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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) in individuals switching from FTC/TDF.

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/descovy/descovy_pi.

Summary

Clinical Data

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

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.[4]

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.[3]

The long-term clinical significance of these renal laboratory changes on adverse reaction frequencies between FTC/TAF and FTC/TDF is not known.[5]

Product Labeling[5]

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.

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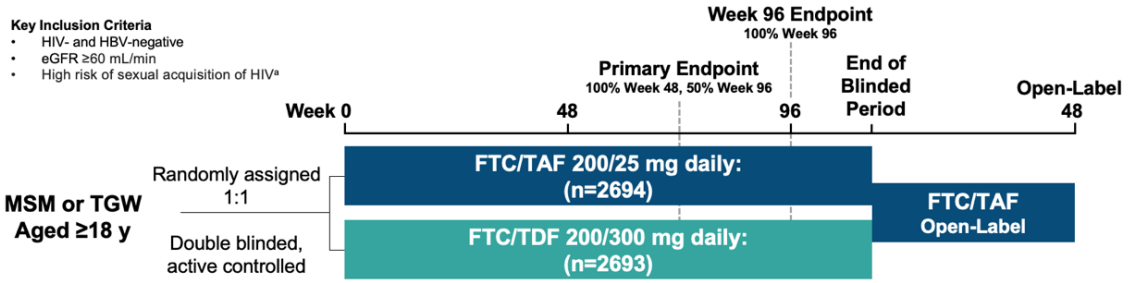
Clinical Data

DISCOVER: Once Daily 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 FTC/TAF vs FTC/TDF for HIV-1 PrEP. Figure 1 below includes the study design and key inclusion criteria. Prior use of FTC/TDF for HIV-1 PrEP was allowed.[1,2,6]

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



[a]High risk 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 PY after all participants had ≥48 weeks of follow-up and ≥50% of participants had 96 weeks of follow-up.[1] 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.[1,6]

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), proportion with >2 condomless anal sex partners in the past 12 weeks (72.0% vs 61.3%), and proportion with rectal chlamydia infection (15.9% vs 12.5%, respectively for all). 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.[4]

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

	Overall		Baseline Use of FTC/TDF	
	FTC/TAF (n=2694)	FTC/TDF (n=2693)	FTC/TAF (n=465)	FTC/TDF (n=440)
Baseline demographics				
Median age, years (range)	34 (18–76)	34 (18–72)	36 (19–73)	36 (19–71)
Race, n (%)				
White	2264 (84)	2247 (84)	391 (84)	379 (87)
Black[a]	240 (9)	234 (9)	41 (9)	28 (6)
Hispanic or Latinx ethnicity, n (%)	635 (24)	683 (25)	81 (17)	73 (17)

Proportion TGW, n (%)	45 (2)	29 (1)	4 (1)	2 (1)
Medical history, n (%)				
Diabetes mellitus	79 (3)	89 (3)	10 (2)	22 (5)
Hypertension	282 (10)	298 (11)	56 (12)	68 (15)
Cariovascular disease	31 (1)	23 (1)	3 (1)	8 (2)
Hyperlipidemia	311 (12)	320 (12)	51 (11)	72 (16)

[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.[2] 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).[4]

There were 8 discontinuations due to renal AEs through Week 96 (2 FTC/TAF vs 6 FTC/TDF)[2], of which all except for one case in the FTC/TAF arm were reported by investigators as related to study drug. In the FTC/TDF arm, 3 out of 6 discontinuations had other risk factors including hypertension, nonsteroidal anti-inflammatory drug use or a prior history of kidney disease, while the remaining 3 discontinuations had no other contributing factors identified. In the FTC/TAF arm, both discontinuations had risk factors such as myocardial infarction, contrast neuropathy, hypertension, and focal segmental glomerulosclerosis discovered by renal biopsy.[7] There were no reported cases of Fanconi syndrome in the FTC/TAF arm vs 1 case in the FTC/TDF arm (Table 2).[2]

Table 2. Renal Safety through Week 96 for All Participants[2]

	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

Abbreviations: 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 F/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

In a subgroup analysis of renal outcomes through Week 96, changes in renal biomarkers were evaluated in participants with baseline use of FTC/TDF for PrEP. Baseline characteristics of participants with baseline use of FTC/TDF for PrEP randomized to either the FTC/TAF and FTC/TDF arm included, respectively: median $eGFR_{CG}$ of 119 mL/min vs 116 mL/min (n=465 vs 439), median RBP:Cr 118 µg/g vs 121 µg/g (n=465 vs 436), and β2M:Cr 106 µg/g vs 118 µg/g (n=464 vs 433).[4]

Similar to the overall study population, renal biomarkers of participants with baseline use of FTC/TDF for PrEP significantly favored those randomized to the FTC/TAF arm compared with those remaining on FTC/TDF (Table 3).[4]

Table 3. Renal Safety through Week 96 for Participants with Baseline Use of FTC/TDF for PrEP[4]

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

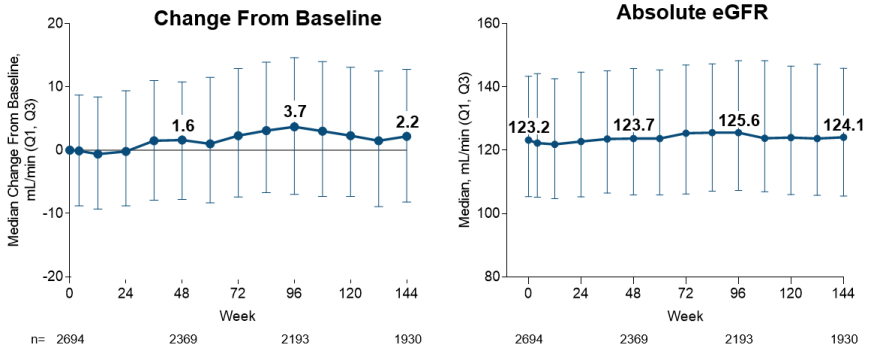
[a]P-value from 2-sided Wilcoxon rank sum test to compare treatment groups., [b]n=406, [c]n=377, [d]n=374, [e]n=402, [f]n=368, [g]n=459, [h]n=435

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 OL phase. Baseline demographics are outlined in the FTC/TAF column of Table 1 above.[9]

Sub-analyses for renal function showed consistent changes in eGFR in FTC/TAF participants through Week 144, as shown in Figure 2 below.[9]

Figure 2. 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).[3]

Table 4. OLE Renal Safety from OL Baseline to OL Week 48[3]

	Stay on FTC/TAF	Switch from FTC/TDF	P-value[a]
$eGFR_{CG}$, median change from OL baseline, mL/min	-2.8[b]	+0.3[c]	<0.001
RBP:Cr, median % change from OL baseline	-9.9[d]	-26.8[e]	<0.001
β2M:Cr, median % change from OL baseline	-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 adverse reaction frequencies between FTC/TAF and FTC/TDF is not known.[5]

References

1. Mayer KH, Molina JM, Thompson MA, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. *Lancet.* 2020;396(10246):239-254.
2. Ogbuagu O, Ruane PJ, Podzamczer D, et al. Long-term safety and efficacy of emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis: week 96 results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet HIV.* 2021;8:e397-e407.
3. Wohl DA, Spinner CD, Flamm J, et al. HIV-1 infection kinetics, drug resistance, and long-term safety of pre-exposure prophylaxis with emtricitabine plus tenofovir alafenamide (DISCOVER): week 144 open-label extension of a randomised, controlled, phase 3 trial. [Supplementary Appendix] *Lancet HIV.* 2024;11(8):508-521.
4. Campbell T, Clarke A, Trottier B, et al. Safety and Efficacy of F/TAF and F/TDF for PrEP in DISCOVER Participants Taking F/TDF for PrEP at Baseline [Poster 995]. Paper presented at: IDWeek Virtual; 21-25 October, 2020.
5. Enclosed. Gilead Sciences Inc, DESCOVY® (emtricitabine and tenofovir alafenamide) tablets, for oral use. U. S. Prescribing Information. Foster City, CA.
6. ClinicalTrials.gov. Safety and Efficacy of Emtricitabine and Tenofovir Alafenamide (F/TAF) Fixed-Dose Combination Once Daily for Pre-Exposure Prophylaxis in Men and Transgender Women Who Have Sex With Men and Are At Risk of HIV-1 Infection (DISCOVER). ClinicalTrials.gov Identifier: NCT02842086. Last Updated: 22 October 2024. Available at: https://clinicaltrials.gov/ct2/show/NCT02842086. Accessed: 23 December 2024.
7. Mills A, Workowski K, Campbell T, et al. Renal Outcomes for Participants Taking F/TAF vs. F/TDF for HIV PrEP in the DISCOVER Trial [Presentation]. Paper presented at: IDWeek; 05 October, 2019; Washington, D.C.
8. Food and Drug Administration (FDA). FDA Briefing Document: Meeting of the Antimicrobial Drugs Advisory Committee. DESCOVY (emtricitabine 200 mg and tenofovir alafenamide 25 mg) Tablets. 07 August. 2019.
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
CG=Cockcroft-Gault
Cr=creatinine
eGFR=estimated glomerular filtration rate
FTC=emtricitabine
MSM=men who have sex with men
OL=open-label

OLE=open-label extension
PrEP=pre-exposure prophylaxis
RBP=retinol-binding protein
TAF=tenofovir alafenamide
TDF=renofovir disoproxil fumarate
TGW=transgender women

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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