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GILEAD | Medical Information

Descovy for PrEP® (FTC/TAF) Switching From FTC/TDF for PrEP

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

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; www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Summary

Product Labeling

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.[1]

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.[1]

FTC/TDF is indicated in at-risk adults and adolescents weighing ≥35 kg for PrEP to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test immediately prior to initiating FTC/TDF for HIV-1 PrEP.[2]

Clinical Data on Switching From FTC/TDF to FTC/TAF for PrEP

FTC/TAF demonstrated noninferior efficacy to FTC/TDF for HIV-1 PrEP among adult MSM and TGW in the phase 3 DISCOVER trial at both the primary and Week 96 analyses.[3-6]

- HIV incidence rates were low through Week 48 of the OL phase (FTC/TAF: 0.09 per 100 PY; FTC/TDF→FTC/TAF: 0.05 per 100 PY).[6]
- Improvements in bone and renal biomarkers were also observed in those who switched from FTC/TDF→FTC/TAF in the OL phase.[5,6]

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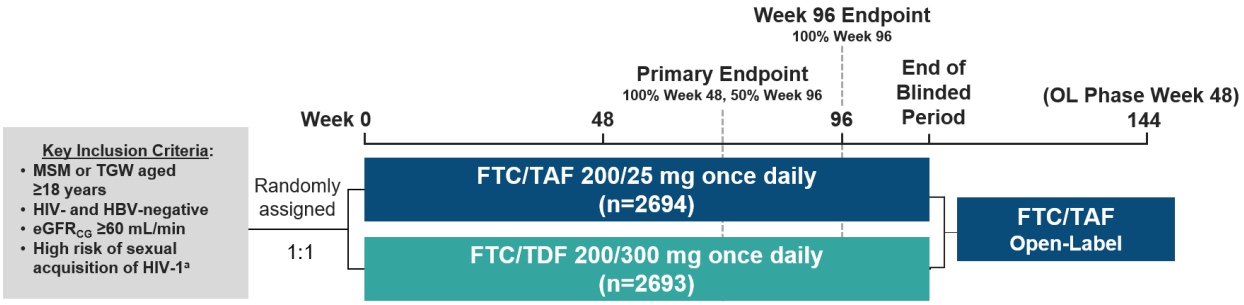
Clinical Data on Switching From FTC/TDF to FTC/TAF for PrEP

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

Study design and demographics

DISCOVER was a phase 3, multinational study in 5387 HIV-negative adult MSM and TGW that evaluated the safety and efficacy of FTC/TAF vs FTC/TDF for HIV-1 PrEP (Figure 1). The primary 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. 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. Prior use of FTC/TDF for HIV-1 PrEP was allowed.[3,5,7]

Figure 1. DISCOVER: Study Design[3,5,7]



[a]Included ≥1 of the following: condomless anal intercourse with ≥2 unique male partners of HIV-positive or unknown HIV status within the previous 12 weeks; a documented history of syphilis, rectal gonorrhea, or rectal chlamydia in the previous 24 weeks.

Participant baseline characteristics were similar between the FTC/TAF and FTC/TDF arms, including risk factors for HIV acquisition (Table 1).[3]

Table 1. DISCOVER: Baseline Demographics and HIV Risk Factors[3,4]

Key Demographics and Characteristics		FTC/TAF (n=2694)	FTC/TDF (n=2693)
Age, median (range), years		34 (18–76)	34 (18–72)
Race, n (%)	White	2264 (84)	2247 (84)
	Black or mixed Black	240 (9)	234 (9)
	Asian	113 (4)	120 (4)
Ethnicity, Hispanic or Latinx, n (%)		635 (24)	683 (25)
TGW, n (%)		45 (2)	29 (1)
Sexual orientation, %	Gay	92	91
	Bisexual	6	8
	Straight	1	1
	Other	1	<1

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Key Demographics and Characteristics		FTC/TAF (n=2694)	FTC/TDF (n=2693)
Region, %	USA	59	60
	EU	34	33
	Canada	7	6
HIV risk factors, %	Recreational drug use in the past 12 weeks	67	67
	Receptive condomless anal sex with ≥2 unique partners in the past 12 weeks	62	60
	Binge drinking[a]	23	22
	Taking FTC/TDF for HIV-1 PrEP at baseline	17	16
	Rectal chlamydia in the past 24 weeks	13	12
	Rectal gonorrhea in the past 24 weeks	10	10
	Syphilis in the past 24 weeks	9	10

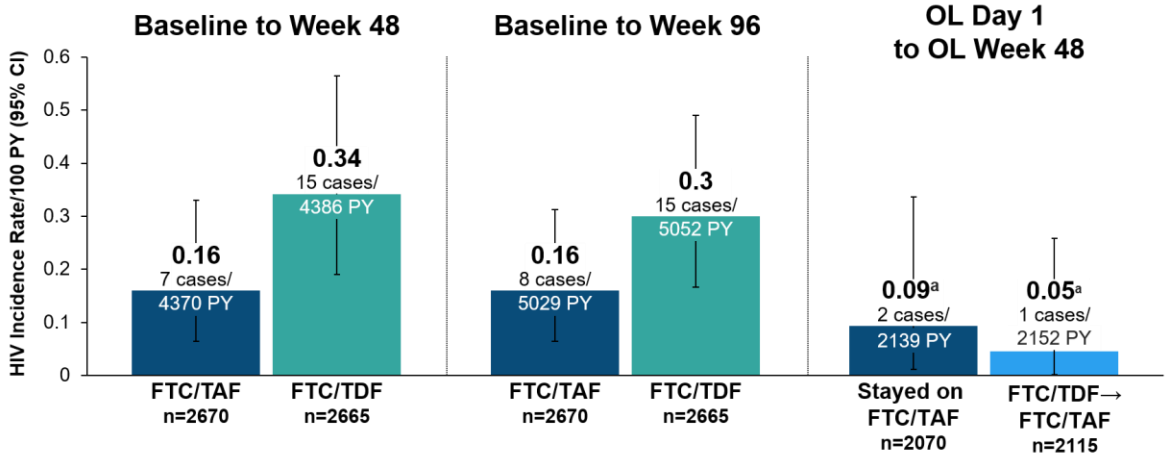
[a]Defined as consuming ≥6 drinks on ≥1 occasion at least once per month.

Efficacy results

The primary analysis had a total follow-up of 8756 PY (FTC/TAF, 4370 PY; FTC/TDF, 4386 PY). Overall, there were 22 incident HIV cases (FTC/TAF, n=7; FTC/TDF, n=15; incidence rate: 0.16 per 100 PY and 0.34 per 100 PY, respectively). The incidence rate ratio of incident HIV cases between the FTC/TAF and FTC/TDF arms was 0.47 (95% CI: 0.19–1.15); the upper bound of the 95% CI was less than the noninferiority margin of 1.62, thus the noninferiority criteria was met.[3]

From Day 1 of the OL phase to Week 48 of the OL phase, there were a total of 3 incident HIV cases (FTC/TAF, n=2; FTC/TDF→FTC/TAF, n=1), for an HIV incidence rate of 0.09 per 100 PY in the FTC/TAF group and 0.05 per 100 PY in the FTC/TDF→FTC/TAF group (Figure 2). The HIV incidence rates were similar between the two study arms.[6] Among all incident HIV cases from baseline to Week 144, 5 participants had suspected HIV at baseline, and 19 participants had low levels of tenofovir diphosphate per dried blood spot analysis.[8,9]

Figure 2. DISCOVER: Incidence Rates of New HIV Cases From Baseline to OL Week 48[6]



[a]During the OL phase, 1 additional participant in each group had a positive quantitative HIV nucleic acid amplification test that was later confirmed to be a false positive.

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Safety results

Bone safety

Among participants who had previously received FTC/TDF for PrEP, there were no significant differences between the FTC/TAF and FTC/TDF groups in the change in hip and spine BMD from baseline to Week 96. Mean percent BMD changes in hip and spine from baseline to Week 96 favored FTC/TAF use without baseline FTC/TDF use (Table 2).[10]

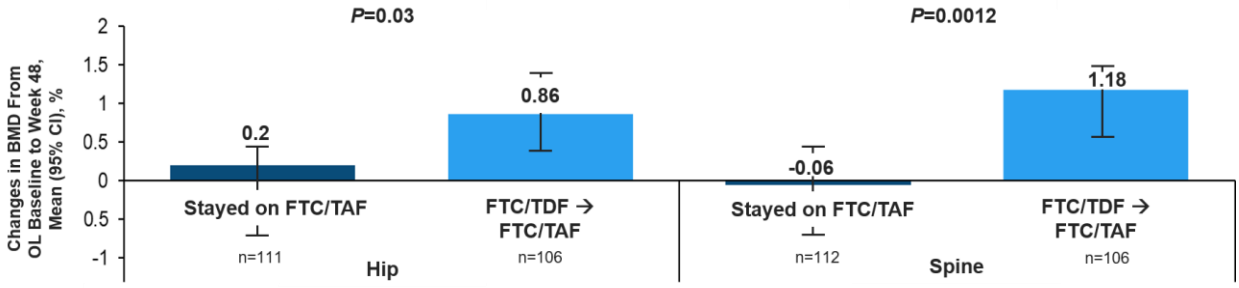
Table 2. DISCOVER: Analysis of BMD Mean Percent Change From Baseline at Week 96[10]

BMD Cohort	Location	n	FTC/TAF	FTC/TDF	*P*-Value
Baseline FTC/TDF use	Hip	20[a]	+1.8	+1.4	0.75
	Spine	20[b]	+0.9	-1.2	0.13
No baseline FTC/TDF use	Hip	124[c]	+0.4	-1.4	<0.001
	Spine	125	+0.8	-1.5	<0.001

[a]n=20 in baseline FTC/TDF→FTC/TAF group, n=16 in baseline FTC/TDF→FTC/TDF group.
[b]n=20 in baseline FTC/TDF→FTC/TAF group, n=17 in baseline FTC/TDF→FTC/TDF group.
[c]n=124 in no baseline FTC/TDF→FTC/TAF group, n=122 in no baseline FTC/TDF→FTC/TAF group.

On Day 1 of the OL phase, which began 96 weeks after the blinded phase, hip and spine BMDs were not significantly different between study arms. At Week 48 of the OL phase, participants who switched from FTC/TDF to FTC/TAF had statistically significant increases in hip and spine BMD compared with those who remained on FTC/TAF (Figure 3).[6]

Figure 3. DISCOVER: Changes in BMD From OL Baseline to Week 48[6]



Please note, the long-term clinical significance of the BMD changes is not known.[1]

Renal safety

On Day 1 of the OL phase, there were significant differences in renal biomarkers between participants who received FTC/TAF and those who received FTC/TDF during the blinded phase of the study (Table 3).[6]

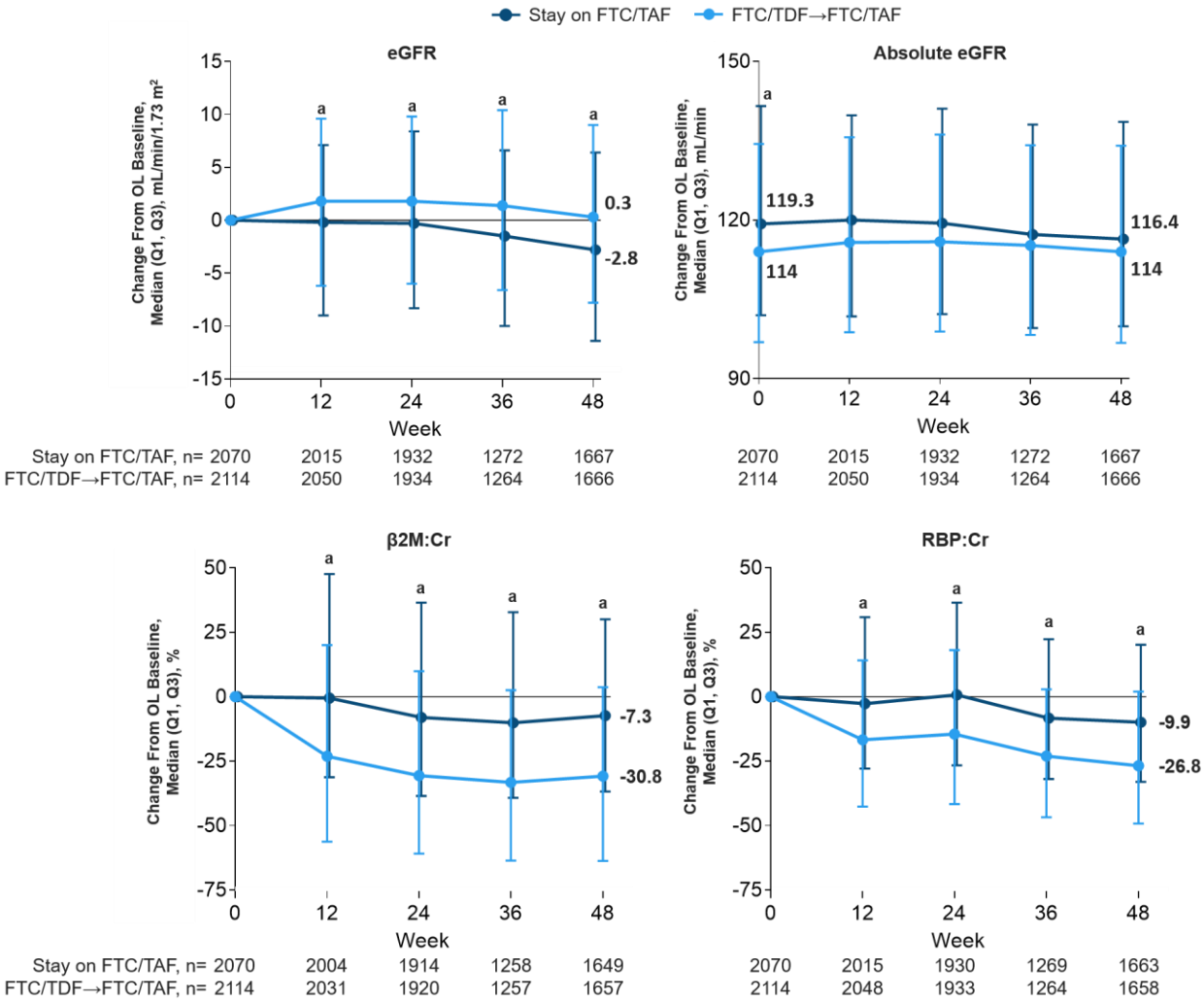
Table 3. Renal Biomarkers on Day 1 of the OL Phase[6]

Renal Biomarkers, Median (Q1, Q3)	Stayed on FTC/TAF	FTC/TDF→FTC/TAF	*P*-Value[a]
$eGFR_{CG}$, mL/min	119.3 (102, 141.6)	114 (96.9, 134.4)	<0.0001
β2M:Cr, mcg/g	72.2 (51.1, 106.6)	99.3 (63.8, 202.9)	<0.0001
RBP:Cr, mcg/g	102 (74.9, 146.8)	124.8 (88.6, 192.8)	<0.0001

[a]*P*-values were calculated using the Cochran–Mantel–Haenszel test.

At Week 48 of the OL phase, participants who switched from FTC/TDF to FTC/TAF had significantly greater improvements in renal biomarkers compared with participants who stayed on FTC/TAF (Figure 4).[6]

Figure 4. DISCOVER: Renal Outcomes Through Week 48 of the OL Phase[6]



[a]*P*-values were calculated using the Cochran–Mantel–Haenszel test with mean scores to compare the two study arms.

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.[1]

Hepatic safety

On Day 1 of the OL phase, HDL and LDL levels were significantly higher in participants who received FTC/TAF compared with those who received FTC/TDF during the blinded phase of the study (Table 4).[6]

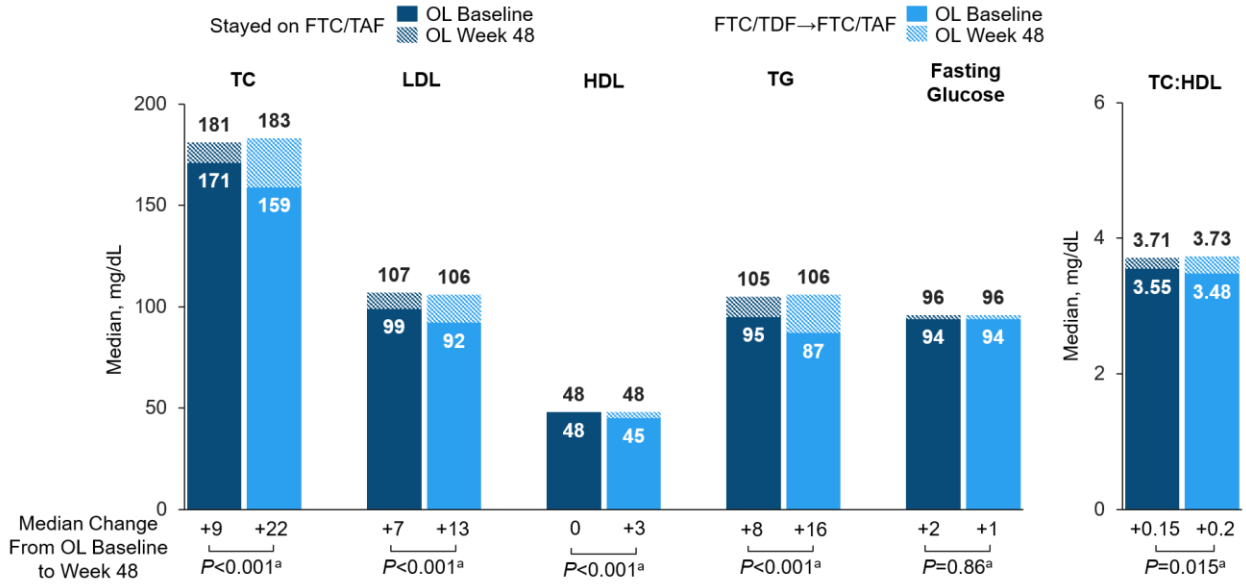
Table 4. DISCOVER: Lipid Levels on Day 1 of the OL Phase[6]

Lipid Levels, Median (Q1, Q3), mg/dL	Stayed on FTC/TAF	FTC/TDF→FTC/TAF	*P*-Value[a]
LDL	99 (80, 120)	92 (75, 113)	<0.0001
HDL	48 (40, 57)	45 (38, 54)	<0.0001

[a]*P*-values were calculated with a 2-sided Wilcoxon rank sum test.

At Week 48 of the OL phase, median changes from baseline in TC, LDL, HDL, TG, and TC:HDL ratio were significantly greater in participants switching from FTC/TDF to FTC/TAF compared to those remaining on FTC/TAF (Figure 5).[6]

Figure 5. DISCOVER: Median Changes in Fasting Lipid Levels From OL Baseline to Week 48[6]



[a]*P*-values were calculated with a 2-sided Wilcoxon rank sum test.

Weight change

In both arms, approximately 50% of participants had a BMI in the overweight category at baseline. Median weight changes for participants in the FTC/TAF and FTC/TDF arms were +1 kg and 0 kg, respectively, at Week 48 (*P*<0.001), and +1.7 kg and +0.5 kg at Week 96 (*P*<0.0001).[5,11] Weight increase was observed across all study arms regardless of baseline PrEP use.[5] From baseline of the OL phase through Week 48, participants who stayed on FTC/TAF had a median weight change of +1.2 kg, and participants who switched from FTC/TDF to FTC/TAF had a median weight change of +2 kg (*P*<0.001).[6]

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Abbreviations

β2M=β2-microglobulin
CG=Cockcroft-Gault
FTC=emtricitabine
MSM=men who have sex with men
OL=open-label
PrEP=pre-exposure prophylaxis
PY=patient years
Q=quartile
RBP=retinol-binding protein
TAF=tenofovir alafenamide
TC=total cholesterol
TDF=tenofovir disoproxil fumarate
TG=triglycerides
TGW=transgender women

Product Label

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

Follow Up

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🖱 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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