Characterization of HIV Acquisitions on Long-Acting Cabotegravir PrEP from ImPrEP CAB Brasil

987

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BACKGROUND

- HIV acquisition during long-acting cabotegravir (CAB) PrEP is rare but poses significant challenges for HIV detection and monitoring within prevention programs.
- We present the first analysis of HIV-1 acquisitions on CAB PrEP in routine public health settings in Brazil.

METHODS

- ImPrEP CAB Brasil is an implementation study of same-day CAB initiation at oral PrEP clinics in individuals aged 18-30 years across 6 Brazilian cities.
- Individuals are enrolled after negative Ab RDT and undetectable Gene Xpert.

Point-of-Care Tests
Antibody (Ab) Rapid Diagnostic Test (RDT)
Gene Xpert

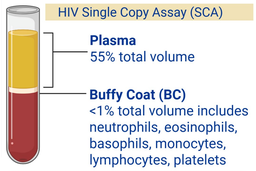
Retrospective Testing at Local Lab
HIV-1 RNA (Roche COBAS)
Ab/Antigen (Ag) RDT
4th gen Abbott Architect
Sanger Sequencing (if HIV-1 confirmed)
Geenius (with any positive/detectable test)

Research Tests (Sensitive Detection)
5th gen BioPlex Ag/Ab
Single Copy Assay (SCA), LOD ≥3 c/mL
Cell-Associated HIV LTR DNA Assay (CAD)
Single Genome Sequencing of *int* (SGS)
Whole HIV-1 Genome NGS (WGS)

Frozen plasma, serum, PBMC and/or buffy coat shipped to the University of Pittsburgh for specialized testing.



ImPrEP Study Sites



Cell-Associated DNA Assay (CAD) performed from 1 mL of buffy coat.

RESULTS

Table 1. Participant Characteristics, Concomitant Infections, and Self-Reported Behavioral History

	Pt A	Pt B	Pt C	Pt D
Participant Characteristics				
Age, in years	25	25	19	19
Sex	Male	Male	Male	Male
Population	MSM	MSM	MSM	MSM
Sexually Transmitted Infection (STI) Screening at Study Enrollment (Prior to CAB-LA Initiation)/At Time of or After HIV-1 Confirmation				
Syphilis	Neg/Neg	Neg/Treated	Neg/Neg	Neg/Neg
CT/NG	Neg/Neg	Pos/Neg	Pos/Neg	Neg/Pos
HBV	Neg/Neg	Neg/Neg	Neg/Neg	Neg/Neg
HCV	Neg/Neg	Neg/Neg	Neg/Neg	Neg/Neg
Self-Reported Behavioral History in the Past Six Months				
Condomless anal intercourse	Yes	Yes	Yes	Yes
Number of partners	1[a]	10	8	5

[a] Partner reported to be living with HIV with detectable HIV-1 RNA levels

In an implementation study of long-acting cabotegravir PrEP across six Brazilian cities, only 4 HIV-1 acquisitions occurred among 1,220 participants, characterized by low-level viremia, delayed antibody seroconversion (2–9 months after detectable RNA), and infrequent integrase resistance, confirming very high PrEP effectiveness. Rare breakthrough infections were detected by sensitive assays, highlighting the need for better point-of-care diagnostics.

Table 2. Serology, HIV-1 RNA and/or DNA Results at Each CAB-LA PrEP Injection

			CAB-LA Injection	1	2	3	4	5	6	7	8	
PPT	Test Type	Test Name		M0	M1	M3	M5	M7	M9	M11	M13	M13.1
A	Serology	Ab RDT		NR	NR	NR	NR	NR	R			
		Geenius		Neg	Neg	Neg	-	-	Inconcl.			
		Ag/Ab RDT		NR	NR	NR	NR	NR	NR			
		Abbott Architect		NR	NR	NR	NR	NR	NR			
		BioPlex		NR	NR	NR	NR	NR	-			
	HIV-1 RNA	Gene Xpert (cp/mL)		TND	-	-	-	-	49			
		Gene Xpert (2X) (cp/mL)		-	-	-	-	-	63			
		Roche COBAS (cp/mL)		<20,det.	<20,det.	51.1	TND	TND	102			
		Roche COBAS (2X) (cp/mL)		TND	26.8	-	-	-	182			
		Single Copy Assay (cp/mL)		TND	-	-	-	-	-			
	HIV-1 DNA	LTR CAD (cp/5x10^6 cells)		TND*	3	4	-	-	3			
B	Serology	Ab RDT		NR	NR	NR	NR	NR	NR	NR	NR	NR
		Geenius		-	-	-	-	-	-	-	Neg	Neg
		Ag/Ab RDT		NR	NR	NR	NR	NR	NR	NR	-	NR
		Abbott Architect		NR	NR	NR	NR	NR	NR	NR	R	R
		BioPlex		-	-	-	-	-	-	NR	NR	Ab R
	HIV-1 RNA	Gene Xpert (cp/mL)		TND	-	-	-	-	-	-	-	≥40
		Roche COBAS (cp/mL)		TND	TND	TND	TND	TND	TND	TND	655	28
		Roche COBAS (2X) (cp/mL)		-	-	-	-	-	-	-	490	-
		Single Copy Assay (cp/mL)		-	-	-	-	-	-	TND	-	-
	HIV-1 DNA	LTR CAD (cp/5x10^6 cells)		-	-	-	-	-	-	-	-	11
C	Serology	Ab RDT		NR	NR	NR	NR	NR	NR	NR	NR	NR
		Geenius		-	-	-	-	-	-	Neg	Inconcl.	Pos
		Ag/Ab RDT		NR	NR	NR	NR	NR	NR	NR	NR	NR
		Abbott Architect		NR	NR	NR	NR	NR	NR	NR	R	R
		BioPlex		-	-	-	-	-	-	NR	Ab R	-
	HIV-1 RNA (c/mL)	Gene Xpert (cp/mL)		TND	-	-	-	-	-	-	-	≥40
		Gene Xpert (2X) (cp/mL)		-	-	-	-	-	-	-	-	23,700
		Roche COBAS (cp/mL)		TND	TND	TND	TND	TND	TND	<20,det.	79,500	55,100
		Roche COBAS (2X) (cp/mL)		-	-	-	-	-	-	<20,det.	-	-
		Single Copy Assay (cp/mL)		-	-	-	-	-	-	1.9	-	-
	HIV-1 DNA	LTR CAD (cp/5x10^6 cells)		-	-	-	-	-	-	-	343	-
D	Serology	Ab RDT		NR							R	
		Geenius		-							Pos	
		Ag/Ab RDT		NR							Ab R	
		Abbott Architect		NR							R	
	HIV-1 RNA	Gene Xpert (cp/mL)		TND							≥40	
		Gene Xpert (2X) (cp/mL)		-							481,000	
		Roche COBAS (cp/mL)		-							1,140,000	

Loss to follow-up for 407 days.
No injections received after initial injection.

*Limited sampling depth due to poor DNA recovery (1x10^6 BC cells assayed)

Point-of-Care | Local Lab | Research

Abbreviations: cp, copies; CT/NG, Chlamydia trachomatis/Neisseria gonorrhoeae; det., Detected; HBV, hepatitis B; HCV, hepatitis C; M, month; MSM, men who have sex with men; Neg, Negative; NR, Non-Reactive; Pos, Positive; Pt, participant; R, Reactive; TND, Target Not Detected; -, no data

Table 3. HIV Drug Resistance Mutations by Standard and Sensitive Genotyping

PT (Month)	Sanger Genotype Gene Region: mutation	Mutation (frequency in genomes sequenced) by SGS or WGS
A (M9)	Not done – HIV-1 RNA too low	SGS: S230R (accessory) (100%, 7/7)
B (M13)	NRTI: none; NNRTI: K103N; PI: none; INSTI: none	SGS: No mutations (100%, 53/53)
C (M13)	NRTI: none; NNRTI: none; PI: none; INSTI: Q148QR, N155NH	WGS: L74I (100%); Q148R (50%); N155H (53%)
D (M13)	NRTI: none; NNRTI: K103N; PI: none; INSTI: none	Not done – no sample available

RESULTS, con't

Among 1220 participants (ppt) enrolled in the ImPrEP incidence cohort between 11/2023-9/2024, 4 HIV-1 acquisitions occurred on CAB (all MSM, ages 19–25).

- **Ppt A**: HIV-1 RNA retrospectively detected at CAB initiation (<20 cp/mL); not detected by SCA, repeat RNA
  - CAD not detected (in 1x10^6 buffy coat cells) until M1
  - RDT reactive at month 9 post-CAB initiation
- **Ppt B, C**: HIV-1 RNA 1.9 – 655 at time of detection
  - CAD detected (in 11 – 343 cp/5x10^6 buffy coat cells)
  - RDT non-reactive at time of HIV diagnosis; retrospectively found to be reactive by BioPlex, Architect, and/or Geenius
- **Ppt D:** HIV-1 RNA detected 13 months after CAB initiation and no subsequent injections.

SUMMARY/CONCLUSIONS

- Among 4 CAB-LA PrEP users in Brazil who acquired HIV-1, 3 had HIV-1 RNA <1000 c/mL at diagnosis, and delayed Ab detection (2-9 months after first detectable RNA).
- Major INSTI mutations were observed only in 1 individual despite continued use of CAB prior to HIV confirmation.
- These findings confirm CAB's high efficacy for PrEP and the rarity of breakthrough infections, while underscoring the need for sensitive point-of-care diagnostics and additional data on responses to INSTI-based ART in such clinical scenarios.

PLAIN LANGUAGE SUMMARY

Long-acting injectable cabotegravir PrEP was highly effective in an implementation study of same-day CAB initiation. Rare HIV-1 infections were difficult to detect, suggesting better point-of-care HIV testing methods may be needed.

Acknowledgements: This project was made possible thanks to Unitaid's funding and support. Unitaid accelerates access to innovative health products and lays the foundation for their scale-up by countries and partners. Unitaid is a hosted partnership of WHO.

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