Real-World HIV Renal Outcomes With TDF to TAF Switch

Kaiser Permanente Research

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Conclusions

- **In this real-world study of PLWH who switched their ART from TDF to TAF based backbone while maintaining the same third agent, we observed an improvement in adjusted mean eGFR and eGFR slope calculations upon switch to TAF, with the largest change seen in those PLWH who had a lower baseline eGFR**

Background

Tenofovir alafenamide (TAF) was introduced in 2016 to provide a potentially safer renal profile than tenofovir disoproxil fumarate (TDF) in people living with HIV (PLWH). We sought to evaluate changes in renal function in patients who changed from TDF to TAF within a large integrated healthcare system.

Aim

Evaluated eGFR (CKD-EPI) renal outcomes associated with TDF to TAF switch.

Methods

Overview:

- Retrospective study in PLWH, identified through the KPSC HIV registry, that switched TDF to TAF (01/01/2016 to 01/01/2019), while maintaining the same third agent
- Data were collected while participants were taking TDF and TAF, up to 18 months both before / after switch
- For eGFR slope calculations, eGFR data were collected in 6 month intervals with mean eGFR calculated when ≥ 1 eGFR were available during each time period

Inclusion Criteria:

- Age ≥ 18 years at time of TDF to TAF switch
- ≥ 6 months of therapy on each TDF and TAF regimen
- Participants have ≥ 2 eGFR's available, which are ≥ 6 months apart, during both the TDF and TAF 18 month review period
- Among the available TDF eGFR's, each participant had a baseline eGFR (≥ 1 eGFR) available within 6 months before TDF to TAF switch

Exclusion Criteria:

- Concurrent prescription with any other HIV medication outside of regimen switch of interest
- eGFR slope change of +/- 50 mL/min/1.73m^2 per year
- ER / Hospitalization during study period with:
  - Diagnosis of dehydration and/or sepsis

TDF to TAF Regimen Switch:

- EVG/c/FTC/TDF → EVG/c/FTC/TAF
- RPV/FTC/TDF → RPV/FTC/TAF
- FTC/TDF + ETR → FTC/TAF + ETR
- FTC/TDF + RAL → FTC/TAF + RAL
- FTC/TDF + DRV/c → FTC/TAF + DRV/c
- FTC/TDF + DRV/r → FTC/TAF + DRV/r
- FTC/TDF + DTG → FTC/TAF + DTG
- FTC/TDF + NVP → FTC/TAF + NVP

Covariates:

- Individual and clinical characteristics:
  - Gender; Age at regimen switch; Race (African American / other); BMI (>30 mg/kg2)
  - Baseline eGFR (<90 and ≥90 mL/min/1.73m^2)
  - Cumulative known overall TDF exposure (years)
- Co-morbidities:
  - HTN, DM2, CVD
- Concurrent Medications of Influence:
  - ACE-I / ARB, NSAID's, Cotrimoxazole

Outcomes:

- Mean eGFR comparison (TAF – TDF)
- Mean eGFR slope calculations (annual eGFR change)
  - eGFR TDF Baseline to first available eGFR TAF
  - eGFR TDF Baseline to last available eGFR TAF

Statistical Analysis:

- Multivariable linear regression or mixed model analysis was used to adjust for individual and clinical characteristics, comorbidities, concomitant medications and was stratified by baseline eGFR (≥90 and <90)

Limitations

- Determining the long-term clinical relevance of the improvements observed in eGFR outcomes with the real-world TDF to TAF switch is beyond the scope of this study and may be the focus of future studies.

Results

Demographics (Individual and Clinical Characteristics):

Individual & Clinical Characteristics	Baseline eGFR ≥ 90 (N = 426)	Baseline eGFR <90 (N = 611)		Total (N = 1037)
		eGFR 60 to <90 (N = 524)	eGFR <60 (N = 87)	
Age at Conversion				
• Mean Age (Years)	42.1	51.1	60.5	48.2
Gender				
• Male	391 (91.8%)	469 (89.5%)	75 (86.2%)	935 (90.2%)
Self-Reported Race/Ethnicity				
• African American	72 (16.9%)	73 (13.9%)	10 (11.5%)	155 (15%)
BMI				
• BMI ≥ 30 (kg/m2)	104 (24.4%)	120 (22.9%)	17 (19.5%)	241 (23.2%)
Co-Morbidities				
• Hypertension	68 (16%)	143 (27.3%)	44 (50.6%)	255 (24.6%)
• Diabetes Mellitus 2	40 (9.4%)	47 (9%)	11 (12.6%)	98 (9.5%)
• Cardiovascular Disease	26 (6.1%)	63 (12%)	30 (34.5%)	119 (11.5%)
Concurrent Medications of Influence				
• ACE-I / ARB	57 (13.4%)	109 (20.8%)	29 (33.33%)	195 (18.8%)
• NSAID's	144 (33.8%)	166 (31.7%)	21 (24.1%)	331 (31.9%)
• Cotrimoxazole	46 (10.8%)	45 (8.6%)	7 (8.1%)	98 (9.5%)
TDF and TAF Exposure During Study (Up to 18 Months Before / After Regimen Switch)				
• TDF – Mean Days (SD)	512.8 (71.4)	521.7 (60.7)	527 (59.8)	518 (65.3)
• TAF – Mean Days (SD)	537.5 (39.9)	539.9 (35)	542.2 (24.2)	539.1 (36.3)
Known Cumulative TDF Exposure (All TDF Exposure Before Regimen Switch)				
• TDF – Mean Days (SD)	1,443 (1,089.6)	1915.1 (1346.5)	2140.8 (1,281.9)	1740.1 (1,266.5)
Baseline Mean eGFR (mL/min/1.73m2) - Within 6 months before TDF to TAF Switch				
• eGFR – Mean (SD)	103.2 (9.8)	76.7 (8.4)	53.6 (6)	85.7 (18.2)
TAF Conversion Group				
• RPV	173 (40.6%)	208 (39.7%)	31 (35.6%)	412 (39.7%)
• EVG/c	184 (43.2%)	193 (36.8%)	27 (31%)	404 (39%)
• DTG or RAL	29 (6.8%)	57 (10.9%)	18 (20.7%)	104 (10%)
• NVP or ETR	20 (4.7%)	41 (7.8%)	6 (6.9%)	67 (6.5%)
• DRV/(c or RTV)	20 (4.7%)	25 (4.8%)	5 (5.8%)	50 (4.8%)

Adjusted[1] eGFR TAF Slope Calculations:

Individuals with baseline eGFR < 90 had a significant improvement in calculated eGFR slope after TDF to TAF switch

eGFR TDF Baseline[2]	N	eGFR TAF Slope[3] (TAF First Available)	p-Value	95% CI	Mean (SD) Days[5]
≥ 90	426	+0.54	0.820	(-4.2, 5.2)	270.2 (79.3)
< 90	611	**+6.51**	<0.001	(3.1, 11)	268.6 (75.3)
Entire Cohort	1037	**+3.57**	<0.01	(0.9, 6.3)	269.3 (76.9)
eGFR TDF Baseline[2]	**N**	**eGFR TAF Slope[4] (TAF Last Available)**	**p-Value**	**95% CI**	**Mean (SD) Days[5]**
≥ 90	426	-0.77	0.520	(-3.1, 1.6)	517.9 (77)
< 90	611	**+3.23**	<0.001	(1.6, 4.9)	524.4 (72.8)
Entire Cohort	1037	**+1.51**	0.025	(0.2, 2.8)	521.7 (74.6)

1) eGFR TAF slope calculations were adjusted for individual and clinical characteristics, comorbidities, concomitant medications and were stratified by baseline eGFR (≥90 and <90). 2) eGFR (mL/min/1.73m2). 3) Annualized eGFR slope calculation is between the mean baseline eGFR before TAF switch and the first available mean TAF eGFR after switch. 4) Annualized eGFR slope calculation is between the mean baseline eGFR before TAF switch and the last available mean TAF eGFR after switch. 5) Mean days between eGFR TDF Baseline and eGFR TAF.

Adjusted[1] Mean eGFR Difference:

There was an overall improvement in mean eGFR after switch to TAF, particularly in PLWH with lower baseline eGFR

Regimen	Mean eGFR	p-Value	95% CI
Mean eGFR (Entire Cohort); n = 1,037			
TAF	88.4	<0.001	(87.5, 89.2)
TDF	85.6	<0.001	(84.8, 86.3)
TAF - TDF	**2.8**	<0.001	(2.2, 3.4)
Mean eGFR (Baseline eGFR ≥ 90); n = 426			
TAF	102.45	<0.001	(101, 103.9)
TDF	103.03	<0.001	(101.7, 104.4)
TAF - TDF	-0.58	0.202	(-1.5, 0.3)
Mean eGFR (Baseline eGFR < 90); n = 611			
TAF	79.2	<0.001	(78.2, 80.2)
TDF	73.7	<0.001	(72.8, 74.5)
TAF - TDF	**5.5**	<0.001	(4.8, 6.3)

Regimen	Mean eGFR	p-Value	95% CI
Mean eGFR (Baseline eGFR ≥ 60 to < 90); n = 524			
TAF	82.6	<0.001	(81.5, 83.7)
TDF	77.4	<0.001	(76.4, 78.4)
TAF - TDF	**5.2**	<0.001	(4.4, 6)
Mean eGFR (Baseline eGFR < 60); n = 87			
TAF	60.5	<0.001	(58.5, 62.4)
TDF	53	<0.001	(51.7, 54.3)
TAF - TDF	**7.5**	<0.001	(5.6, 9.3)

1) Mean eGFR Difference was adjusted for individual and clinical characteristics, comorbidities, concomitant medications and were stratified by baseline eGFR (≥90 and <90).

Abbreviations:

PLWH = People living with HIV; ART = Antiretroviral therapy; eGFR = Estimated glomerular filtration rate (CKD-EPI, mL/min/1.73m^2); KPSC = Kaiser Permanente Southern California; TDF = Tenofovir disoproxil fumarate; TAF = Tenofovir Alafenamide;; EVG = Elvitegravir; c = Cobicistat; RPV = Rilpivirine; ETR = Etravirine; RAL = Raltegravir; DRV = Darunavir; r = Ritonavir; DTG = Dolutegravir; NVP = Nevirapine; HTN = Hypertension; DM2 = Diabetes Mellitus II; CVD = Cardiovascular disease; ACE-I = Angiotensin-converting enzyme (ACE) inhibitors; ARB = Angiotensin receptor blocker; NSAIDs = Non-steroidal anti-inflammatory drugs

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