GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Efficacy by Adherence Subgroups

This document is in response to your request for information regarding the efficacy of the single-tablet regimen (STR) Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in people with HIV (PWH) by adherence subgroups.

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

Clinical Data on Efficacy of BIC/FTC/TAF by Adherence Subgroups

In a pooled analysis of 5 trials evaluating BIC/FTC/TAF vs DTG + 2 NRTIs, PWH who were treated with BIC/FTC/TAF had high rates of virologic suppression (96–99%, using LOCF imputation) at Weeks 48, 96, and 144, regardless of the level of adherence.[1]

In a phase 3 study that evaluated the safety and efficacy of switching to BIC/FTC/TAF in VS PWH who identified as Black American, high rates of virologic suppression (98–100% using a LOCF imputation) were maintained through Week 72 in all adherence subgroups.[2]

Real-World Data on Efficacy of BIC/FTC/TAF by Adherence Subgroups

In a retrospective study of VS PWH who switched to BIC/FTC/TAF or DTG-containing STRs or MTRs in the Trio Health HIV EMR and dispensing database, viral suppression rates remained high and were similar between all groups despite the differences in adherence.[3]

A retrospective cohort study in Italy evaluating BIC/FTC/TAF forgiveness reported that a PDC as low as 0.75 was sufficient for >90% of patients to obtain a VL of <50 or <200 c/mL.[4]

Clinical Data on the Efficacy of BIC/FTC/TAF by Adherence Subgroups

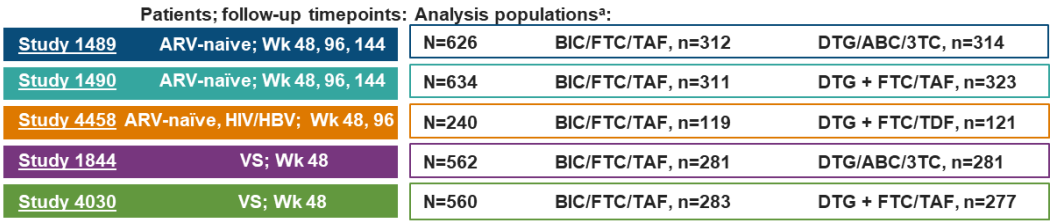
Pooled Analysis of Adherence in Studies of BIC/FTC/TAF vs DTG + 2 NRTIs

Study design and demographics

A retrospective analysis of studies that included PWH who received BIC/FTC/TAF (n=1306) or DTG + 2 NRTIs (n=1316) was performed to determine rates of adherence and the effect of adherence on virologic outcomes. Adherence was analyzed at Weeks 48, 96, or 144 and

was categorized into three subgroups: high (≥95%), intermediate (≥85% to <95%), and low (<85%). Adherence was calculated by dividing the number of pills taken (imputed from unreturned pills) by the total number of pills prescribed. Virologic outcomes were evaluated using the last available on-treatment VL using the last available on-treatment VL (LOCF imputation). Participants underwent postbaseline resistance testing if they had confirmed virologic failure (defined as VL ≥50 c/mL at two consecutive visits) and a VL ≥200 c/mL at the confirmation visit, or if they had VL ≥200 c/mL at the Week 48 study visit or the last visit and were not resuppressed (VL <50 c/mL) while on the study drug. Baseline demographics were generally similar between treatment groups.[1]

Figure 1. Pooled Analysis: Studies Included and Analysis Populations[5]



[a]Included participants who returned ≥1 pill bottle and had ≥1 postbaseline VL measurement.

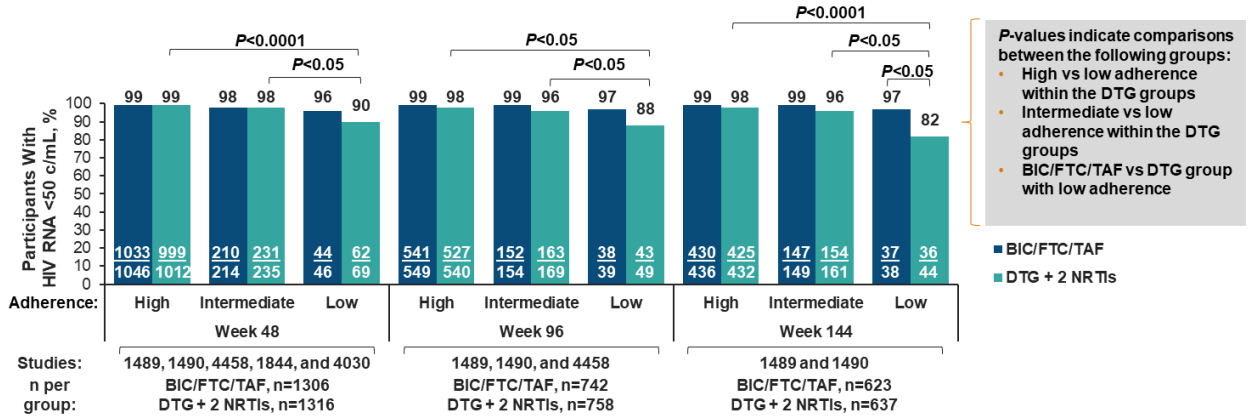
Results

At each analysis time point, overall rates of virologic suppression at last visit were high in both treatment groups (BIC/FTC/TAF, 99%; DTG + 2 NRTIs, 97–98%).[6]

Through Week 48, low adherence (<85%) was observed in 4% of participants in the BIC/FTC/TAF group and 5% in the DTG + 2 NRTI group. Among these participants with low adherence, median adherence was 78% for the BIC/FTC/TAF group and 80% for the DTG + 2 NRTI group through Week 48. Compared to participants with high and intermediate adherence, those with low adherence were younger, more often Black, and more often ARV-naive ($P \leq 0.02$).[1]

Participants who received BIC/FTC/TAF had high rates of virologic suppression, regardless of the level of adherence, whereas virologic suppression rates were significantly lower among participants treated with DTG + 2 NRTIs who had <85% adherence than among those with intermediate or high adherence (Figure 2). Among participants with low adherence, the virological suppression rate at Week 144 was significantly higher in those who received BIC/FTC/TAF than in those who received DTG + 2 NRTIs ($P<0.05$).[1]

Figure 2. Pooled Analysis: Virologic Suppression in Treatment Groups by Time Point and Adherence Category[1]



Note: Adherence subgroups were defined as follows: high, ≥95%; intermediate, ≥85% to <95%; low, <85%.

No participants who received BIC/FTC/TAF had treatment-emergent resistance. Two participants who received DTG/ABC/3TC had emergent M184V identified (adherence through Week 144: 93% and 86%); both were resuppressed after being switched to open-label BIC/FTC/TAF.[1]

Safety outcomes were not provided for this pooled analysis[5]; safety data for the individual studies included in this summary are reported elsewhere (Studies 1489,[7] 1490,[7] 4458,[8] 1844,[9] and 4030[10]).

Adherence Analysis in the BRAAVE 2020 Study

A phase 3, randomized, active-controlled study evaluated the safety and efficacy of switching to BIC/FTC/TAF (n=330) or continuing a baseline regimen of 2 NRTIs plus a third agent (n=165) in PWH who were VS; located in the US; and self-identified as Black, Black American, or mixed race, including Black. The primary efficacy endpoint was the proportion of participants with plasma VL ≥50 c/mL at Week 24 by FDA Snapshot analysis. After Week 24, participants in the continuing baseline regimen group were switched to BIC/FTC/TAF.[11]

Switching to BIC/FTC/TAF was noninferior to continuing the baseline regimen of 2 NRTIs plus a third agent at Week 24.[11] High rates of virologic suppression (98–100%, using an M=E analysis) were maintained through Week 72 in participants who received BIC/FTC/TAF, regardless of adherence levels. Through Week 72, 100% of participants (363/363) with ≥95% adherence, 98% of participants (102/104) with ≥80% to 95% adherence, and 100% of participants (15/15) with <80% adherence had a VL <50 c/mL at their last visit (LOCF). No treatment-emergent resistance-associated mutations were detected.[2]

Through Week 72, all-grade AEs that occurred in ≥5% of participants who received BIC/FTC/TAF at any time (n=493) included upper respiratory tract infection, syphilis, headache, pain in extremity, arthralgia, hypertension, and nasopharyngitis. There were 12 participants who reported AEs that led to study drug discontinuation through Week 72.[12]

Real-World Data on the Efficacy of BIC/FTC/TAF by Adherence Subgroups

Trio Health Study[3]

A retrospective observational study evaluated data on HIV suppression from the Trio Health HIV EMR and dispensing database in VS stable patients switched to STRs (BIC/FTC/TAF, DTG/3TC/ABC) or MTRs (DTG + FTC/TAF, DTG + FTC/TDF, DTG + 3TC + ABC). PDC ≥80% and ≥95% were used to measure adherence. At baseline, there were significant differences across treatment groups in gender, race, and proportion of patients with CD4 <200 cells/mcL.

The study evaluated 2229 patients: 51% (n=1130) switched to BIC/FTC/TAF, 23% (n=520) switched to DTG/3TC/ABC, and 26% (n=579) switched to DTG MTRs. Patients who switched to BIC/FTC/TAF were found to be significantly more adherent at PDC ≥80% and PDC ≥95% than DTG/3TC/ABC and DTG MTR. At Month 6, viral suppression rates remained high (86–96%) and were similar between all groups despite the differences in adherence. Accounting for differences within groups at baseline in adjusted models, an association was found between adherence and viral suppression for DTG regimens but not for BIC/FTC/TAF.

BIC/FTC/TAF Forgiveness to Imperfect Adherence[4]

A retrospective cohort study in Italy was conducted to assess overall adherence in PWH treated with BIC/FTC/TAF and to determine rates of virologic suppression associated with different levels of adherence. Patients who were treated with BIC/FTC/TAF from January 2020 to August 2022 and who had obtained a minimum of 2 refills were eligible for inclusion (N=420). Adherence was assessed by PDC (number of days with available medication divided by the number of days between 2 consecutive refills), and VLs were obtained from EMRs. Patients were categorized according to virologic response: TND (undetectable), VL <50 c/mL, or VL <200 c/mL. Forgiveness in this study was calculated as the possibility to reach and maintain one of the three virologic thresholds for any degree of imperfect adherence.

Most patients were male (73.1%), and the median (IQR) age was 51 (45–57) years. Although 26 PWH were ARV naive prior to starting BIC/FTC/TAF, the median (IQR) duration of HIV infection was 7.9 (4–18) years, and the median (IQR) CD4 nadir was 277 (100–513) cells/mcL. The cohort had a median follow-up of 873 PY.

Overall adherence was high, with a median (IQR) PDC of 0.97 (0.91–1). The mean adherence rate among patients with a steady VL <50 or <200 c/mL was 0.94 (95% CI: 0.93–0.95). Overall virologic success rate was also high, with only 17 measures (2.2%) of VL >200 c/mL and 56 measures (7.11%) of VL >50 c/mL over 873 PY.

Forgiveness with BIC/FTC/TAF was observed with a PDC as low as 0.75. An adherence level of 0.75 was sufficient to achieve a VL of <50 or <200 c/mL in >90% of patients and to reach the TND threshold in >60% of patients.

In a logistic regression analysis, PDC significantly correlated with the VL <200 c/mL threshold (P<0.0001) and with achieving and maintaining a VL <50 c/mL (P-value not reported). Achievement of a TND VL was significantly associated with PDC (P<0.0001), number of chronic pathologies (P<0.001), and duration of time with HIV (P=0.05).

References

1. Andreatta K, Sax PE, Wohl D, et al. Efficacy of bictegravir/emtricitabine/tenofovir alafenamide versus dolutegravir-based three-drug regimens in people with HIV with varying adherence to antiretroviral therapy. *Journal of Antimicrobial Chemotherapy.* 2024.
2. Andreatta K, D'Antoni ML, Chang S, et al. High Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide in African-American Adults With HIV Including Those with Preexisting Resistance, Viral Blips, and Suboptimal Adherence [Poster 629]. Paper presented at: IDWeek Virtual; 29 Sept-03 Oct, 2021.
3. Sax PE, Althoff KN, Eron JJ, et al. Impact of Adherence on Viral Suppression with Bictegravir- and Dolutegravir (DTG)- Containing Triple Therapy in Clinical Practice. [Poster P029]. Paper presented at: HIV Drug Therapy Glasgow; October 5-8, 2020; Virtual.
4. Maggiolo F, Taramasso L, Valenti D, et al. B/F/TAF forgiveness to non-adherence. *Sex Transm Infect.* 2024;100(7):418-422.
5. Andreatta K, Sax PE, Wohl D, et al. Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) Versus Dolutegravir (DTG)-Based 3-Drug Regimens in Adults With HIV Who Have Suboptimal Antiretroviral Adherence [Poster 1613188]. Paper presented at: ID Week 2023; October 11-15, 2023; Boston, MA.
6. Andreatta K, Sax PE, Wohl D, et al. Efficacy of bictegravir/emtricitabine/tenofovir alafenamide versus dolutegravir-based three-drug regimens in people with HIV with varying adherence to antiretroviral therapy [Supplementary Material]. *Journal of Antimicrobial Chemotherapy.* 2024.
7. 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.
8. Avihingsanon A, Lu H, Leong CL, et al. Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, emtricitabine, and tenofovir disoproxil fumarate for initial treatment of HIV-1 and hepatitis B coinfection (ALLIANCE): a double-blind, multicentre, randomised controlled, phase 3 non-inferiority trial [Main Article + Supplementary Appendix]. *The Lancet HIV.* 2023:1-13.
9. Molina JM, Ward D, Brar I, et al. Switching to fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide from dolutegravir plus abacavir and lamivudine in virologically suppressed adults with HIV-1: 48 week results of a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. *The Lancet HIV.* 2018;5(7):e357-365. http://www.ncbi.nlm.nih.gov/pubmed/29925489
10. Sax PR, J. Luetkemeyer, A. Yazdanpanah, Y. Ward, D. Trottier, B. Rieger, A. Liu, H. Acosta, R. Collins, S. Brainard, D. Martin, H. Investigators. Switching to Bictegravir, Emtricitabine, and Tenofovir Alafenamide in Virologically Suppressed Adults With Human Immunodeficiency Virus. *Clinical Infectious Disease.* 2021.
11. 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.
12. 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
c/mL=copies per mL
CD4=clusters of differentiation 4
DTG=dolutegravir
EMR=electronic medical record
FTC=emtricitabine
LOCF=last observation carried forward
M=E=missing=excluded
MTR=multitablet regimen
NRTI=nucleos(t)ide reverse transcriptase inhibitor
PDC=proportion of days covered
PWH=people with HIV
PY=person years
STR=single-tablet regimen
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TE=treatment experienced
TND=target not detected
VL=viral load
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 privacy@gilead.com.