PDB0303

Sexually Transmitted Infections in the DISCOVER HIV PrEP Trial

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Introduction

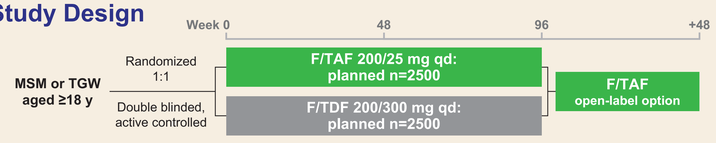
- DISCOVER (ClinicalTrials.gov NCT02842086) is an ongoing, randomized, controlled trial comparing emtricitabine/tenofovir alafenamide (F/TAF) with emtricitabine/tenofovir disoproxil fumarate (F/TDF) for pre-exposure prophylaxis (PrEP) in men who have sex with men (MSM) and transgender women (TGW)
- The burden of sexually transmitted infections (STIs) is high worldwide[1]
  - Some MSM and TGW face a disproportionately high burden of STIs, which may increase the risk of acquiring HIV[2]
  - Rectal gonorrhea incidence is directly correlated with HIV infection and has been proposed as a predictor of HIV incidence[3]
- Most clinical studies of PrEP have reported stable or decreasing STI rates during follow-up[4]

Objective

- To report STI outcomes in DISCOVER through 96 wk of follow-up

Methods

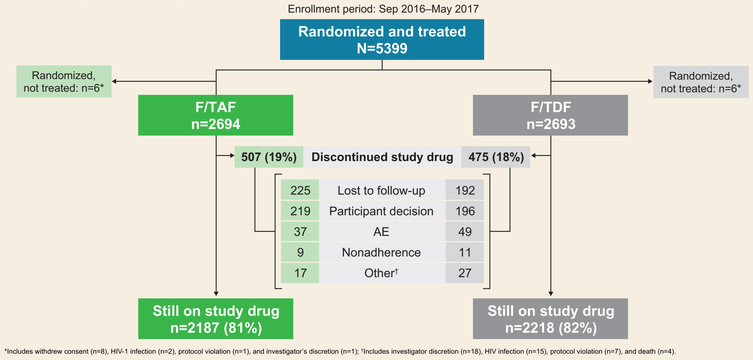
Study Design



- 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 (Cockcroft-Gault equation) ≥60 mL/min
  - Prior use of PrEP allowed
- Study conducted in Europe and North America in cities/sites with high HIV incidence
- STI assessments were performed at screening and each postbaseline visit
  - Gonorrhea and chlamydia rates were assessed by central laboratory testing (nucleic acid amplification) and investigator-reported adverse events (AEs)
  - Gonorrhea and chlamydia testing was performed from 3 anatomic sites: rectum, oropharynx, and urethra (urine)
  - Syphilis testing was performed by local laboratories in accordance with local guidelines

Results

Participant Disposition



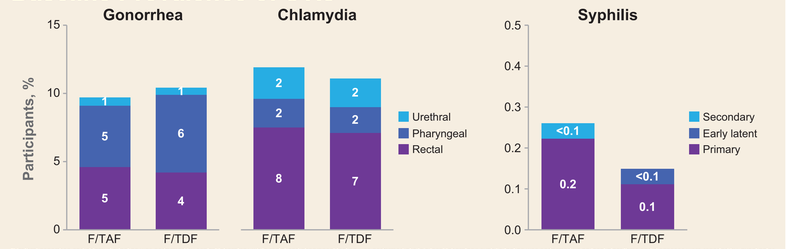
*Includes withdrew consent (n=8), HIV-1 infection (n=2), protocol violation (n=1), and investigator's discretion (n=1); †Includes investigator discretion (n=18), HIV infection (n=15), protocol violation (n=7), and death (n=4).

Demographics and Baseline Characteristics

		F/TAF n=2694	F/TDF n=2693
Demographics	Median age, y (range)	34 (18–76)	34 (18–72)
	Race, n (%)		
	White	2264 (84)	2247 (84)
	Black*	240 (9)	234 (9)
	Asian	113 (4)	120 (4)
	Hispanic or Latinx, n (%)	635 (24)	683 (25)
	Proportion TGW, n (%)†	45 (2)	29 (1)
HIV risk factors, n (%)	≥2 condomless receptive anal sex partners in past 12 wk	1616 (62)	1569 (60)
	Rectal gonorrhea in past 24 wk	**274 (10)**	**262 (10)**
	Rectal chlamydia in past 24 wk	**342 (13)**	**333 (12)**
	Syphilis in past 24 wk	**230 (9)**	**263 (10)**
	Recreational drug use in past 12 wk	1785 (67)	1786 (67)
	Binge drinking‡	618 (23)	599 (22)
	Taking F/TDF for PrEP at baseline	465 (17)	440 (16)

*Includes mixed black race; †Identified by self-report; ‡≥6 drinks on ≥1 occasion at least monthly.

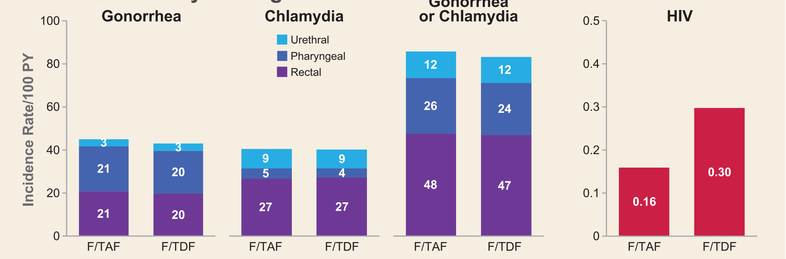
Baseline Prevalence of STIs*



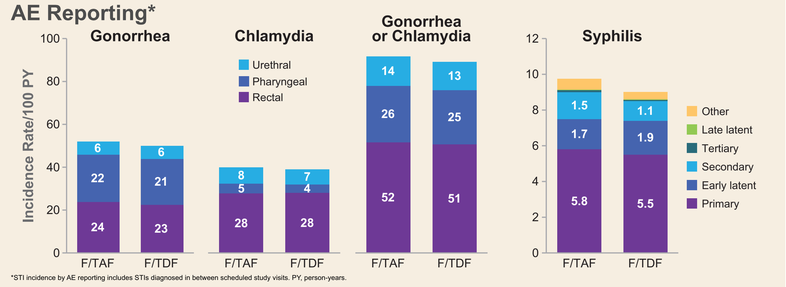
*Urethral gonorrhea and chlamydia testing was performed by central laboratory, while rectal and pharyngeal testing was performed at site's local laboratory; syphilis testing was performed using local algorithms and diagnoses were reported by investigator.

- 16.1% of participants in F/TAF arm and 15.8% in F/TDF arm tested positive for gonorrhea or chlamydia at any anatomic site; a corresponding 11.3% and 10.5% tested positive for gonorrhea or chlamydia at rectum

Incidence of STIs Through Week 96
Central Laboratory Testing

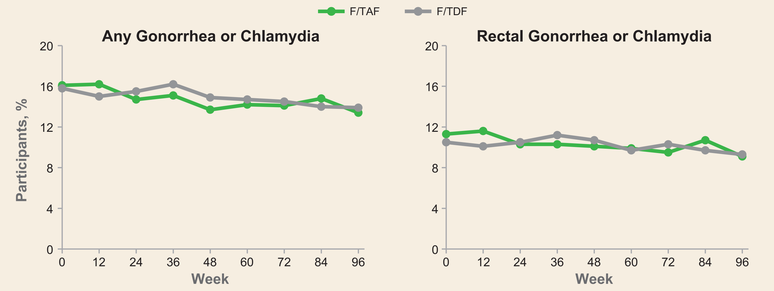


AE Reporting*



*STI incidence by AE reporting includes STIs diagnosed in between scheduled study visits. PY, person-years.

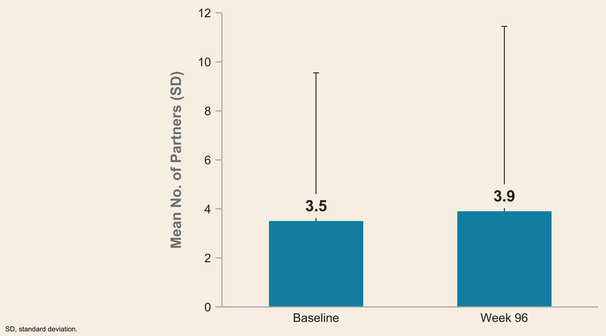
Longitudinal Prevalence of Gonorrhea and Chlamydia*



*Central laboratory diagnosed; trend estimates, 95% confidence intervals (CIs), and p-values were from generalized log-linear model, with treatment and visit as fixed effects; within-participant covariance matrix was assumed to be compound symmetric.

- Gonorrhea or chlamydia prevalence by visit declined at a rate of -9.9%/y (95% CI -14.1, -5.4; p <0.001)
- Rectal gonorrhea or chlamydia prevalence by visit declined at a rate of -11.3%/y (95% CI -16.4, -5.9; p <0.001)

Participant-Reported Condomless Receptive Anal Sex



SD, standard deviation.

STI Incidence Rates in Participants Who Acquired HIV

Events, n (incidence rate/100 PY)	HIV Cases n=23	No HIV n=5312	p-Value
Gonorrhea			
Any	23 (118)	4417 (44)	<0.001
Rectal	11 (56)	2030 (20)	<0.001
Pharyngeal	10 (51)	2050 (20)	0.004
Urethral	2 (10)	337 (3)	0.12
Chlamydia			
Any	22 (113)	4044 (40)	<0.001
Rectal	14 (72)	2703 (27)	<0.001
Pharyngeal	2 (10)	454 (5)	0.25
Urethral	6 (31)	887 (9)	0.002
Syphilis	6 (31)	964 (10)	0.004

- The rate of HIV acquisition was higher in participants with history of rectal gonorrhea, rectal chlamydia, or syphilis at screening (0.57 vs 0.11/100 PY; p <0.001)

Conclusions

- Gonorrhea and chlamydia incidence rates were high during DISCOVER, with the rectum being the most commonly affected anatomic site
- STI prevalence remained high through 96 wk, but demonstrated a small decrease over time
- Participants who acquired HIV during DISCOVER had a higher historical rate of rectal STIs and a higher incidence rate of rectal STIs during the trial vs participants who did not acquire HIV
- In combination with participant-reported sexual behavior findings, these results suggest risk compensation did not occur in DISCOVER

References: 1. World Health Organization. Report on global sexually transmitted infection surveillance. 2018; 2. Patheia P, et al. Clin Infect Dis 2013;57:1203-9; 3. Mullick C, Murray J. J Infect Dis 2020;221:214-7; 4. Werner RN, et al. PLoS One 2018;13:e0208107.

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