Abstract 975

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Urine Assay for Tenofovir to Monitor Adherence to Tenofovir/Emtricitabine as PrEP

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Background

- Tenofovir/Emtricitabine (TDF/FTC) reduces HIV transmission and is approved for pre-exposure prophylaxis (PrEP).
- PrEP for HIV prevention is at least 92% effective when taken daily.[1-4]
- Adherence is critical for the success of PrEP.
- Current adherence measurements, self-report, and plasma tenofovir (TDF) levels are inadequate tools for monitoring adherence in real-time.[2]

Objective

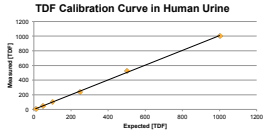
- Our goal was to develop and validate a urine assay to measure TDF levels to objectively monitor adherence to PrEP.

Methods

- We conducted 3 cohort studies to validate the assay:
  1. Qualitative evaluation of the relationship of urine TDF to plasma TDF in 10 HIV+ subjects with undetectable HIV viral loads on a TDF-based regimen
  2. Quantitative evaluation of TDF clearance in plasma and urine over 7 days in 10 HIV-negative subjects who received a single dose of TDF/FTC
  3. Concordance between plasma and urine TDF levels over time was assessed in a 16 week study of 10 HIV-negative individuals on daily TDF/FTC for PrEP

Results

The assay



Tenofovir (TDF) calibration curve in human urine over a concentration range of 10 to 1000 ng/mL. A known concentration of TDF was injected into a human urine sample (x axis) and measured using LC-MS/MS (y axis). [TDF] = tenofovir concentration.

- We developed a semi-quantitative liquid chromatography-tandem mass spectrometry (LC-MS/MS) urine assay with high sensitivity/specificity for TDF.
- This assay allowed us to determine TDF concentrations in log categories between <10 ng/ml to > 10,000 ng/ml.

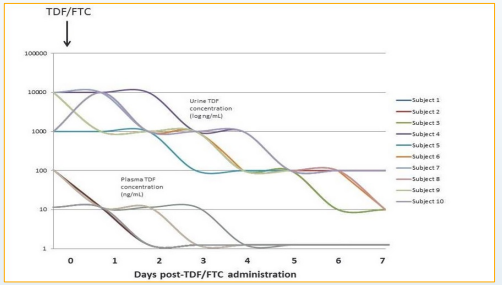
Results

Cohort 1 (Relationship between urine and plasma concentration in well-controlled individuals)

- 100% concordance btw presence of TDF in plasma & urine (PPV 100%, 95 CI,0.63-1; NPV 100%, 95 CI, 0.05-1)
- TDF concentration 3-4 logs higher in urine than plasma

Results

Cohort 2 (Clearance of TDF in plasma & urine)

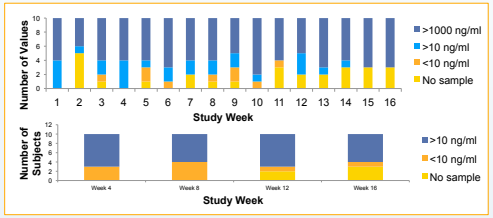


- TDF is detected for >7 days in urine and 2-4 days in plasma after a single dose of Truvada
- Urine TDF is cleared in a log-linear fashion, with a direct correlation of urine levels to time since last dose
- Urine assay is 2 logs more sensitive than serum over 7 days

References

1. Grant RM et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 363.27 (2010): 2587-99.
2. K. R. Amico et al. Adherence Support Approaches in Biomedical HIV Prevention Trials: Experiences, Insights and Future Directions from Four Multisite Prevention Trials, AIDS. Behav. (2013)
3. M. C. Thigpen et al, Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana, N. Engl. J. Med. 367 (2012) 423-34.
4. J. M. Baeten et al, Antiretroviral prophylaxis for HIV prevention in heterosexual men and women, N. Engl. J. Med. 367 (2012) 399-410.

Cohort 3 (Urine assay in patients on PrEP)



- TDF detected in 93% of urine samples (concentration range: >10 ng/mL to >10,000 ng/mL)
- TDF detected in 74% of plasma samples (concentration range: >10 ng/mL to >100 ng/mL)
- Urine TDF concentration > 1000 ng/mL highly predictive of presence of TDF in plasma (>10 ng/mL) (PPV 0.88, 95%CI, 0.69-0.97; NPV 0.88, 95%CI, 0.47-0.99)

Conclusions

- The urine assay correlates highly with plasma TDF levels and is more sensitive for TDF over 7 days.
- Levels of urine TDF could be used to distinguish between recent adherence with a dose of TDF in last 48 hours (>1000ng/mL), low adherence (>100ng/mL), and non-adherence with >1 week since the last dose (<10 ng/mL).

Future Steps

- Will real-time adherence monitoring with the urine assay lead to clinically significant and sustained increase in adherence to PrEP?
- Can the urine assay be further developed into a point of care test?