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DISCOVER: 96-Week Follow-up of Black and Hispanic/Latinx Study Participants

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Introduction

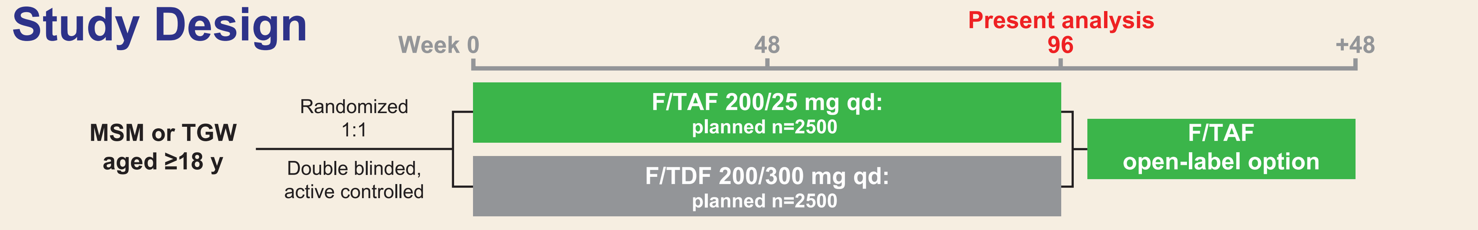
- DISCOVER (NCT02842086) is an ongoing Phase 3, multicenter, randomized, controlled trial evaluating the efficacy and safety of emtricitabine/tenofovir alafenamide (F/TAF) vs emtricitabine/tenofovir disoproxil fumarate (F/TDF) for HIV pre-exposure prophylaxis (PrEP) in cisgender men who have sex with men (MSM) and transgender women (TGW) at risk of HIV infection
- In the full DISCOVER cohort:
  - F/TAF demonstrated noninferior efficacy vs F/TDF for HIV PrEP[1]
  - F/TAF was superior to F/TDF with respect to biomarkers of renal function and bone mineral density (BMD)[1]

Objectives

- To evaluate efficacy, adherence, and safety-related outcomes in black and Hispanic/Latinx (H/Lx) participants treated with F/TAF vs F/TDF through 96 wk in DISCOVER

Methods

Study Design



- Eligibility: high sexual risk of HIV
  - 2+ unique condomless anal sex partners 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
- Location: European and North American cities/sites with high HIV incidence
- Assessments:
  - Safety: adverse events (AEs), BMD, and renal biomarkers
  - Adherence: self-report, pill counts, and drug levels in dried blood spots (DBS)
  - HIV lab testing: rapid HIV testing on site and central lab
  - HIV risk: confidential computer-aided self-interview (CASI) and sexually transmitted infection testing (gonorrhea, chlamydia, and syphilis)
- Comparisons: efficacy and safety measures for F/TAF vs F/TDF in participants who self-identified as black, nonblack, H/Lx, or non-H/Lx

Results

Participant Disposition Through Week 96

	F/TAF Black* n=240	F/TAF H/Lx n=635	F/TDF Black* n=234	F/TDF H/Lx n=683
Discontinued study drug, n (%)	70 (29)	114 (18)	52 (22)	117 (17)
Lost to follow-up	41 (17)	59 (9)	28 (12)	56 (8)
Participant decision	14 (6)	48 (8)	14 (6)	45 (7)
AE	7 (3)	4 (1)	4 (2)	6 (1)
Nonadherence	2 (1)	1 (<1)	1 (<1)	4 (1)
Other†	6 (3)	2 (<1)	5 (2)	6 (1)
Still on study drug	n=170 (71%)	n=521 (82%)	n=182 (78%)	n=566 (83%)

*Includes black/mixed race; †Includes protocol violation (n=4), investigator discretion (n=6), HIV infection (n=8), and death (n=1).

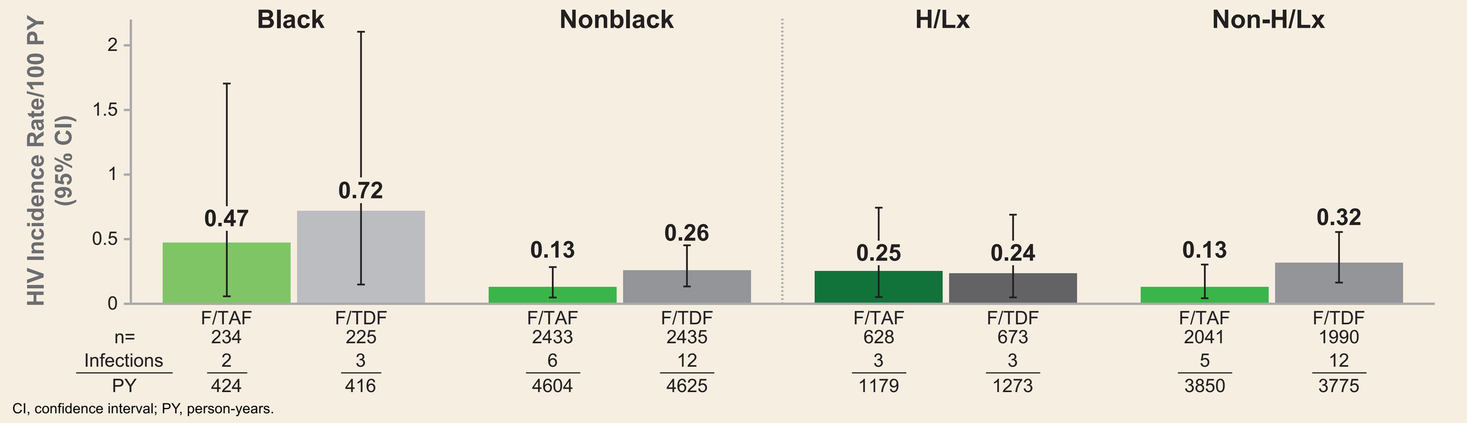
- A greater percentage of black vs nonblack participants were lost to follow-up (15% vs 7%; p <0.001)

Baseline Demographics and HIV Risk

	Black F/TAF n=240	Black F/TDF n=234	Nonblack F/TAF n=2451	Nonblack F/TDF n=2454	H/Lx F/TAF n=635	H/Lx F/TDF n=683	Non-H/Lx F/TAF n=2058	Non-H/Lx F/TDF n=2008
Baseline Demographics and Medical Characteristics								
Median age, y (range)	30 (19–67)	29 (18–72)	34 (18–76)	35 (18–72)	32 (18–74)	32 (18–65)	35 (18–76)	35 (18–72)
MSM, n (%)	228 (95)	228 (97)	2418 (99)	2431 (99)	618 (97)	667 (98)	2030 (99)	1995 (99)
TGW, n (%)	12 (5)	6 (3)	33 (1)	23 (<1)	17 (3)	16 (2)	28 (1)	13 (<1)
Sexuality by CASI, n (%)								
Gay/homosexual	194 (82)	172 (75)	2264 (93)	2257 (92)	570 (90)	617 (91)	1890 (92)	1815 (91)
Straight/heterosexual	7 (3)	3 (1)	18 (<1)	13 (<1)	7 (1)	9 (1)	18 (<1)	7 (<1)
Bisexual	34 (14)	55 (24)	137 (6)	159 (7)	49 (8)	49 (7)	122 (6)	165 (8)
Other					8 (1)	6 (<1)	15 (<1)	7 (<1)
Median BMI, kg/m^2 (Q1, Q3)	27.1 (23.6, 30.7)	26 (23.1, 29.4)	25.2 (23.0, 28.3)	25.3 (22.9, 28.2)	25.3 (23.3, 28.5)	25.4 (23.1, 28.6)	25.3 (23.0, 28.5)	25.3 (22.8, 28.2)
Median $eGFR_{CG}$, mL/min (Q1, Q3)	125.8 (103.9, 157.2)	119.1 (102.4, 142.8)	122.7 (105.0, 142.2)	121.2 (103.8, 142.3)	124.2 (107.4, 147.0)	124.5 (107.7, 149.4)	122.4 (104.2, 141.6)	120.0 (102.3, 140.1)
Taking F/TDF for PrEP at BL, n (%)	41 (17)	28 (12)	424 (17)	409 (17)	81 (13)	73 (11)	384 (19)	364 (18)
HIV Risk Factors								
Syphilis in past 24 wk, n (%)	26 (11)	38 (16)	204 (8)	224 (9)	61 (10)	80 (12)	169 (8)	182 (9)
Rectal gonorrhea in past 24 wk, n (%)	26 (11)	9 (4)	248 (10)	252 (10)	65 (10)	79 (12)	209 (10)	183 (9)
Rectal chlamydia in past 24 wk, n (%)	34 (14)	20 (9)	307 (13)	313 (13)	84 (13)	98 (14)	257 (12)	235 (12)
Condomless receptive anal sex, mean no. of partners in 90 d prior to screening (SD)	2.3 (4.4)	1.9 (3.4)	3.7 (6.1)	3.6 (6.4)	3.0 (4.4)	2.9 (5.0)	3.8 (6.3)	3.6 (6.5)

BL, baseline; BMI, body mass index; Q, quartile; SD, standard deviation.

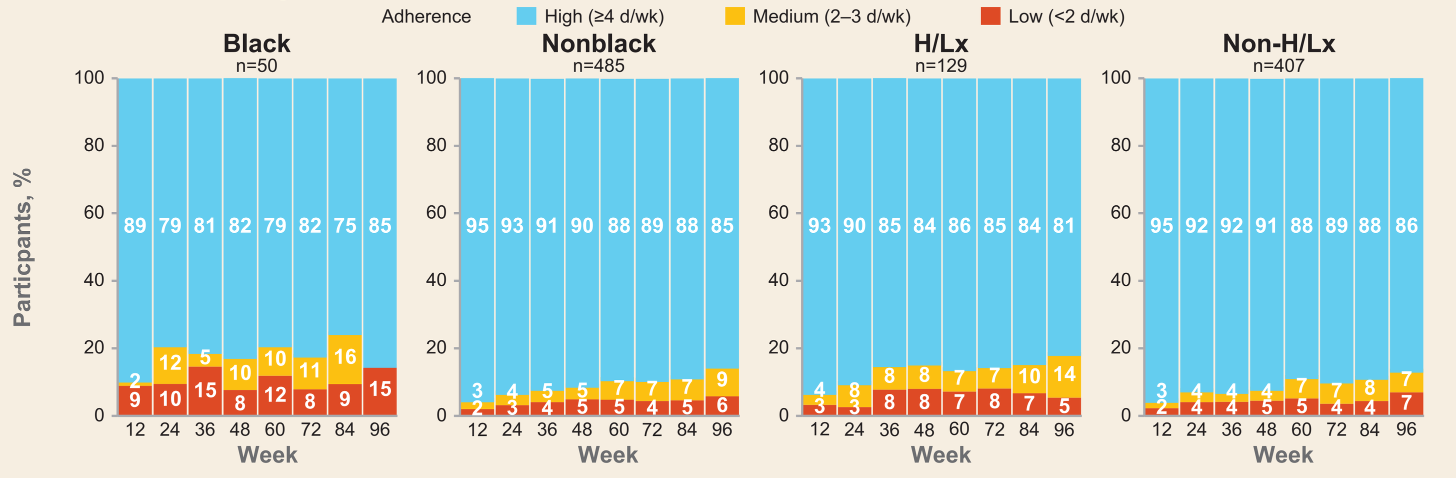
Primary Endpoint Analysis: HIV Incidence



CI, confidence interval; PY, person-years.

- Of 11 infections in black or H/Lx participants, 2 had suspected prebaseline infections
- The remaining 9 participants had low or undetectable DBS drug levels at diagnosis

Adherence by DBS



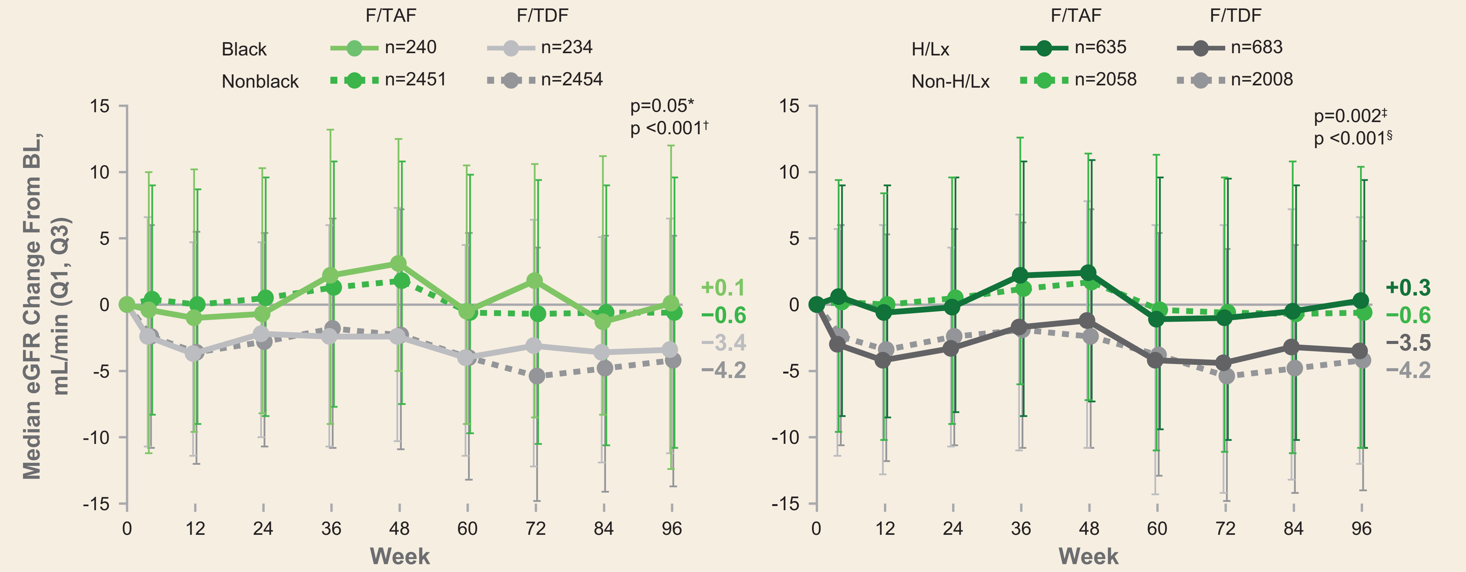
- Odds ratio (95% CI) for low adherence: 2.37 (1.17, 4.79) for black vs nonblack and 1.53 (0.89, 2.66) for H/Lx vs non-H/Lx

Safety

TEAEs Occurring in ≥1% of Participants by Preferred Term, n (%)	Black F/TAF n=240	Black F/TDF n=234	Nonblack F/TAF n=2451	Nonblack F/TDF n=2454	H/Lx F/TAF n=635	H/Lx F/TDF n=683	Non-H/Lx F/TAF n=2058	Non-H/Lx F/TDF n=2008
Study-drug related TEAEs	43 (18)	58 (25)	512 (21)	579 (24)	154 (24)	181 (27)	402 (20)	458 (23)
Diarrhea	9 (4)	16 (7)	127 (5)	144 (6)	35 (6)	47 (7)	101 (5)	113 (6)
Nausea	11 (5)	12 (5)	103 (4)	111 (5)	30 (5)	35 (5)	85 (4)	88 (4)
Headache	6 (3)	4 (2)	53 (2)	53 (2)	19 (3)	15 (2)	40 (2)	42 (2)
Fatigue	0	5 (2)	44 (2)	66 (3)	9 (1)	25 (4)	35 (2)	46 (2)
Abdominal pain	3 (1)	4 (2)	23 (<1)	31 (1)	7 (1)	7 (1)	19 (<1)	28 (1)
Flatulence	1 (<1)	7 (3)	21 (<1)	26 (1)	3 (<1)	7 (1)	19 (<1)	26 (1)
Abdominal discomfort	1 (<1)	0	17 (<1)	30 (1)	11 (2)	15 (2)	7 (<1)	15 (<1)
Abdominal pain upper	2 (<1)	4 (2)	15 (<1)	19 (<1)	2 (<1)	4 (<1)	15 (<1)	20 (1)
Dizziness	1 (<1)	4 (2)	15 (<1)	20 (<1)	5 (<1)	8 (1)	11 (<1)	16 (<1)
Abdominal distension	2 (<1)	7 (3)	17 (<1)	12 (<1)	7 (1)	8 (1)	12 (<1)	11 (<1)
Vomiting	1 (<1)	3 (1)	14 (<1)	9 (<1)	4 (<1)	3 (<1)	11 (<1)	10 (<1)
Insomnia	1 (<1)	3 (1)	10 (<1)	11 (<1)	2 (<1)	5 (<1)	9 (<1)	9 (<1)

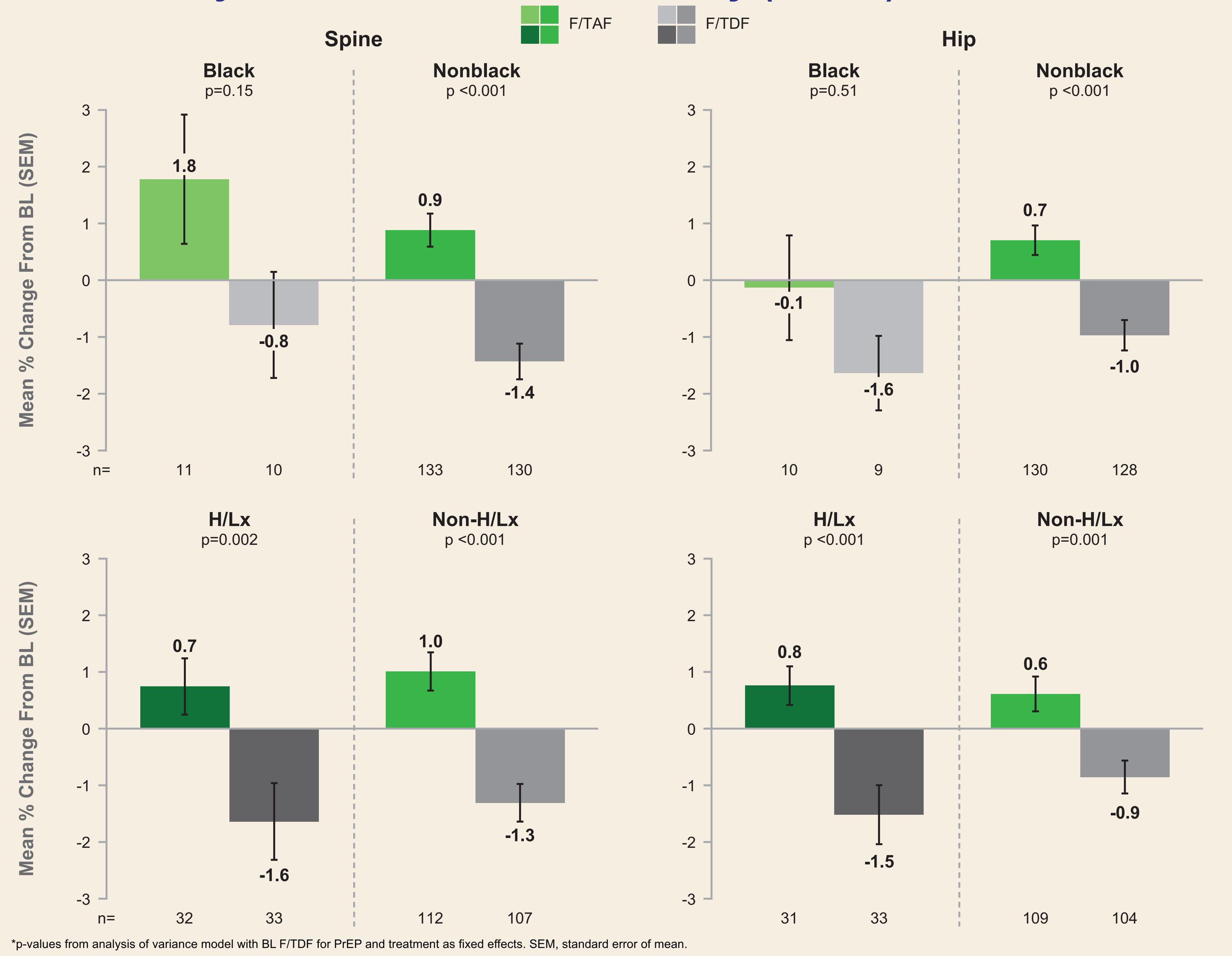
TEAEs, treatment-emergent AEs.

$eGFR_{CG}$ Change Through Week 96



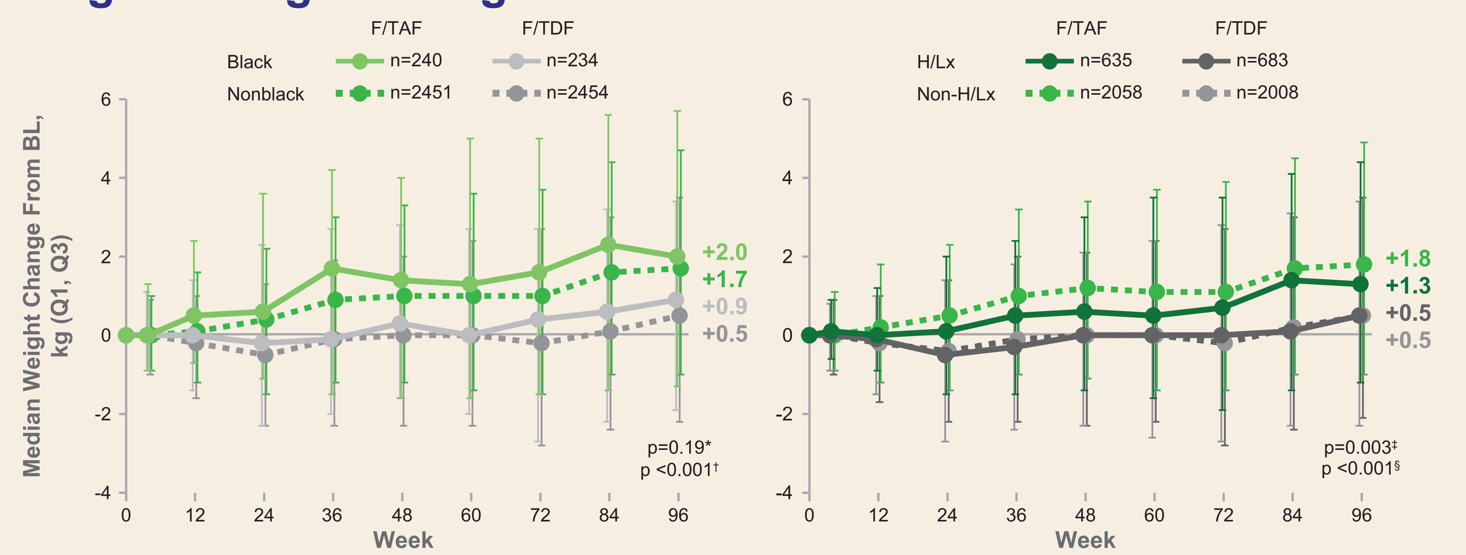
*Comparing treatments within black subgroup; †Comparing treatments within nonblack subgroup; ‡Comparing treatments within H/Lx subgroup; §Comparing treatments within non-H/Lx subgroup.

Bone Safety at Week 96: BMD Substudy (n=375)*



*p-values from analysis of variance model with BL F/TDF for PrEP and treatment as fixed effects. SEM, standard error of mean.

Weight Change Through Week 96



*Comparing treatments within black subgroup; †Comparing treatments within nonblack subgroup; ‡Comparing treatments within H/Lx subgroup; §Comparing treatments within non-H/Lx subgroup.

Fasting Lipids at Week 96*

*p-values from 2-sided Wilcoxon rank-sum test to compare treatment groups. HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Conclusions

- The HIV incidence rate was low in black and H/Lx participants on PrEP in DISCOVER, and was similar in the F/TAF and F/TDF arms
- Adherence to study drug was high in all groups; however, more black participants had medium or low adherence vs nonblack participants
- Study drug-related TEAEs were similar between groups
- eGFR changes were more favorable in the F/TAF arm, including black and H/Lx participants
- Black and H/Lx participants taking F/TAF had either increases or less declines in BMD compared with those taking F/TDF
- Black and H/Lx participants taking F/TAF had stable LDL and HDL cholesterol, whereas those taking F/TDF had proportional declines in LDL and HDL
- Weight increases occurred in black and H/Lx participants in both arms, and were 0.8–1.1 kg greater in those taking F/TAF

References: 1. Hare CB, et al. CROI 2019, abstr 104.
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