GILEAD | Medical Information

Descovy for PrEP® (FTC/TAF) Weight Change

This document is in response to your request for information regarding Descovy for PrEP® (emtricitabine/tenofovir alafenamide [FTC/TAF] for HIV-1 pre-exposure prophylaxis [PrEP]) and weight change. This response 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; www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Product Labeling[1]

Indications and Usage

HIV-1 PrEP

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 the 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 Weight Change With FTC/TAF

DISCOVER Study

Study design and demographics

DISCOVER (NCT02842086) is an ongoing, phase 3, randomized, double-blind, active-controlled, multinational study in adult MSM and TGW without HIV that is evaluating the safety and efficacy of once-daily FTC/TAF (n=2694) vs FTC/TDF (n=2693) for HIV-1 PrEP. Eligible participants were randomly assigned (1:1) to receive either FTC/TAF or FTC/TDF with a corresponding placebo once daily. The primary outcome was the incidence of HIV-1 acquisition per 100 person-years after all participants had ≥48 weeks of follow-up and ≥50% of participants had 96 weeks of follow-up, with a pre-specified non-inferiority margin of 1.62. All participants were unblinded after 96 weeks, and participants in both arms

were offered the opportunity to continue on or switch to open-label FTC/TAF for an additional 48 weeks.[2]

Weight change

Baseline median BMI of participants in both arms was 25.3 kg/m^2, and approximately 50% of participants had a BMI in the overweight/obese category (>25 kg/m^2).[3,4] Median weight changes for participants in the FTC/TAF vs FTC/TDF arm, respectively, were +1 kg vs 0 kg (P<0.001) at Week 48 and +1.7 kg vs +0.5 kg (P<0.001) at Week 96.[3,5] A subgroup analysis assessed long-term outcomes of participants randomly assigned to FTC/TAF who continued on FTC/TAF in the open-label phase. The median weight change from baseline through Week 144 was +2.3 kg, which equated to a mean annualized increase in body weight of 0.83 kg per year.[6]

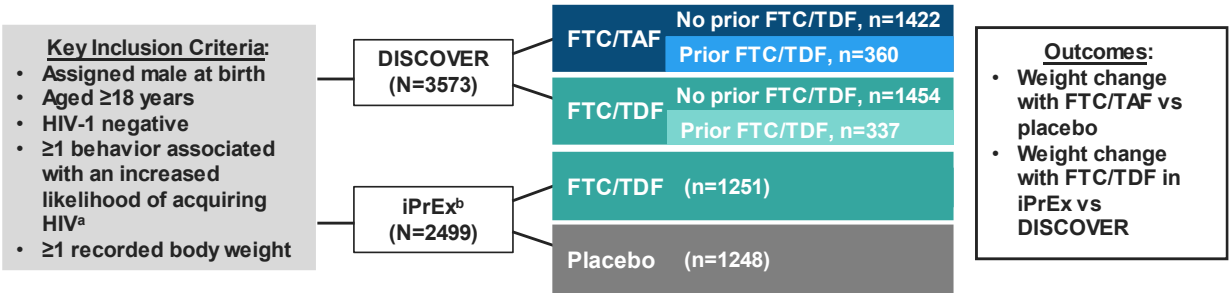
Overall, weight gain was observed in all participants across both arms, regardless of baseline PrEP use. Among baseline PrEP users, the median weight change from baseline to Week 96 was +2.3 kg in the FTC/TAF arm and +1.1 kg in the FTC/TDF arm (difference, 1.2 kg). Among participants with no baseline PrEP use, the median change in weight from baseline to Week 96 was +1.6 kg in the FTC/TAF arm and +0.4 kg in the FTC/TDF arm (difference, 1.2 kg).[7]

Retrospective Analysis of DISCOVER and iPrEx Studies[8]

Study design and demographics

A retrospective analysis compared weight changes in participants who received FTC/TAF for PrEP with those of participants who received placebo using data from DISCOVER and iPrEx, two randomized, double-blind, phase 3 clinical trials (N=6072). Eligible participants for each trial were assigned male at birth, aged ≥18 years, and negative for HIV-1 and had ≥1 behavior that increased the likelihood of acquiring HIV-1 (Figure 1). The main eligibility criteria for this analysis included ≥1 recorded body weight.

Figure 1. Retrospective Analysis of DISCOVER and iPrEx: Study Designs[8]



[a]For iPrEx, the behaviors were the following: no condom use during anal intercourse with a male partner with either HIV or an unknown HIV status in the past 6 months; anal intercourse with >3 male partners in the past 6 months; exchange of money, gifts, shelter, or drugs for anal sex with a male partner in the last 6 months; sex with a male partner and diagnosis of a sexually transmitted infection in the last 6 months or at screening; having a sexual partner with HIV with whom condoms were not consistently used in the last 6 months. In DISCOVER, the behaviors were the following: condomless anal intercourse with ≥2 unique male partners with either HIV or an unknown HIV status in the last 12 weeks; a documented history of syphilis, rectal gonorrhea, or chlamydia in the last 24 weeks.
[b]No participants in iPrEx received FTC/TDF before randomization.

Compared with participants in iPrEx, participants in DISCOVER were more likely to be White, be ≥36 years of age, have a BMI ≥27 kg/m^2, and use more medications associated with weight gain (Table 1).

Table 1. Retrospective Analysis of DISCOVER and iPrEx: Baseline Demographics and Clinical Characteristics[8]

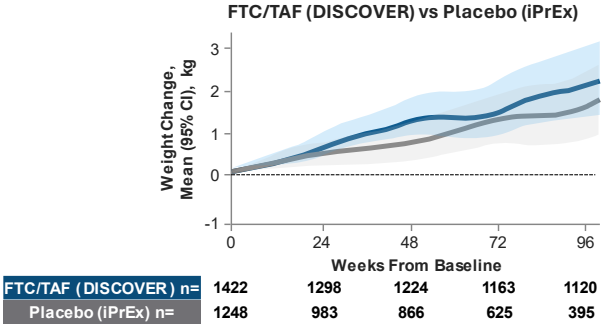
Key Demographics and Characteristics		DISCOVER (FTC/TAF vs FTC/TDF)		iPrEx (FTC/TDF vs Placebo)
		All Participants (N=3573)[a]	Prior FTC/TDF (n=697)[a]	All Participants (N=2499)
Age, mean ± SD, years		36.1±11	37.5±11	27.1±9
Race or ethnicity, n (%)	White	2825 (79)	579 (83)	431 (17)
	Black	405 (11)	55 (8)	214 (9)
	Hispanic or Latine	871 (24)	121 (17)	1806 (72)
	Other[b]	343 (10)	63 (9)	1854 (74)[c]
Medications associated with weight change,[d] n (%)	Gain	516 (14)	131 (19)	63 (3)
	Loss	287 (8)	62 (9)	28 (1)
	Unknown	246 (7)	72 (10)	31 (1)
Body weight, mean ± SD, kg		85±18	84.6±18	68.1±14
BMI, mean ± SD, kg/m^2		27±5	26.7±5	23.8±4

[a]Participants who received FTC/TDF before baseline were counted in both columns and were subsequently randomly assigned to continue FTC/TDF or switch to FTC/TAF.
[b]Included American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, other race, and participants with Not Permitted designation when local regulations did not allow collection of race/ethnicity information.
[c]Most participants self-reported as "mixed race or other."
[d]Included antidepressants/psychoanaleptics, antidiabetics, antiepileptics, antihistamines, antipsychotics, contraceptives, corticosteroids, beta-androgenic blockers, and insulin.

Results

Among participants with no prior use of FTC/TDF, there was no significant difference in mean weight change from baseline between participants who received FTC/TAF in DISCOVER and placebo in iPrEx at Week 24 (mean difference, +0.7 kg), Week 48 (+0.44), Week 72 (+0.13), or Week 96 (+0.53; each, *P*=0.1; Figure 2).

Figure 2. Retrospective Analysis: Estimated Mean Weight Change[a] From Baseline to Week 96 in Participants Who Received FTC/TAF in DISCOVER or Placebo in iPrEx[8]



[a]Data were adjusted for baseline age, country of enrollment, diabetes status, non-fasting glucose, eGFR, ALT levels, race, height, use of medications associated with weight change at baseline and during the trial, and weight.
Note: Solid lines represent means, and shaded areas represent 95% CIs.

Among participants with no prior FTC/TDF use, similar proportions of participants who received FTC/TAF in DISCOVER and placebo in iPrEx had large increases in body weight at 48 weeks (Table 2).

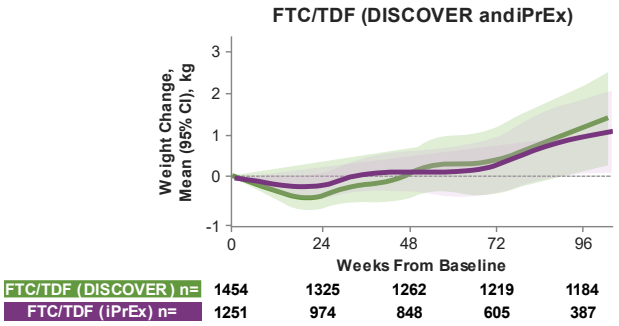
Table 2. Retrospective Analysis: Top Percentiles of Weight Change[a] From Baseline to Week 48 in Participants With No Prior FTC/TDF Use Who Received FTC/TAF in DISCOVER or Placebo in iPrEx[8]

Top Percentiles (95% CI), kg	FTC/TAF (DISCOVER)	Placebo (iPrEx)
80th	4.1 (3.8, 4.4)	4.2 (3.7, 4.7)
85th	4.6 (4.2, 5.1)	5 (4.4, 5.7)
90th	5.8 (5.3, 6.2)	5.7 (5.1, 6.3)
95th	7.9 (7, 8.7)	6.9 (5.8, 8.1)
99th	11.1 (10.1, 12.2)	11.6 (9, 14.2)

[a]Data were adjusted for baseline age, country of enrollment, diabetes status, non-fasting glucose, eGFR, ALT levels, race, height, use of medications associated with weight change at baseline and during the trial, and weight.

Among participants with no prior FTC/TDF use, the estimated mean weight change from baseline was similar between those who received FTC/TDF in DISCOVER or iPrEx (Figure 3).

Figure 3. Retrospective Analysis: Estimated Mean Weight Change[a] From Baseline to Week 96 in Participants With No Prior FTC/TDF Use Who Received FTC/TDF in DISCOVER or iPrEx[8]

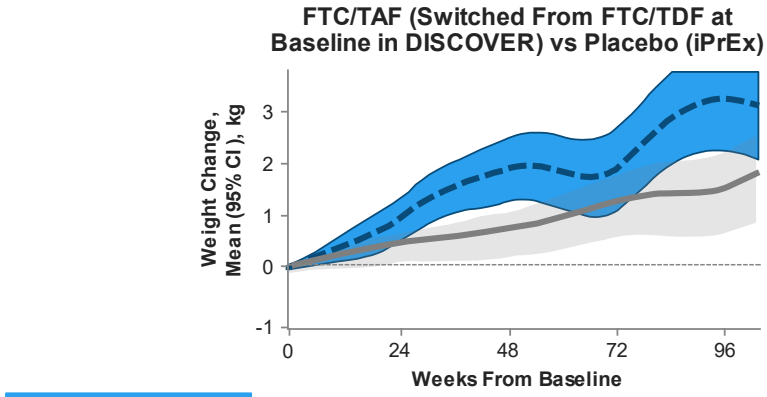


[a]Data were adjusted for baseline age, country of enrollment, diabetes status, non-fasting glucose, eGFR, ALT levels, race, height, use of medications associated with weight change at baseline and during the trial, and weight.

Note: Solid lines represent means, and shaded areas represent 95% CIs.

Among participants in DISCOVER with prior FTC/TDF use who switched to FTC/TAF at baseline, the mean weight gain was similar to that in participants in iPrEx with no prior FTC/TDF use who received placebo, with a mean (95% CI) between-group difference of +0.46 (0.02–0.9) kg at Week 24, +1.15 (0.53–1.77) kg at Week 48, +0.63 (-0.16 to 1.42) kg at Week 72, and +1.74 (0.78–2.7) kg at Week 96 (Figure 4).

Figure 4. Retrospective Analysis: Estimated Mean Weight Change[a] in Participants With Prior FTC/TDF Use Who Switched to FTC/TAF in DISCOVER vs Received Placebo in iPrEx[8]



FTC/TAF (DISCOVER) n=	360	341	338	326	319
Placebo (iPrEx) n=	1248	983	866	625	395

[a]Data were adjusted for baseline age, country of enrollment, diabetes status, non-fasting glucose, eGFR, ALT levels, race, height, use of medications associated with weight change at baseline and during the trial, and weight.

Note: Solid lines represent means, and shaded areas represent 95% CIs.

References

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3. 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.
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5. Ruane P, Clarke A, Post FA, et al. Phase 3 Randomized, Controlled DISCOVER Study of Daily F/TAF or F/TDF for HIV Pre-exposure Prophylaxis: Week 96 Results [Poster PE3/16]. Paper presented at: 17th European AIDS Conference; 06-09 November, 2019; Basel, Switzerland.
6. 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.
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Abbreviations

FTC=emtricitabine
MSM=men who have sex with men
PrEP=pre-exposure prophylaxis
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
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

For any additional questions, please contact Gilead Medical Information at:

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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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