GILEAD | Medical Information

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

This document is in response to your request for information regarding the use of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in patients with baseline (BL) nucleos(t)ide reverse transcriptase inhibitor resistance (NRTI-R).

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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 in adults and pediatric patients weighing ≥14 kg who have 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 Studies: Use of BIC/FTC/TAF in BL NRTI-R

Across multiple clinical studies and at various timepoints, ARV-naive and TE PWH with BL NRTI-R achieved or maintained high rates (90–100%) of virologic suppression on BIC/FTC/TAF.[2-16]

Real-World Data: Use of BIC/FTC/TAF in BL NRTI-R

In real-world studies of BIC/FTC/TAF treatment in ARV-naive and TE PWH with BL NRTI-R, high rates (87.5–100%) of virologic suppression were observed at various timepoints.[17-26]

Clinical Studies: Use of BIC/FTC/TAF in BL NRTI-R

Pooled Analysis: Prevalence of M184V/I Resistance and Efficacy Outcomes in VS Participants[2]

Study design and BL resistance

A pooled analysis was conducted in participants (N=2034) from Studies 4030, 4580 (BRAAVE 2020), 1844, 1878, 4449, and 1474 to evaluate the prevalence of preexisting M184V/I resistance mutation and its effect on virologic outcomes in VS (ie, HIV-1 RNA <50 c/mL for 3 or 6 months) participants who switched to BIC/FTC/TAF.

In Studies 4030 and 4580, participants with BL M184V/I mutations were allowed, but other studies included in the analysis excluded participants if an M184V/I mutation was detected prior to the switch in therapy. Historical genotype reports were collected during enrollment, if available, and HIV-1 proviral DNA genotype testing was conducted retrospectively on any available BL samples.

Most M184V/I mutations were identified by BL proviral DNA genotyping (167/182; 92%). Eighty-one percent of participants with M184V/I mutations (147/182) had ≥1 other resistance substitution.

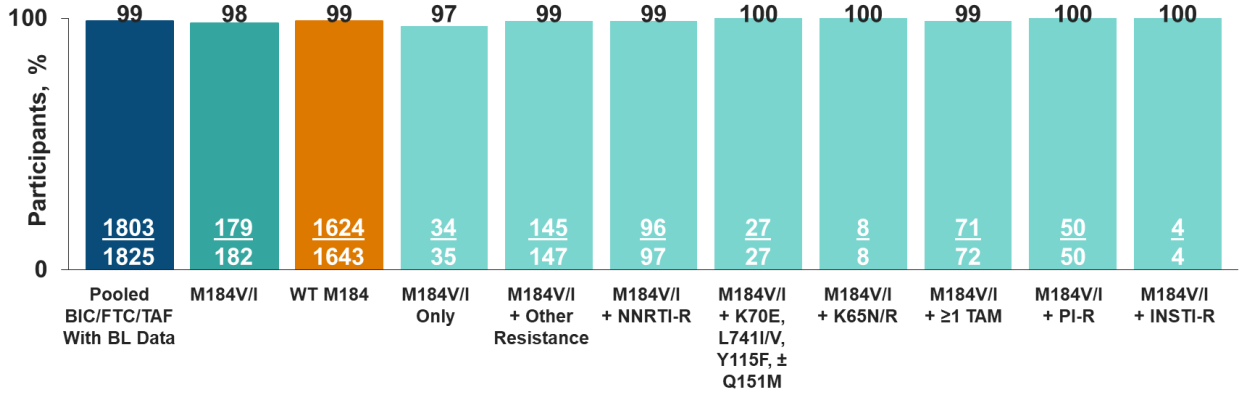
Table 1. Pooled Analysis: Frequency of BL NRTI-R Substitutions in Participants Treated With BIC/FTC/TAF (Sax et al)[2]

BL NRTI-R Substitution, n/N (%)	Pooled BIC/FTC/TAF (N=2034)
PR/RT data available (historical and/or proviral)	1825/2034 (90)
NRTI-R	288/1825 (16)
M184V/I	182/1825 (10)
K65R/N	18/1825 (1)
Any TAM	167/1825 (9)

Efficacy results

High rates (97–100% based on missing=excluded analyses) of virologic suppression (HIV-1 RNA <50 c/mL) were maintained up to 180 weeks after switching to BIC/FTC/TAF, and no treatment-emergent resistance was detected. In participants with preexisting M184V/I who received BIC/FTC/TAF (median duration, 69 weeks), rates of virologic suppression were high (Figure 1). Rates of virologic suppression were similar between participants with and without M184V/I resistance mutations (98% vs 99%, respectively; *P*=0.48).

Figure 1. Pooled Analysis: Virologic Suppression by Preexisting M184V/I in the BIC/FTC/TAF Group (LOCF; Sax et al)[2]



Abbreviation: WT=wild-type allele.

Safety outcomes were not provided for this pooled analysis. Please see product labeling for BIC/FTC/TAF safety information.

Pooled Analysis: Prevalence of Preexisting TAMs and Efficacy Outcomes[3]

Study design and BL resistance

A pooled analysis was conducted in PWH (N=2286) from Studies 4030, 4580, 1844, 1878, and 4449 to evaluate the prevalence of preexisting TAMs and their effect on virologic outcomes after participants switched to BIC/FTC/TAF. Historical genotype reports were collected after enrollment, if available, and HIV-1 proviral DNA genotype testing was conducted on BL samples; participants with previously undetected BL resistance mutations were allowed to remain in the study and were included in all analyses.

In the pooled analysis, 91% of participants who received BIC/FTC/TAF had PR/RT data available, and preexisting TAMs were detected in 10% of these participants (Table 2).

Table 2. Pooled Analysis: BL Resistance Data in Participants Treated With BIC/FTC/TAF (Andreatta et al)[3]

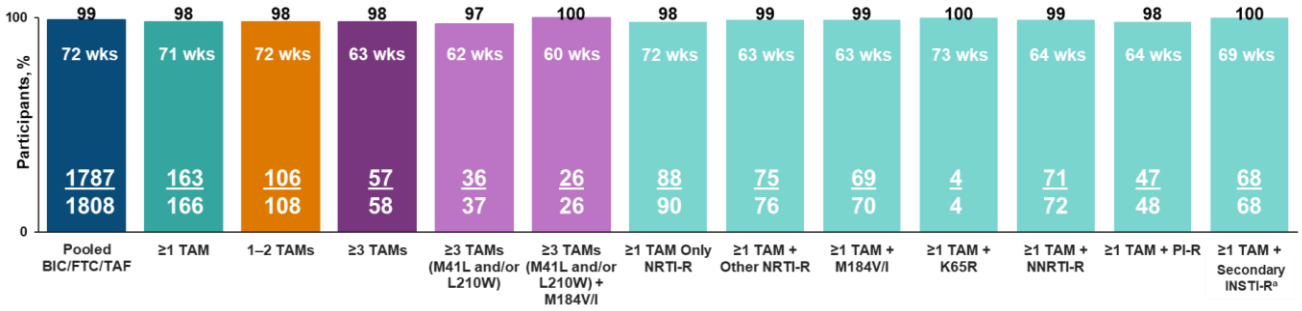
BL Resistance, n (%)	Pooled BIC/FTC/TAF (n=2079)
≥1 TAM	206 (10)[a]
1–2 TAMs	127 (6)
≥3 TAMs	79 (4)
≥3 TAMs, including M41L ± L210W	48 (2)
≥1 TAM-only NRTI-R (no other NRTI-R)	112 (5)
≥1 TAM + other NRTI-R	94 (5)
≥1 TAM + M184V/I	87 (4)

[a]TAMs: K70R, 5%; M41L, 4%; D67N, 4%; K219E/N/Q/R, 4%; T215F/Y, 4%; L210W, 2%.

Efficacy results

High rates of virologic suppression (using LOCF imputation) were maintained after participants switched to BIC/FTC/TAF for a median treatment duration of 72 weeks, and no treatment-emergent resistance was detected (Figure 2).

Figure 2. Pooled Analysis: Virologic Suppression at Last Study Visit by Preexisting TAMs (LOCF; Andreatta et al)[3]



[a]No participants with ≥1 TAM and primary INSTI-R received BIC/FTC/TAF.
Note: The median treatment durations of BIC/FTC/TAF are presented in each bar.

Safety outcomes were not provided for this pooled analysis. Please see product labeling for BIC/FTC/TAF safety information.

Post Hoc Pooled Analysis: Prevalence of K65R/N and Efficacy Outcomes in VS Participants[4]

Study design and BL resistance

A post-hoc pooled analysis assessed VS participants (N=2028 with BL genotype RT data) who received BIC/FTC/TAF in Studies 1474, 1844, 1878, 4030, 4449, and 4580 to evaluate the prevalence of preexisting K65R/N resistance mutation and its effect on virologic efficacy at Week 48 by FDA Snapshot algorithm. All studies except Study 4030 excluded participants with documented K65R/N before enrollment; however, all participants with preexisting K65R/N that was identified after enrollment stayed in the study. Results of historical RNA or proviral DNA genotype testing for PR, RT, and IN were collected when available, and retrospective proviral DNA genotype testing for PR, RT, and IN was performed at BL.

Overall, K65R/N resistance mutations were detected in 1% of participants (20/2028; Table 3).

Table 3. Pooled Analysis: Resistance Profile of Participants With BL K65R/N Resistance Mutations (Boopathy et al)[4]

BL K65R/N Resistance Mutation, n/N (%)	Pooled BIC/FTC/TAF (N=2028)
K65R/N ± other NRTI RAMs[a]	20/2028 (1)
K65R/N + M184V/I ± other NRTI RAMs	9/20 (45)
K65R/N only	6/20 (30)
K65R/N + ≥1 TAMs	6/20 (30)

[a]Other primary NRTI RAMs included Y115F (n=5), L74V/I (n=2), and Q151K/L/M (n=2); secondary NRTI RAMs included A62V (n=4), T69N (n=2), V75V/I (n=2), F116Y (n=2), V118I (n=2), T215I/A (n=2), and F77L (n=1).

Efficacy results

Of the participants with BL K65R/N resistance mutation, 92% of participants (12/13) randomized to BIC/FTC/TAF were VS at Week 48 by FDA Snapshot algorithm, and all (20/20) had HIV-1 RNA <50 c/mL through end of study by LOCF. No VF or treatment-emergent resistance to BIC/FTC/TAF was reported. One participant with K65R/N decided to discontinue BIC/FTC/TAF and had HIV-1 RNA <50 c/mL at their last study visit at Week 24.

Safety outcomes were not provided for this pooled analysis. Please see product labeling for BIC/FTC/TAF safety information.

Studies 1489 and 1490: BL Resistance in ARV-Naive PWH

Study design and BL resistance

An integrated viral resistance analysis of two phase 3 clinical trials in ARV-naive PWH comparing BIC/FTC/TAF to DTG/ABC/3TC (Study 1489) or DTG + FTC/TAF (Study 1490) was conducted. All participants were screened using HIV-1 genotypic data with PR and RT population sequencing data obtained from the GenoSure MG assay.[5,6] Exclusion criteria included resistance to study drugs. BL NRTI resistance-associated substitutions (1–2 TAMs [n=19], K219E/N/Q/R [n=11], M41L [n=4], D67N [n=3], K70R [n=3], K65E/R detected by retrospective deep sequencing [n=2], L74V [n=1]) were identified in 3% of participants in the BIC/FTC/TAF arms (n=634).[5]

Efficacy results

BIC/FTC/TAF demonstrated noninferior efficacy (HIV-1 RNA <50 c/mL) to DTG/ABC/3TC (Study 1489) and DTG + FTC/TAF (Study 1490) by FDA Snapshot analysis at Week 144.[7] Preexisting NRTI-R using a mutation frequency cutoff of ≥15% was discovered in 21 participants who received BIC/FTC/TAF, 8 participants who received DTG/ABC/3TC, and 6 participants who received DTG + FTC/TAF; 100% of these participants were VS at Week 144.[5] Primary NRTI-R mutations were detected at low frequencies (2–15%) using retrospective deep sequencing in an additional 3.7% of ARV-naive participants (47/1270). Using the LOCF method, high rates of virologic suppression (100%) were observed in participants with BL primary NRTI-R, including low-frequency M184V or K65R resistance substitutions, at Week 96 across all treatment arms.[6]

Safety results at Week 144[7]

A safety analysis was not conducted in the subgroup of participants with BL NRTI-R. Overall, the most common all-grade adverse reactions reported in ≥10% of all participants in the BIC/FTC/TAF arms in either study through Week 144 were nausea, diarrhea, URTI, headache, nasopharyngitis, back pain, fatigue, cough, and syphilis. AEs led to study drug discontinuation in no participants in the BIC/FTC/TAF arm in Study 1489 and in 6 participants (2%) in the BIC/FTC/TAF arm in Study 1490.

Studies 1878 and 1844: BL Resistance in VS PWH

Study design[8]

An integrated viral resistance analysis of two phase 3 clinical trials in VS PWH comparing BIC/FTC/TAF to PI + 2 NRTIs (Study 1878) or DTG/ABC/3TC (Study 1844) was conducted. Exclusion criteria included documented or suspected resistance to FTC, TFV, DTG, ABC, or 3TC, including, but not limited to, K65R and M184V/I in RT. The resistance analysis population consisted of participants with confirmed VF with HIV-1 RNA ≥200 c/mL at the confirmation visit or HIV-1 RNA ≥200 c/mL at Week 48 or last visit on study drug; plasma viral RNA genotyping and phenotyping of PR, RT, and IN were attempted for all participants in this population.

Efficacy results at Week 48[8]

Switching to BIC/FTC/TAF demonstrated noninferior efficacy (HIV-1 RNA <50 c/mL) by FDA Snapshot analysis compared with staying on PI + 2 NRTIs or DTG/ABC/3TC at Week 48. Among participants in the BIC/FTC/TAF arms with available BL NRTI genotypic data (n=405), 13% had primary NRTI-R substitutions (K65N/R [n=5], M184I/V [n=30], L74V [n=2], Y115F [n=2], Q151M [n=2]). At Week 48, among participants who switched to BIC/FTC/TAF, 94% of participants (49/52) with BL NRTI-R and 90% (27/30) with BL M184I/V maintained virologic suppression. No treatment-emergent resistance was detected among participants in the BIC/FTC/TAF arm.

Open-label extension phase

In Study 1878, 94/98 participants with BL NRTI-R and 59/62 participants with BL M184V/I who received BIC/FTC/TAF for a median duration of 101 weeks had HIV-1 RNA <50 c/mL at their last visit.[9] In Study 1844, 47/48 participants with BL NRTI-R and 17/17 participants with BL M184V/I who received BIC/FTC/TAF for a median duration of 96 weeks had HIV-1 RNA <50 c/mL at their last visit.[10]

Safety results

A safety analysis was not conducted in the subgroup of participants with BL NRTI-R.
In Study 1878, the most common adverse reactions (all grades) 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.[9] In Study 1844, the most common adverse reactions (all grades) 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.[10]

Study 4030: BL Resistance in VS PWH

Study design[11]

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 VS PWH, including those with known BL resistance mutations. Eligible participants were those 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, and with no documented INSTI-R or confirmed VF during treatment with an INSTI-containing regimen. 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 by NRTI-R category based on historical genotype.

Efficacy results at Week 48

Switching to BIC/FTC/TAF demonstrated noninferior efficacy (HIV-1 RNA ≥50 c/mL) by FDA Snapshot analysis vs staying on DTG + FTC/TAF at Week 48.[11] Rates of virologic suppression were high regardless of preexisting NRTI-R (Table 4). No participant with known or suspected BL NRTI-R in either treatment arm had HIV-1 RNA ≥50 c/mL at Week 48 or their last visit, including 81 participants (BIC/FTC/TAF, n=47; DTG + FTC/TAF, n=34) with BL M184V/I resistance mutations. No treatment-emergent resistance was observed in either arm through Week 48.[12]

Table 4. Study 4030: BL Resistance and Virologic Outcomes at Week 48 by FDA Snapshot Analysis[11,12]

Resistance Category, n/N (%)	Presence of BL Resistance		HIV-1 RNA <50 c/mL		Treatment Difference, % (95% CI)
	At Stratification	Final	BIC/FTC/TAF[a]	DTG + FTC/TAF[a]	
1: High[b]	15/565 (3)	30/565 (5)	15/16 (94)	14/14 (100)	-6.3 (-30.7 to 19.4)
2: Low[c]	63/565 (11)	108/565 (19)	51/55 (93)	51/53 (96)	-3.5 (-14.2 to 6.9)
3: None[d]	487/565 (86)	427/565 (76)	199/213 (93)	191/214 (89)	4.2 (-1.3 to 9.9)

[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: K65R/E/N, ≥3 TAMs, including M41L or L210W, or T69 insertions.
[c]Resistance Category 2: M184V/I, K70E/G/M/Q/S/T, L74V/I, V75A/S/M/T, Y115F, T69D, Q151M, M41L, D67N, K70R, L210W, T215F/Y, or K219Q/E/R/N.
[d]Resistance Category 3: no NRTI RAMs.

Safety results at Week 48[11]

A safety analysis was not conducted in the subgroup of participants with BL NRTI-R. The most commonly reported AEs (≥10%) in either group were nasopharyngitis, diarrhea, and URTI. Drug-related AEs that occurred in ≥2% in either group were diarrhea and headache. Six participants (2%) in each arm discontinued the study because of AEs.

BRAAVE 2020 Study

Study design and BL resistance[13]

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 2 NRTIs plus a third agent (n=165) in VS PWH who were located in the USA 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. Preexisting BL NRTI mutations were detected in 15% of participants (Table 5).

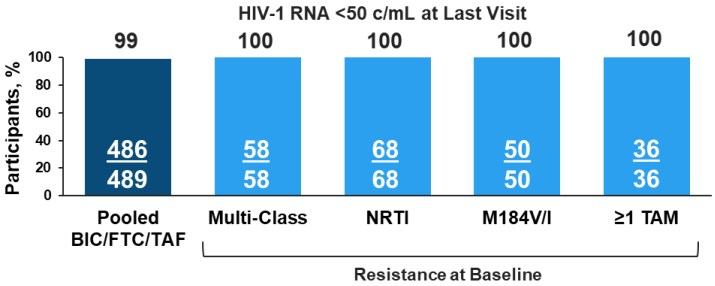
Table 5. BRAAVE 2020: Proportion of Participants With Preexisting NRTI-R Substitutions[13]

Preexisting NRTI RAMs, n (%)	Cumulative BL Genotype (n=468)
NRTI-R	68 (15)
M184V/I	50 (11)
K65R	4 (1)
Any TAM	36 (8)
1–2 TAMs	27 (6)
≥3 TAMs	9 (2)
Other (K70E, L74I/V, Y115F, Q151M)	12 (3)

Efficacy results through Week 72[13]

Switching to BIC/FTC/TAF was noninferior to continuing the BL regimen at Week 24. High rates of virologic suppression (98–100%) were maintained through Week 72 on BIC/FTC/TAF, regardless of preexisting NRTI-R, including M184V/I or ≥1 TAM (Figure 3). All participants with preexisting NRTI-R had virologic suppression at their last study visit. No treatment-emergent resistance was observed.

Figure 3. BRAAVE 2020: Virologic Outcomes at Last Visit Through Week 72[13]



Safety results

A safety analysis was not conducted in the subgroup of participants with BL NRTI-R. Switching to BIC/FTC/TAF was well tolerated, and reported AEs were comparable between the two treatment arms at Week 24.[14] All-grade AEs that occurred 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.[15]

PIBIK: Phase 4 Study of BIC/FTC/TAF vs Boosted PI[16]

Study design and BL resistance

A phase 4, randomized, multicenter, open-label pilot study evaluated the efficacy and safety of switching to BIC/FTC/TAF immediately (n=33) or continuing a boosted PI with a delayed switch to BIC/FTC/TAF (n=39) after 24 weeks in VS PWH with BL NRTI-R.
Eligible participants had HIV-1 RNA <50 c/mL for ≥6 months and had historical genotypes that showed no existing INSTI mutations and the presence of M184V/I alone or with other NRTI-associated mutations and/or ≤2 TAMs with or without M184V/I and/or other major NRTI RAMs. The primary and secondary efficacy endpoints were the pure virologic response rates (HIV-1 RNA <50 c/mL) at Week 24 and Week 48, respectively. Other secondary endpoints included safety and treatment-emergent resistance. NRTI RAMs in BL genotype were present in 13 participants (39.4%) in the immediate switch group and in 20 participants (51.3%) in the delayed switch group (Table 6).

Table 6. PIBIK: BL Drug Resistance Mutations (Historical Genotypes)[16]

BL Mutations,[a] n (%)	Immediate Switch to BIC/FTC/TAF (n=33)	Delayed Switch to BIC/FTC/TAF (n=39)
M184V/I only	12 (36.4)	9 (23.1)
1 TAM	6 (18.2)	10 (25.6)
1 TAM + M184V/I	4 (12.1)	7 (18)
1 NAM + M184V/I	3 (9.1)	2 (5.1)
2 TAMs + M184V/I + 1 NAM	3 (9.1)	1 (2.6)
2 TAMs + M184V/I	2 (6.1)	5 (12.8)
2 TAMs	1 (3)	3 (7.7)
1 TAM + M184V/I + 1 NAM	1 (3)	2 (5.1)
1 TAM + 1 NAM	1 (3)	0

Abbreviation: NAM=NRTI-associated mutation.
[a]NAM mutations could include L74I/V and K70E/G/Q; excluded mutations were K65R/N/E, T69ins, and Q151 ± A62V, V75I, F77L, or F116Y. TAM mutations could include the following: M41L, D67N, K70R, L210W, T215F/Y, and K219Q/E/N.

Efficacy results up to Week 48

At both Week 24 and Week 48, the pure virologic response rates were 100% (33/33) in the immediate switch group and 97.4% (38/39) in the delayed switch group (difference between groups, 2.6%; 95% CI: -2.4% to 7.5%).

Safety results up to Week 48

From BL to Week 24, the most common AEs (≥10%) in the immediate switch group were headaches and hypertension (each 12%), and no AE was experienced by ≥10% of the delayed switch group. One participant in the delayed switch group discontinued due to an AE. From Week 24 to Week 48, no AEs in the immediate switch group and headaches

(10.3%) in the delayed switch group were experienced by ≥10% of participants. From Week 24 to Week 48, 1 participant in the immediate switch group and 3 participants in the delayed switch group discontinued due to AEs.

Real-World Data: Use of BIC/FTC/TAF in BL NRTI-R

Key real-world studies are presented in Table 7. Data may not be all-inclusive.

Table 7. Summary of Real-World Studies[17-26]

Study Type	Study Location	Time Point	Study Size	HIV-1 RNA <50 c/mL		Safety Summary
				Overall	BL NRTI-R	
Retrospective cohort study of TE PWH who switched to BIC/FTC/TAF or DTG/3TC (Lee et al)[17]	Taiwan	48 wk	Overall: N=988 (BIC/FTC/TAF: n=480; DTG/3TC: n=508) BL NRTI-R: BIC/FTC/TAF: n=31; DTG/3TC: n=20	96.5% (BIC/FTC/TAF: 95%; DTG/3TC: 98.2%)	K65R ± M184V/I: BIC/FTC/TAF: n/N=3/3 (100%)[a] DTG/3TC: n/N=3/3 (100%)[a] M184V/I: BIC/FTC/TAF: n/N=15/15 (100%); DTG/3TC: n/N=5/6 (83.3%)	In the overall population,[b] 40 patients (7.7%) receiving BIC/FTC/TAF and 24 patients (4.5%) receiving DTG/3TC reported drug-related AEs or events leading to discontinuation. No significant difference was observed in the discontinuation rates between the two groups (*P*=0.055).
BICSTaR study: prospective, observational study in TN and TE PWH (Sabranski et al)[18]	Germany, France, and Canada	36 mo	Overall (TN and TE): N=781 BL NRTI-R (TE): n=22	97%	100%	In the overall population,[b] drug-related AEs occurring in ≥1% of participants receiving BIC/FTC/TAF at 36 mo consisted of weight increased, depression, nausea, and fatigue.
Retrospective study in TE PWH (Mican et al)[19]	Spain	48 wk	Overall: ITT: N=506 PP: N=445 BL NRTI-R: ITT: n=69 PP: n=65	ITT: 83% PP: 94.4%	ITT: 88.4% PP: 93.8%	In the overall population,[b] 19 patients (3.7%) discontinued BIC/FTC/TAF due to AEs, and 6 patients died due to reasons that were deemed unlikely to be related to treatment.
Retrospective cohort study in VS PWH aged ≥50 y (Rolle et al)[20]	US	48 wk	Overall: N=350 BL NRTI-R: n=35	94%	89%	Any drug-related AE was reported in 15% of all patients and led to discontinuation of BIC/FTC/TAF in 2% of all patients.[b]

Study Type	Study Location	Time Point	Study Size	HIV-1 RNA <50 c/mL		Safety Summary
				Overall	BL NRTI-R	
Single-center, retrospective cohort study in real-world effectiveness of switching to BIC/FTC/TAF in PWH with NRTI-R (Mezzogori et al)[21]	Italy	96 wk	Overall: N=257 Preexisting NRTI RAMs: n=41	97.2% (210/216)	100% (41/41)	No safety data were reported.
BICTARG study: retrospective observational study in PWH with NRTI-R receiving BIC/FTC/TAF (Lamaizón et al)[22]	Argentina	36 and 48 mo	BL NRTI-R: n=117 Single M184V/I: n=50 M184V/I + 1 to ≥3 TAMs: n=32 M184V/I + L74V ± TAMs: n=5	Any NRTI-R: 92% at 36 mo and 48 mo Single M184V/I: 83% at 36 mo M184V/I + 1 to ≥3 TAMs: 92–100% at 36 mo M184V/I + L74V ± TAMs: 100% at 36 mo		No safety data were reported.
BICTARG study: subanalysis of retrospective observational study in PWH with history of VF treated with BIC/FTC/TAF (Lamaizón et al)[23]	Argentina	24 and 48 wk	History of VF: n=185 BL NRTI-R: n=111 M184V/I: n=92 M184V/I + TAM: n=31	Patients with history of VF: Wk 48: 94%	Any NRTI-R: Wk 48: 95% M184V/I: Wk 24: 94% Wk 48: 97% M184V/I + TAM: Wk 24: 96% Wk 48: 95%	No safety data were reported.

Study Type	Study Location	Time Point	Study Size	HIV-1 RNA <50 c/mL		Safety Summary
				Overall	BL NRTI-R	
Single-center, retrospective cohort study of PWH who switched to BIC/FTC/TAF or DTG + 2 NRTIs after a virologic rebound (Chen et al)[24]	Taiwan	48 wk	Overall: N=79 (BIC/FTC/TAF: n=40; DTG + 2 NRTIs: n=39) BL NRTI-R: BIC/FTC/TAF: n=15; DTG + 2 NRTIs: n=15	79.9% (BIC/FTC/TAF: 82.5%; DTG + 2 NRTIs: 76.9%)	BIC/FTC/TAF: 93.8% DTG + 2 NRTIs: 86.7%	No safety data were reported.
Multicenter, retrospective cohort study of VS PWH with K65N/R and prior event of VF who switched to BIC/FTC/TAF (Tsai et al)[25]	Taiwan	48 wk	Overall (K65N/R): N=72 K65N/R + M184V/I: n=43	Overall (K65N/R): 87.5%[c] K65N/R + M184V/I: 100%[c]		No treatment-related AEs were reported. One patient died, and 1 patient discontinued BIC/FTC/TAF due to causes unrelated to treatment.
Retrospective study among PWH with preexisting NRTI-R (Shafran et al)[26]	Canada	Mean (range) of 18.6 (2–29) mo	N=50	96%		One patient discontinued BIC/FTC/TAF after 15 mo with HIV-1 RNA <50 c/mL. Two patients died after 10 mo of BIC/FTC/TAF from causes unrelated to treatment.

Abbreviations: BICSTaR=BIC single-tablet regimen; PP=per protocol.
[a]All patients were VS at BL.
[b]Safety analyses were not conducted in the subgroup of patients with BL NRTI-R.
[c]Represents the percentage of patients who maintained HIV-1 RNA <200 c/mL.

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Abbreviations

3TC=lamivudine
ABC=abacavir
AE=adverse event
ARV=antiretroviral
BIC=bictegravir
BL=baseline
c/mL=copies/mL
DTG=dolutegravir
FTC=emtricitabine
IN=integrase
INSTI=integrase strand transfer inhibitor
INSTI-R=integrase strand transfer inhibitor resistance
LOCF=last observation carried forward
NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor
NNRTI-R=non-nucleos(t)ide reverse transcriptase inhibitor resistance
NRTI=nucleos(t)ide reverse transcriptase inhibitor
NRTI-R=nucleos(t)ide reverse transcriptase inhibitor resistance
PI=protease inhibitor
PI-R=protease inhibitor resistance
PR=protease
PWH=people with HIV
RAM=resistance-associated mutation
RT=reverse transcriptase
TAF=tenofovir alafenamide
TAM=thymidine analog mutation
TDF=tenofovir disoproxil fumarate
TFV=tenofovir
TE=treatment experienced
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.

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