GILEAD | Medical Information

Biktarvy® (BIC/FTC/TAF) Viremic Events on BIC/FTC/TAF

This document is in response to your request for information on viremic events in PWH on Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]).

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The full indication, important safety information, and boxed warning 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 virologically suppressed, with no known or suspected substitutions associated with resistance to the integrase strand inhibitor class, FTC, or TFV, or
- to replace the current ARV regimen in those who are virologically-suppressed (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 Viremic Events on BIC/FTC/TAF

In a pooled analysis of eight phase 3 studies of PWH receiving BIC/FTC/TAF (N=2801), 411 viremic events occurred in 290 participants; subsequent resuppression was achieved with BIC/FTC/TAF in 95.1% of participants (250/263) with evaluable viremic events, with a median time from viremic event to resuppression of 22 days.[2]

Clinical Data on Viremic Events in PWH on BIC/FTC/TAF

Pooled Analysis of Phase 3 Studies[2]

Study design and demographics

A post hoc pooled analysis of eight clinical trials was conducted to assess viremic events and subsequent outcomes in ARV-naive and virologically suppressed, TE PWH who were receiving BIC/FTC/TAF (N=2801). Viremic events were defined as ≥1 HIV-1 VL ≥50 c/mL after virologic suppression (VL <50 c/mL). Viremic events were further classified according

to virologic outcome after the viremic event as follows: virologic suppression (≥1 VL <50 c/mL after the viremic event), continued viremia (all VL measurements ≥50 c/mL after the viremic event), or not evaluable (no VL assessment after the viremic event). The duration of viremic events were analyzed according to time from virologic suppression to viremic event, time from viremic event to resuppression, and duration of continued viremia. Study drug adherence was assessed with pill count, and outcomes associated with ≥85% adherence and <85% (low) adherence were evaluated.

Participants in all studies were assessed for VL at baseline/Day 1, Week 4, Week 8 (except for participants in Studies 4449 and 4580), Week 12, and every 12 weeks through the end of the study and at unscheduled visits. Participants with eGFR <30 mL/min and/or resistance to study drug components were generally excluded (Table 1). Baseline demographics of participants with and without viremic events are presented in Table 2.

Table 1. BIC/FTC/TAF Studies Included in the Pooled Analysis[2]

Study	n[a]	Population	Prior ARV Treatment
First Line			
1489	565	• ARV-naive adults	None
1490	575	• ARV-naive adults	None
Switch Studies			
1474	122	• Virologically suppressed children aged 2 to <18 years • Stable ARV regimen and VL <50 c/mL for ≥6 months	Two NRTIs + third agent
1844	281	• Virologically suppressed adults • Stable ARV regimen and VL <50 c/mL for ≥3 months	DTG + ABC/3TC or ABC/DTG/3TC
1878	289	• Virologically suppressed • Stable ARV regimen and VL <50 c/mL for ≥6 months	Boosted ATV or DRV + either FTC/TDF or ABC/3TC
4030	397	• Virologically suppressed adults • Stable ARV regimen and VL <50 c/mL for ≥6 months[b]	DTG + FTC/TAF or DTG + FTC/TDF
4449	85	• Virologically suppressed adults aged ≥65 years • Stable ARV regimen and VL <50 c/mL for ≥3 months	EVG/COBI/FTC/TAF or FTC/TDF + third agent
4580	487	• Virologically suppressed Black, African American, or mixed-race adults • Stable ARV regimen and VL <50 c/mL for ≥6 months	Two NRTIs + third agent

Abbreviations: 3TC=lamivudine; ABC=abacavir; ATV=atazanavir; COBI=cobicistat; DRV=darunavir; DTG=dolutegravir; EVG=elvitegravir; NRTI=nucleos(t)ide reverse transcriptase inhibitor.
[a]The number of participants receiving BIC/FTC/TAF with ≥1 postbaseline HIV-1 RNA measurement.
[b]If there was suspected or documented NRTI-R prior to screening.

Table 2. Pooled Analysis: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		Viremic Event (n=290)	No Viremic Event (n=2511)	*P*-Value
ARV naive, n (%)		145 (50)	479 (19.1)	<0.0001
Virologically suppressed, n (%)		145 (50)	2032 (80.9)	-
Age, median (IQR), years		36 (25–50)	44 (32–54)	0.001
Sex at birth, male/female, n (%)		239 (82.4)/ 51 (17.6)	2067 (82.3)/ 444 (17.7)	0.2099
Race, n (%)	Black	142 (49.1)	987 (39.4)	0.0005
	White	125 (43.3)	1292 (51.6)	
	Asian	9 (3.1)	66 (2.6)	

Key Demographics and Characteristics		Viremic Event (n=290)	No Viremic Event (n=2511)	*P*-Value
	American Indian, Alaska Native, Native Hawaiian, or Pacific Islander	3 (1)	18 (0.7)	
	Other or reporting not permitted[a]	10 (3.4)	141 (5.6)	
Hispanic/Latinx,[a] n (%)		53 (18.3)	457 (18.3)	0.3037
HIV-1 VL, median (IQR), log_{10} c/mL		3 (1.3–4.7)	1.3 (1.3–1.3)	-
HIV-1 VL <50 c/mL,[b] n (%)		137 (47.2)	2002 (79.7)	0.0003
CD4 count,[b] median (IQR), cells/mcL		523 (341–755)	666 (476–881)	0.007
CD4 count <200 cells/mcL,[b] n (%)		31 (10.7)	78 (3.1)	0.004

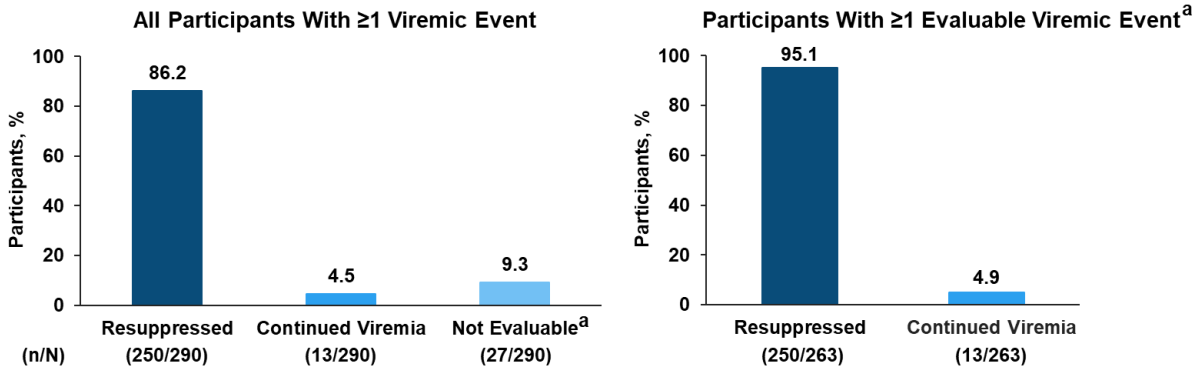
[a]Data were missing for a participant with ≥1 viremic event (race, n=1) and participants without viremic events (ethnicity, n=8; race, n=7) and were excluded from percentage and *P*-value calculations.
[b]Assessed on Day 1 of BIC/FTC/TAF administration.

Results

Overall, 290 participants receiving BIC/FTC/TAF experienced a total of 411 viremic events (1 viremic event, n=219 [75.5%]; 2 viremic events, n=49 [16.9%]; ≥3 viremic events, n=22 [7.6%]); a similar number of ARV-naive and TE participants experienced 1, 2, and ≥3 viremic events. Following BIC/FTC/TAF initiation, the first viremic event occurred at a median (IQR) of 254 (135–541) days after virologic suppression. The median (IQR) VL at the time of any viremic event (n=411) was 2.25 (1.88–3.01) log_{10} c/mL. Compared with participants with no viremic events, those who experienced ≥1 viremic event were more likely to be ARV naive, younger, and Black and to have a baseline HIV-1 VL ≥50 c/mL and CD4 count <200 cells/mcL.

In total, 86.2% of participants (250/290) who experienced ≥1 viremic event achieved resuppression after the last viremic event; when non-evaluable events were excluded, resuppression was achieved in 95.1% of participants (250/263; Figure 1). Of the 91 participants with ≥1 viremic event ≥1000 c/mL, 75 (82.4%) achieved resuppression; 91.5% of participants (75/82) achieved resuppression in the analysis that excluded non-evaluable events.

Figure 1. Pooled Analysis: Virologic Outcomes Following Viremic Events With BIC/FTC/TAF[2]



[a]Participants with viremic events at the last assessment were considered non-evaluable.

Of the 242 participants with a viremic event who had complete VL data from subsequent visits, resuppression was achieved at Week 4, Week 12, and Week 36 by 79.3%, 95.2%, and 100% of participants, respectively. A summary of the duration of viremic events is in

Table 3. Of the 13 participants with continued viremia, 9 (69.2%) had VLs ≥200 c/mL for a median (IQR) duration of 79 (20–127) days; 7 of these participants had continued viremia with VLs ≥1000 c/mL. Discontinuations due to continued viremia were reported in 11 of the 13 participants (84.6%; lost to follow-up, n=4; participant's decision, n=4; lack of efficacy, n=3).

Table 3. Pooled Analysis: Duration of Viremic Events While Receiving BIC/FTC/TAF[2]

Parameter	Number of Events	Median (IQR), Days
Time from virologic suppression to viremic event	411	225 (85–500)
Time from viremic event to virologic resuppression	371	22 (18–36)
Duration of continued viremia	13	72 (43–87)

All 14 participants who had viremia with a comparator ARV regimen before they switched to BIC/FTC/TAF achieved resuppression after a median (IQR) of 25 (21–42) days after they switched to BIC/FTC/TAF; 6 of those participants also experienced viremic events while they were receiving BIC/FTC/TAF.

Data on baseline genotypes were available for 284/290 participants (97.9%) who had viremic events while they were receiving BIC/FTC/TAF (Table 4). Of participants with available data, M184V/I resistance-associated mutations occurred in 4.9% of participants with viremic events and in 6.6% in the overall population.

Table 4. Pooled Analysis: Baseline Resistance Data for Participants With Viremic Events While They Were Receiving BIC/FTC/TAF[2]

	INSTI-R (n=281)	NRTI-R (n=284)	PI-R (n=284)	NNRTI-R (n=284)
Participants with preexisting primary resistance, n (%)	8 (2.8)	29 (10.2)	11 (3.9)	56 (19.7)
Primary resistance substitutions, (n)	T97A (4) E92G/Q (2) R263K (1) Y143C/H/R (1)	M184I/V (14) K219E/N/Q/R (7) T215Y/F (7) K70E/R (6) M41L (6) D67N (3) L210W (3) L741/V (1)	L90M (5) I84V (3) M46I/L (3) D30N (2) I54M/L (1) N83D (1) Q58E (1) V82A/F/L/S/T (1)	K103N/S (28) E138A/G/K/Q/R (16) G190A/E/Q/S (11) Y181C/I/V (7) K101E/P (6) V108I (4) Y188C/H/L (3) M230I/L (2) V106A/M (2) H221Y (1) L100I (1) P225H (1)

Abbreviations: INSTI-R=integrase strand inhibitor resistance; NNRTI-R=non-nucleos(t)ide reverse transcriptase inhibitor resistance; PI-R=protease inhibitor resistance.

Postbaseline resistance testing was performed in 8/13 participants (61.6%) with continued viremia after their last viremic event; none had treatment-emergent resistance to BIC/FTC/TAF.

The adherence rate was 98.2% in participants with no viremic event and 96.6% in participants with any viremic events. Among the participants with low adherence (<85%) to BIC/FTC/TAF, significantly more participants had viremic events (10%) than did not (4.2%; *P*=0.0003).

References

1. Enclosed, Gilead Sciences Inc. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Pozniak A, Orkin C, Yazdanpanah Y, et al. Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) After A Viremic Event: A Pooled Analysis of Studies in People with HIV. *Infect Dis Ther.* 2025.

Abbreviations

ARV=antiretroviral
BIC=bictegravir
CD4=cluster of differentiation 4
FTC=emtricitabine
NRTI-R=nucleos(t)ide reverse transcriptase inhibitor resistance
PWH=people with HIV
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TFV=tenofovir
TE=treatment-experienced
VL=viral load

Product Label

For the full indication, important safety information, and boxed warning, 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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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

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