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DISCOVER in Europe: a Subanalysis of the Phase 3, Randomized, Controlled Trial of Daily Emtricitabine/Tenofovir Alafenamide or Emtricitabine/Tenofovir Disoproxil Fumarate for HIV Pre-exposure Prophylaxis

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Introduction

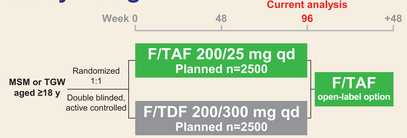
- Emtricitabine/tenofovir alafenamide (F/TAF) was recently approved in the United States for HIV pre-exposure prophylaxis (PrEP)[1]
- Approval was based on results from the DISCOVER study (ClinicalTrials.gov NCT02842086), which was conducted at sites in the European Union (EU) and North America
- Interim data analysis was conducted when 100% of participants completed Week 48 and 50% completed Week 96; results demonstrated that[2]:
  - F/TAF was noninferior to emtricitabine/tenofovir disoproxil fumarate (F/TDF) in preventing HIV infection
  - Both drugs were well tolerated, with low rates of adverse event (AE)–related discontinuations
  - F/TAF had significantly better bone and renal safety outcomes vs F/TDF
- In the EU, there is a continued unmet need for HIV-1 PrEP[3]
- Analyses of data from the 9 EU country subpopulation are reported

Objective

- To assess the incidence of HIV in an EU subpopulation receiving HIV PrEP with F/TAF vs F/TDF

Methods

Study Design



MSM, cis-men who have sex with men; TGW, transgender women.

- Eligibility: high sexual risk of HIV
  - 2+ episodes of condomless anal sex in past 12 wk or rectal gonorrhea/chlamydia or syphilis in past 24 wk
  - HIV and hepatitis B virus negative, and estimated glomerular filtration rate by Cockcroft-Gault ($eGFR_{CG}$) ≥60 mL/min
  - Prior use of PrEP allowed
- Study conducted in the EU and North America in cities/sites with high HIV incidence
- Assessments:
  - Safety: AEs, AE-related discontinuations, bone mineral density (BMD), and renal biomarkers
  - Adherence: self-report, pill counts, drug levels, and dried blood spots (DBS)
  - HIV lab testing: rapid HIV testing on site and central lab
  - HIV risk behavior: confidential computer-aided self-interview questionnaire and sexually transmitted infection (STI) assessment at every visit (gonococcus/chlamydia trachomatis: rectum, urethra, and oropharynx [nucleic acid amplification test], and syphilis testing)
- Primary efficacy endpoint analysis:
  - HIV incidence rate (IR; events/100 person-years [PY]): $\frac{\text{No. of HIV infections}}{\text{PY exposure}} \times (100)$
  - IR ratio: $\frac{\text{HIV IR: F/TAF arm}}{\text{HIV IR: F/TDF arm}}$
  - Noninferiority margin: 1.62; preserves 50% of F/TDF effect vs placebo in 3 prior randomized controlled trials in MSM
  - F/TAF noninferiority to F/TDF established if upper bound of IR ratio 95% confidence interval was <1.62

EU Study Sites

9 EU countries: Austria, Denmark, France, Germany, Ireland, Italy, Netherlands, Spain, UK

- Sites were selected based on having high community incidence of HIV, access to persons at risk of HIV infection, and ability to enroll persons of color and include those with prior PrEP use

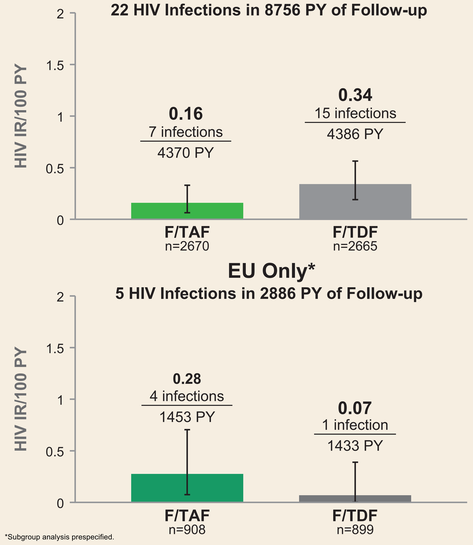
Results

Baseline Demographics and HIV Risk Factors

		Overall		EU Only	
		F/TAF n=2694	F/TDF n=2693	F/TAF n=912	F/TDF n=902
Demographics	Median age, y (range)	34 (18–76)	34 (18–72)	35 (19–65)	35 (19–71)
	Race, n (%)				
	White	2264 (84)	2247 (84)	857 (94)	829 (92)
	Black*	240 (9)	234 (9)	19 (2)	20 (2)
	Asian	113 (4)	120 (5)	26 (3)	38 (4)
	Hispanic or Latinx ethnicity, n (%)	635 (24)	683 (25)	221 (24)	226 (25)
	Proportion TGW, n (%)	45 (2)	29 (1)	6 (0.7)	3 (0.3)
HIV Risk Factors, n (%)	≥2 condomless anal sex (receptive), past 12 wk	1616 (62)	1569 (60)	575 (66)	548 (65)
	Rectal gonorrhea, past 24 wk	274 (10)	262 (10)	148 (16)	136 (15)
	Rectal chlamydia, past 24 wk	342 (13)	333 (12)	128 (14)	124 (14)
	Syphilis, past 24 wk	230 (9)	263 (10)	87 (10)	105 (12)
	Recreational drug use, past 12 wk	1785 (67)	1786 (67)	674 (74)	685 (77)
	Binge drinking†	618 (23)	599 (22)	269 (30)	241 (27)
	Taking F/TDF for PrEP at baseline	465 (17)	440 (16)	105 (12)	103 (11)

*Includes mixed black race; †≥6 drinks on ≥1 occasion, at least monthly.

Primary Endpoint Analysis: HIV Incidence

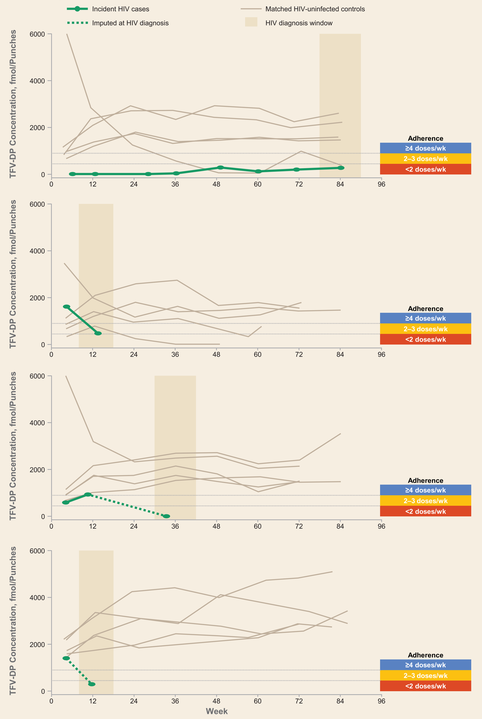


*Subgroup analysis prespecified.

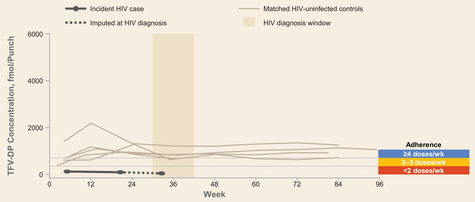
- For the overall population, F/TAF was noninferior to F/TDF for HIV prevention
- For EU regions, 5 HIV diagnoses were reported in Spain (n=3), Germany (n=1), and UK (n=1)

Case Control Adherence by DBS*

Participants on F/TAF With Incident HIV



Participant on F/TDF With Incident HIV



*Values >6000 fmol/punch(es) not shown. TFV-DP, tenofovir-diphosphate.

- TFV-DP levels in DBS were consistent with nonadherence (≤2 doses/wk) at time of HIV diagnosis for all EU cases

Sexually Transmitted Infections Through the Primary Analysis

	Overall			EU Only		
	F/TAF n=2694	F/TDF n=2693	Total N=5387	F/TAF n=912	F/TDF n=902	Total N=1814
Any gonorrhea, chlamydia, or syphilis						
Events (IR/100 PY)	1917 (132)	1794 (125)	3711 (129)	4340 (99)	4227 (96)	8567 (98)
n (%)	634 (70)	652 (73)	1286 (71)	1590 (60)	1643 (62)	3233 (61)
Rectal gonorrhea						
Events (IR/100 PY)	486 (34)	451 (32)	937 (33)	943 (22)	900 (21)	1843 (21)
n (%)	318 (35)	312 (35)	630 (35)	651 (24)	662 (25)	1313 (25)

- On-study STI rates were consistent with rates at baseline
- Spain had the highest IR (158/100 PY) and the UK the lowest (109/100 PY)

Conclusions

- Among DISCOVER participants at EU sites, HIV incidence was low
  - Most HIV infections occurred in participants with low or undetectable drug levels
- Study participants from EU sites had consistent high rates of sexual risk behavior
- HIV IR data from the EU subanalysis are consistent with IRs observed in North America
- F/TAF is an effective option for PrEP in MSM and TGW at risk for HIV infection, including those with high rates of STIs

References: 1. Descovy [package insert]. Foster City, CA: Gilead Sciences, Inc.; 10/2019; **2.** Hare CB, et al. CROI 2019. abstr 104; **3.** Hayes R, et al. Euro Surveillance. 2019 Oct;24.

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