GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Efficacy and Safety in Females

This document is in response to your request for information regarding the efficacy and safety of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in females with HIV-1.

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 the Efficacy and Safety of BIC/FTC/TAF in Females

In a pooled efficacy and safety analysis of the BICSTaR study, 97% of TE females maintained virologic suppression through Month 24. DRAEs were reported in 16% of females and led to discontinuation of BIC/FTC/TAF in 9%.[1]

The efficacy and safety of BIC/FTC/TAF in females with HIV-1 was assessed in a pooled analysis of five phase 2 or 3 clinical studies including ARV-naive and VS participants through 48 weeks (N=373). Rates of virologic suppression were similar between BIC/FTC/TAF and comparator arms. BIC/FTC/TAF was well tolerated.[2]

Study 1961 was a phase 3, open-label study with an OLE phase that compared outcomes in females who switched to BIC/FTC/TAF vs those in the SBR group. Virologic suppression was maintained at Week 96 in 99.5% of females who stayed on BIC/FTC/TAF and in 98.5% who switched to BIC/FTC/TAF at Week 48. BIC/FTC/TAF was well tolerated.[3,4]

Clinical Data on the Efficacy and Safety of BIC/FTC/TAF in Females

BICSTaR Study[1]

Study design and demographics

An ongoing, prospective, multinational, observational study is evaluating the safety and efficacy of BIC/FTC/TAF in ARV-naive and TE participants. Study outcomes include virologic suppression (HIV-1 RNA <50 c/mL), treatment persistence at Months 12 and 24, resistance, DRAEs, and changes in weight, BMI, lipid levels, and renal function. Overall, 13% of ARV-naive (n=135) and 14% of TE (n=703) participants were female.

Efficacy and safety results through Month 24

In the M=E analysis (n=628) at Month 24, 97% of females (62/64) in the TE group achieved HIV-1 RNA <50 c/mL, compared with 95% of males (*P*=0.755). In the TE group through Month 24 (female, n=96; male, n=607):

- 16% of females experienced a DRAE, compared with 15% of males (*P*=0.805);
- No females and <1% of males experienced a serious DRAE; and,
- 9% of females and 7% of males discontinued BIC/FTC/TAF due to DRAEs (ie, weight increase [3%] and depression [1%]).

Weight change

In the TE group, the median (Q1, Q3) weight for the 49 female participants with available data was 65 (59, 74) kg at BL and 65 (58, 78) kg at Month 24 (median [Q1, Q3] change of +0.5 [-1.6, +3] kg), whereas the median (Q1, Q3) weight for the 327 male participants with available data was 78 (69, 88) kg at BL and 79 (70, 90) kg at Month 24 (median [Q1, Q3] change of +1.3 [-1, +4.8] kg; *P*=0.15).

Pooled Analysis in Females

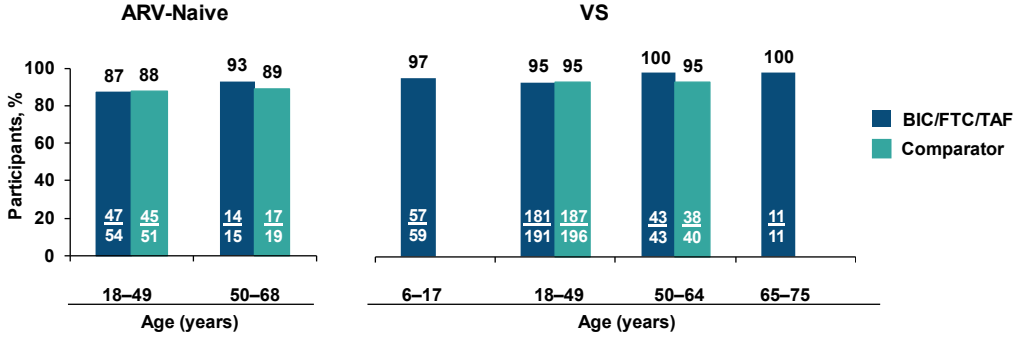
Study design and demographics[2]

The efficacy and safety of BIC/FTC/TAF in females (n=373) were assessed in a pooled analysis of five phase 2 or 3 clinical studies through 48 weeks. Studies 1489 and 1490 were conducted in ARV-naive populations. Studies 1961, 1474, and 4449 were conducted in VS, TE populations. In Studies 1489 and 1490, participants received either BIC/FTC/TAF or an active comparator regimen (DTG/ABC/3TC or DTG + FTC/TAF). In the single-arm Studies 1474 and 4449, participants switched to BIC/FTC/TAF from other ARVs. Efficacy and safety assessments included virological suppression (HIV-1 RNA <50 c/mL), treatment-emergent resistance, AEs, and laboratory parameters. Across all age groups, most female participants who received BIC/FTC/TAF were Black or White race, the range of median CD4 counts was 411 cells/mcL to 848 cells/mcL, and the range of median weights was 40.5 kg to 76.2 kg.

Efficacy results

Participants taking BIC/FTC/TAF achieved or maintained high levels of virologic suppression (Figure 1).[2,5]

Figure 1. Pooled Analysis: HIV-1 RNA <50 c/mL at Week 48[2,5]



No treatment-emergent resistance was reported in participants who received BIC/FTC/TAF. Efficacy results of the pooled analysis were consistent with the results seen in analyses of each study.[2,5]

Safety results[2]

AEs in the female cohorts studied were consistent with overall analyses of both sexes. In participants aged 6 to 17 years old treated with BIC/FTC/TAF, the most common DRAEs (incidence >10%) were upper respiratory tract infection, headache, cough, diarrhea, and influenza. The most common AEs (incidence >10%) reported in adults treated with BIC/FTC/TAF were headache, nausea, and diarrhea. There were no discontinuations related to bone, renal, or hepatic AEs. Grade 3 or 4 laboratory abnormalities that occurred in participants receiving BIC/FTC/TAF were as follows: LDL elevation (range, 0–7%), total cholesterol elevation (range, 0–0.5%), hematuria (range, 0–19%), and neutropenia (range, 0–7%).

Table 1. Pooled Analysis: AEs in Female Participants Treated With BIC/FTC/TAF[2]

	ARV-Naive		VS		
	18–49 Years (n=54)	50–68 Years (n=15)	6–17 Years (n=59)	18–49 Years (n=191)	50–75 Years (n=43)
Any Grade 3 or 4 AE, %	85.2	80	78	62.8	79.6
DRAE, %	18.5	6.7	13.6	8.9	5.6
Any AE leading to study discontinuation, n	0	0	1[a]	0	1

[a]One participant with Grade 2 anxiety and insomnia.

In participants aged ≥18 years and treated with BIC/FTC/TAF, median decreases in eGFR of <5 mL/min/1.73 m^2 were observed from BL to Week 48. VS participants aged 6 to 17 years experienced the greatest change in eGFR (median reduction of 16 mL/min/1.73 m^2). There were no reports of Fanconi syndrome or proximal renal tubulopathy in any of the treatment arms. Among participants aged 18 to 64 years in the VS arm, statistically significant decreases in RBP:Cr and β2M:Cr were observed in those who switched from a TDF-based regimen compared with those who remained on their BL regimen (P<0.001). No other changes in renal biomarkers were statistically significant. Changes in eGFR were consistent with known effects of BIC on OCT-2 and MATE-1.

In Study 1489, the mean decrease in spine BMD from BL to Week 48 in the BIC/FTC/TAF and DTG/ABC/3TC treatment arms was 0.5% and 1.1% (P=0.52), respectively, and changes in hip BMD were 0.7% and 1.7% (P=0.16). At Week 144, slight increases in BMD were observed, with no significant differences between study arms (spine, P=0.91; hip, P=0.29).

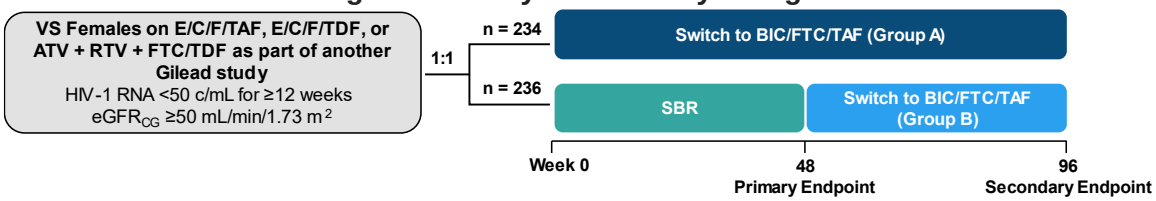
A median weight gain of 1 kg was observed in participants aged 65 to 75 years. In adults, weight gain or loss was uncommon and occurred in 1.2% of BIC/FTC/TAF-treated participants and <1% of participants in the comparator arm. From BL to Week 48, VS participants in the BIC/FTC/TAF arm aged 18 to 64 years gained significantly more weight than those in the comparator arm (median gain, +1.5 kg vs +0.4 kg; P<0.001). In TN participants aged 18 to 68 years in the BIC/FTC/TAF arm, the median weight gain from BL to Week 144 was not significantly different from increases observed with DTG/ABC/3TC (5 kg vs 7.9 kg; P=0.54) and DTG + FTC/TAF (5 kg vs 4.9 kg; P=0.77).

Study GS-US-380-1961

Study design and demographics

A phase 3, prospective, randomized, multicenter, open-label study with an OLE phase was conducted (Figure 2).[3,4] Key inclusion criteria were completion of the Week 48 OLE, Week 96, or Week 144 visits for Gilead-sponsored studies. The primary endpoint was the proportion of participants with HIV-1 RNA ≥50 c/mL at Week 48 according to the FDA Snapshot analysis, with a prespecified noninferiority margin of 4%. BL demographics and disease characteristics were similar between both groups, with a median age of 40 years, most participants were Black and White race, and 53% of participants in each group were on E/C/F/TAF at BL.[4,6]

Figure 2: Study 1961: Study Design[3,4]



Results through Week 48[4]

Efficacy, resistance, bone safety, and renal safety results were consistent with results seen in the pooled analysis.

Extension phase results through Week 96

Using an M=E analysis, virologic suppression was maintained at Week 96 in 99.5% of females (207/208) in Group A who stayed on BIC/FTC/TAF and in 98.5% of females (191/194) in Group B who switched to BIC/FTC/TAF at Week 48.[3]

No treatment-emergent resistance developed in females taking BIC/FTC/TAF in Group A through Week 96 or those in Group B who switched to BIC/FTC/TAF from Week 48 to Week 96. One participant on E/C/F/TAF in the SBR group had virologic failure at Week 48 and emergent M184M/I/V and was subsequently resuppressed when switched to BIC/FTC/TAF.[3]

BIC/FTC/TAF was well tolerated; most AEs reported as Grade 1 or 2 in severity.[3] One participant in Group B discontinued due to Grade 2 elevated AST, ALT, and GGT, all of which were determined to be study-drug related.[7] Study DRAEs occurred in 10% of participants in Group A through Week 96. DRAEs related to BIC/FTC/TAF that occurred in >1 participant in Groups A and B included headache (1%), dyslipidemia, insomnia, iron-deficiency anemia, nausea, and vomiting (each, <1%).[3]

Grade 3 or 4 laboratory abnormalities that occurred in ≥2% of participants receiving BIC/FTC/TAF in Group A through Week 96 were as follows: hematuria, 12% (all related to menses); fasting LDL elevation, 6%; amylase elevation, 3%; and neutropenia, 3%.[3]

There was no proximal renal tubulopathy or discontinuations due to renal AEs through Week 96. A median change from BL in $eGFR_{CG}$ of -1.8 mL/min/1.73 m^2 was observed for all participants on BIC/FTC/TAF in the OLE (Groups A and B) at Week 96. Those switching from BL TDF-containing regimen to BIC/FTC/TAF had a greater percentage decrease in RBP:Cr and β2M:Cr than other groups. Changes in fasting lipid parameters from BL to Week 96 were not clinically relevant in Group A or Group B.[4]

Pregnancy results[3]

Participants in the BIC/FTC/TAF group who became pregnant discontinued the study drug. Among all patients who received BIC/FTC/TAF in the OLE phase (Group A and Group B, n=462), 12 females became pregnant, with 7 live births, 1 fetal death (1 twin pregnancy that resulted in fetal deaths: 1 death in utero and 1 stillbirth; neither was attributed to study drug), 2 elective abortions, and 2 unknown pregnancy outcomes.

References

1. Trottier B, Antinori A, De Wet J, et al. Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) for the Treatment of People Living With HIV: 24-Month Analyses by Age, Race, Sex, Adherence and Late Diagnosis in a Multi-Country Cohort Study [Poster P067]. Paper presented at: HIV Glasgow 23-26 October, 2022; Glasgow, UK.
2. Orkin C, Ajana F, Kityo C, et al. Brief Report: Efficacy and Safety of Bictegravir/Emtricitabine/Tenofovir Alafenamide in Females Living With HIV: An Integrated Analysis of 5 Trials. *J Acquir Immune Defic Syndr.* 2021;88(4):393-398.
3. Kityo C, Hagins D, Koeing E, et al. Longer-term (96-week) Efficacy and Safety of Switching to Bictegravir, Emtricitabine and Tenofovir Alafenamide (B/F/TAF) in Women [Presentation]. Paper presented at: 10th IAS Conference on HIV Science (IAS 2019); 21-24 July, 2019; Mexico City, Mexico.
4. Kityo C, Hagins D, Koenig E, et al. Switching to Fixed-Dose Bictegravir, Emtricitabine, and Tenofovir Alafenamide (B/F/TAF) in Virologically Suppressed HIV-1 Infected Women: A Randomized, Open-Label, Multicenter, Active-Controlled, Phase 3, Noninferiority Trial. *J Acquir Immune Defic Syndr.* 2019;82(3):321-328. https://www.ncbi.nlm.nih.gov/pubmed/31609930
5. Orkin C, Ajana F, Kityo C, et al. Efficacy and Safety of Bictegravir/Emtricitabine/Tenofovir Alafenamide vs Comparators in Women and Girls: an Analysis of 5 Clinical Trials [Presentation]. Paper presented at: EACS; 06-09 November, 2019; Basel, Switzerland.
6. ClinicalTrials.gov. *Safety and Efficacy of Switching to a FDC of B/F/TAF From E/C/F/TAF, E/C/F/TDF, or ATV+RTV+FTC/TDF in Virologically Suppressed HIV-1 Infected Women. ClinicalTrials.gov Identifier: NCT02652624. Last Updated: 06 November.* 2017.
7. Gilead Sciences Inc. Data on File.

Abbreviations

β2M=β-2-microglobulin
3TC=lamivudine
ABC=abacavir
AE=adverse event
ARV=antiretroviral
ATV=atazanavir
BL=baseline
BMD=bone mineral density
c/mL=copies/mL
DRAE=drug-related AE
DTG=dolutegravir
CG=Cockcroft-Gault
E/C/F/TAF=elvitegravir/ cobicistat/emtricitabine/ tenofovir alafenamide
E/C/F/TDF=elvitegravir/ cobicistat/emtricitabine/ tenofovir disoproxil fumarate
GGT=γ-glutamyl transferase
M=E=missing=excluded
OCT-2=organic cation transporter 2
MATE-1=multidrug and toxin extrusion-1 transporters
OLE=open-label extension
Q=quartile
RBP=retinol-binding protein
RTV=ritonavir
SBR=stay on baseline regimen
TDF=tenofovir disoproxil fumarate
TE=treatment experienced
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
🖱 https://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.