

Performance characteristics of HIV RNA screening with CAB-LA PrEP in HPTN 083

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Disclosures

Raphael J. Landovitz reports consulting agreements and/or Scientific Advisory roles for Gilead Sciences, Merck Inc, RedQueen Therapeutics, and ViiV Healthcare (Financial Interest)

- **HPTN 083 is an ongoing phase 3 study of CAB-LA vs daily oral TDF/FTC for PrEP in cisgender men and transgender women**
 - **Stopped early by DSMB for superiority of CAB-LA; continues as an open-label extension (OLE)**
 - **CAB-LA approved by US FDA and other global regulatory agencies**
- **CAB-LA PrEP delays detection of HIV infection compared to standard HIV testing algorithms**
- **In retrospective analyses, RNA testing identified HIV infection earlier and often prior to INSTI resistance**
- **The OLE HIV testing algorithm was designed to evaluate whether prospective HIV RNA testing at each injection could reliably identify HIV infection earlier**

Analysis Period

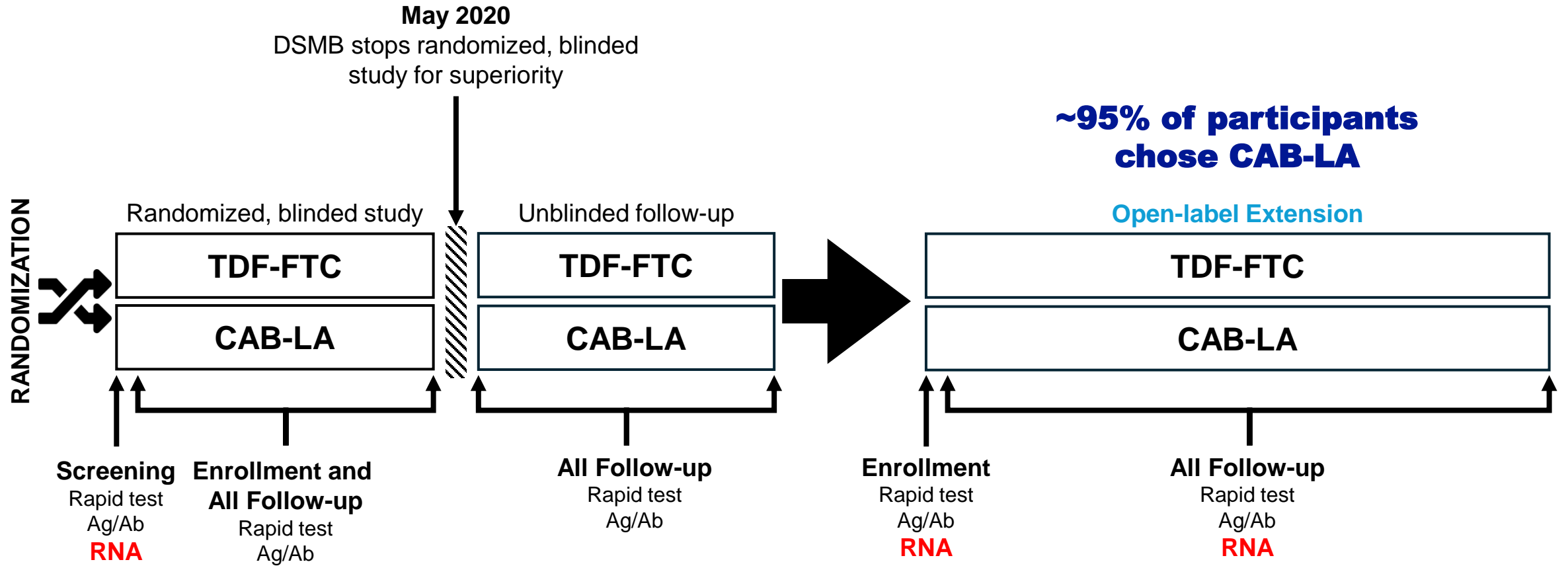
- OLE entry through November 30, 2023
 - OLE activation date varied by site

Testing Procedures in OLE (all visits)

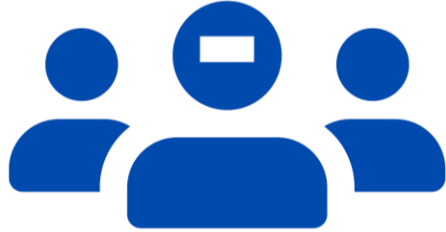
- Site-based rapid testing (RT), antigen/antibody testing (Ag/Ab), and HIV RNA testing
- HIV status determined by an independent committee that reviewed results from site testing and retrospective testing at a central laboratory
 - Review triggered by any positive/reactive HIV test result at site

In this preliminary analysis, we calculated the positive predictive value (PPV) and false positive rate (FPR) of isolated positive RNA results, and assessed the sensitivity of HIV RNA screening

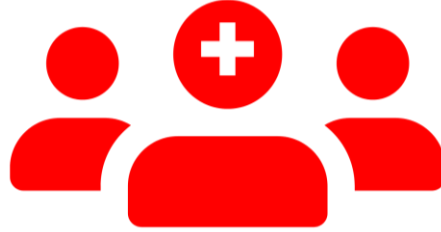
Study Design



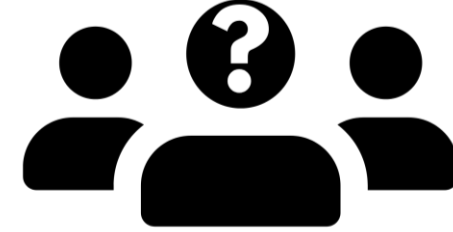
| | Participants | # of visits with an RNA screening test | Person-years of follow-up |
|--|--------------|--|---------------------------|
| Overall | 2,619 | 26,528 | 3,892 |
| Per participant median (min-max) | - - - | 12 (1-22) | - - - |
| Randomization Arm | | | |
| Cabotegravir | 1,334 | 13,268 | 1,998 |
| TDF/FTC | 1,285 | 13,260 | 1,894 |
| Region | | | |
| Africa | 72 | 519 | 141 |
| Asia | 525 | 5,716 | 801 |
| Latin America | 1,213 | 11,831 | 1,733 |
| United States | 809 | 8,462 | 1,217 |
| Participants choosing CAB in OLE | 2,483 | | |
| w/ Visits with CAB-LA in past 6m | 2,461 | 23,300 | 3,684 |
| w/ Visits with no CAB-LA in past 6m | 1,925 | 3,228 | 209 |



**ADJUDICATED
NEGATIVE**



**ADJUDICATED
POSITIVE**



**ADJUDICATION STATUS
NOT DETERMINED**



**POSITIVE HIV
RNA TEST**



**NEGATIVE HIV
RNA TEST**



**POSITIVE NON-RNA
HIV TEST**



**NEGATIVE NON-RNA
HIV TEST**



**NO CAB-LA W/ IN
THE LAST 6 MONTHS**

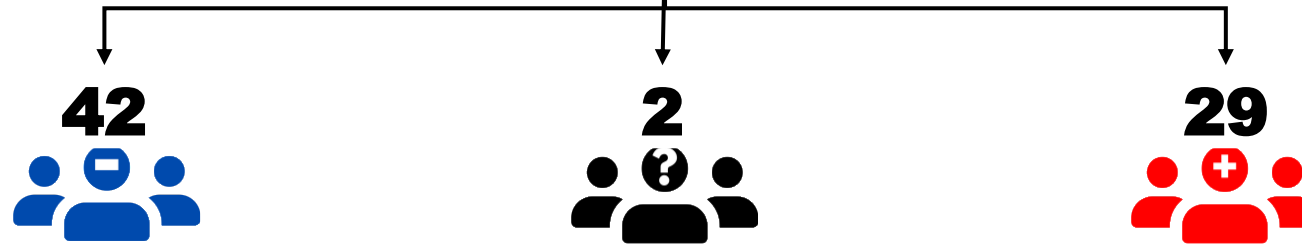


**CAB-LA W/ IN
THE LAST 6 MONTHS**

26,528

Visits with an RNA screening test at sites

73

 (One or more reactive/positive HIV test result)

ADJUDICATED
NEGATIVE



ADJUDICATED
POSITIVE



ADJUDICATION STATUS
NOT DETERMINED



POSITIVE HIV
RNA TEST



NEGATIVE HIV
RNA TEST



POSITIVE NON-RNA
HIV TEST



NEGATIVE NON-RNA
HIV TEST



NO CAB-LA W/ IN
THE LAST 6 MONTHS



CAB-LA W/ IN
THE LAST 6 MONTHS

26,528

Visits with an RNA screening test at sites

73

 (One or more reactive/positive HIV test result)

42



2



29



20



22



ADJUDICATED
NEGATIVE



ADJUDICATED
POSITIVE



ADJUDICATION STATUS
NOT DETERMINED



POSITIVE HIV
RNA TEST



NEGATIVE HIV
RNA TEST



POSITIVE NON-RNA
HIV TEST



NEGATIVE NON-RNA
HIV TEST



NO CAB-LA W/ IN
THE LAST 6 MONTHS

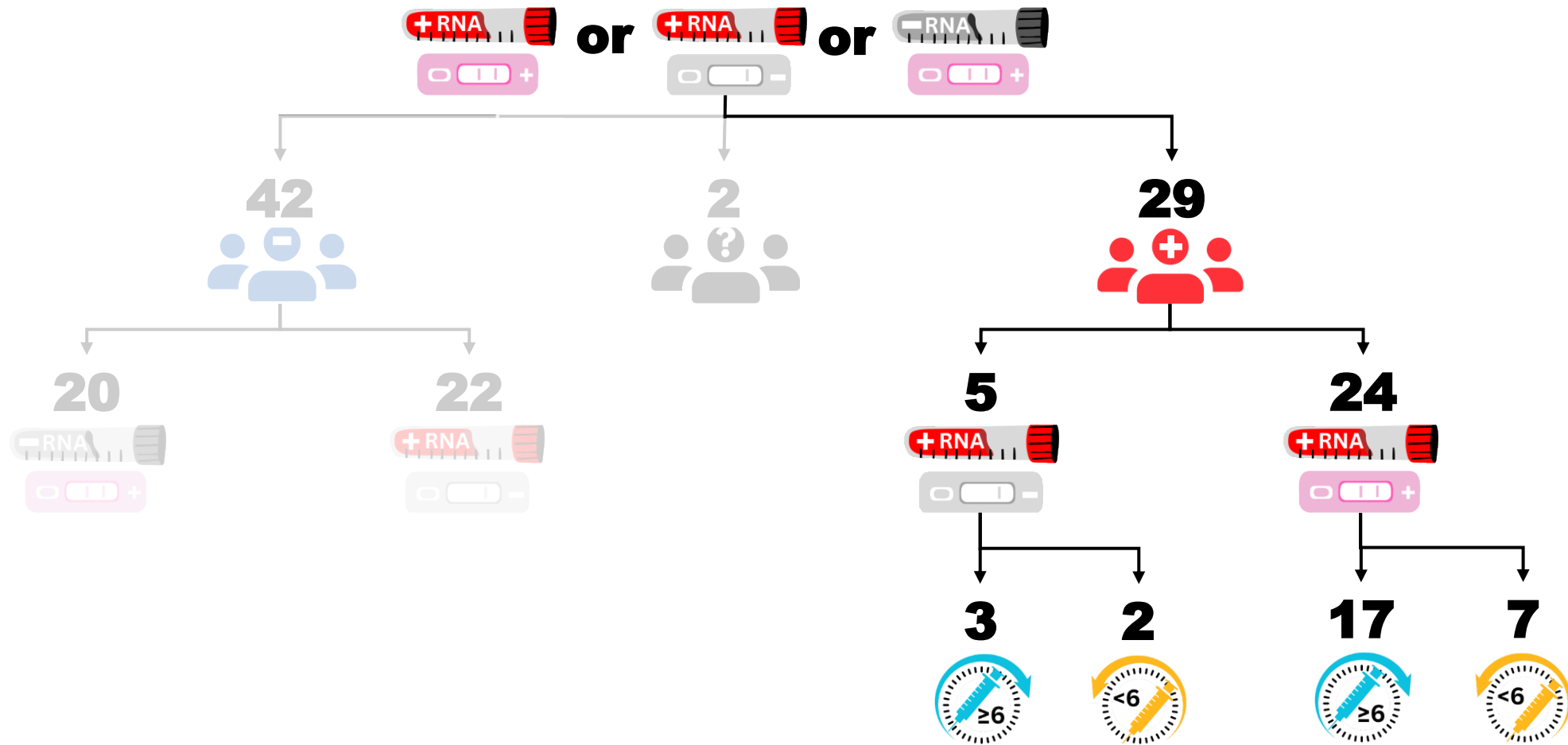


CAB-LA W/ IN
THE LAST 6 MONTHS

26,528

Visits with an RNA screening test at sites

73

 (One or more reactive/positive HIV test result)

| | | | | | | | | |
|--|---|---|--|---|---|---|---|---|
|  |  |  |  |  |  |  |  |  |
| ADJUDICATED NEGATIVE | ADJUDICATED POSITIVE | ADJUDICATION STATUS NOT DETERMINED | POSITIVE HIV RNA TEST | NEGATIVE HIV RNA TEST | POSITIVE NON-RNA HIV TEST | NEGATIVE NON-RNA HIV TEST | NO CAB-LA W/ IN THE LAST 6 MONTHS | CAB-LA W/ IN THE LAST 6 MONTHS |

26,528

Visits with an RNA screening test at sites


73

 (One or more reactive/positive HIV test result)

42



2



29



20



22




False positive

27

Isolated RNA-positive visits

5



True positive

24



3



2



17




7




ADJUDICATED
NEGATIVE




ADJUDICATED
POSITIVE



ADJUDICATION STATUS
NOT DETERMINED



POSITIVE HIV
RNA TEST



NEGATIVE HIV
RNA TEST



POSITIVE NON-RNA
HIV TEST



NEGATIVE NON-RNA
HIV TEST



NO CAB-LA W/ IN
THE LAST 6 MONTHS



CAB-LA W/ IN
THE LAST 6 MONTHS

PPV (95% CI)*



18.5%
(7.0%, 38.7%)



Overall

*Isolated positive RNA results
† RNA screening with other tests

| | PPV (95% CI)* | FPR (95% CI)* |
|--|-------------------------------|--------------------------------|
| | 18.5% (7.0%, 38.7%) | 0.08% (0.05%, 0.13%) |
| | 9.1% (1.6%, 30.6%) | 0.09% (0.05%, 0.14%) |
| | 60% (17%, 92.7%) | 0.06% (0.01%, 0.25%) |



Overall

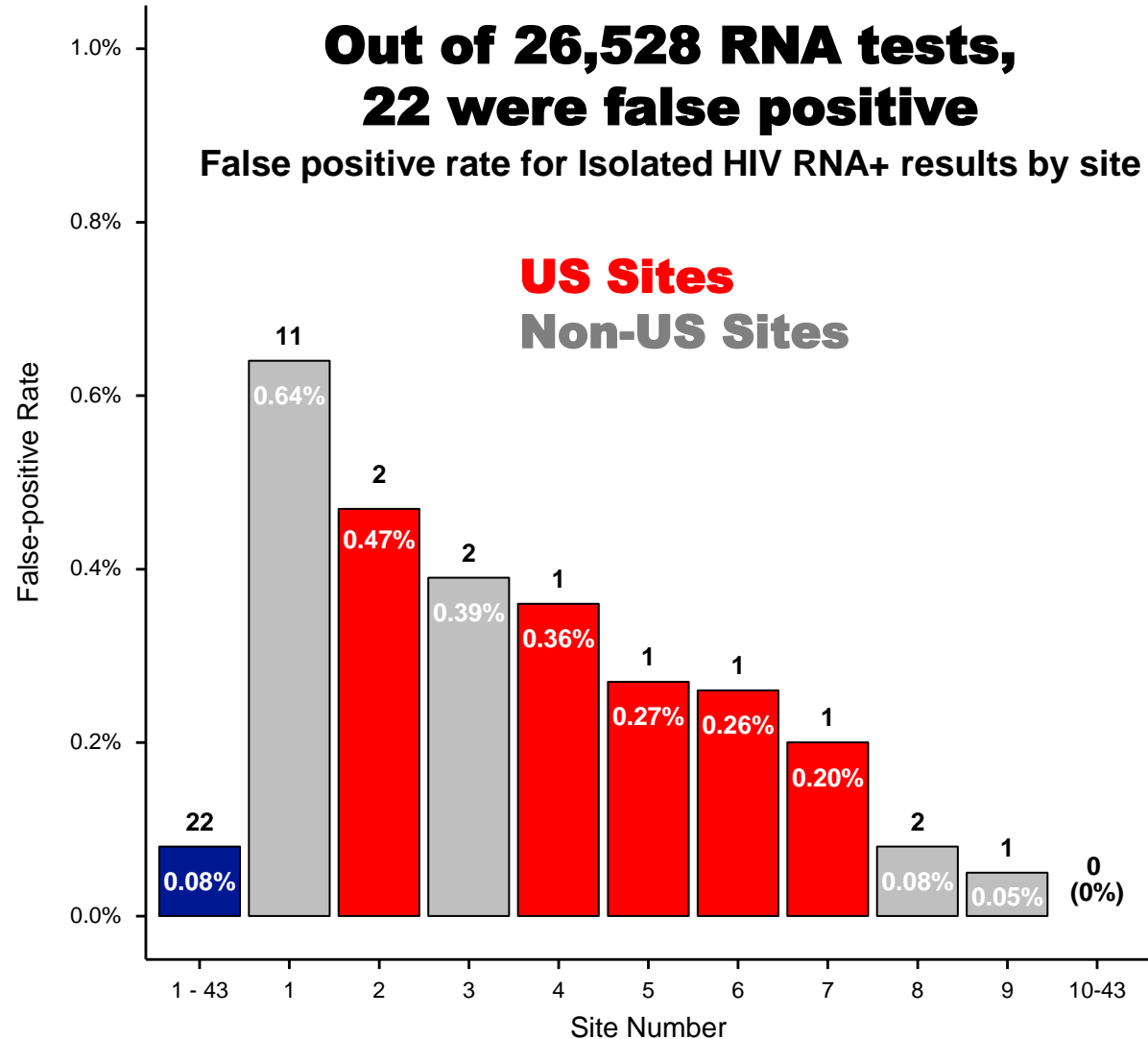


No CAB-LA w/ in the last 6 months



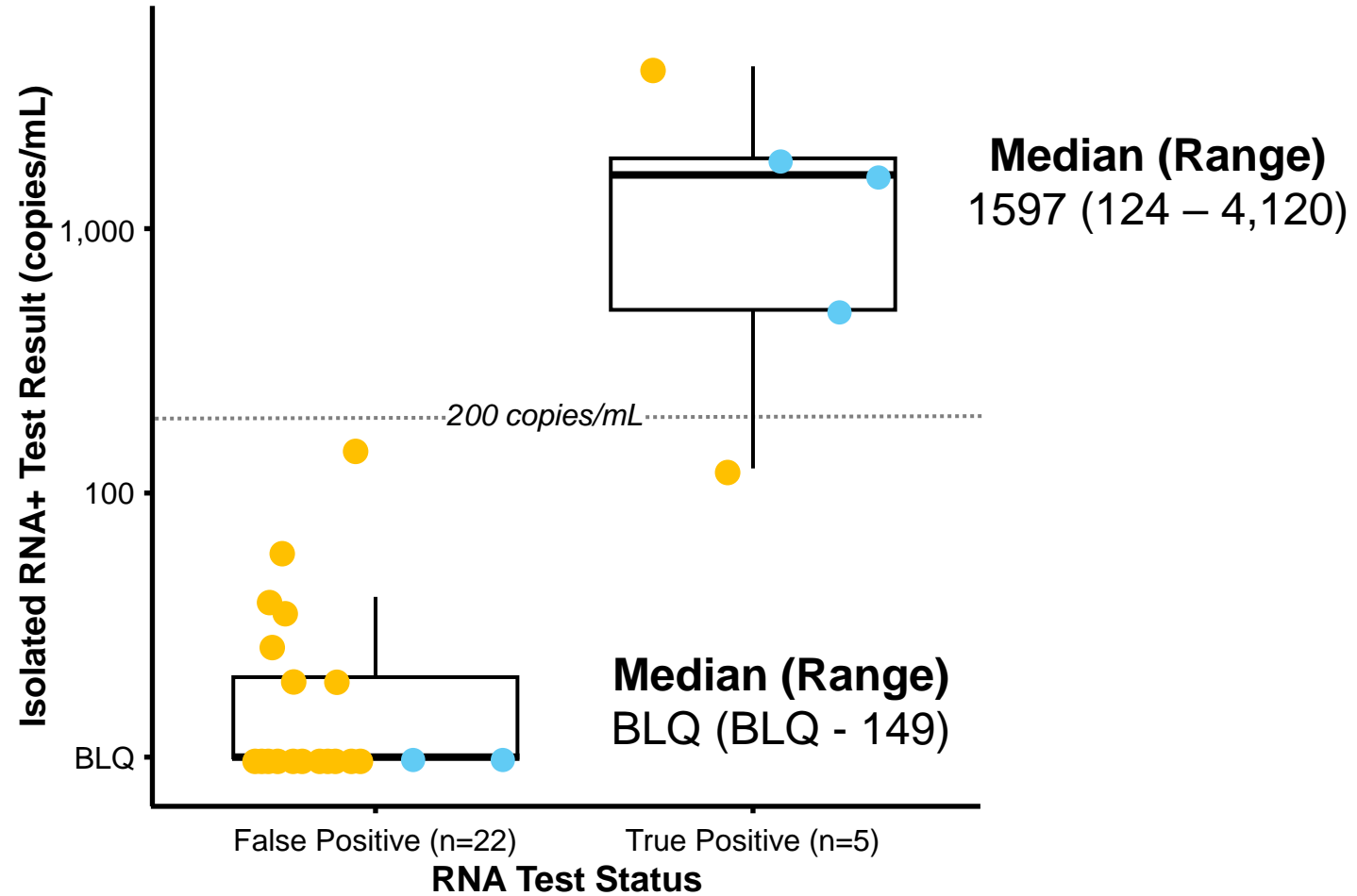
CAB-LA w/ in the last 6 months

Out of 26,528 RNA tests, 22 were false positive
False positive rate for Isolated HIV RNA+ results by site



*Isolated positive RNA results
† RNA screening with other tests

HIV viral load at isolated RNA-positive visits



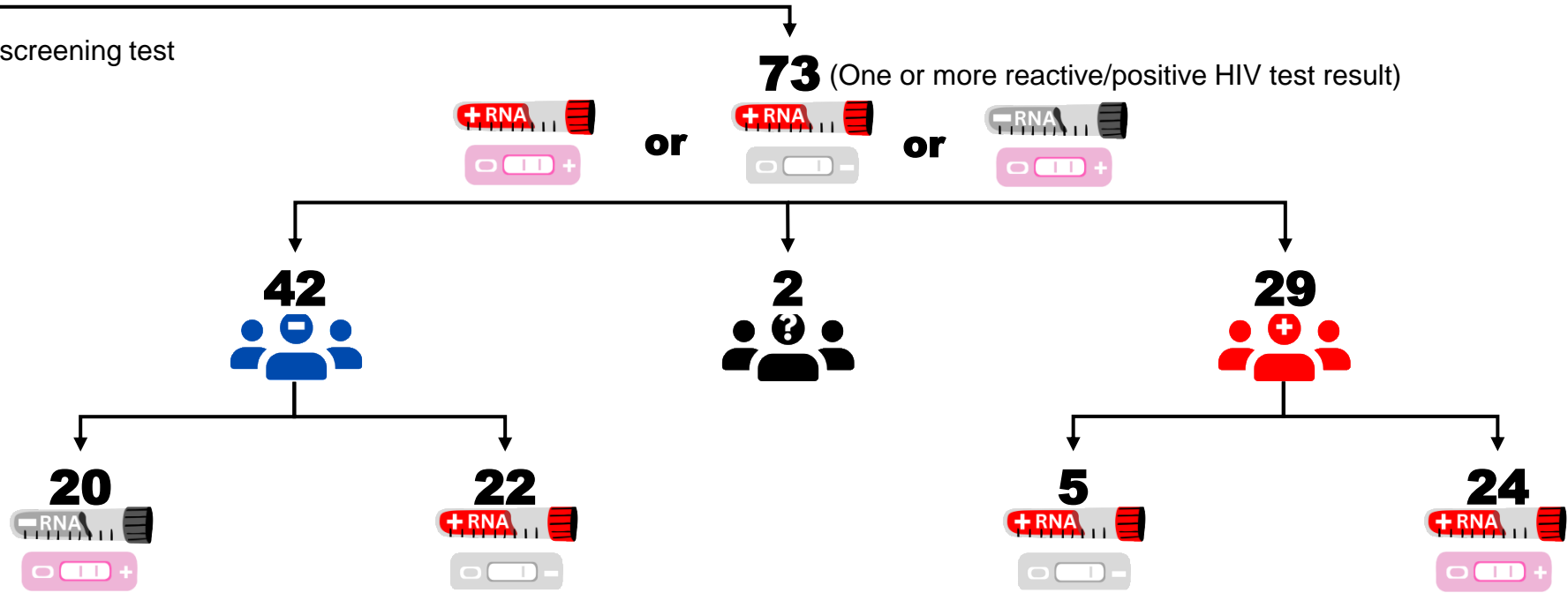
No CAB-LA w/ in
the last 6 months



CAB-LA w/ in
the last 6 months

26,528

Visits with an RNA screening test



ADJUDICATED
NEGATIVE



ADJUDICATED
POSITIVE



ADJUDICATION STATUS
NOT DETERMINED



POSITIVE HIV
RNA TEST



NEGATIVE HIV
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POSITIVE NON-RNA
HIV TEST



NEGATIVE NON-RNA
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NO CAB-LA W/ IN
THE LAST 6 MONTHS

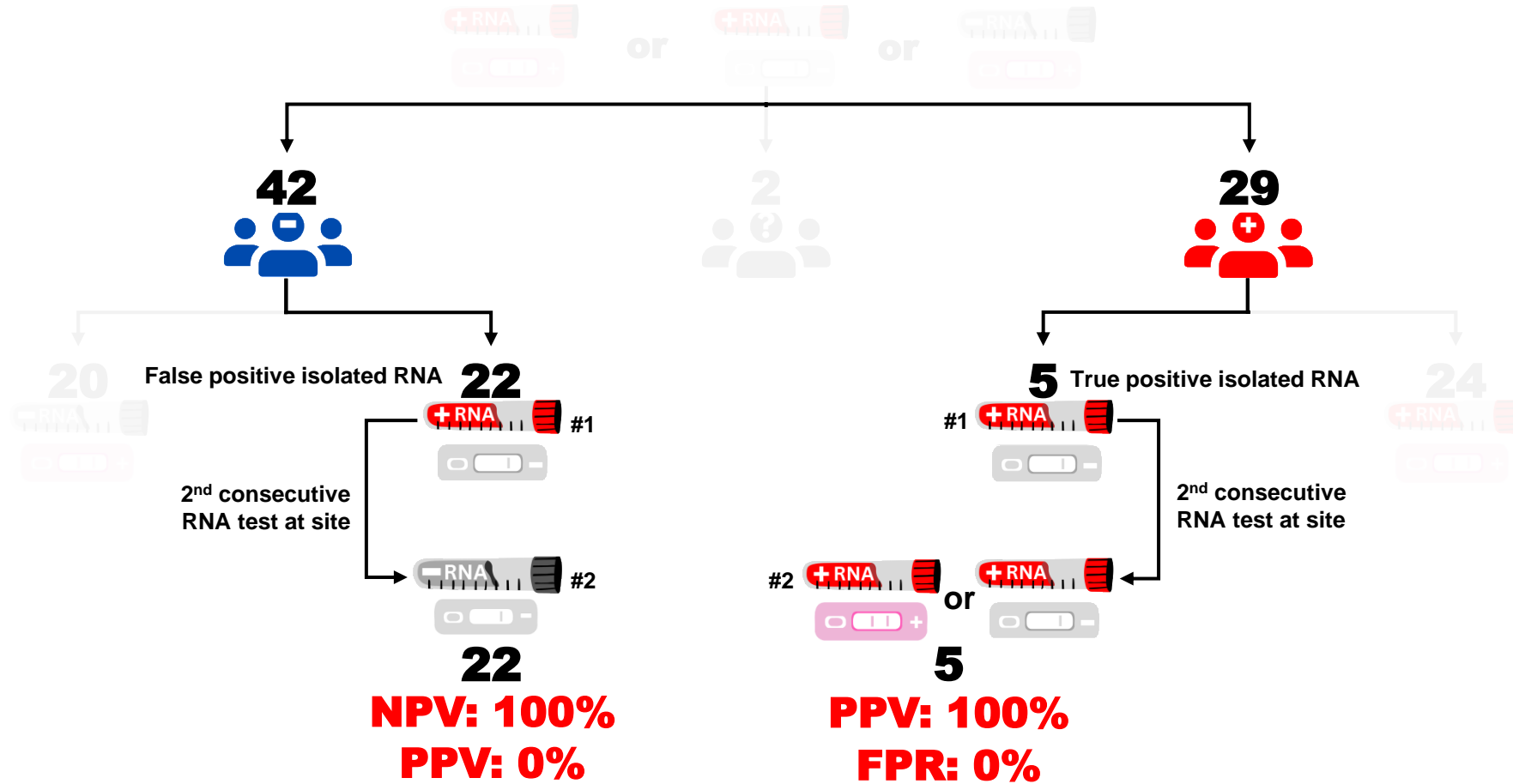


CAB-LA W/ IN
THE LAST 6 MONTHS

26,528

Visits with an RNA screening test at sites

73 (One or more reactive/positive HIV test result)



ADJUDICATED NEGATIVE

ADJUDICATED POSITIVE

ADJUDICATION STATUS NOT DETERMINED

POSITIVE HIV RNA TEST

NEGATIVE HIV RNA TEST

POSITIVE NON-RNA HIV TEST

NEGATIVE NON-RNA HIV TEST

NO CAB-LA W/ IN THE LAST 6 MONTHS

CAB-LA W/ IN THE LAST 6 MONTHS

26,528

Visits with an RNA screening test at sites

73 (One or more reactive/positive HIV test result)



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20

22

5

24

Negative Clinical Outcomes of false positive RNA testing

7

Subsequent CAB Delays
4 CAB-LA >70 days
2 Discontinued
1 26-day oral CAB gap

15

No CAB Delays

To date, none of these 7 individuals has evidence of HIV acquisition

Legend for clinical outcomes and test results:

- ADJUDICATED NEGATIVE
- ADJUDICATED POSITIVE
- ADJUDICATION STATUS NOT DETERMINED
- POSITIVE HIV RNA TEST
- NEGATIVE HIV RNA TEST
- POSITIVE NON-RNA HIV TEST
- NEGATIVE NON-RNA HIV TEST
- NO CAB-LA W/ IN THE LAST 6 MONTHS
- CAB-LA W/ IN THE LAST 6 MONTHS

- In this preliminary analysis, single isolated positive HIV RNA result at sites performed poorly for detecting HIV infection with CAB-LA PrEP
 - Performance was better without CAB-LA in the past 6 months
 - Repeat RNA testing was able to discriminate true from false positive cases
- Although infrequent, most single isolated positive RNA test results were false-positive results
- Guidelines for HIV testing algorithms for detecting HIV infections in the setting of long-acting PrEP should consider these performance characteristics

Sponsors

- U.S. National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Mental Health (NIMH), National Institute on Drug Abuse (NIDA), and the National Institute of Child Health and Human Development (NICHD) all components of the U.S. National Institutes of Health (NIH)
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HIV Prevention Trials Network (HPTN)

- Laboratory Center (Johns Hopkins University)
- SCHARP (Fred Hutchinson Cancer Research Center)
- Leadership and Operations Center (FHI360)

Pharmaceutical Support

- ViiV Healthcare
- Gilead Sciences, Inc.

HPTN 083 Study Team

Community Program Managers Community Educators & Recruiters, CAB Members

Our 43 study sites in 7 countries

And most of all, our study participants