Urine Testing Detects Tenofovir in HIV Patients on Tenofovir Alafenamide-Based Treatment

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Background

- Tenofovir alafenamide (TAF) is approved for ART and is being evaluated for HIV prevention
- Urine tenofovir (TFV) testing has been validated to measure tenofovir disoproxil fumarate (TDF)-based PrEP and ART medication adherence
- Compared to TDF, TAF has approximately 10% of the plasma tenofovir exposure

Koenig *HIV Medicine* 2017

Background: Urine Assay

Urine TFV (ng/mL)	Adherence Level	Date Last Dose	Implication
>1000	Recent adherence	Within 48 hours	HIV protection
10-1000	Low adherence	2-7 days ago	Sub-optimal HIV protection, at risk of resistance
<10	Non-adherence	>7 days ago	No HIV protection, low risk of resistance

- Methods: Liquid chromatography/mass spectrometry assay
- Advantages:
  - Non-invasive, acceptable to target population
  - Affordable, easily incorporated into a variety of settings
  - Low maintenance adherence monitoring strategy
  - Can be collected at the same time as urine STI screening, etc.

Koenig *CROI* 2015

Urine Assay: Performance Characteristics

Analytical Validation	How well does the test perform in the laboratory?	Urine testing vs Plasma (n = 10)	Sensitivity	100%
			Specificity	100%
			PPV	100%
			NPV	100%
		CDC Validation of Urine Test (n = 50)	Sensitivity	94%
			Specificity	91%
			PPV	85%
			NPV	97%
Clinical Validation	How well does the test perform in a clinical setting?	Urine testing (dose in last 48 hrs) vs DBS (>4 doses/wk) (n = 90)	Sensitivity	94%
			Specificity	56%
			PPV	95%
			NPV	50%
Clinical Utility	How useful is the test?	Adherence study in real world setting (n = 50)	Week 4	80%
			Week 12	74%
			Week 24	82%
			Week 36	82%
			Week 48	70%
		Future Studies Planned	Adherence over time	
			HIV infections prevented	

Objectives

- In a proof of concept study, we assessed the urine assay for the detection of TFV in patients taking TAF-based ART

Methods

- Washington University in St. Louis Infectious Diseases Clinic, April – June 2017
- 10 patients were included in this study
- Inclusion criteria: HIV-infection with undetectable viral load ≥ 3 months, on TAF-based ART for ≥ 3 months, ≥ 18 years, not pregnant
- Primary outcome: TFV detection using the urine assay
  - Levels >1000 ng/mL indicate tenofovir use in the previous 48 hours
  - Levels <10 ng/mL indicate no tenofovir use in the previous week
- Patient self-report: 7-day self-reported adherence was recorded
  - How many doses did you miss in the last 7 days?

Results

Table 1. Participant characteristics

Characteristics	n=10 (%)
Median age (years) (IQR)	48 (30-57)
Gender	
Male	7 (70)
Female	3 (30)
Race	
African American	5 (50)
White	4 (40)
Multiracial	1 (10)
Median duration of HIV infection (years) (IQR)	8 (4-16)
TAF-based medication type	
TAF/FTC/EVG/c*	6 (60)
TAF/FTC/RPV**	4 (40)
Median during on TAF-based medication (months) (IQR)	16 (9-19)

*TAF/FTC/EVG/c, tenofovir alafenamide/emtricitabine/elvitegravir/cobicistat

**TAF/FTC/RPV, tenofovir alafenamide/emtricitabine/rilpivirine

Results

- TFV detection
  - 9 participants had urine TFV levels >1000 ng/mL
    - 8 self-reported no missed doses in the last 7 days
    - 1 self-reported 1 missed dose in the last 7 days
  - 1 participant had a level <10 ng/mL
    - Self-reported missing 3 doses in the last 7 days

Results: ART regimen & adherence

Participant	Age (years)	Medication*	TFV** urine level (ng/mL)	Self-reported missed doses in past 7 days
1	47	TAF/FTC/ELR/COBI	> 1,000	0
2	61	TAF/FTC/RIL	> 1,000	0
3	47	TAF/FTC/ELR/COBI	> 1,000	0
4	30	TAF/FTC/RIL	> 1,000	0
5	52	TAF/FTC/ELR/COBI	> 1,000	0
6	55	TAF/FTC/ELR/COBI	< 10	3
7	61	TAF/FTC/ELR/COBI	> 1,000	0
8	48	TAF/FTC/RIL	> 1,000	0
9	26	TAF/FTC/RIL	> 1,000	1
10	28	TAF/FTC/ELR/COBI	> 1,000	0

*TAF/FTC/EVG/c, tenofovir alafenamide/emtricitabine/elvitegravir/cobicistat; TAF/FTC/RPV, tenofovir alafenamide/emtricitabine/rilpivirine
**TFV, tenofovir

Limitations

- Small sample size – proof of concept
- Single clinic site
- Did not account for “day-of” dosing

Conclusions

- We demonstrated that the urine TFV assay can detect TFV in a sample of HIV-infected, virally suppressed participants on TAF-based ART
- Despite known lower plasma levels of TFV in patients taking TAF versus TDF, urine TFV levels are comparable between these two populations
- In the single participant with a urine TFV level <10ng/mL, there was self-reported recent ART non-adherence
- These findings have implications for low-burden clinical monitoring of TAF for HIV treatment and prevention

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