Low Rate of HIV Acquisition on Cabotegravir Pre-Exposure Prophylaxis in OPERA: Possible Long-Acting Early Viral Inhibition Observed

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OPERA® the longitudinal cohort

IDWeek 2026

Oct. 21-24, 2026 | Washington, D.C.

Disclosures

- Research grants: Gilead Sciences, Merck, GSK/ViiV Healthcare
- Speaker honoraria: Gilead Sciences, Merck, GSK/ViiV Healthcare
- Advisory board participation: Gilead Sciences, GSK/ViiV Healthcare, Epividian

This study was supported by ViiV Healthcare

Objectives

1. Estimate the rate of HIV acquisition on cabotegravir long-acting (CAB LA) for PrEP

2. Characterize people diagnosed with HIV on CAB LA PrEP, with a focus on Long-Acting Early Viral Inhibition presentation

Cabotegravir Long-Acting (CAB LA) PrEP



1st long-acting injectable PrEP option



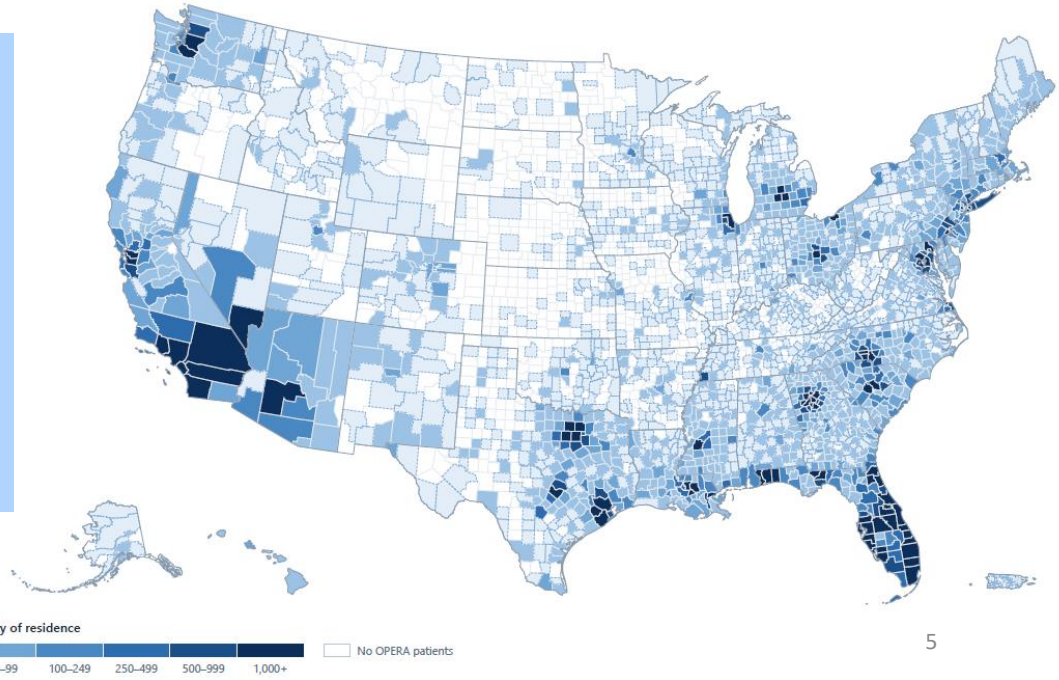
Approved in December 2021 for adults and adolescents, without restriction by exposure route



Superior efficacy compared to daily oral TDF/FTC in cisgender men, cisgender women and transgender women

The Observational Pharmaco-Epidemiology Research & Analysis Cohort

- Collaboration between Epividian and providers since 2013
- Cohort of electronic health records from routine care in primary care clinics and wellness centers throughout the US
- 101 clinics in 23 US states & territories
- > 870,000 people without HIV

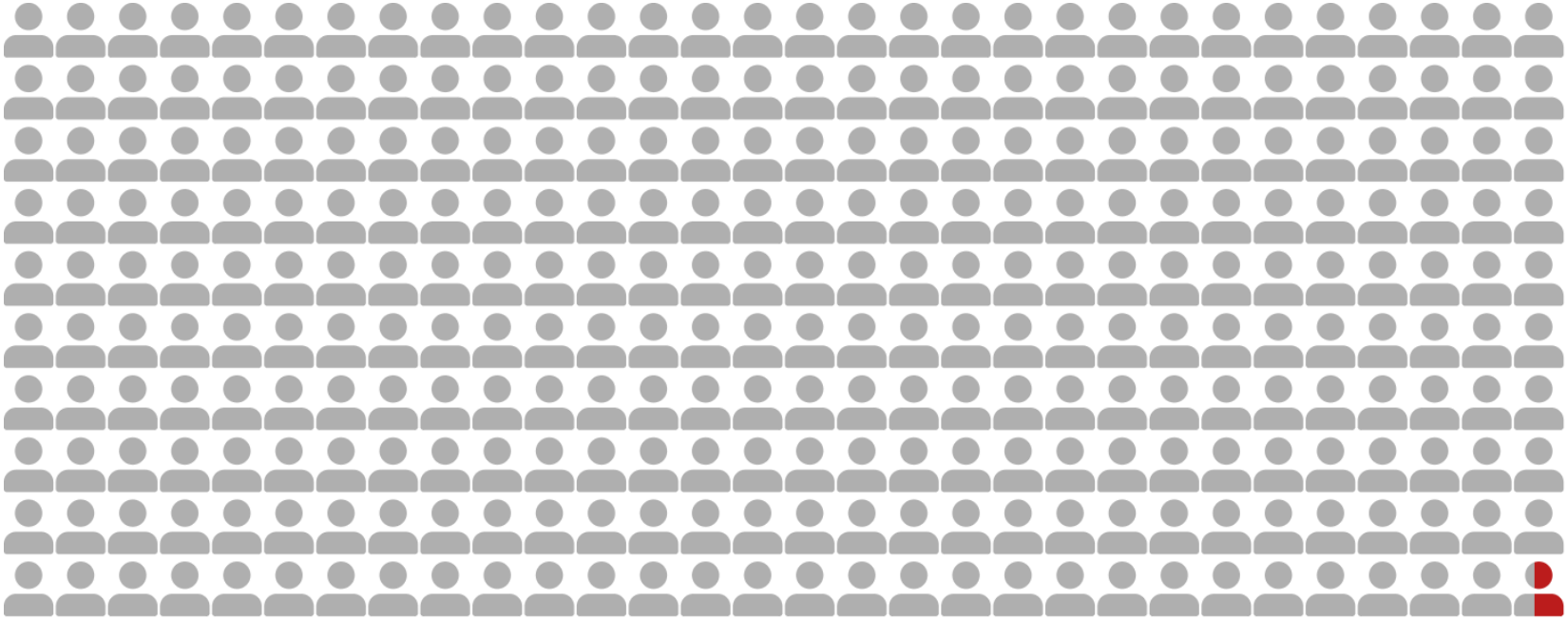


Study Population

Inclusion Criteria	Censoring Criteria
◆ ≥18 years old ◆ No indication of HIV ◆ 1st CAB LA PrEP injection between December 20, 2021 and June 30, 2025 ◆ Did not participate in CAB LA PrEP clinical trials	◆ CAB LA PrEP discontinuation ◆ Lost to follow-up ◆ Death ◆ End of observation period (December 31, 2025)

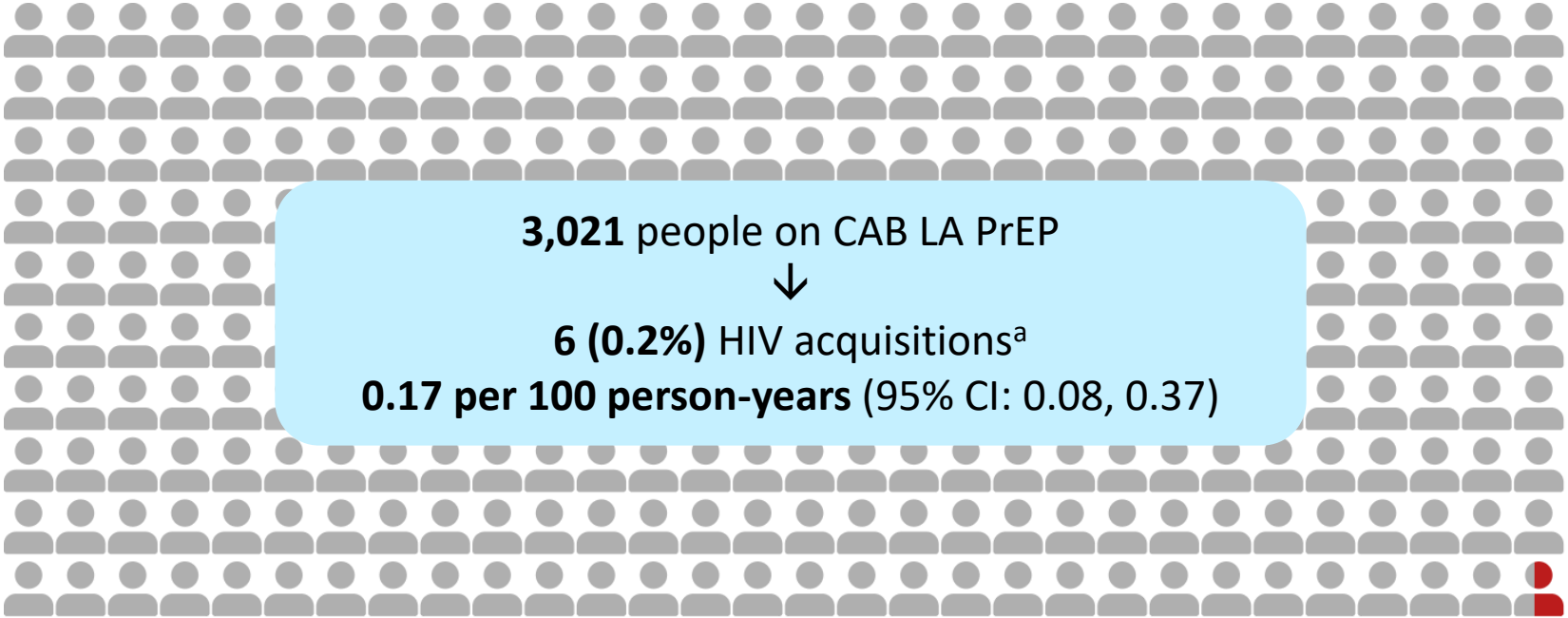
HIV Acquisition on CAB LA PrEP

HIV Acquisition



≈ 10 people on CAB LA PrEP

HIV Acquisition



[a] Includes 2 individuals who have been presented in previous OPERA publications

Characteristics of Individuals who Acquired HIV

	Acquired HIV N = 6[a]
Male	n = 6
Age	Median: 27 (IQR: 23, 53)
Black race	n = 3
Any RNA testing ≤1 week before/at 1st injection	n = 4[b]
Only serology testing ≤1 week before/at 1st injection	n = 1
Every injection received on time	n = 6
Weeks from 1st injection to HIV diagnosis	Median: 44 (IQR: 13, 92); range: 4 to 114
Viral load at HIV diagnosis (copies/mL)	Median: 1,134 (IQR: 209, 1,968)

[a] Includes 2 individuals who have been presented in previous OPERA publications

[b] Prevalent infection cannot be ruled out in 2 individuals without RNA testing at initiation

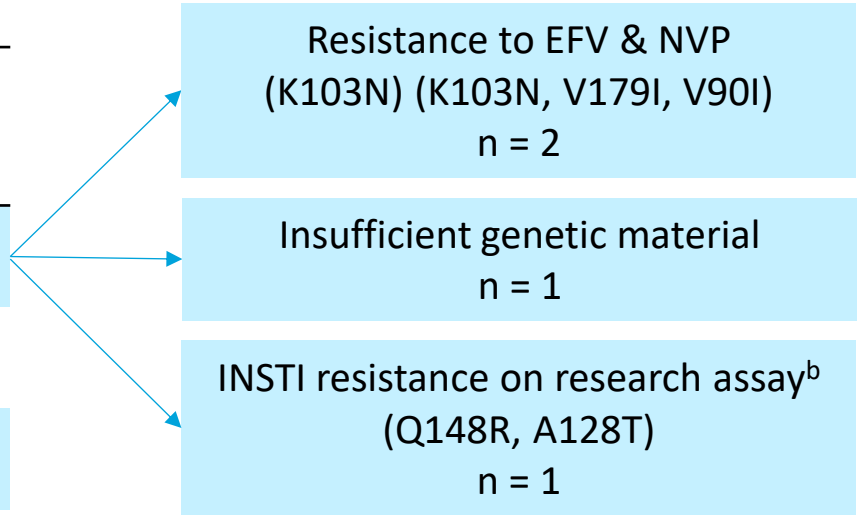
Post HIV Diagnosis

	Acquired HIV N = 6[a]
Observed virologic suppression	n = 4
Awaiting VL testing during ART	n = 1
Transferred care after Dx	n = 1
Observed failure to suppress	n = 0

[a] Includes 2 individuals who have been presented in previous OPERA publications

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[b] This result was not recorded in the EHR. Result from research assay published in Koss, et al. *Open Forum Infect Dis* 2024; 11(9):ofae468

Post HIV Diagnosis

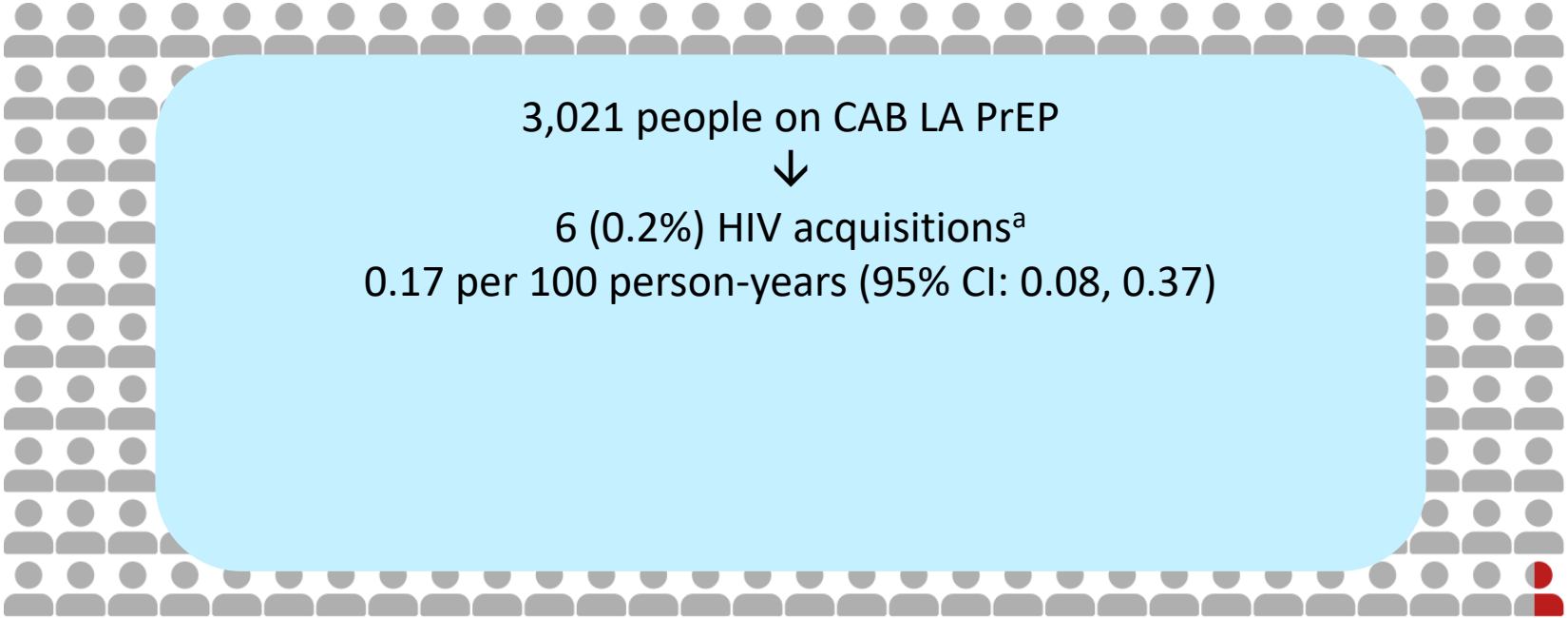
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→ Resistance to 1st gen INSTI, reduced susceptibility to 2nd gen INSTI (Q148Q/K/R, N155N/H, E92E/G)

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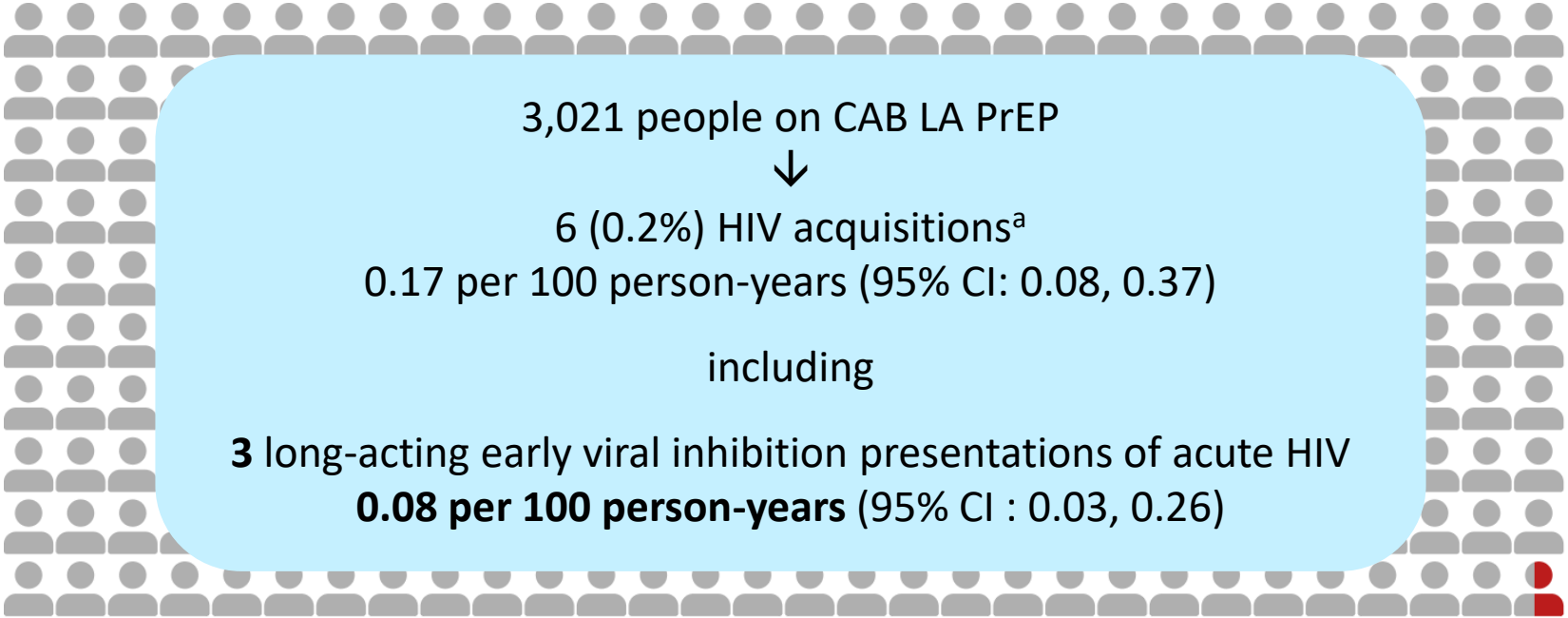
HIV Acquisition with Possible Long-Acting Early Viral Inhibition

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Long-Acting Early Viral Inhibition

1st described in 17/41 (41%) people who acquired HIV among 3,446 participants randomized to CAB LA PrEP (HPTN 083-084)*

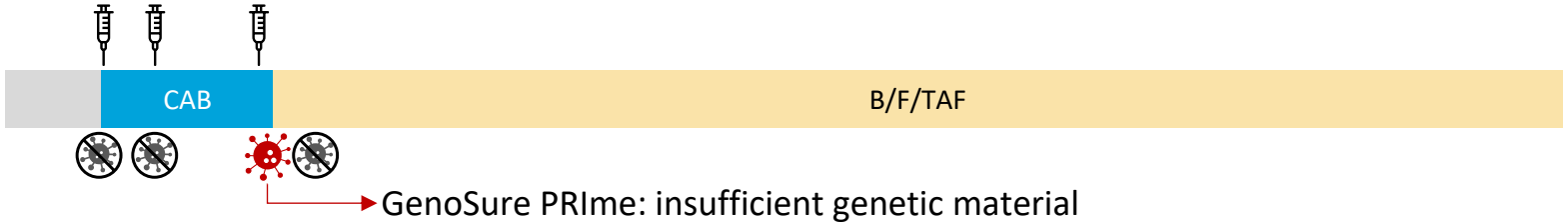
Long-acting early viral inhibition presentation

- Symptoms: minimal, varied, often none reported
- HIV RNA: low or undetectable
- Antibody production: reduced or delayed
- Testing: commonly revert from positive to negative
- Occurs with HIV acquisition both before and after PrEP initiation

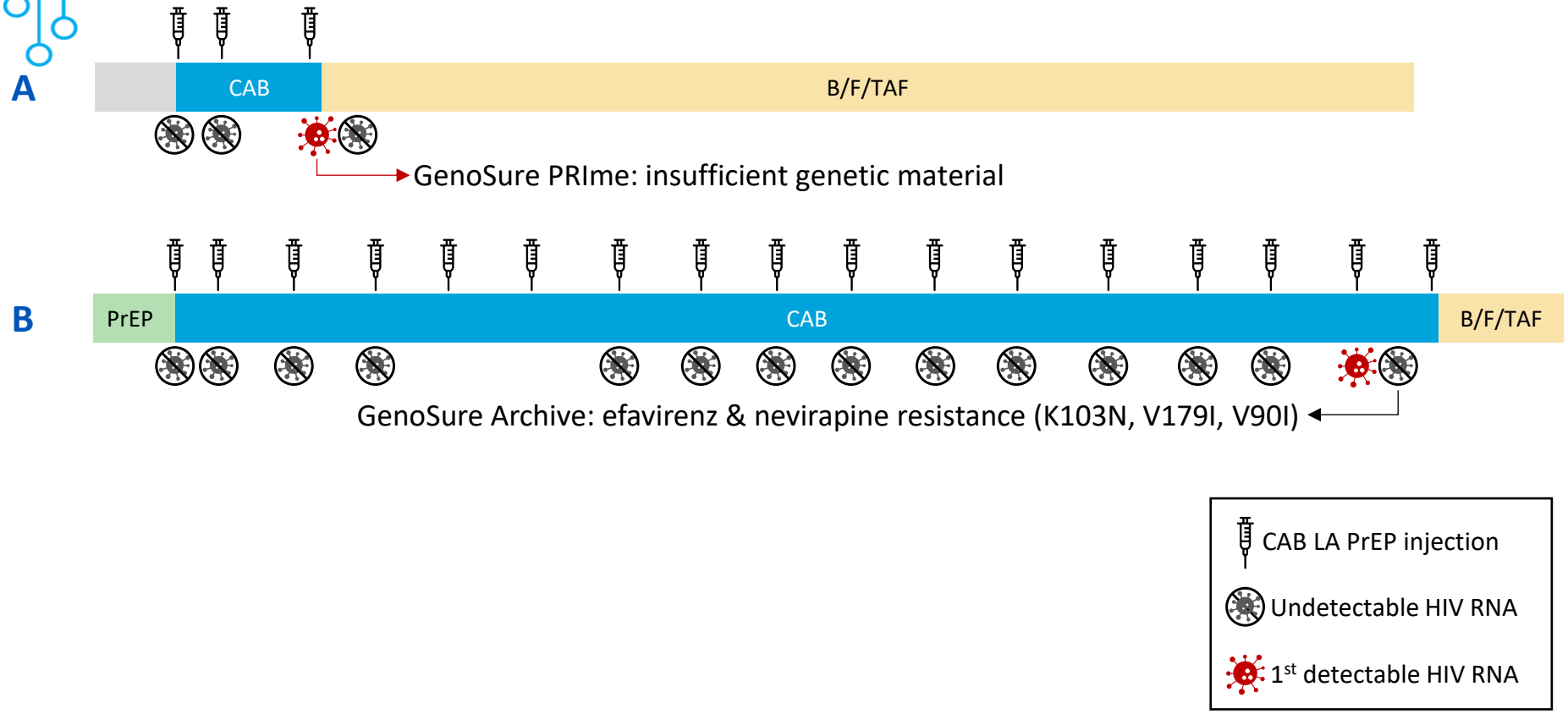
*Landovitz RJ, et al. Features of HIV Infection in the Context of Long-Acting Cabotegravir Preexposure Prophylaxis. *N Engl J Med 2024; 391(13):1253–1256.*

3 Individuals with Possible Long-Acting Early Viral Inhibition

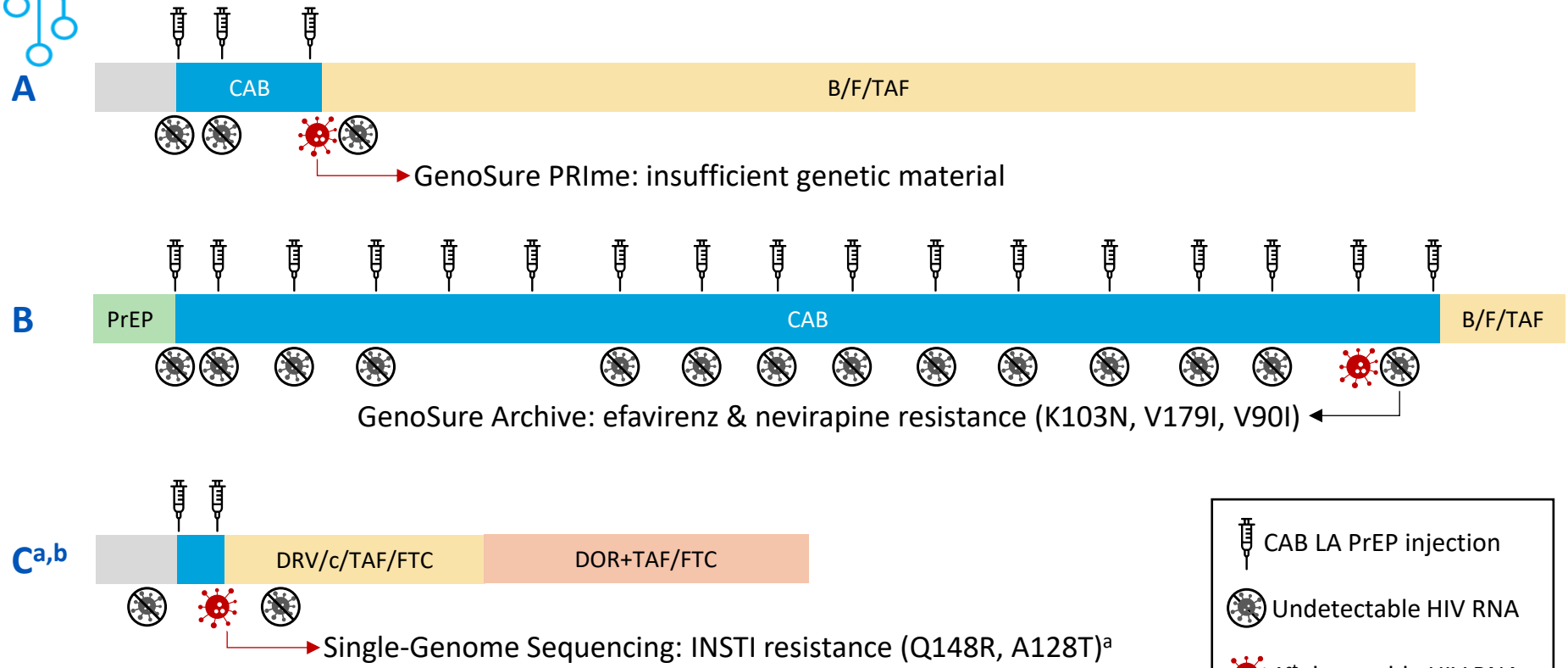
A



3 Individuals with Possible Long-Acting Early Viral Inhibition



3 Individuals with Possible Long-Acting Early Viral Inhibition



[a] Published as a case report: Koss, et al. *Open Forum Infect Dis* 2024; 11(9):ofae468.

[b] Prevalent HIV cannot be ruled out

Summary of Virologic and Serologic Features

Among Individuals with Possible Long-Acting Early Viral Inhibition

Person	Injections	RNA at start	HIV Dx	Post Dx
A	3 on time	D0: RNA-	D96: RNA = 2,018 D99: RNA = 3,767	D99: Start ART; D113: Suppressed; D99-720: Ab/Ag-
B	17 on time	D0: RNA-	D801: RNA = 130 D807: RNA = 80	D856: Start ART, suppressed, Ab/Ag-
C[a]	2 on time	D-20: RNA-[b]	D28: RNA = 447 D30: RNA = 410	D32: Start ART; D70: Suppressed D176: Ab-; D188: Ab+; D394: Ab-

[a] Published as a case report: Koss, et al. *Open Forum Infect Dis* 2024; 11(9):ofae468.

[b] Prevalent HIV cannot be ruled out

Key Findings



CAB LA PrEP is Highly Effective



6 HIV acquisitions out of 3,021 people on CAB LA PrEP (0.17 HIV acquisitions per 100 person-years)

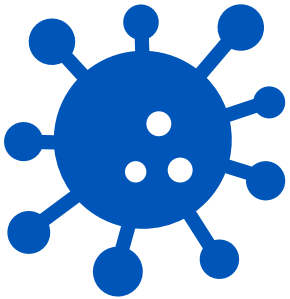
- Potential prevalent HIV in 2 individuals (1 with long-acting early viral inhibition), with uncertain timing of acquisition due to absence of RNA testing at start
- All individuals received every injection on time

Favorable treatment outcomes after HIV acquisition

- Virologic suppression achieved by 4 out of 4 with viral loads
- Out of 5 with genotyping, 2 had resistance mutations to INSTI and 2 had transmitted resistance to EFV & NVP

Presentation of Acute HIV on CAB LA PrEP Not Always Typical

3 out of 6 people with HIV had low RNA and negative serology at diagnosis, consistent with possible Long-Acting Early Viral Inhibition



Negative serology observed as far as 55, 366 and 624 days after RNA was detected

- HIV diagnosis could have been delayed if only serologic tests had been used
- Both CAB LA PrEP and rapid ART initiation can delay or blunt serologic response

Acknowledgements

This research would not be possible without the generosity of people on CAB LA PrEP, their OPERA caregivers, and the organizations that have contributed data to the OPERA cohort.

Authors: Karam Mounzer, Laurence Brunet, Ricky K. Hsu, Jennifer S. Fusco, Anthony Mills, Kevin R. Frost, Gerald Pierone Jr, Michael G. Sension, Philip C. Lackey, Adrienne Guignard, Bryn Jones, Annemiek de Ruiter, Vani Vannappagari, Gregory P. Fusco

We are grateful for the following individuals: Michael Stagner (programming), Bryan Stagner (QA), Bernie Stooks (data architecture), Lisa Lutzi & Nicole Shaw (data management/quality), and Judy Johnson& Quateka Cochran (clinical data categorization).

OPERA® the longitudinal cohort