 [1%] and n=1 [<1%]). The most common TRAEs (>12%) leading to discontinuation in participants with and without preexisting PRMs were weight increased (n=3 [33%] and n=15 [32%], respectively), headache (n=2 [22%] and n=4 [9%]), and fatigue (n=2 [22%] and n=3 [6%]).

Retrospective French Cohort Study in TE PWH With and Without PRMs[7]

Study design and BL demographics

A retrospective French cohort study evaluated the impact of preexisting PRMs on virologic outcomes of TE PWH with and without BL PRMs who received BIC/FTC/TAF using data from the ANRS-CO3-AquiVIH-NA cohort. Included in the analysis were VS and non-VS adults who had ≥1 genotypic resistance test available before initiating BIC/FTC/TAF between 2018 and 2021. Overall, 147/636 patients (23.1%) with available data had preexisting NRTI and/or INSTI mutations, and 489 had none. At BL, 526 patients (82.7%) were VS (HIV-1 RNA <50 c/mL; PRM, n=110; no PRM, n=416), and 110 (17.3%) were not VS (HIV-1 RNA >50 c/mL; PRM, n=37; no PRM, n=73). M184V/I was the most common PRM (Table 2). No major INSTI mutations were reported.

Table 2. Preexisting NRTI Resistance Mutations in >1% of Patients (Bellecave et al)[7]

Preexisting NRTI Resistance Mutations, n (%)	Overall (n=147)	Not VS (n=37)	VS (n=110)
Total M184V/I	131 (89.1)	34 (91.9)	97 (88.2)
M184V/I alone	53 (36.1)	19 (51.4)	34 (30.9)
M184V/I + 1–2 TAMs	30 (20.4)	7 (18.9)	23 (20.9)
M184V/I + 1–2 TAMs + K65R	2 (1.4)	0	2 (1.8)
M184V/I + ≥3 TAMs	37 (25.2)	6 (16.2)	31 (28.2)
M184V/I + ≥3 TAMs + Q151M	3 (2)	0	3 (2.7)
M184V/I + K65R	2 (1.4)	0	2 (1.8)
≥3 TAMs	11 (7.5)	2 (5.4)	9 (8.2)

Effectivness results

Virologic suppression was higher in patients with no preexisting PRMs than in those with preexisting PRMs (92.8% and 86.4%, respectively; *P*=0.0147). Among VS patients at

BIC/FTC/TAF initiation, virologic suppression remained >95%, regardless of the presence of PRMs. Among non-VS patients at BL, 70% achieved virological suppression; among those with preexisting PRMs, the rate was 59.5%.

VF (defined as two consecutive measures of HIV-1 RNA >50 and <1000 c/mL or one measure of HIV-1 RNA >1000 c/mL within 60 months, or failure to achieve HIV-1 RNA <50 c/mL within 12 months among non-VS patients at BL), occurred at a higher rate in patients with preexisting PRMs than in those without preexisting PRMs (12.9% and 7.2%, respectively; *P*=0.0205). In a univariate analysis, PRMs were significantly associated with an increased risk of VF (HR, 1.9; 95% CI: 1.1–3.29; *P*=0.022); the M184V/I mutation was also significantly associated with an increased risk of VF (HR, 2.03; 95% CI: 1.16–3.53; *P*=0.013).

Safety data were not reported.

References

1. Enclosed, Gilead Sciences Inc. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Acosta RK, Chen GQ, Chang S, et al. Three-year study of pre-existing drug resistance substitutions and efficacy of bictegravir/emtricitabine/tenofovir alafenamide in HIV-1 treatment-naive participants. *J Antimicrob Chemother.* 2021.
3. Andreatta K, Willkom M, Martin R, et al. Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide Maintained HIV-1 RNA Suppression in Participants with Archived Antiretroviral Resistance Including M184V/I. *J Antimicrob Chemother.* 2019.
4. 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.
5. 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.
6. Trottier B, Bonnet F, García-Deltoro MG, et al. Real World Effectiveness and Tolerability of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Treatment Experienced People With HIV and a History of Antiretroviral Drug Resistance Mutations [Poster 1628848]. Paper presented at: ID Week 2023; October 11-15, 2023; Boston, MA.
7. Bellecave P, Peyrouny-Mazeau A, Leleux O, et al. Factors associated with virological failure in people with HIV treated with bictegravir/emtricitabine/tenofovir alafenamide. Impact of pre-existing mutations and risk of resistance emergence. ANRS-CO3-AquiVIH-NA cohort. *J Antimicrob Chemother.* 2026;81(9).
8. Orkin C, DeJesus E, Sax PE, et al. Three-Year Outcomes of the Fixed-Dose Combination Bictegravir, Emtricitabine, and Tenofovir Alafenamide vs Dolutegravir-Containing Regimens for Initial Treatment of HIV-1 Infection: Week 144 Results from Two Randomised, Double-Blind, Multicentre, Phase 3, Non-Inferiority Trials. *The Lancet HIV.* 2020;7:e389–400.
9. Andreatta K, Chang S, Delaney M, et al. Long-term Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide After Switch From Boosted Protease Inhibitor-Based Regimens Including in Those With Preexisting Resistance and Viral Blips [Poster PE1/19]. Paper presented at: 18th European AIDS Conference; October 27-30, 2021; London, United Kingdom.
10. Brar I, Ruane P, Ward D, et al. Long-term Follow-up After a Switch to Bictegravir, Emtricitabine, and Tenofovir Alafenamide From Dolutegravir, Abacavir, and Lamivudine [Poster 1028]. Paper presented at: IDWeek Virtual; 21-25 October, 2020.
11. Rockstroh JK, Molina JM, Post F, et al. Long-Term Follow-Up After a Switch to Bictegravir, Emtricitabine, Tenofovir Alafenamide (B/F/TAF) from a Boosted Protease Inhibitor-Based

Regimen [Poster P036]. Paper presented at: HIV GLASGOW Drug Therapy Virtual; 05-08 October, 2020; Glasgow, UK.
12. 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.
13. 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.
14. Kumar P, Stephens JL, Wurapa AK, et al. Week 72 Outcomes and COVID-19 Impact From the BRAAVE 2020 Study: a Randomized Switch to B/F/TAF in Black American Adults With HIV [Poster 802]. Paper presented at: 11th International AIDS Society (IAS) Conference on HIV Science Virtual; 18-21 July, 2021.

Abbreviations

3TC=lamivudine
ABC=abacavir
AE=adverse event
ARV=antiretroviral
BIC=bictegravir
BICStaR=BIC single-tablet regimen
BL=baseline
c/mL=copies per mL
DTG=dolutegravir
FTC=emtricitabine
HR=hazard ratio
IN=integrase
INSTI=integrase strand transfer inhibitor
M=E=missing=excluded
NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor
NRTI=nucleos(t)ide reverse transcriptase inhibitor
PI=protease inhibitor
PR=protease
PRM=primary resistance mutation
PWH=people with HIV-1
RT=reverse transcriptase
TAF=tenofovir alafenamide
TAM=thymidine analogue mutation
TE=treatment-experienced
TFV=tenofovir
TRAE=treatment-related adverse event
URTI=upper respiratory tract infection
VF=virologic failure
VS=virologically suppressed

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 gilead.privacy@gilead.com.

BIKTARVY, GILEAD, and the GILEAD logo are registered trademarks of Gilead Sciences, Inc., or its related companies.
© 2026 Gilead Sciences, Inc.