GILEAD | Medical Information

Descovy for PrEP® (FTC/TAF) Renal Safety Profile of Switching From FTC/TDF

This document is in response to your request for information regarding the renal safety profile of Descovy for PrEP® (emtricitabine/tenofovir alafenamide [FTC/TAF] for HIV-1 pre-exposure prophylaxis [PrEP]) in individuals switching from FTC/TDF. This document was developed according to principles of evidence-based medicine and only contains data from phase 3 clinical trials.

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The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi.

Summary

Product Labeling[1]

FTC/TAF is indicated in at-risk adults and adolescents weighing ≥35 kg for PrEP to reduce the risk of HIV-1 infection from sexual acquisition, excluding individuals at risk from receptive vaginal sex. Individuals must have a negative HIV-1 test immediately prior to initiating FTC/TAF for HIV-1 PrEP.

Limitations of Use: The indication does not include use of FTC/TAF in individuals at risk of HIV-1 from receptive vaginal sex because effectiveness in this population has not been evaluated.

Clinical Data on the Renal Safety Profile of Switching From FTC/TDF to FTC/TAF

Daily FTC/TAF was compared to FTC/TDF for HIV-1 PrEP among adult MSM and TGW in DISCOVER, a phase 3 randomized, active-controlled, clinical trial.[2-4]

- Participants with baseline use of FTC/TDF for PrEP and randomized to the FTC/TAF arm had significant improvements in $eGFR_{CG}$, urine RBP:Cr and β2M:Cr at Week 96 compared with those who remained on FTC/TDF.[5]
- Participants who switched to FTC/TAF during the OLE had significant improvements in $eGFR_{CG}$, urine RBP:Cr and β2M:Cr at Week 48 of the OLE compared with those who were randomized to FTC/TAF at baseline.[4]
- The long-term clinical significance of these renal laboratory changes on adverse reaction frequencies between FTC/TAF and FTC/TDF is not known.[1]

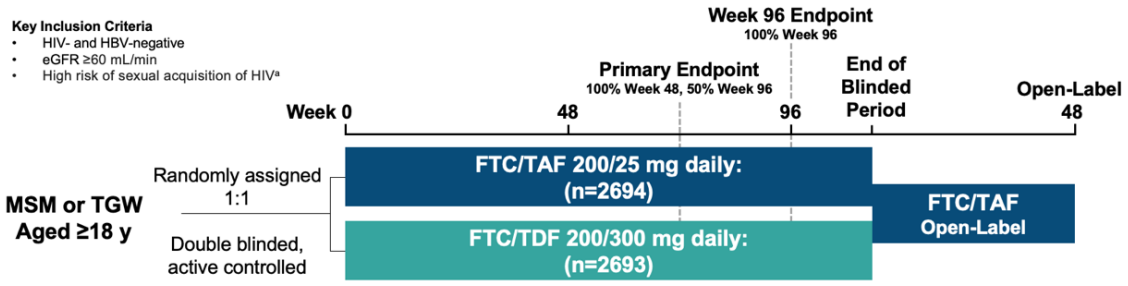
Clinical Data on the Renal Safety Profile of Switching From FTC/TDF to FTC/TAF

DISCOVER: FTC/TAF vs FTC/TDF for HIV-1 PrEP in MSM and TGW

Study design and demographics

DISCOVER is a phase 3, multinational study in 5387 HIV-negative adult MSM and TGW evaluating the safety and efficacy of once-daily FTC/TAF vs FTC/TDF for HIV-1 PrEP (Figure 1). Prior use of FTC/TDF for HIV-1 PrEP was allowed.[2,3,6]

Figure 1. DISCOVER: Study Design[2,3,6]



[a]High risk was defined as ≥2 episodes of condomless anal intercourse with ≥2 unique male partners of HIV-positive or unknown HIV status within the previous 12 weeks, or a documented history of syphilis, rectal gonorrhea, or rectal chlamydia in the previous 24 weeks.

The primary measured outcome was the incidence of HIV-1 per 100 person years after all participants had ≥48 weeks of follow-up and ≥50% of participants had 96 weeks of follow-up.[2] All participants were unblinded after 96 weeks, and participants in both arms were offered the opportunity to continue on or switch to once-daily FTC/TAF for an additional 48 weeks.[2,6]

Participant baseline characteristics were similar between the FTC/TAF and FTC/TDF arms, including medical history (Table 1).[7] The baseline characteristics of the subset of participants with baseline use of FTC/TDF for PrEP differed from the overall population by median age (36 years vs 34 years, respectively), proportion with >2 condomless anal sex partners in the past 12 weeks (72% vs 61.3%), and proportion with rectal chlamydia infection (15.9% vs 12.5%). A similar proportion of participants reported binge drinking (baseline FTC/TDF for PrEP: 22.3%, overall population: 22.8%).[8] For participants taking FTC/TDF for PrEP at baseline, the median duration of PrEP use was 398.5 days.[5]

Table 1. DISCOVER: Baseline Demographics and HIV Risk Factors[7]

Key Demographics and Characteristics		Overall		Baseline Use of FTC/TDF	
		FTC/TAF (n=2694)	FTC/TDF (n=2693)	FTC/TAF (n=465)	FTC/TDF (n=440)
Age, median (range), years		34 (18–76)	34 (18–72)	36 (19–73)	36 (19–71)
Race or ethnicity, n (%)	White	2264 (84)	2247 (84)	391 (84)	379 (87)
	Black[a]	240 (9)	234 (9)	41 (9)	28 (6)
	Hispanic or Latinx	635 (24)	683 (25)	81 (17)	73 (17)
TGW, n (%)		45 (2)	29 (1)	4 (1)	2 (1)

Key Demographics and Characteristics		Overall		Baseline Use of FTC/TDF	
		FTC/TAF (n=2694)	FTC/TDF (n=2693)	FTC/TAF (n=465)	FTC/TDF (n=440)
Medical history, n (%)	Hyperlipidemia	311 (12)	320 (12)	51 (11)	72 (16)
	Hypertension	282 (10)	298 (11)	56 (12)	68 (15)
	Diabetes mellitus	79 (3)	89 (3)	10 (2)	22 (5)
	Cardiovascular disease	31 (1)	23 (1)	3 (1)	8 (2)

[a]Included mixed Black race.

Renal safety results

Overall, through Week 96, the effects on renal biomarkers and $eGFR_{CG}$ significantly favored FTC/TAF compared with FTC/TDF.[3] Participants in the FTC/TAF arm, compared with FTC/TDF, had a similar incidence of quantitative proteinuria, defined as UPCR >200 mg/g (Table 2).[5]

There were 8 discontinuations due to renal AEs through Week 96 (FTC/TAF, n=2; FTC/TDF, n=6),[3] and all but 1 case in the FTC/TAF arm were reported by investigators as related to study drug. In the FTC/TDF arm, 3 of the 6 participants who discontinued treatment had other risk factors (ie, hypertension, nonsteroidal anti-inflammatory drug use, or a prior history of kidney disease), and 3 participants who discontinued treatment had no contributing factors. In the FTC/TAF arm, both participants who discontinued had risk factors: myocardial infarction, contrast neuropathy, hypertension, and focal segmental glomerulosclerosis discovered by renal biopsy.[7] There were no reports of Fanconi syndrome in the FTC/TAF arm and 1 case in the FTC/TDF arm (Table 2).[3]

Table 2. DISCOVER: Renal Safety Through Week 96 in Overall Population[3]

Parameter	FTC/TAF (n=2694)	FTC/TDF (n=2693)	*P*-Value
$eGFR_{CG}$, change from baseline,[a] median, mL/min	+3.7	-0.4	<0.0001[d]
RBP:Cr, change from baseline,[b] mean, %	+0.2	+21.4	<0.0001[e]
β2M:Cr, change from baseline,[c] mean %	-14.6	+14.2	<0.0001[e]
Participants with treatment emergent UPCR >22.6 mg/mmol, %	1	1.3	0.22[f]
Renal AEs that led to study drug discontinuation, n	2	6	NR
Fanconi syndrome, n	0	1	NR

Abbreviation: NR=not reported
[a]FTC/TAF, n=2193; FTC/TDF, n=2217.
[b]FTC/TAF, n=2191; FTC/TDF, n=2216.
[c]FTC/TAF, n=2172; FTC/TDF, n=2200.
[d]*P*-values were from an ANOVA model with baseline FTC/TDF for PrEP and treatment as fixed effects.
[e]*P*-values were from the Van Elteren test stratified by baseline FTC/TDF for HIV-1 PrEP to compare the two treatment groups.
[f]*P*-values for treatment comparison were from the rank ANCOVA adjusting for baseline category and baseline FTC/TDF for PrEP.

Participants with baseline use of FTC/TDF for PrEP

A subgroup analysis evaluated renal outcomes through Week 96 among participants with baseline use of FTC/TDF for PrEP, Baseline characteristics of participants with baseline use of FTC/TDF for PrEP randomly assigned to FTC/TAF and FTC/TDF included the following: median $eGFR_{CG}$ of 119 mL/min vs 116 mL/min (n=465 vs 439), respectively; median RBP:Cr 118 mcg/g vs 121 mcg/g (n=465 vs 436); and β2M:Cr 106 mcg/g vs 118 mcg/g (n=464 vs 433).[5]

Similar to the overall study population, renal biomarkers of participants with baseline use of FTC/TDF for PrEP significantly favored those who were randomly assigned to receive FTC/TAF compared with those who continued FTC/TDF (Table 3).[5]

Table 3. DISCOVER: Renal Safety of Participants With Baseline FTC/TDF for PrEP Use Through Week 96[5]

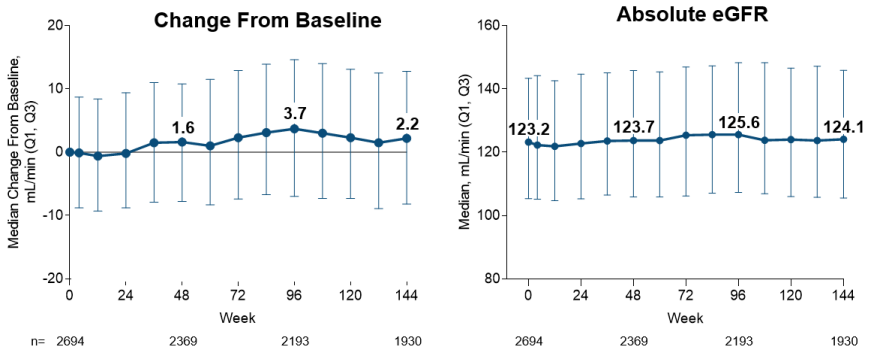
Parameter	Switch to FTC/TAF	Stay on FTC/TDF	*P*-Value[a]
$eGFR_{CG}$ change from baseline, median, mL/min	+6.7[b]	+0.6[c]	<0.001
RBP:Cr change from baseline, median, %	-10.3[b]	+5.5[d]	<0.001
β2M:Cr change from baseline, median, %	-35.5[e]	-11.4[f]	<0.001
Participants with treatment-emergent proteinuria, %	21[g]	24[h]	0.45

[a]*P*-value from 2-sided Wilcoxon rank sum test to compare treatment groups. [b]n=406. [c]n=377. [d]n=374. [e]n=402. [f]n=368. [g]n=459. [h]n=435.

OLE outcomes at Week 144

An analysis assessed outcomes of participants on FTC/TAF based on results at Week 144. The amount of time between Week 96 and the end of blinded phase varied between participants; most reached Week 144 on FTC/TAF during the first 48 weeks of the OLE phase. Subanalyses for renal function showed consistent changes in eGFR in FTC/TAF participants through Week 144, as shown in Figure 2 below.[9]

Figure 2. DISCOVER: Changes in eGFR in FTC/TAF Participants Through Week 144[9]



Participants who switched to FTC/TAF during the OLE had significant improvements in $eGFR_{CG}$, urine RBP:Cr and β2M:Cr at Week 48 of the OLE compared with those who were randomized to FTC/TAF at baseline (Table 4).[4]

Table 4. DISCOVER: Renal Safety Outcomes From OLE Baseline to OLE Week 48[4]

Parameter, Median Change From OLE Baseline	Stay on FTC/TAF	Switch From FTC/TDF	*P*-Value[a]
$eGFR_{CG}$, mL/min	-2.8[b]	+0.3[c]	<0.001
RBP:Cr, %	-9.9[d]	-26.8[e]	<0.001
β2M:Cr, %	-7.3[f]	-30.8[g]	<0.001

[a]*P*-value from Cochran–Mantel–Haenszel test to compare treatment groups. [b]n=1667. [c]n=1666. [d]n=1663. [e]n=1658. [f]n=1649. [g]n=1657.

Please note, the long-term clinical significance of these renal laboratory changes on the frequencies of adverse reactions while receiving FTC/TAF or FTC/TDF is not known.[1]

References

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9. Ramgopal M, Ruane P, Shalit P, et al. Long-term Outcomes of Participants on F/TAF for Pre-Exposure Prophylaxis: Results for 144 Weeks of Follow-Up in the DISCOVER Trial [Poster 854]. Paper presented at: IDWeek Virtual; 29 Sept-03 Oct, 2021.

Abbreviations

β2M=β2-microglobulin
AE=adverse event
ANCOVA=analysis of covariance
ANOVA=analysis of variance
CG=Cockcroft-Gault
FTC=emtricitabine
MSM=men who have sex with men
OLE=open-label extension
PrEP=pre-exposure prophylaxis
RBP=retinol-binding protein
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TGW=transgender women
UPCR=urine protein-creatinine ratio

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Descovy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi.

Follow Up

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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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