Safety and Efficacy of F/TAF and F/TDF for PrEP in DISCOVER Participants Taking F/TDF for PrEP at Baseline

Thomas Campbell,[1] Amanda Clarke,[2] Benoit Trottier,[3] Gordon E. Crofoot,[4] Christoph C. Carter,[5] Alex Kintu,[5] Yongwu Shao,[5] Ramin Ebrahimi,[5] Moupali Das,[5] Diana M. Brainard,[5] Jay Gladstein[6]

[1]University of Colorado School of Medicine, Aurora; [2]Brighton and Sussex University Hospitals, Brighton, UK; [3]Clinique Médicale Urbaine du Quartier Latin, Montréal, Québec, Canada; [4]The Crofoot Research Center, Houston, TX; [5]Gilead Sciences, Inc., Foster City, CA; [6]APLA Health, Los Angeles, CA

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
800-445-3235

Introduction

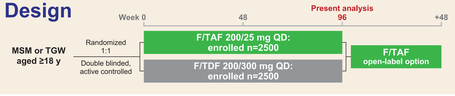
- DISCOVER (NCT02842086) is an ongoing Phase 3, multicenter, randomized, controlled trial evaluating the efficacy and safety of emtricitabine/tenofovir alafenamide (F/TAF) compared with emtricitabine/tenofovir disoproxil fumarate (F/TDF) for HIV pre-exposure prophylaxis (PrEP) in cisgender men who have sex with men (MSM) and transgender women (TGW) at risk of HIV infection
- When all participants had completed 96 wk of follow-up[1]:
  - F/TAF demonstrated noninferior efficacy compared with F/TDF for HIV PrEP
  - F/TAF was superior to F/TDF with respect to biomarkers of renal function and bone mineral density
- F/TAF was approved for HIV PrEP in the USA in Oct 2019[2]

Objectives

- To assess efficacy and safety-related outcomes in participants in the DISCOVER study who were on F/TDF for PrEP at enrollment

Methods

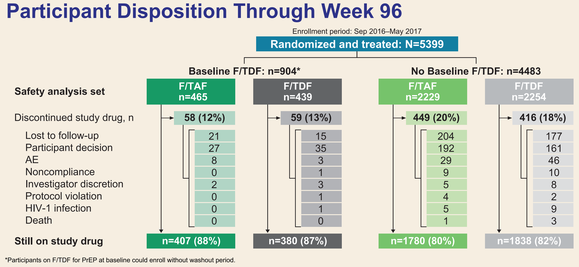
Study Design



- 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 (HBV) negative, and estimated glomerular filtration rate by Cockcroft-Gault ($eGFR_{CG}$) ≥60 mL/min
  - Prior use of F/TDF for PrEP allowed
- Study conducted in Europe and North America in cities/sites with high HIV incidence
- Assessments:
  - Safety: adverse events (AEs), AE-related discontinuations, bone mineral density, and renal biomarkers
  - Adherence: self-report, pill counts, drug levels, and dried blood spots
  - HIV laboratory testing: rapid HIV testing on site and at central laboratory
  - HIV risk behavior: confidential computer-aided self-interview (CASI) questionnaire and sexually transmitted infection assessment at every visit (gonococcus/chlamydia trachomatis: rectum, urethra, and oropharynx [nucleic acid amplification test], and syphilis testing)

Results

Participant Disposition Through Week 96



*Participants on F/TDF for PrEP at baseline could enroll without washout period.

Baseline Demographics and Clinical Characteristics*

	Baseline F/TDF n=905	No Baseline F/TDF n=4482	p-Value
Median duration of PrEP, d (Q1, Q3)	398.5 (148, 763)	—	
Median age, y (Q1, Q3)	36 (30, 45)	34 (27, 43)	<0.001
TGW, n (%)	6 (1)	68 (2)	0.044
Race, n (%)			0.79
White	770 (85)	3741 (84)	
Black	69 (8)	405 (9)	
Asian	39 (4)	194 (4)	
Other	14 (2)	81 (2)	
Hispanix/Latinx ethnicity, n (%)	154 (17)	1164 (26)	<0.001
Sexuality by CASI, n (%)			0.009
Gay/homosexual	850 (94)	4045 (91)	
Bisexual	44 (5)	341 (8)	
Straight/heterosexual	3 (<1)	38 (1)	
Median BMI, kg/m^2 (Q1, Q3)	25.5 (23.1, 28.4)	25.3 (23.0, 28.4)	0.54

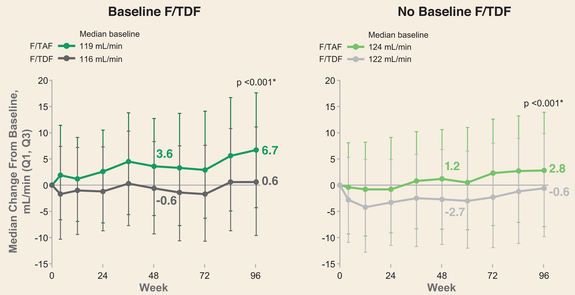
*Trial not designed as switch study; randomization did not take into consideration baseline F/TDF. BMI, body mass index; Q, quartile.

Efficacy

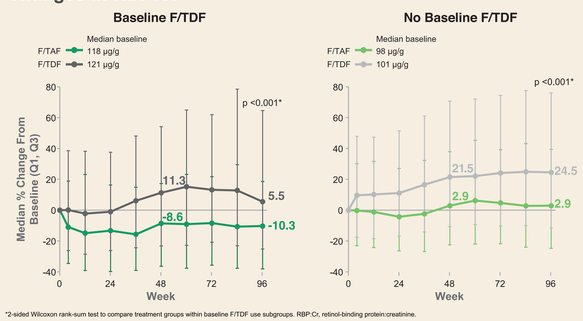
- At Week 96, there was 1 HIV infection among prior F/TDF users who were randomized to F/TDF (incidence rate 0.119/100 person-years [95% confidence interval 0.003, 0.662])
  - The HIV infection was in a participant who had intermittent low adherence
- No infections occurred in prior F/TDF users who were randomized to F/TAF

Renal Safety

Changes in $eGFR_{CG}$

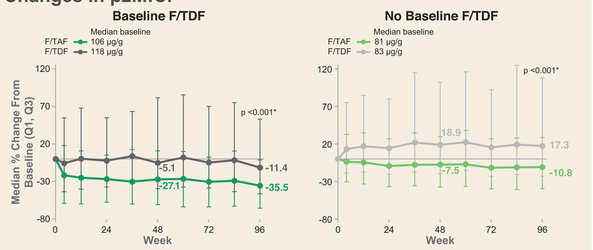


Changes in RBP:Cr

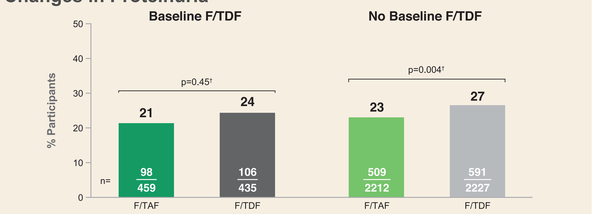


*2-sided Wilcoxon rank-sum test to compare treatment groups within baseline F/TDF use subgroups. RBP:Cr, retinol-binding protein:creatinine.

Changes in β2M:Cr

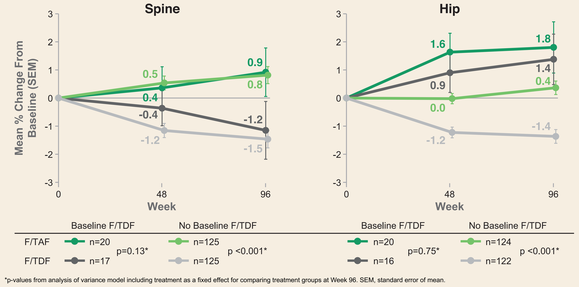


Changes in Proteinuria



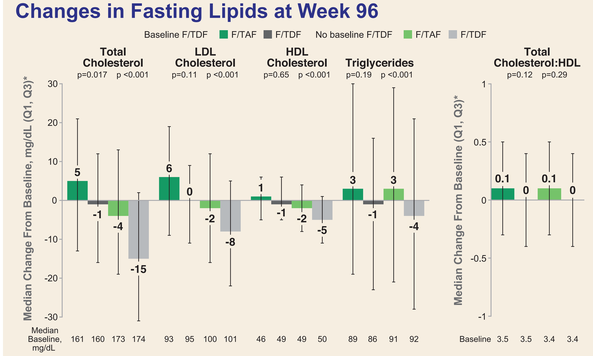
*2-sided Wilcoxon rank-sum test to compare treatment groups within baseline F/TDF use subgroups; †Rank analysis of covariance adjusting for baseline F/TDF use to compare treatment groups. β2M:Cr, β2-microglobulin:creatinine.

Bone Safety: Changes in Bone Mineral Density



*p-values from analysis of variance model including treatment as a fixed effect for comparing treatment groups at Week 96. SEM, standard error of mean.

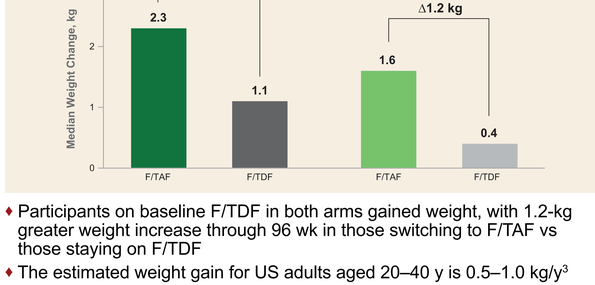
Changes in Fasting Lipids at Week 96



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

- Among baseline F/TDF users, 3% of those who switched to F/TAF started a lipid-modifying agent vs 1% of those who stayed on F/TDF (p=0.03)
- Among those not on baseline F/TDF, the rates of lipid-modifying agent initiation were similar between the F/TAF and F/TDF arms (1.3% vs 1.0%; p=0.27)

Weight Changes at Week 96



- Participants on baseline F/TDF in both arms gained weight, with 1.2-kg greater weight increase through 96 wk in those switching to F/TAF vs those staying on F/TDF
- The estimated weight gain for US adults aged 20–40 y is 0.5–1.0 kg/y[3]

Conclusions

- DISCOVER, the largest randomized, active-controlled, noninferiority, PrEP trial with F/TAF vs F/TDF offered the opportunity to examine clinical efficacy and safety in participants taking F/TDF prior to trial enrollment who were randomized to initiate F/TAF or stay on F/TDF
- HIV incidence was low in participants who were on baseline F/TDF prior to trial enrollment, irrespective of whether they were randomized to switch to F/TAF or remained on F/TDF
- Switching from F/TDF to F/TAF was associated with improvements in renal biomarkers, consistent with studies in HIV and HBV treatment
- The pattern of weight change in prior F/TDF users who switched to F/TAF was similar to that of those who had not used F/TDF before; the weight differences between arms could be explained by the known weight-suppressive effects of F/TDF[4]
- The increases in HDL and LDL cholesterol levels in participants who switched from F/TDF to F/TAF could be explained by removal of F/TDF's lipid-lowering effect[5]
- F/TAF is a safe and effective PrEP option for individuals who switch from F/TDF

References: **1.** Ogbuagu O, et al. CROI 2020, *abstr 092*; **2.** Descovy [package insert]. Foster City, CA: Gilead Sciences, Inc., 10/19; **3.** Hill JO, et al. Science 2003;299:853-5; **4.** Glidden DV, et al. Clin Infect Dis 2018;67:411-9; **5.** Tungsiripat M, et al. AIDS. 2010;24:1781-4. **Acknowledgments:** We extend our thanks to the participants, their families, and all participating study investigators. This study was funded by Gilead Sciences, Inc.