Diagnostic Outcomes after Detectable HIV-1 RNA in Persons on CAB-LA PrEP in Routine Care in the U.S.

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Participants who had a single detected/reactive HIV RNA while on CAB-LA PrEP were not subsequently diagnosed with HIV infection and continued PrEP or resumed it after a short course of ART. One participant with HIV RNA detected in two separate, longitudinal samples was subsequently diagnosed with HIV, suggesting that more than one positive HIV RNA by standard clinical testing may indicate HIV infection, but larger studies are needed.

BACKGROUND

- Long-acting cabotegravir (CAB-LA) PrEP is highly effective but rare instances of HIV acquisition on CAB-LA have occurred in trials and clinical care.
- HIV diagnosis among persons on CAB-LA PrEP can be complicated by suppression of viremia, delayed seroconversion, and false-positive HIV RNA.
- We examined HIV detection, subsequent provider-selected ART or PrEP regimen, and diagnostic outcomes in individuals with detectable but unconfirmed plasma HIV RNA while on CAB-LA PrEP in routine care.

METHODS

- SeroPrEP is an observational study enrolling persons in the U.S. with evidence of potential HIV acquisition during use of PrEP modalities in routine care.
- This analysis includes persons receiving CAB-LA PrEP in routine care who had a detected/reactive HIV-1 RNA and non-reactive Ag/Ab test
  - Participants (ppt) subsequently enrolled in SeroPrEP
  - Ppts remained in routine care, with clinical test results and provider-selected PrEP or ART regimens obtained from records
  - Blood samples were collected for research assays with retrospective testing

Table 1. Laboratory Assays

Assay Type	Clinical Test Results Obtained from Records*	Research Tests in SeroPrEP (More Sensitive Detection)
Serology	4th Gen Lab-based Ag/Ab 4th Gen Rapid Ag/Ab	5th Gen Lab-Based Ag/Ab
HIV RNA	HIV-1/2 Qualitative RNA HIV-1 Quantitative RNA	Single Copy Assay (SCA); Limit of Detection $(LOD)_{95}$ ≥3 c/mL; LOD_{50} <0.7 c/mL
HIV DNA	HIV-1 DNA Qualitative	Cell-Associated HIV-1 LTR DNA (CAD) in 2.5x10⁴-5x10⁵ purified CD4⁺ T cells

* Clinical test selection per provider discretion. Not all tests performed for all participants.

RESULTS

Among 9 male participants on CAB-LA PrEP in routine care in this analysis:

- Median (range): age 33 (29, 56) years; BMI 26.5 (22.4, 41.8) kg/m²
- **7 ppt** (Ppts 1-2,4-8) with a single detectable HIV RNA on clinical testing:
  - Had repeat clinical testing and research assays without evidence of HIV
  - 3/7 temporarily switched to ART; 7/7 resumed or remained on PrEP after
- **1 ppt** (Ppt 3) with a single detectable HIV RNA on clinical testing:
  - Had <1 copy HIV RNA detected by SCA and 3 copies detected by CAD
  - Has remained on CAB-LA with negative clinical HIV tests to date (22 months)
- **1 ppt** (Ppt 9) with two detectable/reactive HIV RNA on separate clinical samples sample 1: HIV-1 qual reactive; sample 2: HIV-1 RNA <20 detected (3 days later)
  - Started ART rapidly; research assays without evidence of HIV
  - Paused ART after 5 months. 3 months later, HIV detected on two clinical HIV RNA tests (290 cp/ml and 140 cp/ml) and ppt resumed ART

Fig 1. Clinical HIV-1 RNA Levels and PrEP/ART Regimen History from the Time of CAB-LA PrEP Initiation

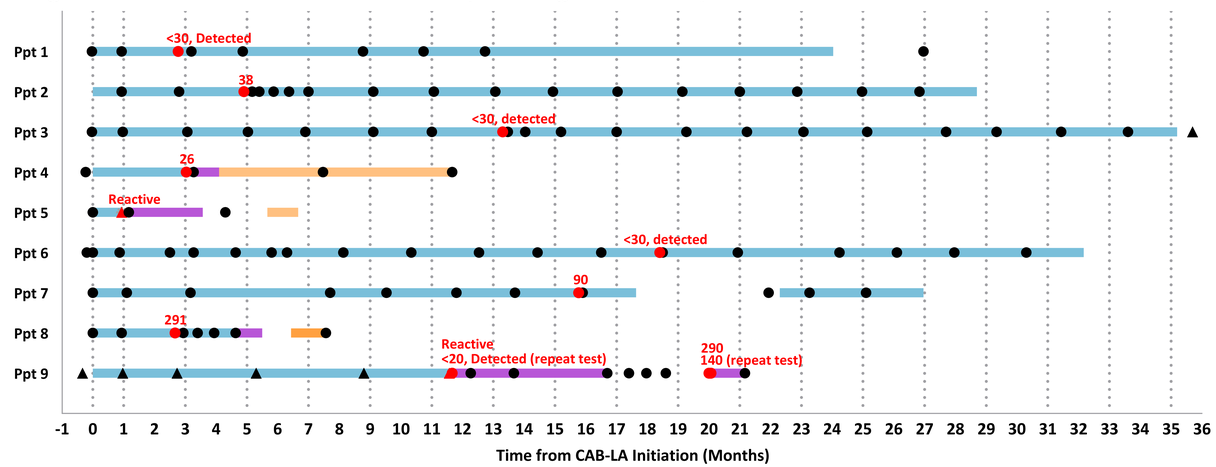


FIGURE KEY

HIV-1 RNA Levels
- ● Undetectable quantitative HIV-1 RNA (<20 or <30 cp/mL)
- ● Detectable quantitative HIV-1 RNA (Result listed on graph in cp/mL)
- ▲ Non-reactive qualitative HIV-1 RNA
- ▲ Reactive qualitative HIV-1 RNA

Antiretroviral Regimen Initiation or Continuation
- Injectable CAB-LA PrEP (Dosing intervals displayed with 56-day post-injection window or until ART initiated)
- DRV/c/F/TAF ART
- Oral F/TAF or F/TDF PrEP

Table 2. Clinical and Research Test Results at Time of Detectable HIV-1 RNA

Ppt	# CAB-LA Injections Prior to 1st Detectable HIV-1 RNA	Clinical Test Results			Research Test Results		Clinical Follow Up
		Ag/Ab	First Detectable HIV-1 RNA	First Repeat HIV-1 RNA (Days after first Detectable RNA)	CAD copies/CD4⁺ T cell equivalents (Days after first detectable RNA)	SCA (HIV-1 RNA copies/mL) (Days after first detectable RNA)	PrEP/ART Regimen After First Detectable HIV-1 RNA
1	2	NR	Detected, <30 cp/mL	ND (13)	ND/2.5x10⁴ (13)	ND (13)	CAB-LA PrEP
2	2	NR	38 cp/mL	ND (8)	ND/2.5x10⁵ (44)	ND (8)	CAB-LA PrEP
3	7	NR	Detected, <30 cp/mL	ND (5)	3/5x10⁵ (5) ND/3x10⁵ (25)	0.4 (5) ND (25)	CAB-LA PrEP
4	1	NR	26 cp/mL	ND (7)	ND/3.5x10⁵ (21)	ND (21)	DRV/c/F/TAF (15 days) → F/TDF PrEP
5	1	NR	Reactive (Qualitative)	ND (7)	ND/5x10⁶ (22)[a] ND/5x10⁴ (133)	ND (22) ND (133)	F/TDF
6	11	NR	Detected, <30 cp/mL	ND (3)	ND/5x10⁵ (13)	ND (13)	CAB-LA PrEP
7	8	NR	90 cp/mL	ND (4)	ND/5x10⁵ (63)	ND (28) ND (63)	Paused CAB-LA PrEP for 6.5 months (mo.), then restarted
8	2	NR	291 cp/mL	ND (8)	ND/3.5x10⁵ (58)	ND (58)	DRV/c/F/TAF (7 days), paused for 8.5 mo. then started F/TAF PrEP
9[b]	6	NR	Reactive (Qualitative)	Detected, <20 cp/mL (3)	ND/2.5x10⁵ (112)	ND (112) 11,933 (231)	DRV/c/F/TAF for 5 mo., paused ART for 3 mo., then restarted ART

[a]CAD was done on PBMC with 3 different targets (GAG, POL and LTR)
[b]Ppt 9 did not have Ag/Ab available at the time of initial or repeat HIV RNA testing or prior to ART start. Ag/Ab was NR 21 days after initial detected HIV RNA. One injection (day 77) was outside of injection window.

CONCLUSIONS

- Of 9 individuals with a detectable plasma HIV-1 RNA while on CAB-LA PrEP in routine clinical care in the U.S., only 1 was subsequently diagnosed with HIV.
  - One other individual had retrospective plasma HIV-1 RNA and DNA detection by research assays at a single time point and remained on LA-PrEP.
- Two separate sample collections with detected or reactive HIV RNA on standard clinical testing should increase clinical suspicion for HIV diagnosis.
- Larger studies are needed to assess the utility and cost of diagnostic testing strategies to resolve ambiguous HIV test results and to inform clinical management of LA-PrEP.

PLAIN LANGUAGE SUMMARY

Sometimes it can be difficult to determine if someone has acquired HIV while on long-acting PrEP because PrEP can suppress detection of HIV or antibody responses to HIV. In this small study, a single positive HIV RNA test was not enough on its own to determine that a person had HIV. One individual who had two positive clinical HIV RNA tests was confirmed to have HIV. More than one positive HIV RNA test may indicate HIV infection, but larger studies are needed.

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