Longer Term Safety of F/TAF and F/TDF for HIV PREP: DISCOVER Trial Week 96 Results

Poster 5296
CONFERENCE CAHR 2020

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Introduction

- The DISCOVER study (ClinicalTrials.gov NCT02842086) is an ongoing Phase 3, randomized, controlled trial evaluating the efficacy and safety of F/TAF for PrEP among cisgender men and transgender women who have sex with men (MSM, TGW) at high risk of HIV infection
- Interim data analysis was conducted when 100% of participants completed Week 48 and 50% completed Week 96, and demonstrated that[1]:
  - F/TAF was noninferior to F/TDF in preventing HIV infection
  - Both drugs were well tolerated, with low rates of AE-related discontinuations
  - F/TAF had significantly better bone and renal safety outcomes vs F/TDF

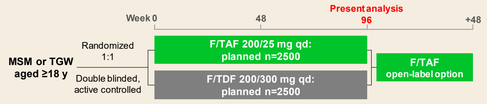
AE, adverse event; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; PrEP, pre-exposure prophylaxis [1]Hare CB, et al. CROI 2019, abstr 104.

Objectives

- To present longer term results conducted after all participants completed the Week 96 visit

Methods

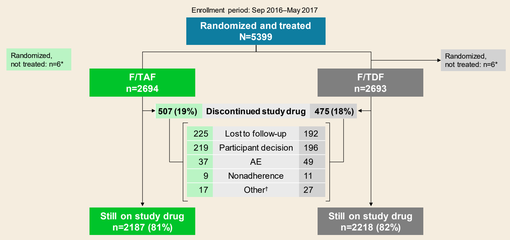
Study Design



BMD, bone mineral density; eGFRcg, estimated glomerular filtration rate by Cockcroft-Gault.

- Eligibility: high sexual risk of HIV
  - 2+ episodes of condomless anal sex in the past 12 wk or rectal gonorrhea/chlamydia or syphilis in past 24 wk
  - HIV and hepatitis B virus negative, and eGFRCG ≥60 mL/min
  - Prior use of PrEP allowed
- Study conducted in Europe and North America in cities/sites with high HIV incidence
- Safety assessments
  - Renal: AEs and renal biomarkers
  - Bone: fracture events and BMD
  - Metabolic: fasting lipids, glucose, and body weight

Participant Disposition Through Week 96



*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).

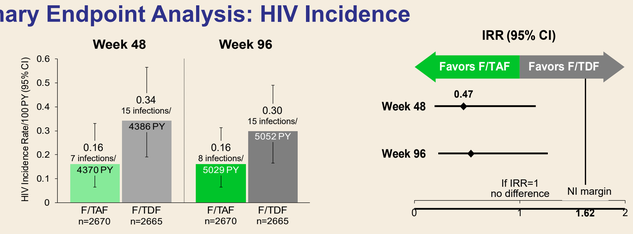
Demographics and Baseline Characteristics*

		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 (5)
	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 BL	465 (17)	440 (16)

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

Results

Primary Endpoint Analysis: HIV Incidence



CI, confidence interval; IRR, incidence rate ratio; NI, noninferiority; PY, person-year.

- Primary analysis: 22 HIV infections in 8756 PY of follow-up
- Week-96 analysis: 23 HIV infections in 10,081 PY of follow-up
- F/TAF was noninferior to F/TDF for HIV prevention as the upper bound of IRR 95% CI was <1.62

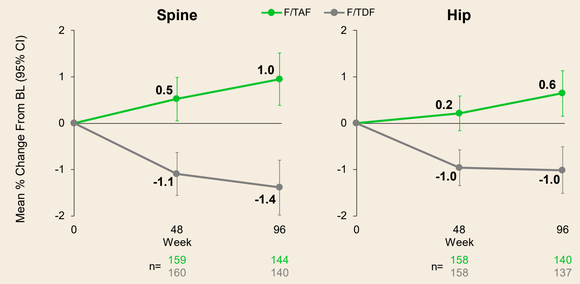
Overall Safety Summary

	F/TAF n=2694	F/TDF n=2693
Any AE, %	93	93
Study drug related	21	24
Grade ≥2 AE, %	49	47
Grade ≥3 AE, %	7	6
Serious AE, %	7	6
Study drug related	0.1	0.2
AE leading to discontinuation, %	1	2
Death*	n=1	n=2

*Reasons: traffic accident, metastatic squamous cell carcinoma, and unknown.

Results (Cont'd)

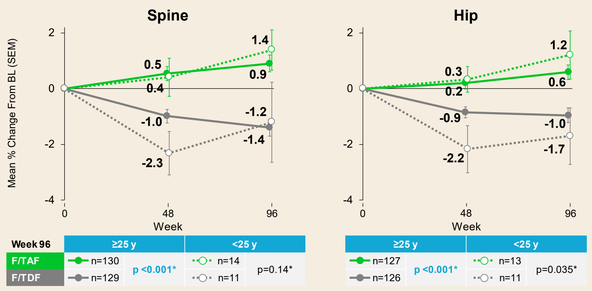
Bone Safety: BMD Substudy (n=375)*



*p-values from analysis of variance model with BL F/TDF for PrEP and study arm as fixed effects. Reported fracture events: F/TAF, n=65; F/TDF, n=64.

Bone Safety: BMD Substudy (n=375)*

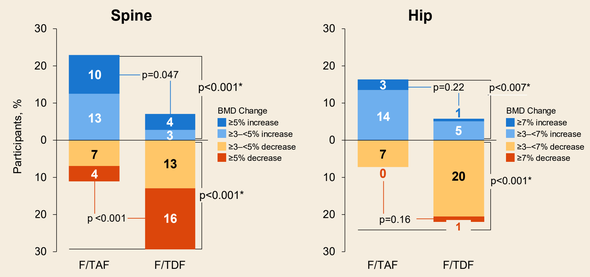
Aged ≥ and <25 y



Week 96	≥25 y		<25 y		≥25 y		<25 y	
F/TAF	n=130	p <0.001*	n=14	p=0.14*	n=127	p <0.001*	n=13	p=0.035*
F/TDF	n=129		n=11		n=126		n=11	

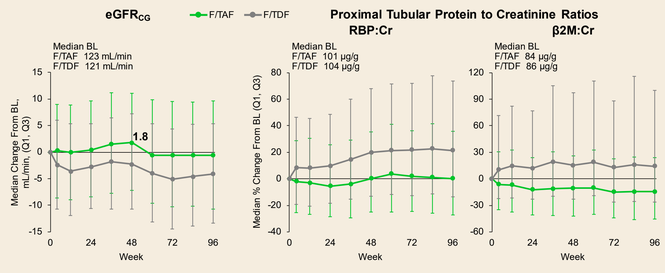
*p-values from analysis of variance model with BL F/TDF for PrEP and study arm as fixed effects. SEM, standard error of mean.

Categorical BMD Changes (By Percent Change) at Week 96



*p-values for ≥3% change include ≥5% change. All p-values based on dichotomized response from Cochran-Mantel-Haenszel test for nominal data (general association statistic) adjusting for BL F/TDF for PrEP.

Renal Safety

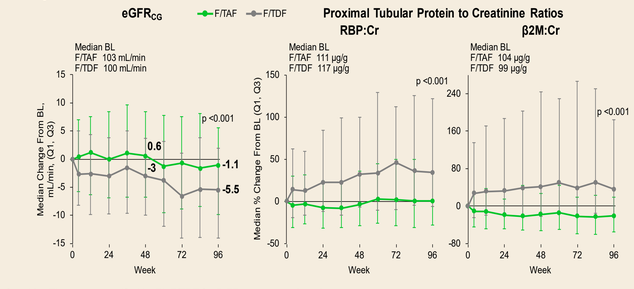


*p-values from Van Elteren test stratified by BL F/TDF for PrEP to compare 2 study arms.β2M, β2-microglobulin; Cr, creatinine; Q, quartile; RBP, retinol-binding protein.

- Renal discontinuations: F/TAF, n=2; F/TDF, n=6
- Fanconi syndrome: F/TAF, n=0; F/TDF, n=1

Renal Safety

Aged ≥50 y

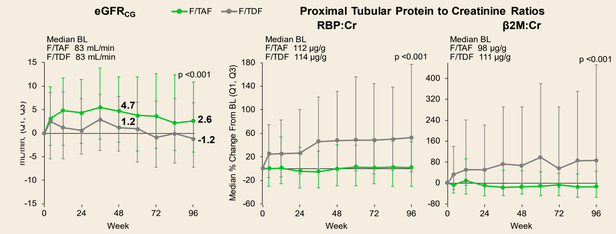


*p-values from Van Elteren test stratified by BL F/TDF for PrEP to compare 2 study arms.

- Renal discontinuations: F/TAF, n=0; F/TDF, n=3

Renal Safety

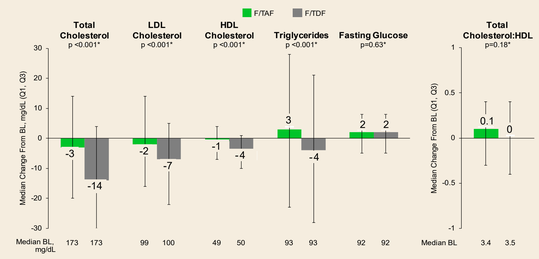
BL eGFR 60–≤90 mL/min



*p-values from Van Elteren test stratified by BL F/TDF for PrEP to compare 2 study arms.

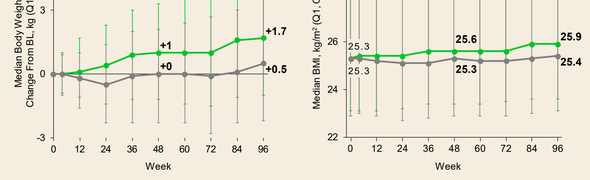
- Renal discontinuations: F/TAF, n=0; F/TDF, n=4

Fasting Lipids and Glucose at Week 96



*p-values from 2-sided Wilcoxon rank sum test to compare 2 study arms.

Body Weight and BMI



p-values for changes from baseline from analysis of covariance model including BL F/TDF for PrEP and study arm as fixed effects and BL body weight or body mass index (BMI) as a covariate.

Conclusions

- F/TAF remained noninferior to F/TDF for HIV PrEP through 96 weeks
- DISCOVER provides the largest, single variable comparison of bone and renal safety parameters between TAF and TDF in the absence of underlying HIV or third antiretroviral agents:
- Differences in BMD between F/TAF and F/TDF increased at week 96; BMD declines of ≥3% were more common in participants taking F/TDF, with more pronounced differences in younger participants
- Renal biomarker changes remained more favorable in participants taking F/TAF, including in older participants and those with reduced eGFR
- F/TDF was associated with greater declines in both LDL and HDL but total cholesterol: HDL ratios or fasting glucose remained similar across both study arms at 96 weeks.
- Weight gain was observed in both arms at 96 weeks, and was approximately 1kg greater in participants taking F/TAF. The weight gain in F/TAF arm was similar to that observed in the placebo arm of iPrEx PrEP trial and the general population[1,2]
- F/TAF is a safe, longer term option for PrEP

[1]Glidden DV, et al. Clin Infect Dis 2018;67:411-9. 2. Hill JO, et al. Science 2003;299:853-5

References & Acknowledgments

We extend our thanks to the participants, their families, and all participating study investigators and staff:

Austria: B Haas, A Rieger; **Canada:** J Brunetta, JJ de Wet, J Szabo, C Tremblay, B Trottier; **Denmark:** J Gerstoft, G Kronborg, C Larsen, D Larsen; **France:** E Cua, J-M Molina, P Philibert, G Pialoux; **Germany:** H Jessen, G Knecht, I Krznaric, C Spinner; **Ireland:** C Bergin, P Mallon; **Italy:** A Antinori, A Lazzarin; **Netherlands:** M Prins; **Spain:** J Coll, M Crespo, J del Romero Gerrero, D Podzamczer; **UK:** V Apea, A Clarke, O Dosekun, R Gilson, S Kegg, C Leen, N Nwokolo, F Post, I Reeves, G Schembri, S Taylor; **USA:** D Asmuth, A Avery, P Benson, M Berhe, I Brar, C Brinson, JH Burack, T Campbell, M Cespedes, M Coleman, CM Creticos, GE Crofoot, FA Cruickshank, E Daar, E DeJesus, W Dinges, S Doblecki-Lewis, T Donovan, J Flamm, JE Gallant, J Gladstein, RM Grant, R Grossberg, J Halperin, WD Hardy, CB Hare, S Hassler, R Hengel, K Henry, T Hodge, S Hosek, M Iandorio, A LaMarca, C Lucasti, S Mannheimer, CT Martorell, M Markowitz, K Mayer, A Mills, S Morris, K Mounzer, O Ogbuagu, O Osiyemi, A Petroll, J Phoenix, MN Ramgopal, B Rashbaum, GJ Richmond, PJ Ruane, L Salazar, AJ Scarsella, M Scott, P Shalit, JL Stephens, MA Thompson, G Voskuhl, BH Wade, DA Wohl, K Workowski, B Young.

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Disclosures

Dr. Jason Szabo is a member of the Quebec guidelines committee for antiretrovirals and has received fees for advisory boards and speaking engagements from Gilead, Merck, Viiv, and Teva. This study was funded by Gilead Sciences, Inc.

Presented at the 29th Annual Canadian Conference on HIV/AIDS Research (CAHR), April 30 - May 3, 2020, Quebec City, Quebec, Canada