



Research Letter | Infectious Diseases

Long-Acting Lenacapavir and Cabotegravir and Viral Suppression Among People With HIV

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Introduction

The field of long-acting injectable antiretroviral therapy for HIV remains in its early stages, with only 1 approved regimen. Cabotegravir and rilpivirine (CAB/RPV) was initially approved in 2021 for patients with viral suppression (VS) but has since been used off label for patients with viremia and adherence challenges. Demonstration projects¹ showed that most patients could attain and sustain VS with long-acting CAB/RPV, prompting the International AIDS Society–USA and Department of Health and Human Services guidelines in the US to endorse this approach.^{2,3} However, implementation remains limited by logistical, financial, and infrastructural barriers, and CAB/RPV is limited by the low genetic barrier to resistance of RPV.⁴

Lenacapavir (LEN), a first-in-class HIV capsid inhibitor, was approved for multidrug-resistant HIV in 2022.⁵ Clinicians are increasingly using LEN with other long-acting agents in these populations, but data on the effectiveness of long-acting LEN/CAB plus RPV are limited.^{6–8} We previously reported outcomes from a 4-clinic case series of 34 patients where viral suppression doubled when taking long-acting LEN/CAB (47% to 94%), with other small case series showing efficacy.^{6–8} Here, we evaluated outcomes among patients with prior adherence challenges, treatment experience, and resistance initiating LEN/CAB.¹

Methods

This retrospective case series was reported in accordance with the [STROBE](#) reporting guideline and was approved by the University of California San Francisco institutional review board, with informed consent waived because data were collected for quality improvement. Using electronic medical record (EMR) data verified through clinician review, we assembled a case series from the Ward 86 HIV Clinic, funded by the Ryan White Program, to evaluate demographics and outcomes among patients who initiated long-acting LEN with other long-acting agents from March 2023 through May 2025, with an extended follow-up through November 2025. Four patients in this analysis were also included in a previously published multicenter case series in which Ward 86 was a participating site.⁷ Self-reported race and ethnicity (categorized as American Indian or Pacific Islander, Black or African American, Hispanic or Latino, non-Hispanic or Latino, multiracial, White, and other [selection of the corresponding standardized EMR race field]) were extracted from the EMR and included to characterize the study population in the context of known disparities in accessing HIV treatment and treatment outcomes. Among patients with baseline viremia (HIV RNA ≥ 200 copies/mL), time to VS (< 200 copies/mL) was estimated using Kaplan-Meier methods. Details of the multidisciplinary infrastructure and implementation support for the long-acting program are provided in the eMethods in [Supplement 1](#). Data were analyzed using R version 4.4.3 (R Project for Statistical Computing). Significance was defined as a 2-sided $P < .05$.

+ Supplemental content

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Table. Demographics of Participants in the Ward 86 LEN/CAB Cohort

Characteristic	Participants, No. (%) (N = 46)
Age, y	
Mean (SD)	47.1 (11.8)
Median (IQR)	48.5 (37.5-56.8)
Gender identity	
Cisgender man	32 (69.6)
Cisgender woman	10 (21.7)
Nonbinary, gender queer, or another gender not listed	3 (6.5)
Transgender woman	1 (2.2)
Ethnicity	
No, not Hispanic, Latino/a, or Spanish origin	30 (65.2)
Yes, Hispanic, Latino/a, or Spanish origin	16 (34.8)
Race and ethnicity ^a	
American Indian or Pacific Islander	2 (4.4)
Black or African American	16 (34.8)
Multiracial	3 (6.5)
Other ^b	14 (30.4)
White	11 (23.9)
Hispanic or Latino	16 (34.8)
Housing status	
Stable (rent or own)	27 (58.7)
Unstable (SRO, shelter, outdoors, or treatment program)	19 (41.3)
Current substance use	
Alcohol use disorder	1 (2.2)
Cocaine use	2 (4.3)
Fentanyl use	1 (2.2)
Methamphetamine or amphetamine use	15 (32.6)
None	27 (58.7)
Viral suppression at initiation	
Suppressed (<200 copies/mL)	22 (47.8)
Viremic (≥200 copies/mL)	24 (52.2)
Injection site reaction	
No	14 (30.4)
Yes	27 (58.7)
Missing	5 (10.9)
Presence of nodules	
Not reported	28 (60.9)
Yes	18 (39.1)
Antiretroviral therapy regimen prior to LEN	
CAB/RPV	3 (6.5)
INSTI-based	26 (56.6)
NNRTI-based	1 (2.2)
Protease inhibitor-based	16 (34.8)
Inclusion of RPV in long-acting LEN/CAB regimen	17 (37.0)
Dosing of CAB/RPV or CAB every 4 wks	18 (39.1)
Reason for switching from prior regimen to LEN	
Baseline INSTI resistance	4 (8.7)
Baseline NNRTI resistance	33 (71.7)
Persistent low-level viremia on CAB/RPV	3 (6.5)
High baseline viral load or slow viral decay	4 (8.7)
Injection site reaction to CAB	1 (2.2)
Suspected resistance	1 (2.2)

Abbreviations: CAB, cabotegravir; INSTI, integrase strand transfer inhibitor; LEN, lenacapavir; NNRTI, nonnucleoside reverse transcriptase inhibitor; RPV, rilpivirine; SRO, single-room occupancy.

^a Race and ethnicity are not mutually exclusive; Hispanic ethnicity is reported independently of race, and patients identifying as Hispanic may also be represented in any race category. Percentages therefore sum to more than 100%.

^b Other reflects selection of the other category from the standardized electronic medical record race fields.

Results

Overall, 46 participants who initiated long-acting LEN/CAB were included in the analyses (mean [SD] age, 47.1 [11.8] years; 32 men [69.6%], 11 women [23.9%], and 3 gender diverse individuals [6.5%]; 16 Black or African American [34.8%], 16 Hispanic or Latino [34.8%], and 11 White [23.9%] individuals) (**Table**). Baseline nonnucleoside reverse transcriptase inhibitor (NNRTI) resistance was high (33 patients [71.7%]), while integrase strand transfer inhibitor resistance was low (4 individuals [8.7%]). At LEN initiation, 22 patients (47.8%) were suppressed, 24 (52.2%) were viremic, and 17 (37.0%) had RPV included in the regimen. Among 24 patients with viremia prior to initiating LEN, more than half (14 patients [58.3%]) had a CD4⁺ count of 200 cells/mm³ or fewer. Patients with baseline VS maintained VS, and all patients without baseline VS achieved VS by 13 weeks. Time to VS estimated among those without baseline VS is shown in the **Figure**. To assess durability of VS, follow-up was extended to a median (IQR) of 100 (63-131) weeks from first LEN injection to the most recent viral load. All patients achieved and maintained VS, with no consecutive viral load greater than 200 copies/mL.

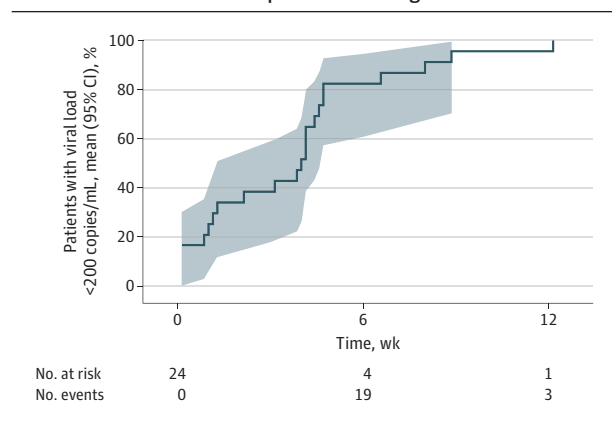
Discussion

In this case series of 46 patients who received long-acting LEN/CAB, patients with baseline VS maintained suppression, and all patients without baseline VS achieved VS by 13 weeks. Rapid achievement of VS was observed among patients viremic at baseline, findings consistent with those from our prior case series of long-acting LEN/CAB⁷ and reports from several smaller series.^{6,8} To our knowledge, this is the largest case series of patients on long-acting LEN/CAB to date.

Although only long-acting CAB/RPV is approved for combination treatment, NNRTI resistance is present in up to 10% of people with HIV globally,⁴ reducing RPV susceptibility. NNRTIs have lower genetic barriers to resistance; in contrast, LEN acts at multiple steps in the HIV viral cycle at several discrete steps,⁹ potentially lending the drug a higher resistance barrier than NNRTIs. A small case series showed persistent VS on unintentional LEN monotherapy, consistent with findings from the LEN licensing trial, which demonstrated high rates of VS, despite optimized background regimens.^{5,8} Accordingly, there is great interest in using long-acting LEN/CAB,⁷ with 2 upcoming trials planned in the Advancing Clinical Therapeutics Globally for HIV/AIDS and Other Infections clinical trials network.

Limitations of our study include retrospective design, sample size, and single-center setting. Ryan White Care-funded clinics have higher rates of VS (91.4%) than the US national average (67.2%), and the infrastructure available at these clinics may limit generalizability¹⁰ and contribute to lower access to and uptake of long-acting injectable therapies. However, our cohort represents the

Figure. Line Graph of Time to Virologic Suppression Among 20 People With HIV Who Initiated Lenacapavir and Cabotegravir While Viremic



Virologic suppression was defined as less than 200 copies/mL.

population for whom long-acting LEN for treatment was initially developed, and the psychosocial barriers faced by this patient population reflect clinical complexity.

In conclusion, long-acting LEN/CAB was initiated in a cohort of treatment-experienced patients with high rates of NNRTI resistance. High VS was achieved regardless of baseline viremia and sustained over a median time of 100 weeks, with no consecutive viral loads greater than 200 copies/mL. This study represents the largest case series of long-acting LEN/CAB and adds to the growing evidence supporting its use for patients with adherence challenges and resistance.

ARTICLE INFORMATION

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SUPPLEMENT 1.

eMethods.

SUPPLEMENT 2.

Data Sharing Statement