Assessment of Longitudinal Changes in Renal Function of HIV-1 Oral Pre-Exposure Prophylaxis Users Using Real-World Data in the United States

TUPEC213

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Conclusions

- In this real-world study, individuals prescribed oral emtricitabine/tenofovir alafenamide (F/TAF) for HIV-1 pre-exposure prophylaxis (PrEP) were less likely to have negatively impacted renal function compared with individuals using oral emtricitabine/tenofovir disoproxil fumarate (F/TDF) for PrEP
- The decrease in estimated glomerular filtration rate (eGFR) from baseline to Week 96 was greater in F/TDF users compared with F/TAF users
- F/TAF users were less likely (40% reduced odds) to have eGFR fall below 60 mL/min/1.73 m^2 compared with F/TDF users
- This is the first study to describe longitudinal changes in renal function among individuals prescribed PrEP in the real world
- Findings are consistent with the DISCOVER trial, which showed that F/TAF users had more favorable renal safety profiles compared to F/TDF

Plain Language Summary

- Medications that prevent the spread of HIV-1 can be taken orally every day or be given by injection every 2 months
- Although HIV-1 prevention medication is well tolerated and effective, some studies have shown it may affect how well your kidneys work
- The DISCOVER trial showed that one type of HIV-1 prevention medication, emtricitabine/tenofovir alafenamide, had less impact on kidney function than another medication, emtricitabine/tenofovir disoproxil fumarate
- To find out whether this result was also seen in the real world, a large healthcare database in the USA was used to explore kidney function over time in people using HIV-1 prevention medication
- The results showed that kidney function in people using emtricitabine/tenofovir disoproxil fumarate decreased more over 96 weeks than in people using emtricitabine/tenofovir alafenamide
- People using emtricitabine/tenofovir alafenamide were also 40% less likely to have reduced kidney function compared with emtricitabine/tenofovir disoproxil fumarate users
- The study supports the findings of the DISCOVER trial in a real-world setting

Background

- Daily oral F/TDF or F/TAF is highly effective at preventing HIV-1 acquisition when used as prescribed[1,2]
- In the Phase 3 randomized, double-blind, non-inferiority DISCOVER trial (NCT02842086), F/TAF for HIV-1 PrEP was associated with an improved renal safety profile versus F/TDF[3]
- However, the effect of oral F/TDF and F/TAF on renal function in the real world is unclear, particularly in people with kidney disease or other predisposing comorbidities (e.g., diabetes and hypertension)[3]
- This study leveraged real-world data from medical and pharmacy claims to assess renal function among individuals prescribed F/TDF and F/TAF for HIV-1 PrEP

Objective

- To assess real-world, longitudinal changes in the renal function of individuals prescribed F/TAF and F/TDF

Methods

Population and Data Source

- Individuals without HIV-1 who initiated F/TAF or F/TDF between January 2015 and December 2023, and had at least one eGFR measurement within 1 year pre- and post-PrEP initiation, were identified using HealthVerity Marketplace™
- For individuals who switched PrEP regimens after PrEP initiation (13%), any eGFR measurements taken after switching were excluded

Analysis of eGFR

- eGFR changes were calculated by subtracting post-PrEP initiation measurements from the pre-initiation 1-year average eGFR and analyzed using multivariable mixed-effects modelling
- Odds ratios (OR) of eGFR <60 mL/min/1.73 m^2 over 96 weeks post-PrEP initiation were calculated for F/TAF versus F/TDF using logistic regression
  - The effect of key covariates on the measure of association was explored by comparing ORs with and without adjustment
- Both mixed and logistic models were adjusted for potential confounders: age at PrEP initiation, baseline eGFR, baseline comorbidities, and use of concomitant medications

Results

Population

- Compared with F/TDF users (mean age, 36.4 years), F/TAF users were older (mean age, 38.6 years) and showed a higher prevalence of baseline comorbidities upon PrEP initiation (**Table 1**)
- At baseline, most F/TAF and F/TDF users had an average eGFR >90 mL/min/1.73 m^2, with a mean eGFR of 101.2 and 103.6 mL/min/1.73 m^2, respectively
  - 593 (25.5%) F/TAF users and 2088 (21.2%) F/TDF users had an average eGFR within the 60–89 mL/min/1.73 m^2 range

Longitudinal Changes in eGFR

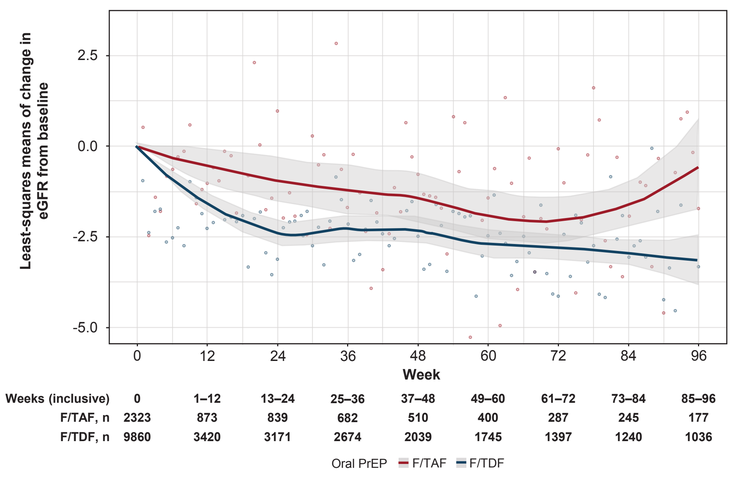
- In the first 6 months of PrEP use, mean eGFR levels decreased more quickly in F/TDF versus F/TAF users
- Compared with F/TAF users, F/TDF users had a greater least-squares mean decrease in eGFR levels through 24 months of use (**Figure 1**)

Results (cont.)

Likelihood of eGFR Falling <60 mL/min/1.73 m^2

- Overall, F/TAF users had 40% reduced odds of eGFR falling <60 mL/min/1.73 m^2 versus F/TDF users after adjusting for multiple factors (**Figure 2**)
  - Contributing factors identified by multivariate logistic regression analysis included age, sex at birth, baseline eGFR, and chronic kidney disease

Figure 1. Least-Squares Mean eGFR Change from Baseline Over Time for F/TAF or F/TDF for HIV-1 PrEP Users



Changes in eGFR from baseline were analyzed using a multivariable mixed-effects model, adjusting for age at PrEP initiation, baseline comorbidities and use of concomitant medications. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.
eGFR, estimated glomerular filtration rate; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; PrEP, pre-exposure prophylaxis.

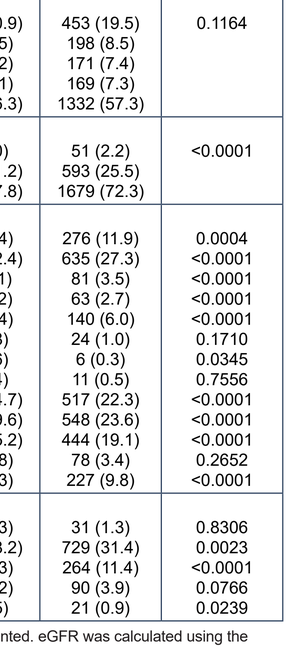
Table 1. Characteristics of PrEP Users at Baseline

n (%)	F/TDF users n=9860	F/TAF users n=2323	Chi-square *P*-value
Sex at birth			
Female	1258 (12.8)	131 (5.6)	<0.0001
Male	8602 (87.2)	2192 (94.4)	
Age (years)			
<40	6513 (66.0)	1421 (61.2)	<0.0001
≥40	3347(33.9)	902 (38.8)	
Race/ethnicity			
White	2057 (20.9)	453 (19.5)	0.1164
Black	739 (7.5)	198 (8.5)	
Hispanic	708 (7.2)	171 (7.4)	
Other	803 (8.1)	169 (7.3)	
Missing	5553 (56.3)	1332 (57.3)	
Baseline eGFR (mL/min/1.73m^2)			
<60	97 (1.0)	51 (2.2)	<0.0001
60-89	2088 (21.2)	593 (25.5)	
≥90	7675 (77.8)	1679 (72.3)	
Comorbidities[a]			
Diabetes	929 (9.4)	276 (11.9)	0.0004
Hypertension	2207 (22.4)	635 (27.3)	<0.0001
Chronic kidney disease	111 (1.1)	81 (3.5)	<0.0001
Acute kidney injury	119 (1.2)	63 (2.7)	<0.0001
Focal segmental glomerulosclerosis	241 (2.4)	140 (6.0)	<0.0001
Hydronephrosis	74 (0.8)	24 (1.0)	0.1710
Pyelonephritis	61 (0.6)	6 (0.3)	0.0345
Eating disorders	42 (0.4)	11 (0.5)	0.7556
Vitamin D deficiency	1445 (14.7)	517 (22.3)	<0.0001
Substance use disorder	1930 (19.6)	548 (23.6)	<0.0001
Tobacco use	1495 (15.2)	444 (19.1)	<0.0001
Methamphetamine use	271 (2.8)	78 (3.4)	0.2652
Alcohol abuse	722 (7.3)	227 (9.8)	<0.0001
Medication			
Lithium	126 (1.3)	31 (1.3)	0.8306
NSAIDs	2778 (28.2)	729 (31.4)	0.0023
Atypical antipsychotics	821 (8.3)	264 (11.4)	<0.0001
Tricyclic antidepressants	310 (3.2)	90 (3.9)	0.0766
Haloperidol	50 (0.5)	21 (0.9)	0.0239

[a]Comorbidities reported in ≥3% of F/TAF or F/TDF users are presented. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.
eGFR, estimated glomerular filtration rate; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; NS, non-significant; NSAIDs, non-steroidal anti-inflammatory drugs PrEP, pre-exposure prophylaxis.

Figure 2. Likelihood of eGFR <60 mL/min/1.73 m^2 for F/TAF Users Versus F/TDF Users Through 96 Weeks After PrEP Initiation

	F/TAF users with any eGFR <60 mL/min/1.73 m^2, n/N	F/TDF users with any eGFR <60 mL/min/1.73 m^2, n/N	Partially-adjusted OR[a] (95% CI)	Fully-adjusted OR[b] (95% CI)
All PrEP users	57 / 1658	248 / 7382	0.81 (0.59, 1.11)	0.60 (0.42, 0.86)
Age <40 years	12 / 1034	54 / 4886	1.06 (0.55, 2.04)	0.79 (0.38, 1.65)
Age ≥40 years	45 / 624	194 / 2496	0.71 (0.50, 1.03)	0.55 (0.36, 0.83)
Female	4 / 100	36 / 772	0.90 (0.29, 2.76)	0.61 (0.19, 1.96)
Male	53 / 1558	212 / 6610	0.82 (0.58, 1.14)	0.59 (0.41, 0.87)
Baseline eGFR 60–90 mL/min/1.73 m^2	35 / 424	150 / 1538	0.69 (0.46, 1.04)	0.59 (0.38, 0.91)
Baseline eGFR >90 mL/min/1.73 m^2	8 / 1209	46 / 5770	0.84 (0.39, 1.80)	0.73 (0.33, 1.62)
Had hypertension	35 / 412	112 / 1535	0.90 (0.58, 1.37)	0.64 (0.39, 1.06)
Had diabetes	23 / 177	43 / 640	1.56 (0.83, 2.93)	1.25 (0.63, 2.48)



n/N represent the proportion of individuals with eGFR <60 mL/min/1.73 m^2 at any time/total number of individuals with eGFR data. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.
[a]Partially adjusted ORs were adjusted with a logistic regression model for baseline comorbidities (yes/no; including diabetes, hypertension, acute kidney injury, focal segmental glomerulosclerosis, hydronephrosis, pyelonephritis, acute tubular necrosis, renal tubular acidosis, acute interstitial nephritis, diffuse cortical necrosis, renal papillary necrosis, eating disorders, vitamin D deficiency, sickle cell disease, tobacco use, and substance use disorder), substance abuse (yes/no; including methamphetamine abuse, cocaine abuse, alcohol abuse), and use of concomitant medications (yes/no; including lithium, non-steroidal anti-inflammatory drugs, atypical antipsychotics, tricyclic antidepressants, and haloperidol.
[b]Fully adjusted ORs were adjusted for all factors included in the partial adjustment, and were additionally adjusted for age, sex at birth, baseline chronic kidney disease, and baseline eGFR.
CI, confidence interval; eGFR, estimated glomerular filtration rate; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; OR, odds ratio; PrEP, pre-exposure prophylaxis.

Limitations

- Renal function assessment relied on availability of laboratory test results in datasets, and individuals may not have been consistently tested on a fixed schedule
  - A mixed-effect model was used to impute and adjust for the uneven distribution of missing data among individuals
- Claims based research may not capture clinically relevant factors affecting renal function (e.g., lifestyle, behavior, over-the-counter medication use, comorbidities)
- The absence of controls for baseline conditions and monitoring of other medical issues could introduce bias, thus cautioning against causal inference from the study's findings
- Individual-level adherence data were not available for this study

References: **1**. Centers for Disease Control and Prevention. PrEP Medication Guide: Reduce Your Risk of Getting HIV. Available at: https://www.cdc.gov/stophivtogether/library/topics/prevention/brochures/cdc-lsht-prevention-brochure-prep-medication-guide-patient.pdf (Accessed June 2024). **2**. Centers for Disease Control and Prevention. Pre-Exposure Prophylaxis (PrEP). Available at: https://www.cdc.gov/hiv/risk/prep/ (Accessed June 2024).
3. Mayer KH, et al. *Lancet.* 2020;396(10246):239–54.

Disclosures: **Xiwen Huang, Valentina Shvachko, Brett Shannon, Chris Nguyen, Joshua Gruber**, and **Li Tao** are all employees and shareholders of Gilead Sciences, Inc.

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