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 participants with baseline (BL) resistance.

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 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 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]

Clinical Data on the Use of BIC/FTC/TAF in 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[7]

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 drug-related AEs 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 virological failure. 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.[8] In Study 1844, 99% of participants with any primary BL resistance mutation who received BIC/FTC/TAF maintained HIV-1 RNA <50 c/mL.[9]

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.[10] 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 treatment-related AEs (mostly Grade 1) in the BIC/FTC/TAF group, and AEs led to discontinuation in 7 participants.[9]

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.[11]

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.[11] High rates (98–100%) of virologic suppression were observed in participants with BL resistance in both treatment groups.[4]

Safety results at Week 48[11]

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-R or NRTI-R (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).[12] 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.[12] 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.[13]

Real-World Data on the Use of BIC/FTC/TAF in 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 efficacy, 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 efficacy and tolerability of 12 months of BIC/FTC/TAF in TE PWH with BL PRMs were assessed.

Efficacy 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), DRAEs (n=9 [9%] and n=47 [5%]), and lack of efficacy (n=1 [1%] and n=1 [<1%]). The most common DRAEs (>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%]).

References

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Abbreviations

3TC=lamivudine
ABC=abacavir
AE=adverse event
ARV=antiretroviral
BIC=bictegravir
BICSTaR=BIC single-tablet regimen
BL=baseline
c/mL=copies/mL
DRAE=drug-related adverse event
DTG=dolutegravir
FTC=emtricitabine
IN=integrase
INSTI=integrase strand transfer inhibitor
INSTI-R=integrase strand transfer inhibitor-resistance
M=E=missing=excluded
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
PR=protease
PRM=primary resistance mutation
PWH=people with HIV
RT=reverse transcriptase
TAF=tenofovir alafenamide
TAM=thymidine analogue mutation
TE=treatment-experienced
TFV=tenofovir
URTI=upper respiratory tract infection
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

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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

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