GILEAD | Medical Information

Biktvary® (BIC/FTC/TAF) Use in Renal Transplant Patients

This document is in response to your request for information regarding the use of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in individuals who have had a renal transplant.

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.

Product Labeling[1]

There is no information in the BIC/FTC/TAF US Prescribing Information about the use of BIC/FTC/TAF in individuals who have had a renal transplant.

Dosage and Administration

Not recommended in patients with severe renal impairment

BIC/FTC/TAF is not recommended in individuals with severe renal impairment (estimated CrCl of 15 to <30 mL/min); or ESRD (estimated CrCl <15 mL/min) who are not receiving chronic hemodialysis; or no ARV treatment history and ESRD who are receiving chronic hemodialysis.

Warnings and Precautions

New onset or worsening renal impairment

Postmarketing cases of renal impairment, including acute renal failure, proximal renal tubulopathy, and Fanconi syndrome, have been reported with TAF-containing products; while most of these cases were characterized by potential confounders that may have contributed to the reported renal events, it is also possible these factors may have predisposed patients to TFV-related adverse events.

Patients taking TFV prodrugs who have impaired renal function and those taking nephrotoxic agents including non-steroidal anti-inflammatory drugs are at increased risk of developing renal-related adverse reactions.

Prior to or when initiating BIC/FTC/TAF, and during treatment with BIC/FTC/TAF, assess SCr, estimated CrCl, urine glucose and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, also assess serum phosphorus. Discontinue BIC/FTC/TAF in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

Clinical Data on BIC/FTC/TAF Use in Renal Transplant Patients

BIK-Switch: Single-Arm, Open-Label Study[2]

Study design and demographics

BIK-Switch, a single-arm, open-label study, evaluated the PK of BIC/FTC/TAF in VS (HIV VL <50 c/mL) PWH (N=19) who switched from their prior ARV regimen after renal transplantation. Eligible participants were followed for 72 weeks; HIV VL was assessed at several timepoints over the study. Intensive PK sampling of BIC, FTC, TAF, and TFV levels was performed at the Week 12 study visit; samples were collected at predose, and 0.5, 1, 2, 4, and 24 hours post dose. These values were compared with those of PWH with normal renal function (CrCl ≥90 mL/min) or renal function approximately similar to that in package inserts (CrCl 30–59 mL/min). Additionally, levels of TFV-DP and FTC-TP in PBMC were collected predose and at Hours 4 and 24 post dose at Week 12, and levels from DBS were collected predose at Weeks 12, 24, 36, 48 and 72. TFV-DP and FTC-TP values were compared with values obtained during the QUANTI-TAF study (N=19).

In the BIK-Switch and QUANTI-TAF studies, baseline demographics were as follows: median (IQR) ages were 57 (48–63) years and 58 (47–61) years, respectively; 68% and 79% were male; 89% and 42% were Black; 21% and 11% were Hispanic or Latinx; median (IQR) CrCls were 52 (45–67) mL/min and 75 (61–102) mL/min (*P*=0.0004); and median (IQR) BMIs were 26 (22–29) kg/m^2 and 27 (22–33) kg/m^2.

PK results

At Week 12, relative to controls described in the FTC/TAF package insert, who had CrCls of 30–59 mL/min, participants had similar plasma AUC values for FTC, TAF, and TFV (Table 1). The BIC AUC range in the BIK-Switch study was within the same range of the BIC AUC reported for controls described in the BIC/FTC/TAF package insert with normal renal function (Table 1). Levels of TFV-DP in DBS and PBMC and of FTC-TP in PBMC among participants in the current study were significantly higher than the levels reported in the QUANTI-TAF study (Table 2).

Table 1. BIK-Switch: Plasma PK at Week 12 in Study Participants and Package Insert Controls With Different Levels of Renal Function[2]

Component	BIK-Switch Study (n=18), Mean (Range)			Controls From Package Inserts, Mean (CV%)	
	C_{max}, ng/mL	C_{trough}, ng/mL	AUC, ng·h/mL	AUC,[a] CrCl 30–59 mL/min	AUC, CrCl ≥90 mL/min
BIC	5045 (1432–9027)	1855 (404–3852)	74,627 (22,222–144,395)	N/A	102,000 (27)[b]
FTC	2505 (1448–5512)	355 (110–1385)	22,758 (13,796–32,844)	23,000 (23.6)	12,300 (29)[b]
TAF	287.3 (11–891)	Not quantifiable	389.5 (45.8–1406.9)	260 (58.8)	142 (17)[b]
TFV	32.1 (10.5–58.8)	23.5 (8.7–44.5)	613 (211–1140)	610 (28.4)	290 (27)[a]

Abbreviation: C_{max}=peak concentration.
[a]FTC/TAF package insert. [b]BIC/FTC/TAF package insert.

Table 2. BIK-Switch: TFV-DP and FTC-TP Levels in DBS and PBMS in Study Participants and Controls From the QUANTI-TAF Study[2]

Component	Matrix	Study Group	GM (95% CI)	GMR[a] (95% CI)	*P*-Value
TFV-DP	DBS, fmol/punches	BIK-Switch (test)	5408 (4391–6662)	1.45 (1.11–1.89)	0.0083
		QUANTI-TAF (reference)	3738 (3110–4491)		
	PBMC, fmol/10^6 cells	BIK-Switch (test)	1475 (1055–2064)	2.38 (1.61–3.51)	<0.0001
		QUANTI-TAF (reference)	621 (497–776)		
FTC-TP	DBS, pmol/punches	BIK-Switch (test)	6.34 (5.27–7.62)	1.09 (0.82–1.44)	0.54
		QUANTI-TAF (reference)	5.82 (4.64–7.3)		
	PBMC, pmol/10^6 cells	BIK-Switch (test)	14.98 (11–20.4)	2.67 (1.89–3.78)	<0.0001
		QUANTI-TAF (reference)	5.6 (4.69–6.68)		

Abbreviations: GM=geometric mean; GMR=geometric mean ratio.
[a]Test/reference.

Efficacy and safety

All participants remained VS, CrCl remained stable through the end of the study, and tacrolimus levels also remained stable without the need for dose adjustments.

Case Series and Case Reports

There are limitations in the interpretation of case reports. Case reports cannot be generalized. Unlike controlled clinical trials, causality cannot be inferred based on uncontrolled observational data. In addition, incidence or prevalence cannot be estimated due to the lack of a representative population sample. Other limitations of case reports include the retrospective design and publication bias.[3]

A single-center observational study of PWH undergoing solid organ transplantation between January 2017 and April 2022 reported outcomes with DTG- or BIC-containing ARV regimens. Of the kidney transplant recipients (n=8), all had a last on-treatment VL <200 c/mL, were aged between 45 and 64 years, and identified as Black, and 2 were female. All PK enhancers were discontinued due to drug interaction concerns with anti-rejection medications. BIC/FTC/TAF was the most recent post-transplant ARV regimen for 4 patients, including 1 patient who was on BIC/FTC/TAF pre-transplant and continued post-transplant. For the 4 patients on BIC/FTC/TAF post-transplant, no ARV-related adverse events, rejection, or other serious infectious complications were documented. All 8 kidney transplant recipients maintained HIV RNA <200 c/mL at the time of report.[4]

A 61-year-old female presented with HIV and chronic kidney disease with polycystic kidneys. Almost 2 years after a right nephrectomy, she was considered eligible for a kidney transplant because of an undetectable HIV VL and CD4 count of 530 cells/mcL with no ongoing infection. Post-transplant, 1500 mg mycophenolate mofetil and 2 mg of tacrolimus were added to the baseline ARV regimen of RAL + ETR + DRV/r. A high tacrolimus concentration (35.5 mcg/L, above the expected therapeutic window of 6–10 mcg/L) was reported 12 hours after a single dose. As there was a drug-drug interaction with the current ARV regimen and tacrolimus that led to continued high tacrolimus concentrations despite dose adjustment, the patient was switched to BIC/FTC/TAF. The PK profile of each component of BIC/FTC/TAF represented a low-risk drug-drug interaction, with no or minimal impact on tacrolimus transport. After the switch, tacrolimus doses were adjusted to maintain a therapeutic concentration with a tacrolimus dose of 2.5 mg. Eighteen months post-transplant, the patient remained VS on the BIC/FTC/TAF regimen and maintained a therapeutic concentration of tacrolimus. However, an increase in the C_{trough} of TFV (0.039 mg/L) was reported.[4]

References

1. Enclosed, Gilead Sciences Inc. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, for oral use. US Prescribing Information. Foster City, CA.
2. Coppinger C, Cooper S, Witting B, et al. Pharmacokinetics of Switching to B/F/TAF in PWH Post-Renal Transplant: BIK-Switch Study [Poster #650]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); March 9-12, 2025; San Francisco.
3. Nissen T, Wynn R. The Clinical Case Report: A Review of Its Merits and Limitations. *BMC Res Notes.* 2014;7:264. https://www.ncbi.nlm.nih.gov/pubmed/24758689
4. Lagoutte-Renosi J, Flammang M, Ducloux D, et al. Bictegravir/emtricitabine/tenofovir alafenamide combination in the management of kidney transplant patients with HIV receiving immunosuppressants. *J Chemother.* 2021:1-4.

Abbreviations

ARV=antiretroviral
AUC=area under the concentration-time curve
BIC=bictegravir
c/mL=copies/mL
CD4=cluster of differentiation 4
C_{trough}=trough concentration
DBS=dried blood spots
DRV/r=darunavir/ritonavir
DTG=dolutegravir
ESRD=end stage renal disease
ETR=etravirine
FTC=emtricitabine
FTC-TP=emtricitabine triphosphate
PBMC=peripheral blood mononuclear cells
PK=pharmacokinetic(s)
PWH=people with HIV
TAF=tenofovir alafenamide
TFV=tenofovir
TFV-DP=tenofovir diphosphate
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

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