Biktarvy® (BIC/FTC/TAF) Lipid Safety Profile

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

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

Lipid Safety Profile of BIC/FTC/TAF in Comparative Studies

In a pooled analysis of Studies 1489 and 1490 through Week 144, fasting lipids increased in all groups after treatment initiation.[1] Small changes in fasting lipid levels were reported in participants on BIC/FTC/TAF in the OLE phase up to Week 240.[2,3]

Lipid Safety Profile of BIC/FTC/TAF in Switch Studies

In clinical trials of virologically suppressed participants who switched to BIC/FTC/TAF vs remaining on their baseline regimens, most lipid parameters remained stable through Week 48.[4-6]

Lipid Safety Profile of BIC/FTC/TAF in Comparative Studies

Studies GS-US-380-1489 and GS-US-380-1490

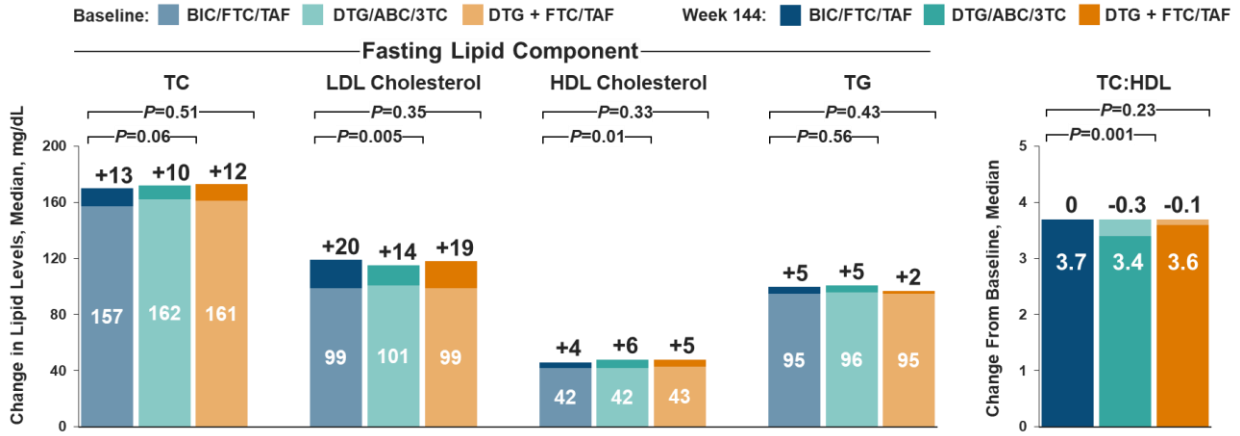
Studies 1489 and 1490 were two phase 3, prospective, randomized, double-blind, active-controlled clinical trials that compared BIC/FTC/TAF (n=314 in Study 1489; n=320 in Study 1490) with DTG/ABC/3TC (n=315) and DTG + FTC/TAF (n=325) in antiretroviral-naïve, adult PWH. Baseline demographics and characteristics were similar between treatment groups in both studies.[7]

At Week 144, LDL elevations were reported as a Grade 3 or 4 laboratory abnormality in 5% of participants in each group in Study 1489, in 4% of participants in the BIC/FTC/TAF group, and in 6% of participants in the DTG + FTC/TAF group in Study 1490. In Study 1489 at Week 144, 5% of participants in each group initiated lipid-modifying medications during the study (P=1).[7]

In a pooled analysis of Studies 1489 and 1490 with data through Week 144, fasting lipids increased in all groups after initiating treatment. Differences between groups in changes in

fasting lipids from baseline to Week 144 were not considered clinically relevant (Figure 1). Similar percentages of participants in each group initiated lipid-modifying medications through Week 144: BIC/FTC/TAF, 4.7%; DTG/ABC/3TC, 5.1%; and DTG + FTC/TAF, 4.9%.[1]

Figure 1. Studies 1489 and 1490: Changes in Fasting Lipids From Baseline to Week 144[1]



Note: *P*-values from 2-sided Wilcoxon rank-sum test to compare changes from baseline between treatment groups.

Extension phase results

Participants who completed the 144-week blinded treatment phase were given the option to continue on or switch to BIC/FTC/TAF for an additional 96-week OLE.[3]

In participants who were initially randomized to receive BIC/FTC/TAF, median (Q1, Q3) lipid changes from baseline to Week 240 were 21 (1, 42) mg/dL for TC, 19 (2, 40) mg/dL for LDL, 4 (-2, 11) mg/dL for HDL, 10 (-16, 46) mg/dL for TG, and 0.1 (-0.5, 0.6) mg/dL for TC:HDL ratio. Lipid-lowering agents were initiated between baseline and Week 240 in 7.4% of participants.[3]

In participants who switched to BIC/FTC/TAF at Week 144, minimal changes in lipid panel values were observed for each subgroup (Table 1).[2]

Table 1. Studies 1489 and 1490: Lipid Parameters at Weeks 144 and 240 According to the DTG-Based Regimen Received During the Double-Blind Phase[2]

Parameter		DTG/ABC/3TC→ BIC/FTC/TAF (n=254)		DTG + FTC/TAF→ BIC/FTC/TAF (n=265)	
		Week 144	Week 240	Week 144	Week 240
Fasting lipid parameters	TC, median, mmol/L	4.3	4.5	4.4	4.5
	LDL, median, mmol/L	2.9	3	3.1	3
	HDL, median, mmol/L	1.2	1.2	1.2	1.2
	TG, median, mmol/L	1.1	1.1	1.1	1.2
	TC:HDL ratio	3.3	3.5	3.5	3.7
Receiving lipid-lowering agents at BIC/FTC/TAF start, %		7		10	
Began lipid-lowering agents while on BIC/FTC/TAF, %		2		5	

Lipid Safety Profile of BIC/FTC/TAF in Switch Studies

Study GS-US-380-1878

A phase 3, prospective, randomized, open-label clinical trial compared switching to BIC/FTC/TAF (n=290) vs staying on a baseline regimen of boosted DRV or ATV + 2 NRTIs (n=287) in virologically suppressed, adult PWH. Baseline demographics and characteristics were similar for the two treatment groups.[4]

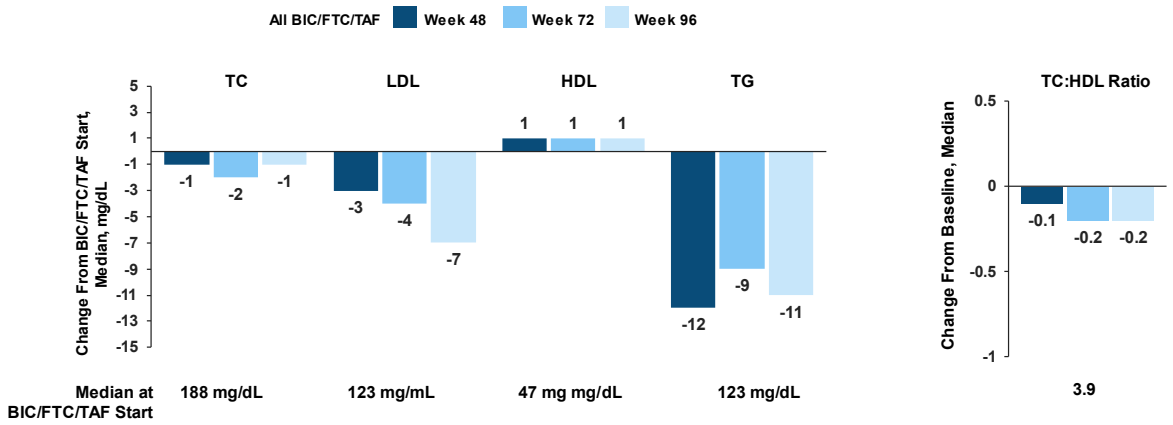
Switching to BIC/FTC/TAF was associated with small, significant decreases in TG (median change from baseline: BIC/FTC/TAF, -6 mg/dL; boosted DRV or ATV + 2 NRTIs, +4 mg/dL; *P*=0.002) and TC:HDL ratio (median change from baseline: BIC/FTC/TAF, -0.2; boosted DRV or ATV + 2 NRTIs, 0; *P*=0.033). At baseline, 16.2% of participants treated with BIC/FTC/TAF and 15.7% of participants treated with boosted DRV or ATV + 2 NRTIs were taking lipid-lowering agents (*P*=0.91). Lipid-lowering medications were initiated by 3% of participants in both groups (*P*=0.64). LDL elevations were reported as a Grade 3 or 4 laboratory abnormality in 4% of participants in both groups through Week 48.[4]

Extension phase results

After the Week 48 primary endpoint, participants were given the option to continue on or switch to BIC/FTC/TAF in the OLE.[8]

Through Week 96, there were numeric declines in TC, LDL, TG, and TC:HDL ratio in virologically suppressed participants who switched to BIC/FTC/TAF (Figure 2).[8]

Figure 2. Study 1878 OLE: Changes in Fasting Lipids Following Switch to BIC/FTC/TAF[8]



Study GS-US-380-1844

A phase 3, randomized, double-blind study evaluated the safety and efficacy of switching to BIC/FTC/TAF (n=282) vs staying on a baseline regimen of DTG + ABC/3TC or DTG/ABC/3TC (n=281) in virologically suppressed, adult PWH. Baseline demographics and characteristics were generally similar between the groups, except for baseline CD4 cell counts, which were higher in the BIC/FTC/TAF group than in the DTG/ABC/3TC group.[5]

At Week 48, switching to BIC/FTC/TAF was associated with similar changes in fasting lipid parameters compared to remaining on DTG/ABC/3TC, though there was a small, statistically significant decrease in TG (median change from baseline: BIC/FTC/TAF, -5 mg/dL vs

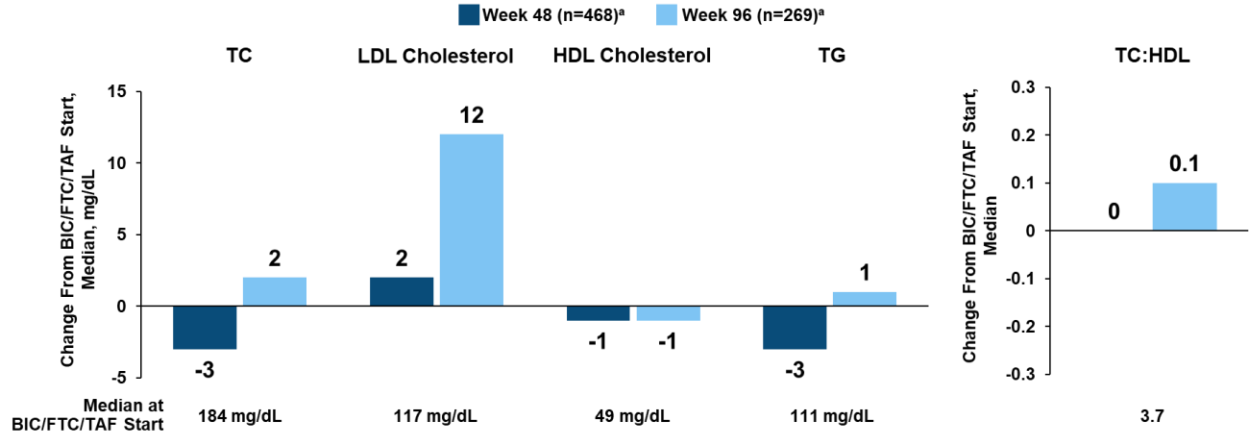
DTG/ABC/3TC, +3 mg/dL; *P*=0.028). Lipid-lowering medications were initiated by 1% of participants in the BIC/FTC/TAF group and 4% of participants in the DTG/ABC/3TC group (*P*=0.033). LDL elevation was reported as a Grade 3 or 4 laboratory abnormality in 5% of participants in each group.[5]

Extension phase results

After the Week 48 primary endpoint, participants were given the option to continue on or switch to BIC/FTC/TAF in the OLE.[9]

Through Week 96, most fasting lipid parameters remained stable, except for an increase in LDL, in virologically suppressed participants who switched to BIC/FTC/TAF (Figure 3).[9]

Figure 3. Study 1844 OLE: Changes in Fasting Lipids Following Switch to BIC/FTC/TAF[9]



[a]Weeks after switch to BIC/FTC/TAF.

Study GS-US-380-1961[6]

A phase 3, prospective, randomized, multi-center, open-label clinical trial compared switching to BIC/FTC/TAF (n=234) vs staying on a baseline regimen of EVG/COBI/FTC/(TAF or TDF) or ATV + RTV + FTC/TDF (n=236) in virologically suppressed adult women with HIV-1. Baseline demographics and characteristics were balanced between the treatment groups.

At Week 48, switching to BIC/FTC/TAF was associated with similar changes in fasting lipid parameters compared with remaining on the baseline regimen, although there was a small, statistically significant decrease in TG (median change from baseline: BIC/FTC/TAF, -10 mg/dL vs those who remained on baseline regimen, +4 mg/dL; *P*<0.001). Lipid-lowering medications were initiated by 2% of participants in the BIC/FTC/TAF group and 4% of participants who remained on their baseline regimen (*P*=0.42). LDL elevations were reported as a Grade 3 or 4 laboratory abnormality in 3% of participants on BIC/FTC/TAF and 6% of participants who remained on their baseline regimen through Week 48.

References

1. Orkin C, Sax PE, Arribas J, et al. Long-term Efficacy and Safety of Bictegravir/Emtricitabine/Tenofovir Alafenamide in ART-Naïve Adults [Poster PE3/14]. Paper presented at: 17th European AIDS Conference; 06-09 November, 2019; Basel, Switzerland.

2. Orkin C, Antinori A, Rockstroh J, et al. Outcomes After Switching From 144 Weeks of Blinded DTG/ABC/3TC or DTG+F/TAF to 96 Weeks of Open-label B/F/TAF [Poster P088]. Paper presented at: HIV Glasgow 23-26 October, 2022; Glasgow, UK.
3. Sax PE, Arribas JR, Orkin C, et al. Bictegravir/emtricitabine/tenofovir alafenamide as initial treatment for HIV-1: five-year follow-up from two randomized trials. *EClinicalMedicine.* 2023;59:101991. https://www.ncbi.nlm.nih.gov/pubmed/37200995
4. Daar ES, DeJesus E, Ruane P, et al. Efficacy and safety of switching to fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide from boosted protease inhibitor-based regimens in virologically suppressed adults with HIV-1: 48 week results of a randomised, open-label, multicentre, phase 3, non-inferiority trial [Main Article + Supplementary Appendix]. *The Lancet HIV.* 2018;5(7):e347-e356. http://www.ncbi.nlm.nih.gov/pubmed/29925490
5. 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 [Main Article + Supplementary Appendix]. *The Lancet HIV.* 2018;5(7):e357-365. http://www.ncbi.nlm.nih.gov/pubmed/29925489
6. 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 [Main Article + Supplementary Appendix]. *J Acquir Immune Defic Syndr.* 2019;82(3):321-328. https://www.ncbi.nlm.nih.gov/pubmed/31609930
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 [Main Article + Supplementary Appendix]. *The Lancet HIV.* 2020;7:e389–400.
8. 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.
9. 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.

Abbreviations

3TC=lamivudine
ABC=abacavir
ATV=atazanavir
BIC=bictegravir
CD4=cluster of differentiation 4
COBI=cobicistat
DRV=darunavir
DTG=dolutegravir
EVG=elvitegravir
FTC=emtricitabine
NRTI=nucleos(t)ide reverse transcriptase inhibitor
OLE=open-label extension
PWH=people with HIV-1
Q=quartile
RTV=ritonavir
TAF=tenofovir alafenamide
TC=total cholesterol
TDF=tenofovir disoproxil fumarate
TG=triglycerides

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.