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DISCOVER Study for HIV Pre-exposure Prophylaxis: No Evidence of Risk Compensation in Participants Taking F/TDF or F/TAF for PrEP Through 96 Weeks

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Introduction

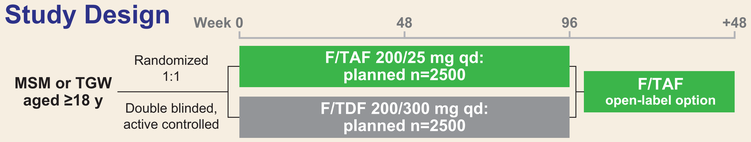
- DISCOVER (ClinicalTrials.gov NCT02842086) is an ongoing randomized controlled trial comparing emtricitabine/tenofovir alafenamide (F/TAF) with emtricitabine/tenofovir disoproxil fumarate (F/TDF) for pre-exposure prophylaxis (PrEP) in men who have sex with men (MSM) and transgender women (TGW)
  - Eligibility criteria for DISCOVER included condomless sex with multiple partners and/or history of rectal sexually transmitted infection (STI)
- Risk compensation is a behavioral theory postulating that people may increase risky behavior in response to a protective intervention
  - The risk compensation theory raises the possibility that some PrEP users may engage in more condomless sex, increasing their STI risk
  - Some studies have reported evidence of risk compensation in PrEP users,[1] while others have not[2-4]

Objectives

- To explore baseline prevalence and longitudinal trends in sexual behaviors during the DISCOVER trial through 96 wk to assess for evidence of risk compensation

Methods

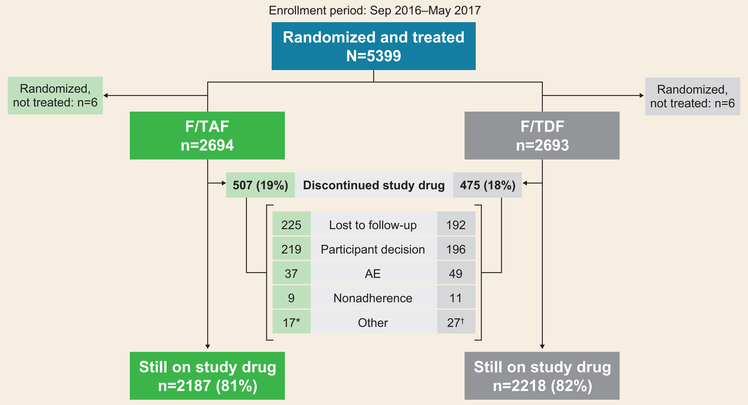
Study Design



- 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 ≥60 mL/min
  - Prior use of PrEP allowed
- Study conducted in Europe and North America in cities/sites with high HIV incidence in MSM
- 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
- All participants responded to a computer-assisted self-interview (CASI) questionnaire throughout the double-blind phase of DISCOVER, assessing number of sexual partners by type of sexual activity:
  - All sex partners (since last study visit)
  - Condomless insertive anal sex (CIAS) partners (study participant was top during sex)
  - Condomless receptive anal sex (CRAS) partners (study participant was bottom during sex)
- Study sites performed risk-reduction counseling, including provision of condoms and lubricant
- Assessment of sexual behavior compared data from CASI reports on number of sex partners during the study through 96 wk using descriptive statistics

Results

Participant Disposition



*Includes investigator's discretion (n=7), HIV-1 infection (n=5), protocol violation (n=4), and death (n=1); †Includes investigator's discretion (n=11), HIV-1 infection (n=10), protocol violation (n=3), and death (n=3).

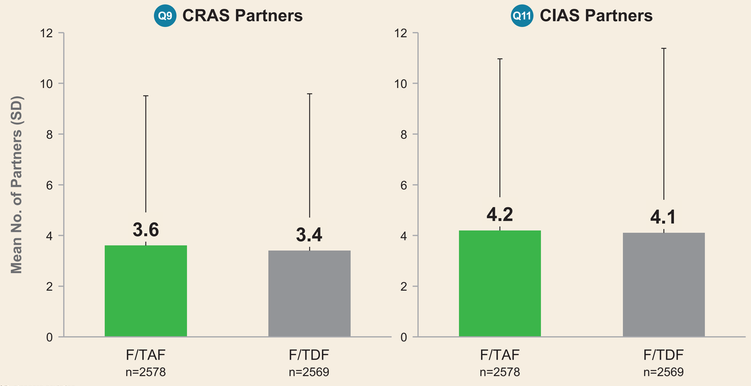
Demographics and Baseline Characteristics

		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 (5)
	Hispanic or Latinx, n (%)	635 (24)	683 (25)
	TGW, n (%)	45 (2)	29 (1)
HIV risk factors, n (%)	**≥2 CRAS 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; ‡≥15% of all participants: poppers (46%), cannabis (40%), cocaine (23%), Viagra (23%), ecstasy (18%), and γ-hydroxybutyrate (GHB; 17%); §≥6 drinks on ≥1 occasion at least monthly.

Number of Condomless Anal Sex Partners
Screening Visit: Last 90 Days

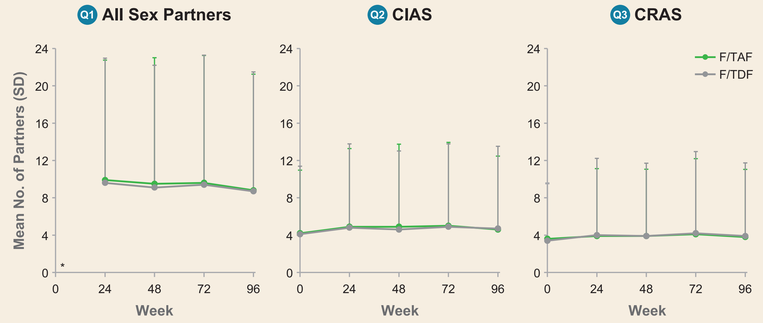
"Screening Visit" Questionnaire
Q8. With how many different men have you been bottom (passive) during anal sex in the last 90 days?
Q9. Of the men in Q8, with how many were you bottom without using a condom?
Q10. With how many different men have you been top (active) during anal sex in the last 90 days?
Q11. Of the men in Q10, with how many were you top without using a condom?



SD, standard deviation.

Longitudinal Sexual Behaviors

"Follow-up" Questionnaire:
Q1. How many different men did you have sex with since your last study visit? *If 0, go to question 7*
Q2. With how many different men have you been top during anal sex without condom since your last study visit?
Q3. With how many different men have you been bottom during anal sex without condom since your last study visit? *If 0, go to question 7*



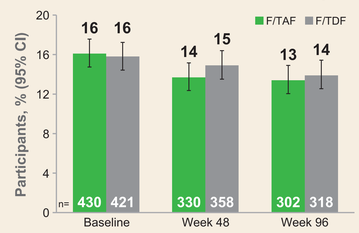
F/TAF, n=	2385	2331	2247	2182	2578	2385	2331	2247	2182	2578	2385	2331	2247	2182
F/TDF, n=	2371	2343	2271	2210	2569	2371	2343	2271	2210	2569	2371	2343	2271	2210

*No. of total sex partners was not queried at screening visit.

- Annual changes in no. of partners:
  - All sex partners: -0.6
  - CIAS: +0.2
  - CRAS: +0.2

Incidence of Sexually Transmitted Infections

Lab-Assessed Gonorrhea or Chlamydia



STI Incidence

n (rate/100 PY)	F/TAF	F/TDF
Lab test incidence		
Gonorrhea (any site)	2269 (45.1)	2171 (43)
Rectal	1048 (20.8)	993 (19.7)
Chlamydia (any site)	2041 (40.6)	2025 (40.1)
Rectal	1343 (26.7)	1374 (27.2)
AE-reported incidence		
Gonorrhea, chlamydia, or syphilis	7179 (142.7)	6916 (136.9)
Syphilis	612 (12.2)	583 (11.5)

CI, confidence interval; PY, patient-years.

Conclusions

- Participants in DISCOVER reported large numbers of sexual partners and condomless sex was commonly reported
- Sexual behaviors in DISCOVER remained largely constant through 96 wk of follow-up
  - Annual changes in total number of sexual partners (-0.6) and number of condomless partners (+0.2) were stable through 96 wk of follow-up
- Diagnosis of STIs did not increase through 96 wk of follow-up
- These data show that risk compensation did not occur in DISCOVER through 96 wk in study participants taking PrEP

References: 1. Lal L, et al. AIDS 2017;31:1709-14. 2. Fonner VA, et al. AIDS 2016;30:1973-83. 3. Grant RM, et al. N Engl J Med 2010;363:2587-99. 4. Smith DK, et al. Morb Mortal Wkly Rep 2012;61:586-9.

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