Poster # P030

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Long-term Outcomes of Participants on F/TAF for Pre-Exposure Prophylaxis: Results for 144 Weeks of Follow-Up in the DISCOVER Trial

Moti Ramgopal,[1] Peter Ruane,[2] Peter Shalit,[3] Yongwu Shao,[4] Ramin Ebrahimi,[4] Alex Kintu,[4] Christoph C. Carter,[4] Moupali Das,[4] Jared Baeten,[4] Iain Reeves,[5] Karam Mounzer[6]

[1]Midway Research Center, Fort Pierce, FL; [2]Ruane Clinical Research Group, Inc., Los Angeles, CA; [3]Peter Shalit MD & Associates, Seattle, WA; [4]Gilead Sciences, Inc., Foster City, CA; [5]Homerton Hospitals NHS trust, London, UK; [7]Philadelphia FIGHT Community Health Centers, Philadelphia, PA

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
Tel: (650) 574-3000

Introduction

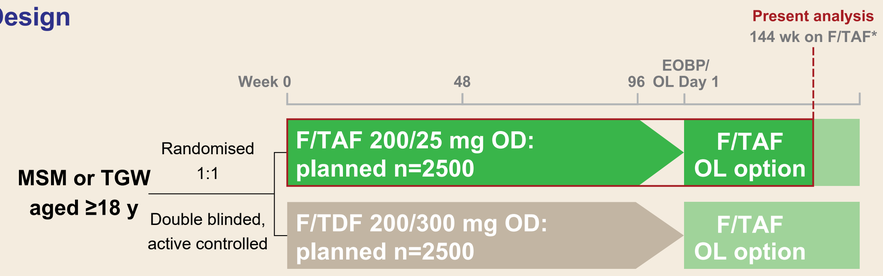
- The DISCOVER study (NCT02842086) is a Phase 3, randomised, controlled trial of the efficacy and safety of emtricitabine/tenofovir alafenamide (F/TAF) vs emtricitabine/ tenofovir disoproxil fumarate (F/TDF) for pre-exposure prophylaxis (PrEP) among cisgender men who have sex with men (MSM) and transgender women who have sex with men (TGW)
- At both the primary analysis (when 100% of participants completed Week 48 and 50% completed Week 96) and Week 96[1,2]:
  - F/TAF was noninferior to F/TDF in preventing HIV infection
  - F/TAF had significantly better bone and renal safety markers vs F/TDF
  - F/TDF was associated with reductions in high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, while F/TAF was associated with minimal lipid changes
- F/TDF was associated with weight loss at Week 24, and less weight gain than F/TAF at Weeks 48 and 96
- Following participants randomised to F/TAF into the open-label (OL) phase allowed for long-term assessment of F/TAF outcomes

Objective

- To assess Week 144 outcomes for participants who were randomised to F/TAF and continued F/TAF in the OL phase

Methods

Study Design

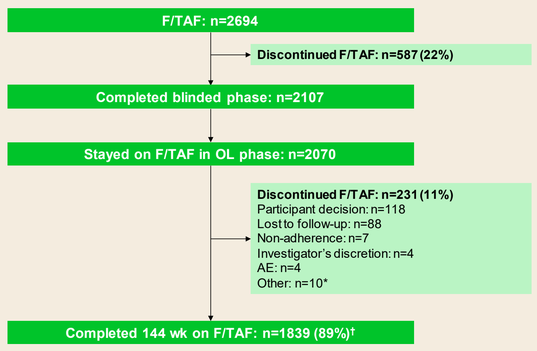


*Blinded phase did not end at Week 96; amount of time between Week 96 and end of blinded phase (EOBP) varied between participants; most reached Week 144 on F/TAF during first 48 wk of OL phase.

- Eligibility: high sexual risk of HIV
  - 2+ episodes of condomless anal sex in past 12 wk, or rectal gonorrhoea/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
- Study conducted in Europe and North America in cities/sites with high HIV incidence
- Assessments:
  - Efficacy: HIV incidence rate and dried blood spot (DBS) tenofovir-diphosphate (TFV-DP) levels to assess adherence
  - Safety: bone mineral density (BMD), renal biomarkers, and metabolic parameters

Results

Participant Disposition Through Week 144



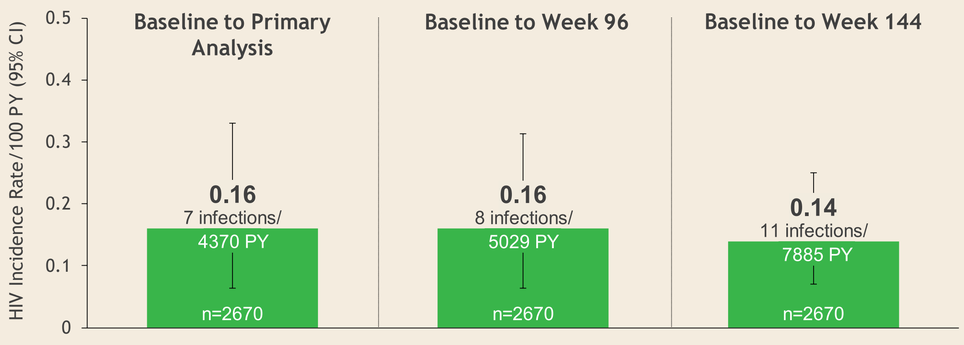
*3 deaths, 3 protocol violations, 1 terminated by sponsor, and 3 HIV infections; †% of participants entering OL phase. AE, adverse event.

Demographics and Baseline Characteristics

		F/TAF n=2694
Demographics	Median age, y (range)	34 (18–76)
	Race, n (%)	
	White	2264 (84)
	Black*	240 (9)
	Asian	113 (4)
	Hispanic or Latinx, n (%)	635 (24)
	TGW, n (%)†	45 (2)
HIV risk factors,n (%)	≥2 condomless receptive anal sex partners in past 12 wk	1616 (62)
	Rectal gonorrhoea in past 24 wk	274 (10)
	Rectal chlamydia in past 24 wk	342 (13)
	Syphilis in past 24 wk	230 (9)
	Recreational drug use in past 12 wk	1785 (67)
	Binge drinking‡	618 (23)
	Taking F/TDF for PrEP at BL	465 (17)

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

Efficacy Analysis: HIV Incidence Rate

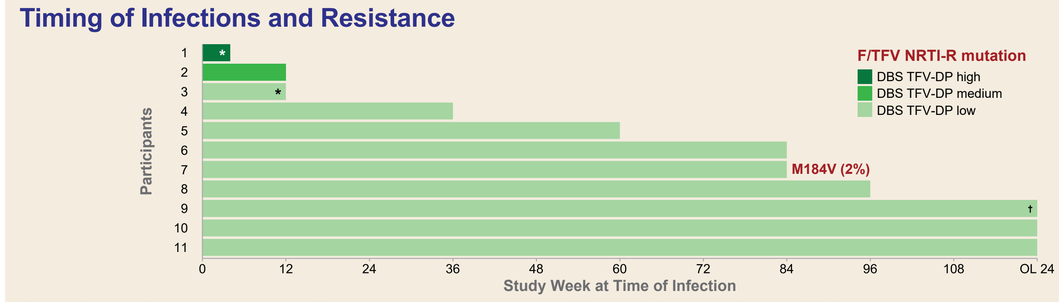


BL, baseline; CI, confidence interval; PY, person-years

- 10 of 11 participants had DBS TFV-DP collected on the day of HIV diagnosis:
  - 8 had TFV-DP levels consistent with low adherence (<2 tablets/wk), 1 consistent with medium adherence (2–3 tablets/wk), and 1 consistent with high adherence (≥4 tablets/wk), but suspected of having HIV at BL
- All infections occurred in MSM aged 21–48 y: 3 of these participants were Black, 8 were White, and 4 self-identified as Hispanic

Results

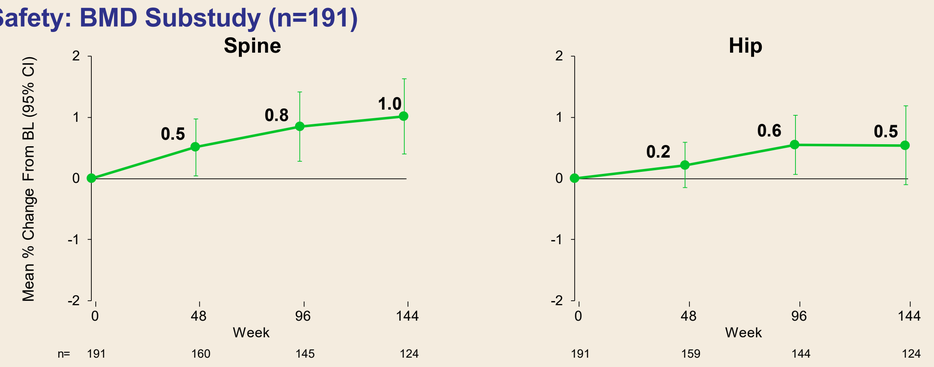
Timing of Infections and Resistance



*Samples did not amplify for unique molecular identifier–next-generation sequencing; †Imputed; DBS not available at time of diagnosis. NRTI-R, nucleoside reverse-transcriptase inhibitor–resistant.

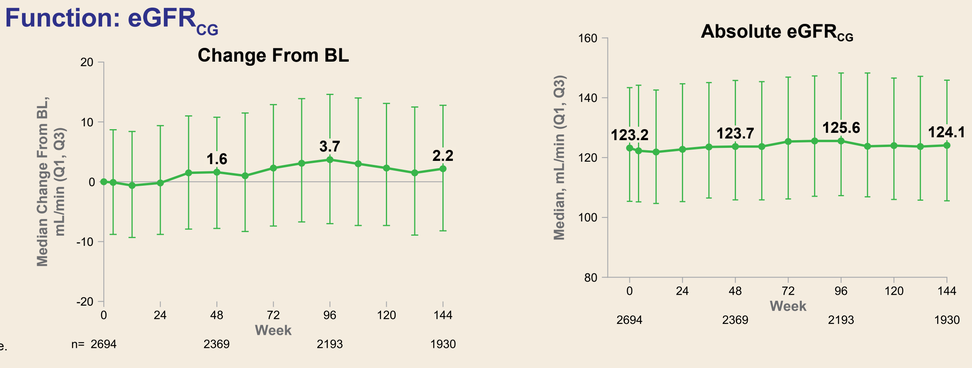
- All infections were in participants with suboptimal adherence
- One participant in the F/TAF arm had M184V mutation, which was detectable by ultra-deep sequencing and not by standard genotypic resistance testing

Bone Safety: BMD Substudy (n=191)



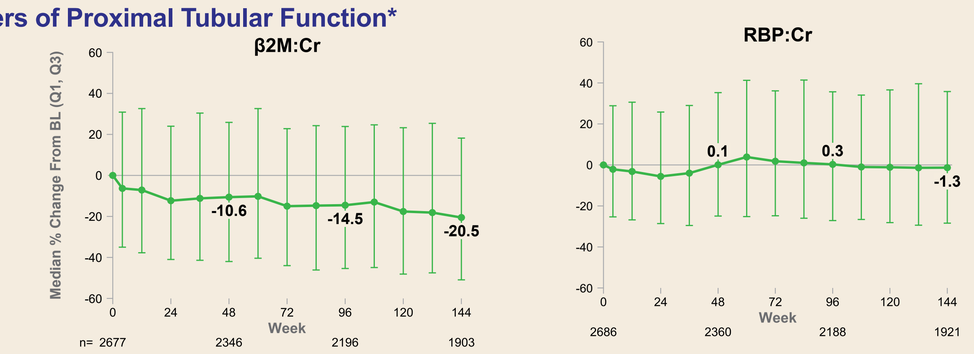
- These changes are consistent with expected BMD increases in the study population's age range[3]

Renal Function: $eGFR_{CG}$



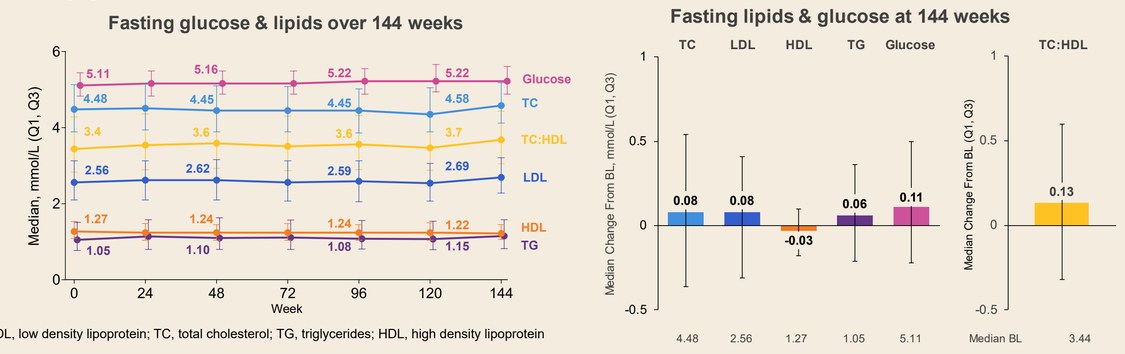
Q, quartile.

Markers of Proximal Tubular Function*



*Increases in β2-microglobulin:creatinine (β2M:Cr) or retinol-binding protein:creatinine (RBP:Cr) ratio are associated with proximal tubular dysfunction since these tests are not routinely used in clinical practice.

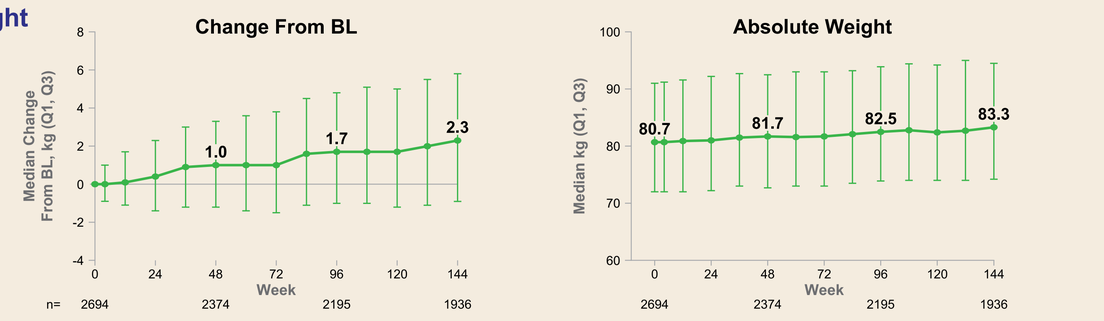
Fasting glucose & lipids over 144 weeks



LDL, low density lipoprotein; TC, total cholesterol; TG, triglycerides; HDL, high density lipoprotein

- 133 participants (4%) on F/TAF were taking lipid-modifying medications at study entry
- Through Week 144, 61 participants (2%) initiated lipid-modifying therapy

Weight



- Mean annualised increase in body weight at Week 144 was 0.83 kg/y; estimated weight gain for US adults aged 20–40 y is 0.5–1.0 kg/y[4]

Conclusions

- The DISCOVER open label phase allowed for long-term assessment (144 wk) of F/TAF for PrEP and demonstrated:
  - A low HIV incidence rate
  - Stable markers of glomerular and proximal tubular function
  - Increases in BMD consistent with expected changes in the study population's age range
  - Minimal changes in cholesterol
  - An increase in weight similar to average annual trends observed in the general US population
- F/TAF is a well tolerated and effective option for long-term use in people who would benefit from PrEP

References: 1. Mayer K, et al. Lancet. 2020;396:239-54; 2. Ogbuagu O, et al. Lancet HIV 2021;8:e397-e407.020; 3. Looker AC, et al. 2005–2008. National Center for Health Statistics. Vital Health Stat 11(251); 2012; 4. Hill JO, et al. Science 2003;299:853-5.

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