GILEAD | Medical Information

Descovy for PrEP® (FTC/TAF) Time to Protection for HIV-1 Pre-Exposure Prophylaxis

This document is in response to your request for information regarding the time needed to achieve protection with the use of Descovy for PrEP® (emtricitabine/tenofovir alafenamide [FTC/TAF] for HIV-1 pre-exposure prophylaxis [PrEP]).

This document includes content from, or references to, clinical practice guidelines, and inclusion should not be interpreted as a treatment recommendation or an endorsement of the guidelines by Gilead Sciences, Inc.

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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]

The time from initiation of FTC/TAF for HIV-1 PrEP to maximal protection against HIV-1 infection is unknown; this 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 the Time to Protection From HIV-1 With FTC/TAF for PrEP

DISCOVER is a phase 3, randomized, double-blind, active-controlled study in HIV-uninfected adult MSM and TGW that is evaluating the safety and efficacy of FTC/TAF (n=2694) vs FTC/TDF (n=2693) for HIV-1 PrEP. Median PBMC TFV-DP levels exceeded EC_{90} within 1 to 2 hours after a single dose of FTC/TAF vs 3 days of once-daily doses needed to exceed this level with FTC/TDF.[2]

Clinical Data on the Time to Protection From HIV-1 With FTC/TAF for PrEP

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

Study design and demographics

DISCOVER (NCT02842086) is an ongoing phase 3, randomized, double-blind, active-controlled, multinational study in 5387 adult MSM and TGW without HIV that is

evaluating the safety and efficacy of FTC/TAF (n=2694) vs FTC/TDF (n=2693), both of which are fixed-dose combination products administered once daily for HIV-1 PrEP. Key inclusion criteria were individuals aged ≥18 years, HIV- and HBV-uninfected, with eGFR ≥60 mL/min, and at high risk of sexual acquisition of HIV (defined as ≥2 episodes of condomless anal intercourse with ≥2 unique male partners with HIV 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).[3,4]

Eligible participants were randomly assigned 1:1 to receive either FTC/TAF 200/25 mg or FTC/TDF 200/300 mg with a corresponding placebo once daily and were instructed to initiate study drug within 24 hours after the Day 1 visit.[5] Follow-up visits occurred at baseline and every 12 weeks and included the following: comprehensive screenings for sexually transmitted infections; HIV screening; and assessment of adverse events, renal function, sexual behavior, and adherence measured by pill counts, questionnaires, plasma tenofovir levels, and TFV-DP levels in dried blood spots.[4]

Prior use of FTC/TDF for HIV-1 PrEP was allowed. Participants using FTC/TDF for HIV-1 PrEP at baseline were allowed to continue until start of study, after receiving an HIV test and meeting other eligibility requirements, as to not eliminate the protective benefit of FTC/TDF prior to study entry.[5]

PK results

TFV-DP concentrations in PBMCs were compared with PK data from historical phase 1 studies to estimate the onset and duration of HIV protection between the two arms. Based on those phase 1 studies, median PBMC TFV-DP levels exceeded EC_{90} within 1 to 2 hours after a single dose of FTC/TAF vs 3 days of once-daily doses needed to exceed this level with FTC/TDF.[2] However, the impact of these data has not been established in any clinical study. EC_{90} has not been shown to correlate with efficacy.

The clinical relevance of these PK data and the correlate of HIV protection is unknown.

Clinical Practice Guidelines on Time to Protection From HIV-1 With FTC/TAF PrEP

Per CDC clinical guidelines, data from exploratory PK studies conducted with HIV-uninfected adult men and women suggest that maximum intracellular concentrations of TFV-DP are reached in blood PBMCs after approximately 7 days of daily oral dosing, in rectal tissue at approximately 7 days, and in cervicovaginal tissues at approximately 20 days. No data are yet available about intracellular drug concentrations in penile tissues susceptible to HIV infection to inform considerations of protection for male insertive sex partners.[6]

References

1. Enclosed. Gilead Sciences Inc, DESCOVY® (emtricitabine and tenofovir alafenamide) tablets, for oral use. U. S. Prescribing Information. Foster City, CA.
2. Spinner CD, Brunetta J, Shalit P, et al. DISCOVER STUDY for HIV Pre-Exposure Prophylaxis: F/TAF has a more Rapid Onset and Longer Sustained Duration of HIV Protection Compared with F/TDF [Presentation]. Paper presented at: IAS 2019; 21-24 July, 2019; Mexico City, Mexico.

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. *The lancet. HIV.* 2021;8:e397-e407.
4. 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.
5. Gilead Sciences Inc. Data on File.
6. Centers for Disease Control and Prevention (CDC). *US Public Health Service: Preexposure Prophylaxis for the Prevention of HIV Infection in the United States—2021 Update: Clinical Providers' Supplement.* December 2021.

Abbreviations

EC_{90}=90% effective concentration
FTC=emtricitabine
MSM=men who have sex with men
PBMC=peripheral mononuclear blood cells
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TFV-DP=tenofovir diphosphate
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

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 Pharmacovigilance and Epidemiology ☎ 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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