Cabotegravir LA for PrEP: Progress in HIV Prevention from Three Years of OPERA Data

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Background

- CAB LA was approved for HIV prevention by the FDA on 20DEC2021
  - 2 initiation injections administered one month apart, followed by 1 maintenance injection every 2 months
- CAB LA is highly effective at preventing HIV
  - Superior efficacy over daily oral TDF/FTC among cisgender men and cis- or transgender women in clinical trials
  - High effectiveness in routine clinical care in the US in early OPERA and TRIO cohort studies
- Adherence to the CAB LA injection schedule has been shown to be suboptimal in early real-world studies

Objectives

- To assess CAB LA PrEP usage and adherence over three years in the OPERA Cohort
- To estimate the real-world incidence of HIV acquisition during CAB LA PrEP use

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
  - ≥1 CAB LA PrEP injection between 21Dec2021 and 30Jun2024
  - No evidence of HIV prior to CAB LA PrEP initiation
  - ≥18 years old
- Censoring criteria
  - CAB LA discontinuation
  - Loss to follow-up (12 months after last clinical contact)
  - Death
  - Study end (31DEC2024)

CAB LA PrEP usage and adherence

- Complete initiation: 2 initiation injections received ≤67 days apart
- Adherence to maintenance injections schedule (Table 1)

Table 1. Patterns of maintenance injection dosing

	Time between injections
On-time maintenance injections	53-67 days
Late maintenance injections	68-127 days
Short delay not requiring reinitiation	68-97 days
Long delay requiring reinitiation	98-127 days
Discontinuation	>127 days

HIV acquisition

- Any new HIV diagnosis or positive HIV test result was assessed through chart review to confirm HIV acquisition after CAB LA PrEP initiation
- Incidence rate: univariate Poisson regression

Results

Figure 1. CAB LA PrEP usage in the OPERA cohort

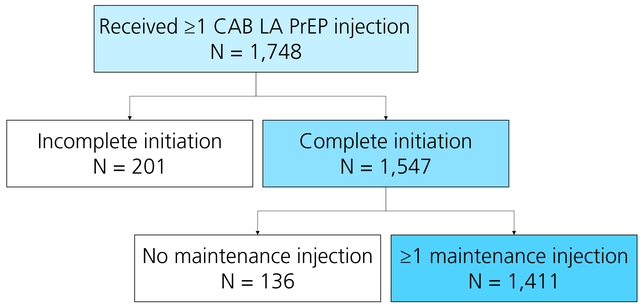


Table 2. Characteristics at the time of the first injection

	CAB LA PrEP recipients N=1,748
Age	Median: 33 (IQR: 27, 40)
Women	200 (11%)
Transgender	150 (9%)
Race	
Black	477 (27%)
White	885 (51%)
Other/unknown	386 (22%)
Hispanic ethnicity	514 (29%)
BMI ≥30 kg/m^2	435 (25%)
Any STI in previous 12 months	693 (40%)

Table 3. Follow-up among complete initiators

	Complete initiators N=1,547
Months from first injection to censoring	Median: 13 (IQR: 9, 19)
Total number of injections	11,068
Number of injections per person	Median: 7 (IQR: 4, 10)

Table 4. CAB LA PrEP discontinuation among complete initiators

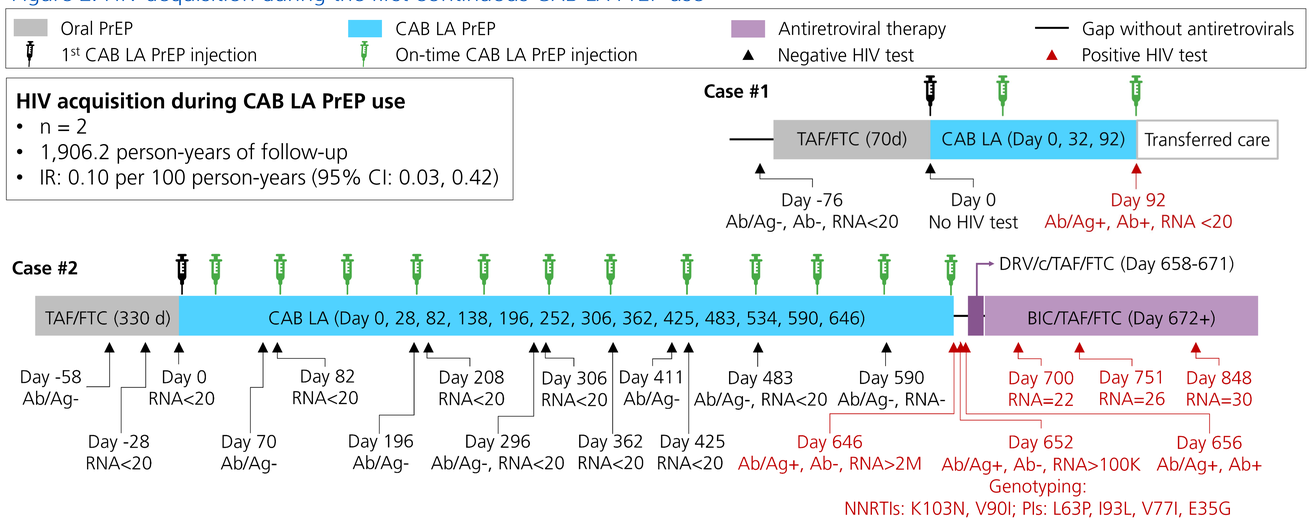
	Complete initiators N = 1,547
Discontinuation	488 (32%)
Resumption of CAB LA PrEP injections after discontinuation	138 (28%)
Months without injection[a]	Median: 7 (IQR: 5, 10)

[a] Potential oral bridging could not be assessed due to incomplete data

Table 5. Adherence to maintenance injection dosing among complete initiators with ≥1 maintenance injection

	Complete initiators with ≥1 maintenance injection N = 1,411
Individuals with all on-time injections	838 (59%)
Individuals with any late injections	573 (41%)
Number of late injections per person	Median: 1 (IQR: 1, 2)
Individuals with any short delays	501 (36%)
Individuals with any long delays	113 (8%)
Total number of late injections	828
Short delay not requiring reinitiation	705 (85%)
Days past the target window	Median: 4 (IQR: 2, 10)
Long delay requiring reinitiation	123 (15%)
Days past the target window	Median: 50 (IQR: 39, 55)

Figure 2. HIV acquisition during the first continuous CAB LA PrEP use



Abbreviations: Ab, antibody; Ag, antigen; BIC, bictegravir; BMI, body mass index; D, days; CAB LA, cabotegravir long-acting; CI, confidence interval; DRV/c, darunavir/cobicistat; EFV, efavirenz; FTC, emtricitabine; IQR, interquartile range; IR, incidence rate; N, number; NVP, nevirapine; PrEP, pre-exposure prophylaxis; STI, sexually transmitted illness; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; VL, viral load

Discussion

- Over the first three years of CAB LA PrEP use in the US,1,748 individuals received CAB LA PrEP injection(s) in the OPERA cohort; 88% completed initiation (**Fig 1**)
  - A high proportion of CAB LA PrEP recipients were young, men, white, and had a recent history of STI (**Table 2**)
- A third of CAB LA PrEP complete initiators discontinued CAB LA PrEP use during the study period (**Table 4**)
  - 28% received additional injection(s) after a median gap of 7 months
- 59% of individuals with maintenance injection(s) adhered to the recommended dosing schedule (**Table 5**)
  - Most injection delays were short
- Incomplete oral bridging records may have contributed to the overestimation of injection delays and discontinuation
- Only 2 cases of HIV acquisition were observed during the first continuous use of CAB LA PrEP (**Fig 2**)
  - Both individuals received all their injections on-time
  - Case #1 (reported at IDWeek 2024)
    - HIV diagnosis: 3 months after CAB LA PrEP initiation
    - Timing of seroconversion cannot be determined (last negative HIV test before oral PrEP start)
  - Case #2 (newly identified)
    - HIV diagnosis: 21 months after CAB LA PrEP initiation
    - K103N mutation detected, indicating high-level resistance to EFV and NVP, but not RPV
- 2 additional HIV acquisitions were observed after CAB LA PrEP discontinuation (4 and 6 months after their last CAB LA PrEP injection, respectively)

Key Findings

- HIV acquisition during CAB LA PrEP was rare, and comparable to trial results, reinforcing its real-world effectiveness as a prevention strategy
- Injection delays were common, but generally of short duration
- Discontinuation and reinitiation patterns suggest continued interest in CAB LA PrEP, and may highlight variability in perceived need for PrEP or care continuity

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