1962. Renal Outcomes for Participants Taking F/TAF vs. F/TDF for HIV PrEP in the DISCOVER Trial

Anthony Mills, MD1, Kimberly Wroblewski, MD1, Thomas Campbell, MD1, Paul Benson, DO2, Gordon Crofoot, MD1, Laura Salazar, MD3, Oyemwa Ogbugua, MD1; Peter Shalit, MD, PhD1; Benoit Trottier, MD1; Christoph C. Carter, MD1; Pamela Wong, MPH1; Diana M. Brainard, MD1, Scott McCallister, MD1; Moupali Das, MD1, and Susanne Dobelecki-Lewis, MD, MSPh1; Men’s Health Foundation, Los Angeles, California; Emory University, Atlanta, Georgia; University of Colorado Denver School of Medicine, Denver, Colorado; "Be Well Medical Center, Berkley, Michigan; "Crofoot Research Center, Houston, Texas; "St Joseph Heritage Healthcare, Newport Beach, California; "Yale School of Medicine, New Haven, Connecticut; "Peter Shalit, MD, PhD, Seattle, Washington; "Clinique de Medicine Urbaine du Quartier Latin, Montreal, Qc, Canada, "Gilead Sciences Inc., Foster City, California, "Gilead Sciences, Foster City, California, "University of Miami Miller School of Medicine, Miami, Florida.

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Background. In the DISCOVER PrEP trial, emtricitabine/tenofovir alafenamide (F/TAF) was noninferior to emtricitabine/tenofovir disoproxil fumarate (F/TDF) for HIV prevention. Here, we report on the renal outcomes of F/TAF and F/TDF among all DISCOVER participants and on those on baseline F/TDF PrEP who were randomized to F/TAF.

Methods. In total, 5387 men who have sex with men (MSM) and transgender women (TGW) at risk for HIV were randomized 1:1 to receive blinded F/TDF or F/TAF taken once daily (full cohort). Of these, 905 were on F/TDF PrEP at enrollment; of whom, 465 were randomized to F/TAF. Renal function and safety assessments included urinalysis (UA), estimated glomerular filtration rate (eGFR Cr), urinary protein:creatinine (Cr) ratio (UPCR), markers of proximal tubular function (β2-microglobulin:Cr ratio [β2M:Cr] and retinol-binding protein:Cr ratio [RBP:Cr]) and investigator-reported renal adverse events (AEs). Week 48 data are presented.

Results. In the full cohort, F/TAF was associated with more favorable changes in eGFR Cr, β2M:Cr, and RBP:Cr compared with F/TDF (Table 1). Treatment-emergent proteinuria by UA was more common with F/TDF than F/TAF (24.3% vs. 21.3% P = 0.005), as were treatment-emergent elevations in UPCR >200 mg/g [35 (1.5%) vs. 16 (0.7%); P = 0.005]. Compared to F/TDF, UPCR was lower in those randomized to F/TAF. Urinary protein:creatinine ratio (Cr) was also significantly lower in those randomized to F/TAF (P = 0.005) (Figure 1). No significant increases in β2M or RBP were observed in those randomized to F/TAF. The effect of treatment was more apparent in the full cohort.

Conclusion. Treatment-emergent proteinuria by UA was more common with F/TDF than F/TAF. Week 48 data show more favorable changes in renal function and proteinuria with F/TAF compared with F/TDF. Considering the superior safety profile of F/TAF, PrEP with F/TAF is effective and has a superior renal safety profile compared with F/TDF.

Table 1. Renal biomarker changes at week 48 compared to baseline.

| Event | F/TAF | F/TDF | p value |
|-------|-------|-------|--------|
| F/TDF median change (QL 03) | 4373 | 1.8 (−2.12, 11.3) | −2.3 (−10.8, 7.2) | <0.001 |
| β2M:Cr median % change (QL 03) | 6898 | −1.14 (−21.5) | 19.3 (−29.7) | <0.001 |
| RBP:Cr median % change (QL 03) | 4718 | 0.2 (−24.9, 35.4) | 19.9 (13.6, 82) | <0.001 |

Table 2. Renal adverse events at week 48.

| Event | Number of participants [%] |
|-------|---------------------------|
| any | F/TAF | F/TDF |
| Renal AE leading to discontinuation | 2 | (<0.1%) | 6 (0.2%) |
| Proximal tubulopathy | 0 | 1 (<0.1%) | 2 |

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1963. PrEP Significantly Reduces the Rate of New HIV Diagnoses in US Metropolitan Statistical Areas Independent of Treatment as Prevention (2012–2017)

Robertino M. Mera-Giler, MD PhD1, Moupali Das, MD1, Trevor Hawkins, MD1, David Magnuson, PharmD1, Julius Asuotong, PhD1 and Scott McCallister, MD1; 1PVE, Foster City, California, 2Gilead Sciences Inc., Foster City, California; 3Gilead Sciences, Foster City, California, 4University of Miami Miller School of Medicine, Miami, Florida.

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Background. Tenofovir/Emtricitabine (TVD) was approved for a Pre-exposure Prophylaxis (PrEP) indication in the United States in July 2012. Biomedical HIV prevention tools can impact the rate of new HIV diagnoses but their relative contributions have not been described.

Methods. The analysis utilized CDC published data on HIV diagnoses in 105 US metropolitan statistical areas (MSAs), a Treatment as Prevention (TasP) proxy of HIV suppressed individuals from 38 US states and DC, and a national pharmacy and medical claims databases to track TVD PrEP use from 2012 to 2017. The calculation of person time at risk excluded time of those taking PrEP as well as those who became HIV positive. TVD PrEP use was categorized in quintiles. A multilevel Poisson regression model which considers changes over time of each MSA was utilized. Rates and rate ratios plus corresponding 95% confidence intervals were obtained for quintiles of PrEP utilization after adjusting for the effect of treatment as prevention and calendar time.

Results. The US MSA rate of HIV diagnoses decreased significantly at a rate of 5.1% (95% CI −4.8 to −5.3%) per year in the period 2012–2017. PrEP use increased from an average of 1.64+1.3 per 100 subjects with a PrEP indication in 2012 to 5.4+3.2 in 2017. HIV viral suppression also increased by 1.3% per year (95% CI 1.1 to 1.6%) during the period of observation among HIV treated subjects. A multivariate model showed that PrEP use was significantly associated with the decline in the rate of new HIV cases, independent of a significant TasP effect. During the period of observation, the lowest quintile of PrEP utilization saw a decline of −0.23% (95% CI −0.2 to −0.43%), while the highest quintile of PrEP utilization showed a statistically significant decline of −4.24% (95% CI −3.9 to −8.01%) per year. Treatment as prevention had a significant and independent effect of −1.56% (−1.1 to −2.1%) per each percent increase of the proportion of HIV subjects with suppression.

Conclusion. From 2012 to 2017, HIV diagnoses declined most steeply in MSAs where PrEP use was the highest. The effect of PrEP use was significantly associated with this decline and was independent of treatment as prevention.

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