# Uptake, adherence and effectiveness over four years of cabotegravir long-acting pre-exposure prophylaxis in the US OPERA Cohort

P013

Ricky K Hsu,[1] Laurence Brunet,[2] Anthony Mills,[3] Kevin R Frost,[2] Gerald Pierone,[4] Michael Sension,[5] Philip C Lackey,[6] Karam Mounzer,[7] Michael B Wohlfeiler,[8] Jennifer S. Fusco,[2] Todd McKeon,[9] Piotr Budnik,[10] Adrienne Guignard,[11] Vani Vannappagari,[9] Gregory P. Fusco[2]

[1]AIDS Healthcare Foundation, NYU Langone Medical Center, New York, New York, USA; [2]Epividian, Raleigh, NC, USA; [3]Men's Health Foundation, West Hollywood, CA, USA; [4]Whole Family Health Center, Vero Beach, FL, USA; [5]CAN Community Health, Fort Lauderdale, FL, USA; [6]No affiliation; [7]Philadelphia FIGHT, Philadelphia, PA, USA; [8]AIDS Healthcare Foundation, Miami, FL, USA; [9]ViiV Healthcare, Durham, NC, USA; [10]ViiV Healthcare, London, UK; [11]ViiV Healthcare, Wavre, Belgium;

## Background

- CAB LA PrEP for HIV prevention consists of 2 initiation injections given one month apart, followed by 1 maintenance injection every 2 months
  - Superior efficacy over daily oral TDF/FTC among cisgender women (HTPN 084), and cisgender men & transgender women who have sex with men (HTPN 083)[1,2]
  - High effectiveness in routine clinical care in the US[3-5]
  - In early real-world studies, most injections were administered on time, although many individuals experienced at least one late injection[3-5]

## Objective

Describe CAB LA PrEP use, effectiveness and adherence over its first 4 years of availability in the US

**Abbreviations:** **Ab**, antibody; **Ag**, antigen; **CAB LA**, cabotegravir long-acting; **CI**, confidence interval; **IQR**, interquartile range; **IR**, incidence rate; **N**, number; **PrEP**, pre-exposure prophylaxis; **STI**, sexually transmitted infection; **TDF/FTC**, tenofovir disoproxil fumarate/emtricitabine

## Methods

### Study Population

- OPERA Cohort: Prospectively captured, routine clinical data from electronic health records in the US (101 clinics, 23 US states/territories)
- Inclusion criteria: (a) ≥18 years old; (b) no evidence of HIV; (c) ≥1 CAB LA PrEP injection between December 20, 2021, and June 30, 2025
- Censoring criteria: first of (a) CAB LA PrEP discontinuation; (b) HIV acquisition; (c) death; (d) loss to follow-up (12 months without clinical contact); (e) study end (December 31, 2025)

### STI and HIV testing and diagnoses

- STI diagnoses:
  - New lab result or diagnosis consistent with syphilis, gonorrhea, chlamydia, trichomoniasis, genital warts
  - New lab result consistent with human papilloma virus, hepatitis B, hepatitis C, herpes simplex-2, without any known history prior to CAB LA PrEP start
  - Incidence rate for any STI diagnosis: unadjusted Poisson regression (person-time censored at first STI diagnosis)
- HIV testing:
  - Ab test, Ag/Ab test, RNA test (qualitative or quantitative)
  - Multiple HIV tests on the same day count as a single testing event
  - Incidence rate for all HIV testing events: unadjusted Poisson regression
- HIV diagnoses:
  - A chart review was conducted to confirm all positive HIV test results and diagnosis codes/title text
  - While timing of HIV acquisition cannot always be determined with precision, all individuals with a confirmed HIV diagnosis during CAB LA PrEP use were included
  - Incidence rate for HIV diagnosis: unadjusted Poisson regression

### Adherence Measures

- Complete initiation: received 2 initiation injections, ≤67 days apart
- Incomplete initiation: only the 1st injection was received with ≥68 days without an injection after the 1st
- Discontinuation: 2 injection cycles without an injection (≥128 days)
- On-time maintenance injection: injection received 53-67 days after the previous injection
- Late maintenance injection: injection received 68-127 days after the previous injection
  - Short delay not requiring reinitiation: injection received 68-97 days after the previous injection
  - Long delay requiring reinitiation: injection received 98-127 days after the previous injection

## Results

### Table 1. Characteristics at CAB LA PrEP start among people with ≥1 CAB LA injection (N = 3,021)

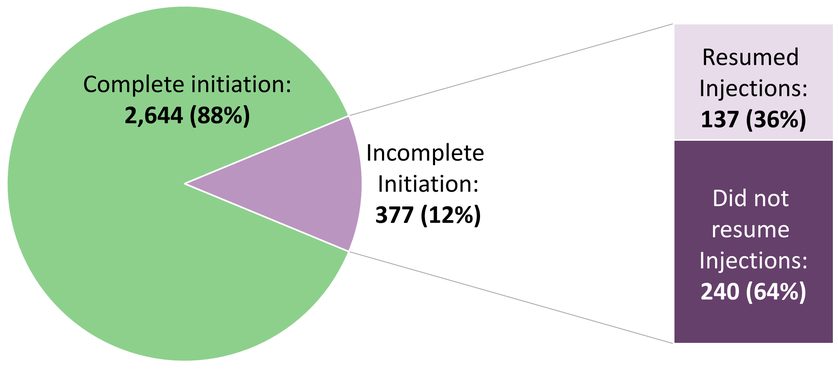
| | CAB LA PrEP users N = 3,021 |
|---|---|
| Age, n (%) | |
| 18-28 | 1,075 (36) |
| 30-39 | 1,102 (36) |
| 40-59 | 729 (24) |
| ≥60 | 115 (4) |
| Female sex, n (%) | 367 (12) |
| Transgender, n (%) | 210 (7) |
| Black Race, n (%) | 882 (29) |
| Hispanic ethnicity, n (%) | 875 (29) |
| Medicaid recipient, n (%) | 630 (21) |
| Medicare recipient, n (%) | 137 (4) |
| Any STI in the past 12 months, n (%) | 1,172 (39) |
| Any prior oral PrEP use, n (%) | 2,201 (73) |
| Any HIV test ≤1 week before/at the 1st injection, n (%) | 2,402 (80) |
| Both Ag/Ab & RNA tests, n (%) | 1,563 (65) |
| Ag/Ab test only, n (%) | 615 (26) |
| RNA test only, n (%) | 224 (9) |

### Table 2. STI diagnoses, HIV diagnoses and HIV testing during CAB LA PrEP use among people with ≥1 injection (N = 3,021)

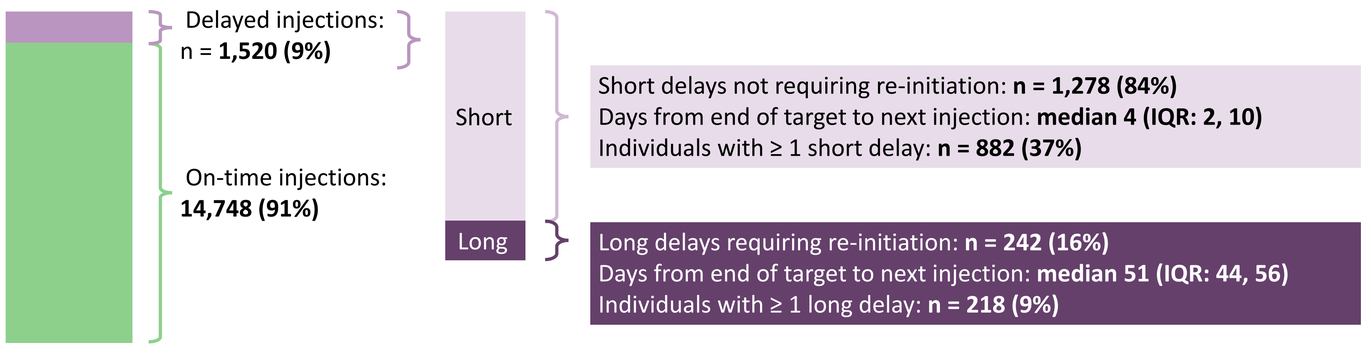
| | CAB LA PrEP users N = 3,021 |
|---|---|
| STI diagnosis during CAB LA PrEP use | |
| Individuals with any STI diagnosis, n (%) | 1,080 (36) |
| Syphilis, n (%)[a,b] | 470 (44) |
| Gonorrhea, n (%)[b] | 614 (57) |
| Chlamydia, n (%)[b] | 375 (35) |
| Other, n (%)[b,c] | 106 (10) |
| Person-years (censored at first STI) | 2,379 |
| IR per 100 person-years (95% CI) | 45.39 (42.77, 48.18) |
| HIV diagnosis during CAB LA PrEP use | |
| n (%) | 6 (0.2%)[d,e,f,g] |
| Months from first CAB LA PrEP injection to HIV acquisition, median (IQR) | 10 (3, 21) |
| Person-years | 3,572 |
| IR per 100 person-years (95% CI) | 0.17 (0.08, 0.37) |
| HIV testing during CAB LA PrEP use | |
| Tests per person, median (IQR) | 6 (3, 11) |
| Person-years | 3,572 |
| IR per person-year (95% CI) | 6.3 (6.2, 6.4) |

[a] Syphilis was identified through serology, and distinction between past and new infection may not have been possible
[b] STI categories are not mutually exclusive; percentages calculated out of people with any STI
[c] Human Papillomavirus and/or genital warts (5%), Herpes simplex-2 (3%), trichomoniasis (1%), hepatitis B virus (1%), hepatitis C virus (<1%)
[d] Includes 2 individuals who have been presented in previous OPERA publications (CROI 2024 & 2026, IDWeek 2024 & 2025, ACTHIV 2025)
[e] Includes 2 individuals with possible prevalent HIV infection (no RNA testing ≤ 1 week before/at CAB LA PrEP start)
[f] All received every injection on time
[g] First laboratory findings indicative of HIV acquisition observed on or within 1 week of a CAB LA PrEP injection

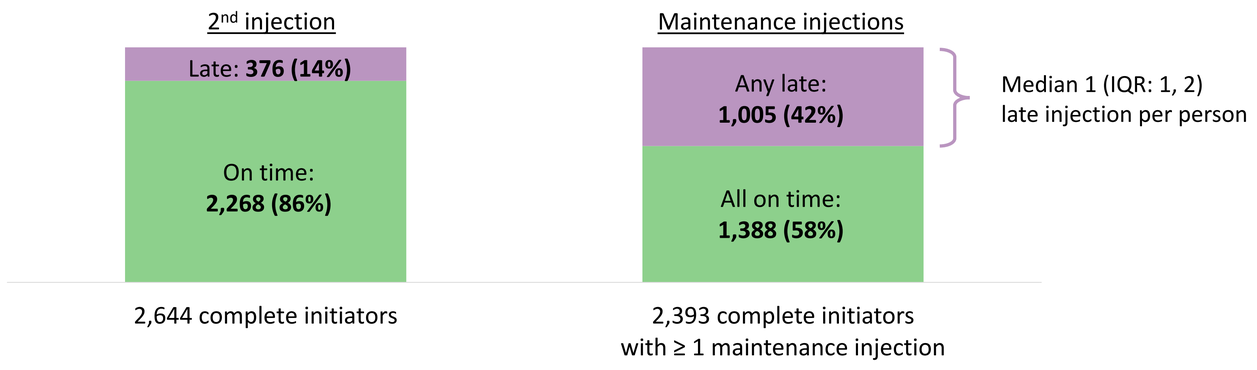
### Figure 1. Completion of the initiation sequence among people with ≥1 CAB LA injection (N = 3,021)




### Figure 2. Injection-level timing of maintenance injections (N = 16,268)




### Figure 3. Person-level timing of injections among complete initiators (N = 2,644)




### Table 3. Follow-up among complete initiators (N = 2,644)

| | Complete initiators N = 2,644 |
|---|---|
| Months of follow-up, median (IQR) | 13 (8, 22) |
| Number of injections (initiation & maintenance) received per person, median (IQR) | 7 (4, 11) |
| Received ≥1 maintenance injection, n (%) | 2,393 (90) |
| Discontinued, n (%) | 1,138 (43) |
| Months from 1st injection to discontinuation, median (IQR) | 10 (7, 15) |
| Resumed injections, n (%) | 237 (21) |
| Months from last injection to resumption, median (IQR) | 7 (5, 10) |

## Discussion

- Over the first 4 years of CAB LA PrEP use in the US, 3,021 individuals received ≥ 1 CAB LA PrEP injection in the OPERA cohort
  - Most were ≤39 years old and had a history or oral PrEP use; many had a recent history of STI **(Table 1)**
- Demonstrated CAB LA PrEP effectiveness despite ongoing risk of HIV exposure **(Table 2)**
  - Low rate of HIV acquisition: 0.17 HIV diagnoses per 100 person-years
  - High rate of STI diagnoses: 45 STI diagnoses per 100 person-years
  - High rate of HIV testing: 6.3 HIV tests per person-year
- High adherence to the dosing schedule
  - Most (91%) maintenance injections were received on time **(Fig 2)**
  - Delays tended to be short, with 84% of delayed injection not requiring re-initiation **(Fig 2)**
  - Although 42% of individuals experienced ≥ 1 late injection, delays were infrequent at the individual level, with a median of 1 late injection per person **(Fig 3)**
- CAB LA PrEP injections were resumed after an interruption by 36% of incomplete initiators **(Fig 1)** and 21% of discontinuers **(Table 3)**
  - Oral bridging use was not assessed because it is not consistently recorded in the electronic health records, which may lead to an overestimation of discontinuations
  - Reasons for interruption and resumption were not captured

## Key Findings

Over the first 4 years of CAB LA PrEP availability in the US:

- High effectiveness of CAB LA PrEP for HIV prevention, with a very low rate of HIV acquisition despite ongoing risk demonstrated by a high rate of STI diagnoses
- Excellent adherence to CAB LA PrEP injections, with rare injection delays tending to be short
- Continued interest in CAB LA PrEP, even after incomplete initiation or discontinuation, which may reflect the dynamic nature of PrEP needs over time

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### References

[1] Delany-Moretlwe (2022), *Lancet*. [2] Landovitz (2023), *The Lancet HIV*. [3] Traeger (2026), *J Acquir Immune Defic Syndr*. [4] Hsu (2026), *CROI*. [5] Elion (2026), *CROI*.

### Support

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Contact: Laurence Brunet; laurence.brunet@epividian.com