Urine Tenofovir Concentrations Correlate with Plasma Tenofovir and Distinguish High, Moderate and Low PrEP Adherence:
A Randomized Directly-observed Pharmacokinetic Trial

TARGET

Tenofovir Adherence to Rapidly Guide and Evaluate PrEP and HIV Therapy

Paul K. Drain, Matthew Spinelli, Rachel W. Kubiak, Oraphan Siriprakaisil, Virat Klinbuayaem, Justice Quame-Amaglo, Pra-ornsuda Sukrakanchana, Suriyan Tanasri, Pimpinun Punyati, Wasna Sirirungsi, Ratchada Cressey, Peter Bacchetti, Hideaki Okochi, Jared M. Baeten, Monica Gandhi, Tim R. Cressey

June 18, 2019

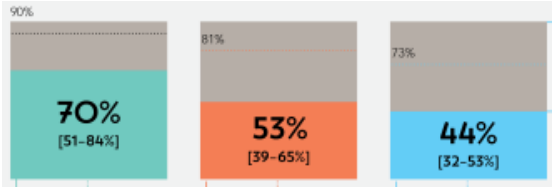
Funded by US National Institute of Allergy and Infectious Disease (AI127200)

UNIVERSITY OF WASHINGTON
INTERNATIONAL CLINICAL RESEARCH CENTER

UCSF Division of HIV, Infectious Diseases & Global Medicine
Department of Medicine

Background & Objective

- Efficacy of daily PrEP and ART highly dependent on sufficient adherence to maintain protective or therapeutic drug concentrations



- Existing tools to monitor PrEP and ART adherence (self-report, pill counts) have limitations

- In a directly observed therapy (DOT) study, we assessed correlation between urine and plasma TFV concentrations and the impact of adherence patterns on TFV concentrations

TARGET
Tenofovir Adherence to Rapidly Guide and Evaluate PrEP and HIV Therapy

UNAIDS, 2018.

Methods

- TARGET (**T**enofovir **A**dherence to **R**apidly **G**uide and **E**valuate PrEP and HIV **T**herapy) was an open-label, three arm randomized controlled trial in Chiang Mai, Thailand
- Enrolled adults ages 18-49 years, if HIV and Hep B negative, and with normal renal function
- **3 study arms** for TDF/FTC (300/200 mg) dosing given DOT:
  - Perfect adherence **-** TDF/FTC 7 days/week
  - Moderate adherence - TDF/FTC 4 days/week
  - Low adherence – TDF/FTC 2 days/week

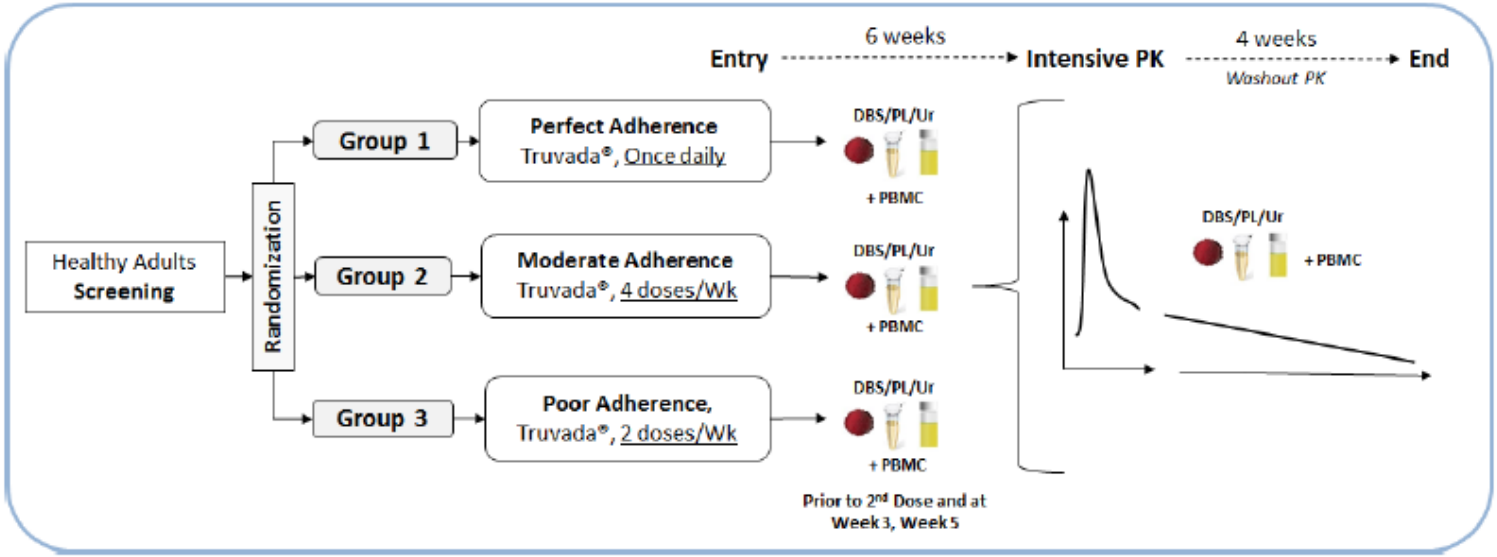
TARGET
Tenofovir Adherence to Rapidly Guide and Evaluate PrEP and HIV Therapy

Protocol: Cressey TR, et al. BMC ID, 2017.

Methods

Three study phases with sampling

- Lead-in TDF/FTC dosing for 6-week period
- Intensive 24-hour pharmacokinetic period
- Drug washout for a 4-week period



Protocol: Cressey TR, et al. BMC ID, 2017.

Methods – Analyses

All tenofovir drug testing perform by liquid chromatography tandem mass spectrometry (LC-MS/MS):

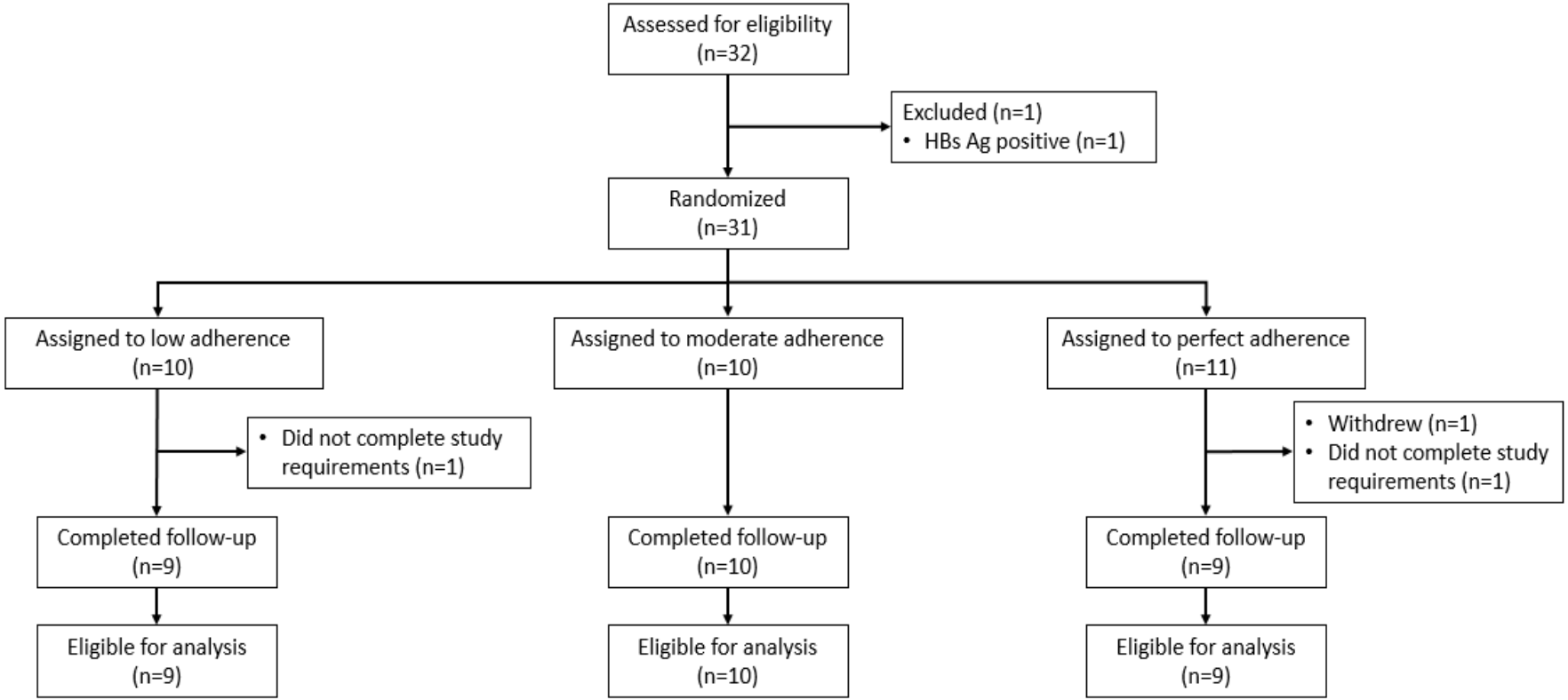
- **Urine** – validated over range of 50 – 50,000 ng/mL
- **Plasma** – validated over range of 3 – 2,500 ng/mL

Statistical Analyses:

- Spearman's correlation coefficient (*r*)
- One-way repeated measures analysis of variance (ANOVA)
- Cox proportional hazard models

Protocol: Cressey TR, et al. BMC ID, 2017.

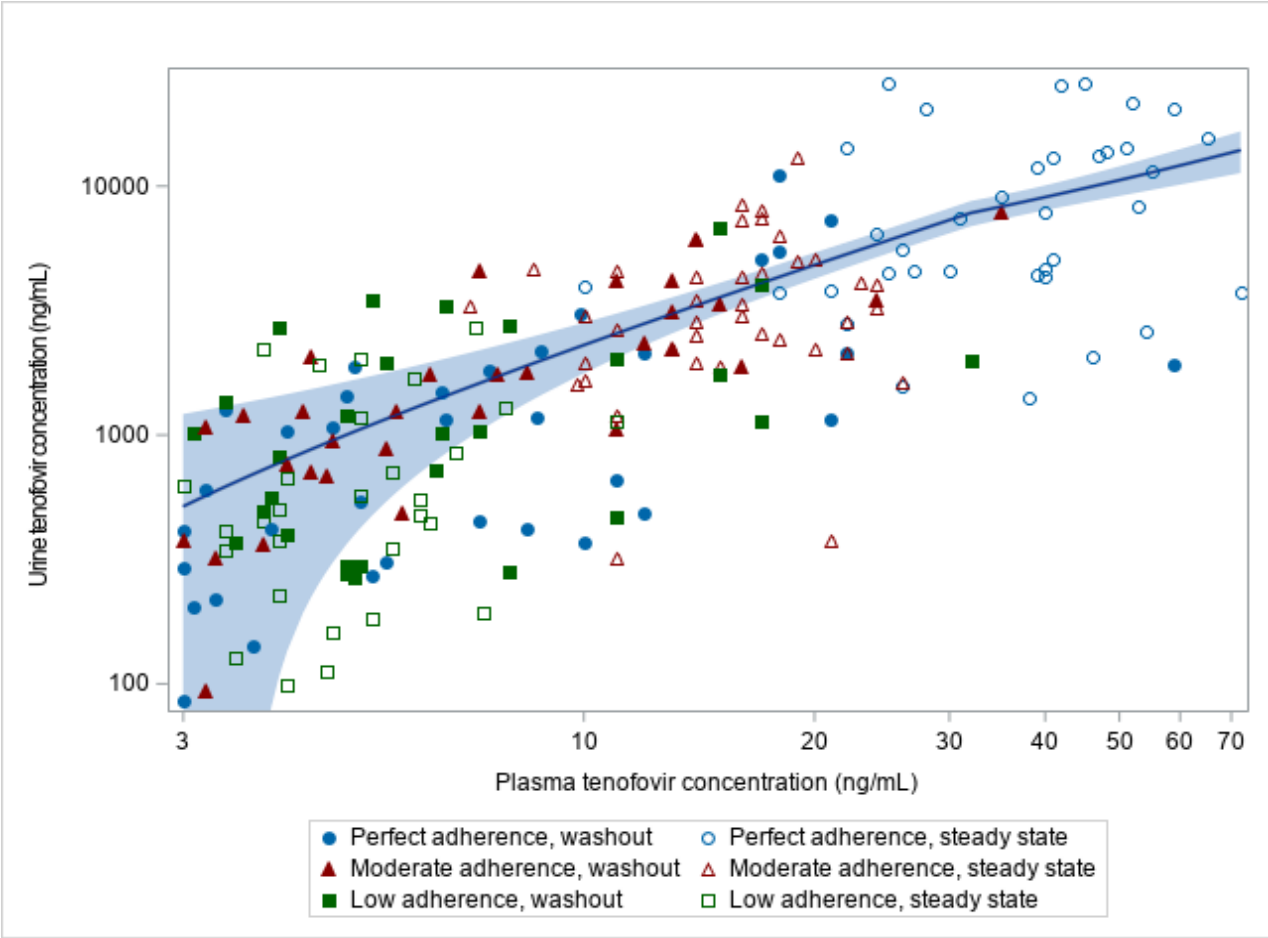
Results – Consort



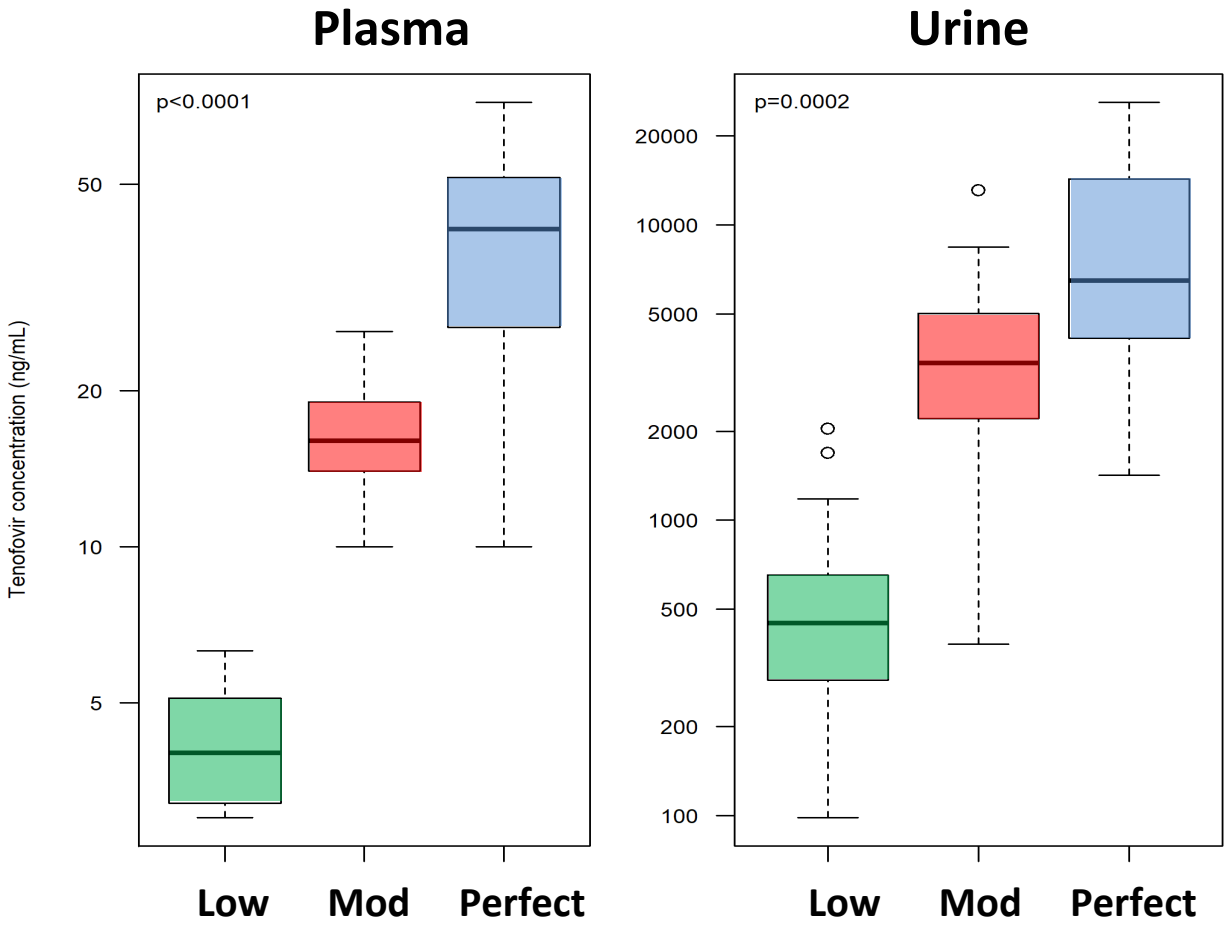
Results – Participant Characteristics

	Adherence Arm		
	Low	**Moderate**	**Perfect**
	(N=9)	(N=10)	(N=9)
	Median (interquartile range)		
Sociodemographic and Clinical			
Male – N (%)	3 (33)	8 (80)	5 (56)
Age (years)	38 (27-40)	32 (28-33)	34 (31-39)
Body Mass Index (kg/m^2)	23.1 (20.2-28.4)	24.0 (22.1-25.1)	20.2 (19.1-24.3)
Laboratory Measures			
White blood cells ($cells/mm^3$)	6,700 (5200-7700)	7,950 (5800-8800)	6,500 (5900-6900)
Hemoglobin (g/dL)	13.3 (13.3-15.0)	14.5 (14.4-15.2)	12.4 (11.9-13.2)
eGFR (Cockcroft-Gault equation)	108 (102-115)	124 (98-132)	91 (87, 108)

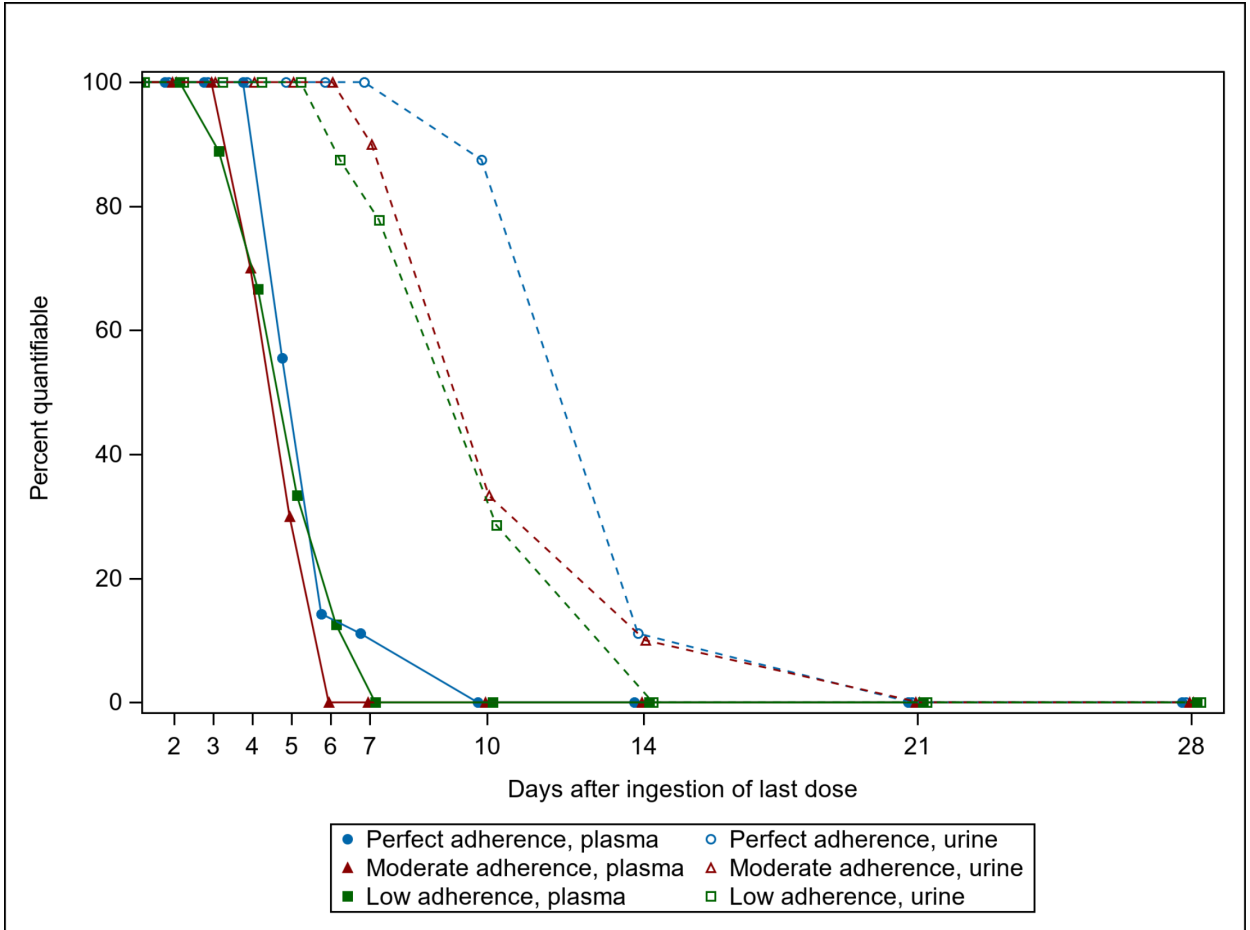
Results – Correlation of TFV between Urine and Plasma



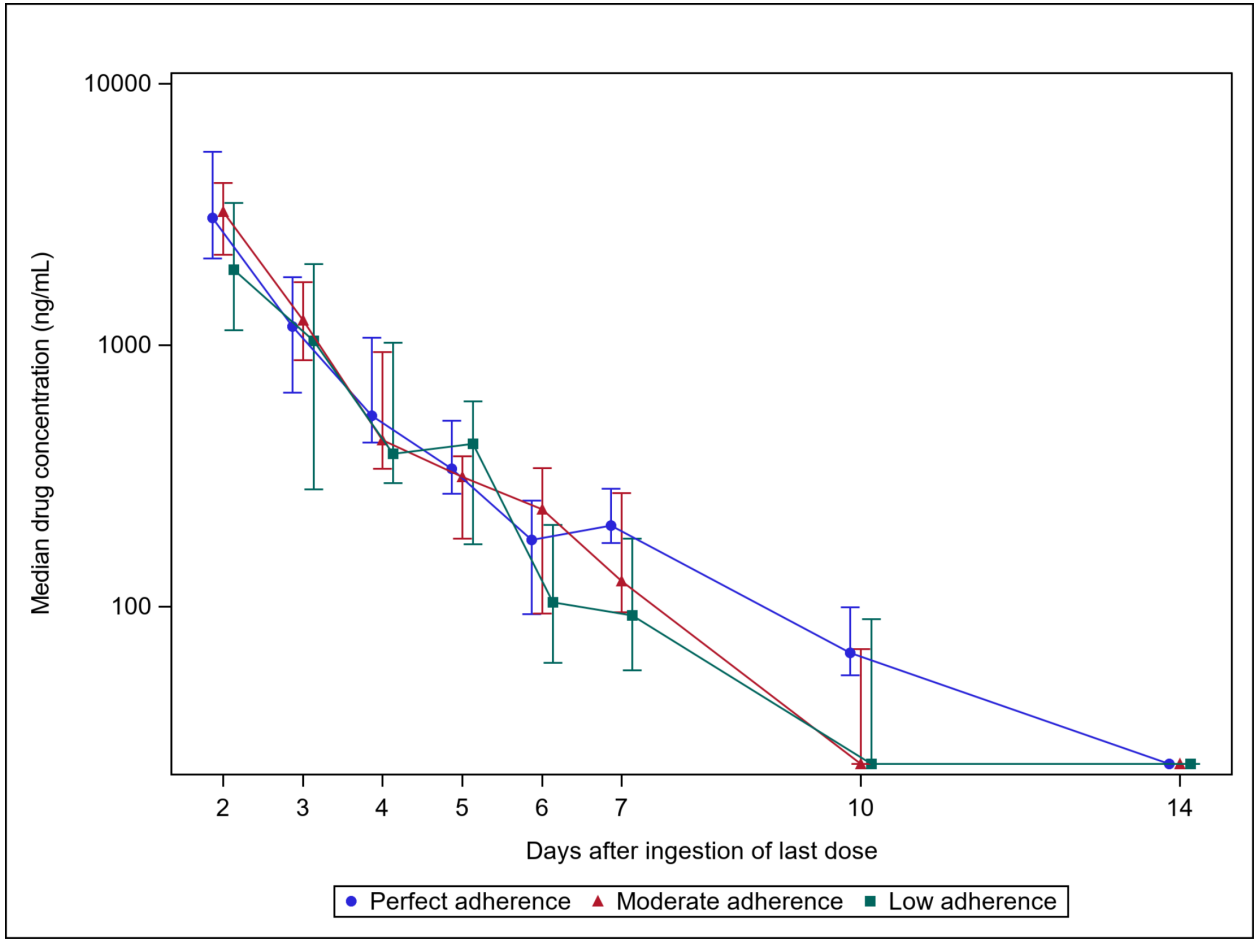
Results – TFV levels at Steady State



Results – Washout of TFV for Plasma (solid) and Urine (dashed)



Results – Washout of TFV in Urine by Adherence Arm



Conclusions

TARGET
Tenofovir Adherence to Rapidly Guide and Evaluate PrEP and HIV Therapy

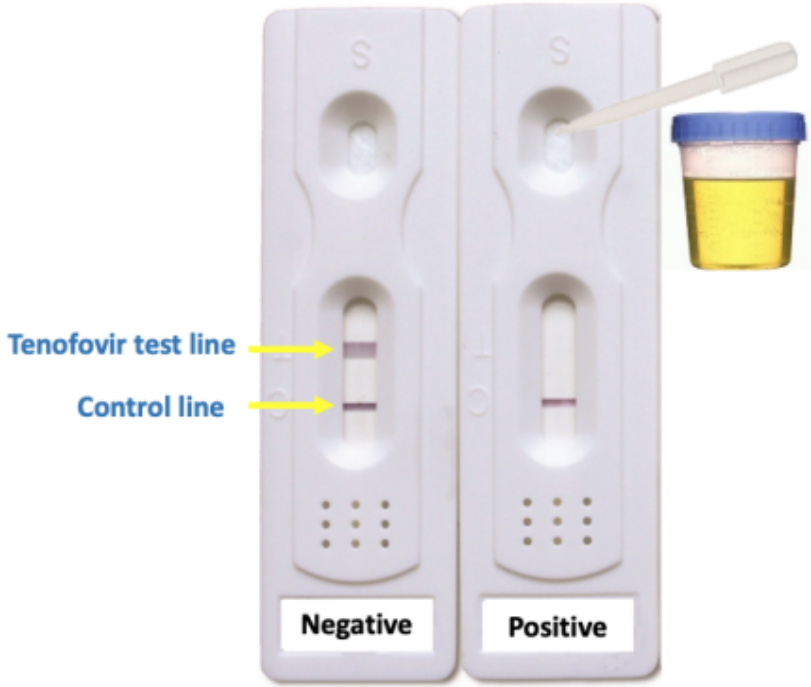
- Urine TFV concentrations correlated with plasma TFV during steady-state and washout period in adults receiving TDF/FTC

- Spot urine and plasma TFV concentrations were significantly different among the 3 adherence arms at steady-state

- Urine TFV concentrations did not differ between the 3 adherence arms during the washout period, suggesting that POC TFV urine testing could provide useful information about timing of recent dosing

Conclusions

- Results suggest plasma and spot urine TFV samples suitable for objectively evaluating recent adherence to PrEP and TDF-based ART
- This data will inform the interpretation of recently-developed point-of-care immunoassays
- Data contributed to development of new tenofovir LFA now launched and ready for further testing in treatment and PrEP



Acknowledgements

TARGET
Tenofovir Adherence to Rapidly Guide and Evaluate PrEP and HIV Therapy

We thank all the TARGET Study participants

University of Washington:
Paul Drain (PI)
Rachel Kubiak
Justice Quame-Amaglo
Jared Baeten

Chiang Mai University:
Tim Cressey
Oraphan Siriprakaisil
Virat Klinbuayaem
Pra-ornsuda Sukrakanchana
Suriyan Tanasri
Pimpinum Punyati
Wasna Sirirungsi
Ratchada Cressey

University of California-San Francisco:
Monica Gandhi
Matthew Spinelli
Peter Bacchetti
Hideaki Okochi

We thank the funders and collaborators

National Institute of Allergy and Infectious Diseases **(AI127200)**

UNIVERSITY OF WASHINGTON
INTERNATIONAL CLINICAL RESEARCH CENTER