GILEAD | Medical Information

Descovy for PrEP® (FTC/TAF) Development of Resistance

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) and development of resistance.

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

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 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.

Resistance Data from DISCOVER Study[2]

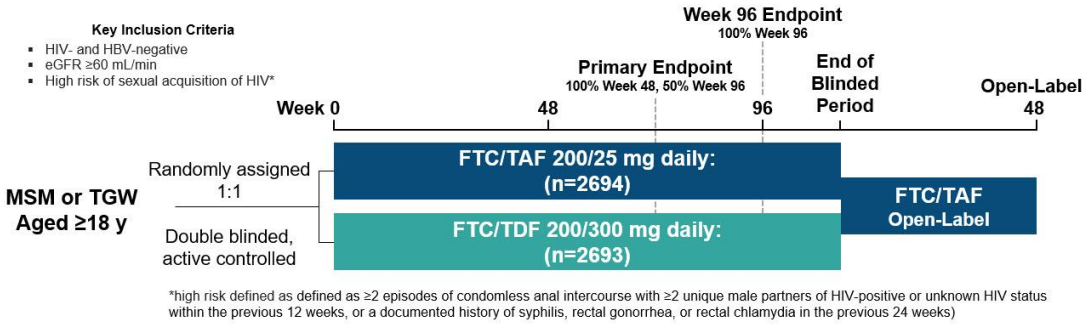
A subanalysis of resistance outcomes through Week 144 in participants from the DISCOVER study showed overall low rates of resistance in the FTC/TAF group, with the majority of HIV cases occurring in patients with low adherence (<2 tablets/week) or suspected baseline infection.

Resistance Data from Discover Study

Study Design and Demographics

DISCOVER was 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.[3,4]

Figure 1. Study Design[3,4]



The primary measured outcome was evaluated by 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.[3] Efficacy was evaluated by a rate ratio with upper bound of the 95% CI below the prespecified 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, once-daily FTC/TAF for an additional 48 weeks. Participant baseline characteristics were similar between the FTC/TAF and FTC/TDF arms, including risk factors for HIV.[4]

Table 1. Select Baseline Demographics and HIV Risk Factors[4]

	FTC/TAF (n=2694)	FTC/TDF (n=2693)
Baseline demographics		
Median age, years (IQR)	34 (28–43)	34 (28–44)
Race, n (%)		
White	2264 (84)	2247 (84)
Black[a]	240 (9)	234 (9)
Asian	113 (4)	120 (5)
Hispanic or Latinx ethnicity, n (%)	635 (24)	683 (25)
Proportion TGW, n (%)	45 (2)	29 (1)
HIV risk factors, %		
≥2 receptive condomless anal sex, past 12 weeks	62	60
Syphilis, past 24 weeks	9	10
Received FTC/TDF for HIV-1 PrEP at baseline	17	16

Abbreviation: IQR=interquartile range.
[a]Included mixed Black race.

Efficacy Results

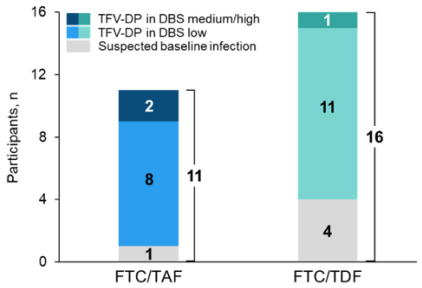
The primary endpoint had a total follow-up of 8756 PY (4370 PY of FTC/TAF and 4386 PY of FTC/TDF) and included data from all participants with ≥48 weeks of follow-up and ≥50% of participants with 96 weeks of follow-up. Across FTC/TAF and FTC/TDF arms, there were a total of 22 HIV diagnoses (7 vs 15, respectively) for an HIV incidence rate of 0.16/100 PY vs 0.34/100 PY, respectively. The incidence rate ratio between the FTC/TAF and FTC/TDF arms was 0.47 (95% CI: 0.19–1.15), establishing non-inferiority of FTC/TAF to FTC/TDF.[3]

When all participants reached Week 96, there was a total follow-up of 10,081 PY (5029 PY of FTC/TAF and 5052 PY of FTC/TDF), with 23 total HIV cases (8 vs 15, respectively) for an HIV incidence rate of 0.16/100 PY vs 0.30/100 PY, respectively. The incidence rate ratio

was 0.54 (95% CI: 0.23–1.26), maintaining non-inferiority of FTC/TAF to FTC/TDF at 96 weeks.[4]

At Week 144, 27 total HIV diagnoses were reported (11 in the FTC/TAF arm vs 16 in the FTC/TDF arm). Five participants had suspected baseline infections and low levels of TFV-DP were found in 19 participants on DBS analysis (Figure 2).[5,6]

Figure 2. Adherence and Resistance Analyses of HIV Diagnoses[a5]



[a]Updated with data cut through Week 118; adherence cutoffs, fmol/punches: FTC/TAF: low, <450; medium, ≥450-<900; high, ≥900; FTC/TDF: low, <350; medium ≥350-<700; high ≥700.

Using standard sequencing, the development of FTC resistance-associated substitutions, M184I and/or M184V, was observed in 4 participants who seroconverted in the FTC/TDF group who had suspected baseline HIV. Ultrasensitive sequencing had similar resistance data with the addition of a M184V mutation detected in one participant in the FTC/TAF arm who had low DBS TFV-DP level at the time of diagnosis, and a possible low level K65R mutation in the FTC/TDF arm.[7] Out of 13 participants who seroconverted with drug resistance and initiated an antiretroviral therapy regimen, 10 achieved virologic suppression while the remaining 3 participants were lost to follow up.[5] In a sensitivity analysis that excluded five participants with suspected baseline HIV, FTC/TAF non-inferiority to FTC/TDF was maintained (incidence rate ratio: 0.64; 95% CI: 0.25–1.65).[4]

Safety Results

Based on AE reporting through Week 96, the incidence of gonorrhea, chlamydia, or syphilis were similar between the two arms. Common AEs reported by ≥10% of participants in either arm included diarrhea, nasopharyngitis, and URTI (Table 2). In the FTC/TAF and FTC/TDF arms, AEs leading to study drug discontinuation occurred in 1% vs 2% of participants, respectively. There were a total of five deaths reported through Week 96 (3 in FTC/TAF and 2 in FTC/TDF).[4]

Table 2. Commonly Reported AEs and STIs in ≥10% of Participants in Either Arm at Week 96[4]

	FTC/TAF (n=2694)	FTC/TDF (n=2693)
Rectal chlamydia, %	33	33
Oropharyngeal gonorrhea, %	32	31
Rectal gonorrhea, %	30	30
Exposure to communicable disease, %	21	20
Diarrhea, %	18	17
Nasopharyngitis, %	15	15
Syphilis, %	15	15
URTI, %	15	13
Urethral chlamydia, %	13	12
Urethral gonorrhea, %	10	9

References

1. Descovy, Gilead Sciences Inc. DESCOVY® (emtricitabine and tenofovir alafenamide) tablets, for oral use. U.S. Prescribing Information. Foster City, CA. Revised January. 2022.
2. 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. *Lancet HIV*. 2024;11(8):508-521.
3. 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*. Jul 25 2020;396(10246):239-254. doi:10.1016/S0140-6736(20)31065-5
4. 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.
5. Cox S. Ultrasensitive HIV-1 Drug Resistance Analysis in the Discover Prep Trial [Presentation]. 2021:
6. Gilead Sciences Inc. Data on File.
7. Cox S, Parikh UM, Heaps AL, et al. HIV-1 Drug Resistance in the DISCOVER Pre-exposure Prophylaxis Trial [Poster 1002]. 2020:

Abbreviations

AE=adverse event
DBS=dried blood spots
FTC=emtricitabine
MSM=men who have sex with men
PrEP=pre-exposure prophylaxis
PY=person-years
STI=sexually transmitted infection
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TFV=tenofovir
TFV-DP=tenofovir diphosphate
TGW=transgender women
URTI=upper respiratory tract infection

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

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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