SITE-BASED HIV TESTING ASSAY PERFORMANCE FOR CABOTEGRAVIR AND TDF-FTC PREP FAILURE IN HPTN 083

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Disclosures: Raphael J. Landovitz has served on Advisory/Monitoring Boards for Merck and RedQueen Therapeutics, and as a consultant to ViiV Healthcare and Gilead Sciences

HPTN 083 ABSTRACT CO-AUTHORS

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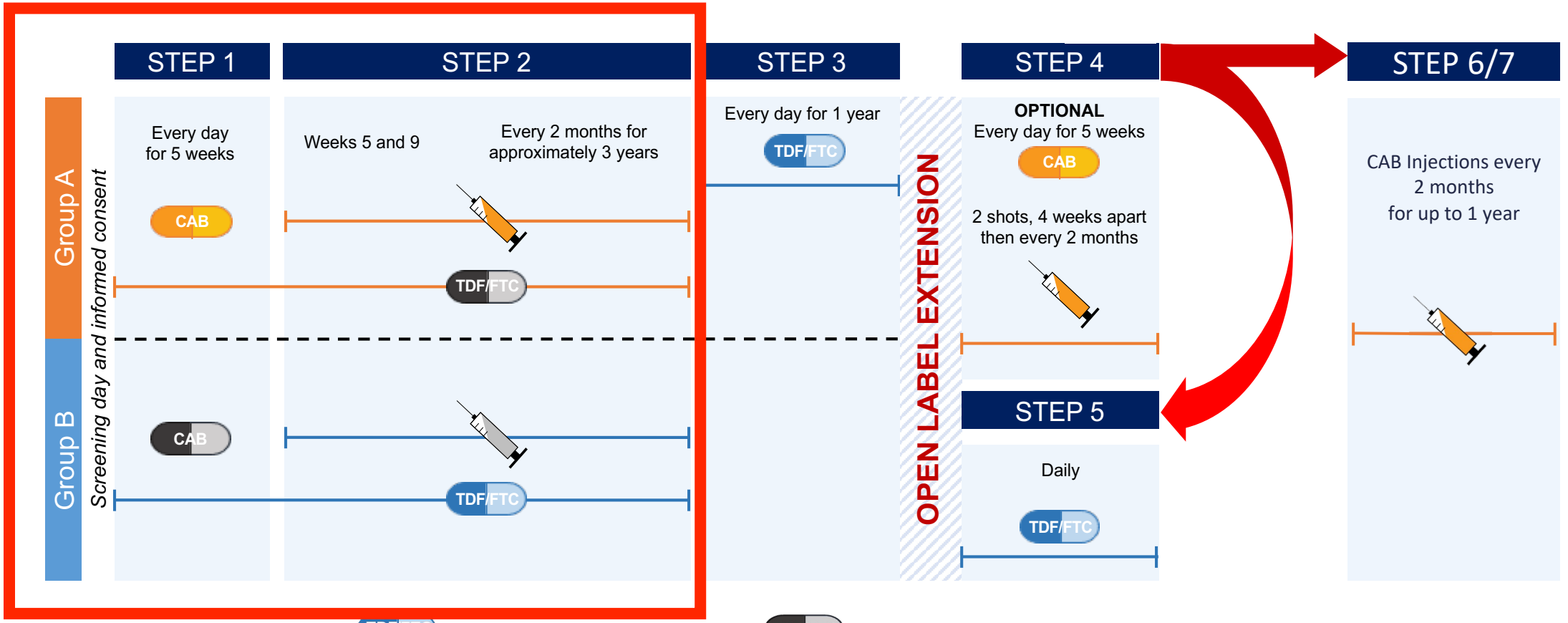
BACKGROUND

- **HPTN 083 is an ongoing RCT of Injectable Cabotegravir (CAB-LA) Compared to Daily Oral Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC), for Pre-Exposure Prophylaxis in Cisgender Men and Transgender Women**
- **CAB-LA was approved by the US FDA for prevention of sexually transmitted HIV in December 2021, and in additional geographies**
- **During the blinded study and for the first year after unblinding, site-based HIV testing algorithms included a US FDA-cleared rapid Ab test (RT) and a laboratory-based antigen/antibody assay (Ag/Ab)**
- **Post-hoc observations identified delays in Ag and Ab-based test reactivity with CAB-LA PrEP failure, often with low-level viremia (LEVI), leading US FDA and CDC to recommend VL testing as part of screening for CAB-LA PrEP failure**

STUDY DESIGN



ANALYSIS CONTEXT & AIM

- **Absence of consensus on the optimal HIV testing algorithm to screen for PrEP failure**

- **We aimed to evaluate the positive predictive value (PPV) of various HIV testing combinations**
  - **Cisgender men and transgender women**
  - **Using RT and Ag/Ab testing only**

METHODS

Study Site Procedures

- Required a negative HIV RNA result within 14 days of study entry, and performed RTs and Ag/Ab tests at all study visits
- Some sites conducted two RTs prior to product administration, as per local practice

HIV Status Determination

- Determined by an external adjudication committee
- Based on site HIV testing and retrospective testing at a central laboratory

Assessment of Predictive Value

- Period of analysis: Blinded and first unblinded year of follow-up
- PPV, 95% Confidence Intervals [CI]) for initial site-based testing was assessed for various combinations of site test results

ANALYSIS POPULATION

	No reactive visits (n=4322)	Adjudicated HIV+ (n=130)	Visit with false + result (n=48)
AGE, mean (SD)	28.3 (8.2)	24.2 (6.4)	27.8 (7.2)
ARM, n (%)			
TDF/FTC	2144 (49.6%)	87 (66.9%)	21 (43.8%)
CAB	2178 (50.4%)	43 (33.1%)	27 (56.2%)
COHORT, n (%)			
MSM	3775 (87.3%)	113 (86.9%)	46 (95.8%)
TGW	544 (12.6%)	16 (12.3%)	2 (4.2%)
REGION, n (%)			
Africa	138 (3.2%)	6 (4.6%)	2 (4.2%)
Asia	720 (16.7%)	18 (13.8%)	11 (22.9%)
Latin America	1854 (42.9%)	68 (52.3%)	17 (35.4%)
US	1610 (37.3%)	38 (29.2%)	18 (37.5%)

Note: Participants with no HIV testing after enrollment (n=67), reactive test results at enrollment (n=1), or unknown HIV status (n=2) were excluded from from this table and all subsequent analyses.
Columns are *not* mutually exclusive, as participants could have both a false reactive visit and a true reactive visit. Although they cannot contribute an initial reactive visit, the person who seroconverted soon after a false reactive visit is included in the HIV-positive column.

VISIT DISPOSITION

Rapid Testing (POC)

Initial reactive visit
n=177

≥1 reactive RTs
- n=72 (1 RT)
- n=33 (2 RTs, both reactive)
- n=1 (2 RTs, discordant)

No reactive RTs
- n=63 (1 RT)
- n=7 (2 RTs)

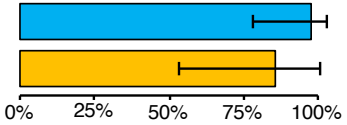
Ag/Ab Testing (Laboratory)

Reactive Ag/Ab
n=92

Non-reactive Ag/Ab
n=12

Reactive Ag/Ab
n=70

3 participants were missing one or more protocol-specified tests

Test Type	CAB HIV+ / Total Reactive	CAB PPV (95% CI)	TDF/FTC HIV+ / Total Reactive	TDF/FTC PPV (95% CI)		PPV (95% CI) Difference CAB vs TDF/FTC
	38/45	84% (71%,94%)	86/94	91% (84%,96%)		-7% (-21%, +7%)

 Reactive Rapid Test

 Non-reactive Rapid Test

 Reactive Ag/Ab Test

 Non-reactive Ag/Ab Test

CAB

TDF/FTC

Test Type	CAB HIV+ / Total Reactive	CAB PPV (95% CI)	TDF/FTC HIV+ / Total Reactive	TDF/FTC PPV (95% CI)		PPV (95% CI) Difference CAB vs TDF/FTC
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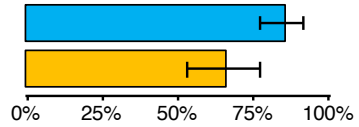
	42/64	66% (53%, 77%)	85/99	86% (77%, 92%)		-20% (-35%, -5%)

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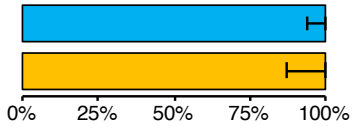
	27/27	100% (87%,100%)	65/65	100% (94%,100%)		0% (-14%, +6%)

Reactive Rapid Test | Non-reactive Rapid Test | Reactive Ag/Ab Test | Non-reactive Ag/Ab Test | CAB | TDF/FTC

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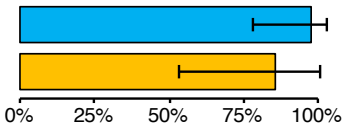
	10/12	**83% (52%, 98%)**	**20/21**	**95% (76%, 100%)**		**-12% (-42%, +11%)**

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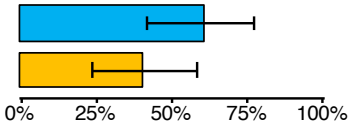
	14/36	**39% (23%, 57%)**	**20/34**	**59% (41%, 75%)**		**-20% (-46%, +6%)**

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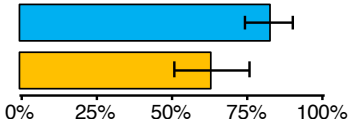
/	43/70	61% (49%, 73%)	86/107	80% (72%, 87%)		-19% (-34%, -4%)

Reactive Rapid Test

Non-reactive Rapid Test

Reactive Ag/Ab Test

Non-reactive Ag/Ab Test

CAB

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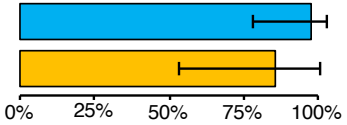
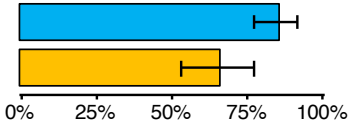
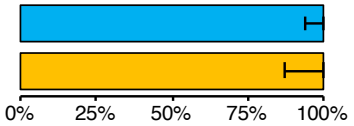
	38/45	84% (71%,94%)	86/94	91% (84%,96%)		-7% (-21%, +7%)
	42/64	66% (53%, 77%)	85/99	86% (77%, 92%)		-20% (-35%, -5%)
	27/27	100% (87%,100%)	65/65	100% (94%,100%)		0% (-14%, +6%)
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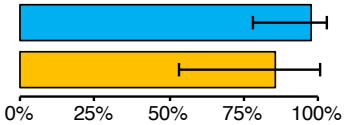
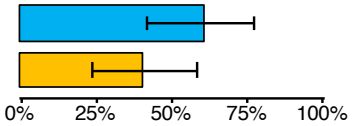
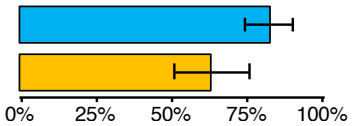
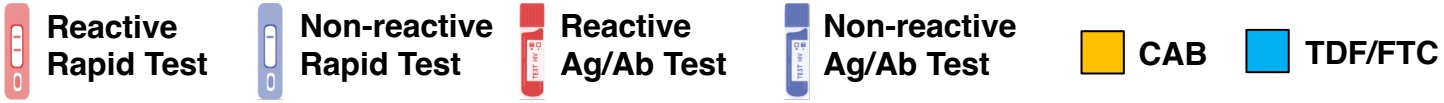
	10/12	83% (52%, 98%)	20/21	95% (76%, 100%)		-12% (-42%, +11%)
	14/36	39% (23%, 57%)	20/34	59% (41%, 75%)		-20% (-46%, +6%)
	43/70	61% (49%, 73%)	86/107	80% (72%, 87%)		-19% (-34%, -4%)



CONCLUSIONS

- **A reactive RT plus a reactive Ag/Ab test, or two reactive RTs had robust PPV**
- **Combinations of reactive RTs and Ag/Ab tests had high PPV, and non-reactive combinations of RT and Ag/Ab tests had high NPV in the context of MSM/TGW PrEP**
  - **In settings where sensitive VL testing is not available or feasible, RT and Ag/Ab tests, when concordant, are sufficient screening in the setting of CAB-LA PrEP**
  - **RT and Ag/Ab tests have excellent performance in the setting of TDF/FTC PrEP**
- **Prospective evaluation of sensitive VL screening for PrEP failure is ongoing in HPTN 083 and 084 OLE's**

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- Statistical Center for HIV/AIDS Research and Prevention (SCHARP)
- Leadership and Operations Center, FHI 360
- HPTN Leadership

Pharmaceutical Support

- ViiV Healthcare
- Gilead Sciences, Inc.

HPTN 083 Study Team

Community Program Managers
Community Educators &
Recruiters, CAB Members

Our 43 Sites in 7 countries

Ryan Kofron

And most of all, our Study Participants