Long-Term Effectiveness of Lenacapavir in Heavily Treatment-Experienced People with HIV-1 in the US

Poster #539

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Conclusions

- In this retrospective, real-world study, long-term lenacapavir (LEN) effectiveness remained high over an 18-month follow-up period in people with HIV-1 with an extensive history of antiretroviral (ARV) resistance and high levels of comorbidity and polypharmacy
- The proportion of people with HIV-1 with HIV-1 RNA <50 copies/mL and <200 copies/mL by missing=excluded analysis increased from 36% and 48% at LEN initiation to 67% and 83% at 18 months, respectively
- Approximately half of people with HIV-1 had a change in their optimized background regimens (OBRs) when LEN was incorporated into treatment
- Median adherence to LEN was high (83.5%) and all-cause LEN discontinuation rate was 14.1%, suggesting LEN was well tolerated in real-world clinical practice in the US
- Renal and laboratory biomarkers remained stable through the 18-month follow-up period

Plain Language Summary

- People with HIV who have taken many HIV medicines may have fewer treatment options; this can happen when the virus stops responding to some medicines (called virus resistance) or when side effects become a concern
- Lenacapavir is a medicine given as an injection every 6 months and approved for treatment of HIV in people who have tried many other HIV medicines
- We looked at how well lenacapavir worked and how it was used in everyday clinical practice outside of clinical trials over 18 months in a group of people with HIV from the US. Many people starting lenacapavir in this study no longer responded well to several HIV medicines
- We found that lenacapavir is an effective and well-tolerated HIV treatment option in real-world care for people with HIV, including those with treatment resistance or a long history of HIV medication use

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Background

- Heavily treatment-experienced (HTE) people with HIV-1 may have limited treatment options due to multidrug resistance or concerns around the safety and tolerability of available ARVs[1]
  - — Novel ARV therapies are urgently needed to address these unmet needs[1]
- LEN is a first-in-class, long-acting capsid inhibitor approved for the treatment of HIV-1 in HTE adults in combination with other ARVs and for HIV-1 prevention as monotherapy[2–4]
- The efficacy and safety of LEN plus an OBR among HTE people with multidrug-resistant HIV-1 have been investigated in the Phase 2/3 CAPELLA study (NCT04150068)[5]
  - — LEN plus an OBR resulted in high and sustained rates of virologic suppression (84.6% with HIV-1 RNA <50 copies/mL by missing=excluded analyses) at Week 156[5]
  - — LEN was well tolerated and very low rates of LEN discontinuation were observed[5]
- To help support translation of these findings into clinical practice, we evaluated the real-world effectiveness and use of LEN in a population of HTE people with HIV-1

Objective

- To describe the sample demographic and clinical characteristics of HTE people with HIV-1 on LEN, LEN resistance at baseline, HIV-1 viral suppression, OBR patterns pre- and post-LEN initiation, LEN adherence, LEN discontinuations, and laboratory measures (including renal function, liver function, lipid levels, and immune status)

Methods

- We retrospectively examined participant characteristics, LEN uptake since US authorization, HIV-1 viral suppression, OBR patterns, adherence, laboratory measures, and ARV therapy resistance among HTE people with HIV-1 who were prescribed LEN
  - — Administrative data were sourced from the HealthVerity Marketplace, including 368,173 people with an HIV-1 diagnosis at any point between Jan 1, 2023 to Sept 30, 2025 (the cut-off date up to which data were collected and included in the analysis)
- Inclusion criteria were age ≥18 years, pharmacy claim of ≥1 LEN injection, and ≥1 HIV-RNA test during the 12-month pre-index or 1-month post-index, with the index date defined as the date of first LEN injection
  - — Following a refresh of the data source, additional participants met inclusion requirements that resulted in numbers that differ from those reported in the abstract
- Descriptive statistics were used to summarize demographics, clinical characteristics, viral suppression (missing=excluded analysis), OBRs, LEN adherence, and discontinuations for participants who received LEN oral loading plus injections (referred to as LEN injection throughout)
- OBR patterns were assessed at two timepoints: 2 months before and 2 months after the first LEN injection
  - — Core ARV classes comprised all ARV therapy classes other than nucleoside reverse transcriptase inhibitors (NRTIs)
- Adherence was calculated as 100% minus the proportion of days during the follow-up period that the participant was not considered "on treatment" (**Figure 1**)
  - — Participants were considered on treatment for 182 days following any LEN injection

Figure 1. Adherence Calculation

$$\text{Adherence \%} = \frac{([\text{Days from first injection}] + [\text{days covered by each maintenance LEN injection}^{a}]) - (\text{days exceeding 196 days from previous injection})}{\text{Total days of follow-up from LEN index date}^{b}}$$

[a]182 days; if maintenance injections occurred within +/– 14 days of the due date, adherence was considered 100%; if maintenance injections occurred 15 days after the due date (196+1 days), these were deducted from the total days covered by LEN (numerator).
[b]Denominator takes into account +/– 14 days; for instance, if a participant has their maintenance injection 10 days prior their due date, 10 days are deducted from the denominator.
LEN, lenacapavir.

- Discontinuations were defined as participants who stopped taking LEN and moved on to a different regimen
- Estimated glomerular filtration rate (eGFR) was derived using the Chronic Kidney Disease Epidemiology Collaboration 2021 algorithm; serum creatinine was used to calculate eGFR where missing
- Resistance was tabulated for those with resistance data available prior to starting LEN and for those who had resistance testing performed after starting LEN

Results

Study Population

- Out of the people with HIV-1 from the HealthVerity Marketplace ever exposed to LEN (n=542), n=93 met the inclusion criteria and received LEN oral initiation plus injections
  - — A high proportion of LEN-exposed people with HIV-1 were excluded from this analysis due to not having any insurance cover post-LEN injection (n=40) or due to missing HIV-1 RNA results, either 12 months before LEN injection (n=243) or 1 month post-LEN injection (n=33)
- Median (interquartile range [IQR]) age was 51 years (36–59), 39% were assigned female at birth, 46% were non-Hispanic, 26% were Black, and 50% had Medicaid (**Table 1**)
- Median (IQR) follow-up from LEN index date until end of enrollment was 502 (285–687) days

Table 1. Baseline Demographics and Clinical Characteristics

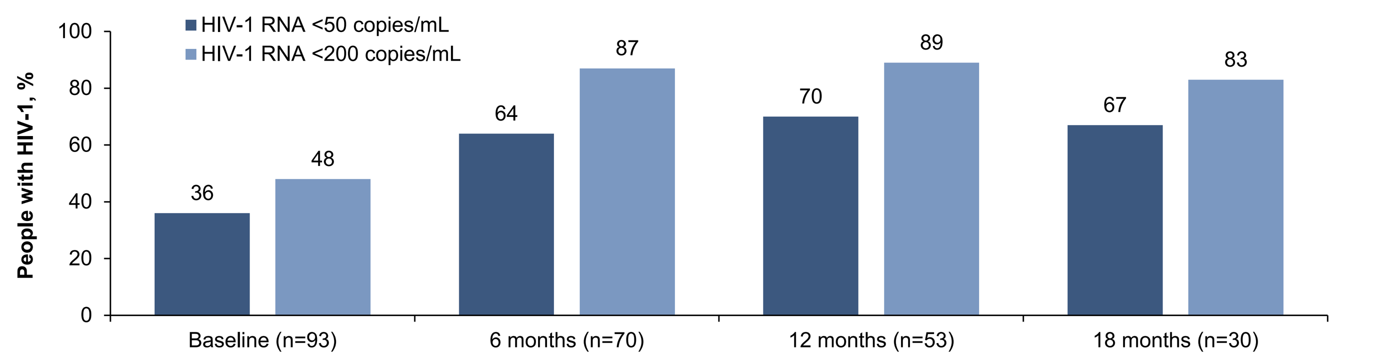
	LEN injection (n=93)
Median (IQR) age, years	51 (36–59)
Assigned female at birth, n (%)	36 (38.7)
Race, n (%)	
White	15 (16.1)
Black	24 (25.8)
Asian	1 (1.1)
Other	15 (16.1)
Missing	38 (40.9)
Non-Hispanic ethnicity, n (%)	43 (46.2)
Payer, n (%)	
Medicare	6 (6.5)
Medicaid	46 (49.5)
Commercial	29 (31.2)
Multiple	12 (12.9)
Missing	0
CD4 cell count distribution, n (%)	18 (19.4)
Median (IQR) CD4 cell count, cells/μL	261 (51–458)
Charlson Comorbidity Index score information availability, n (%)	80 (86.0)
Median (IQR) Charlson Comorbidity Index score	4.0 (3.0–9.0)
Concomitant medication class count availability, n (%)	89 (95.7)
Median (IQR) medication class count	10.0 (6.0–15.0)
ART class resistance information availability, n (%)	38 (40.9)
Resistance to major classes, n/N (%)	
NRTI	26/38 (68.4)
NNRTI	20/38 (52.6)
INSTI	18/38 (47.4)
PI	14/38 (36.8)
Participants with resistance to two major classes, n/N (%)	10/38 (26.3)
Participants with resistance to three major classes, n/N (%)	9/38 (23.7)
Participants with resistance to four major classes, n/N (%)	4/38 (10.5)

ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; LEN, lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

HIV-1 Viral Suppression

- The proportion of people with HIV-1 with HIV-1 RNA <50 copies/mL and <200 copies/mL by missing=excluded analysis increased from baseline (n=93; 36% and 48%, respectively) to 18 months (n=30; 67% and 83%, respectively) (**Figure 2**)

Figure 2. Proportion of HTE People with HIV-1 with HIV-1 RNA <50 copies/mL and <200 copies/mL at Baseline and During Follow-Up (Missing=Excluded Analysis)

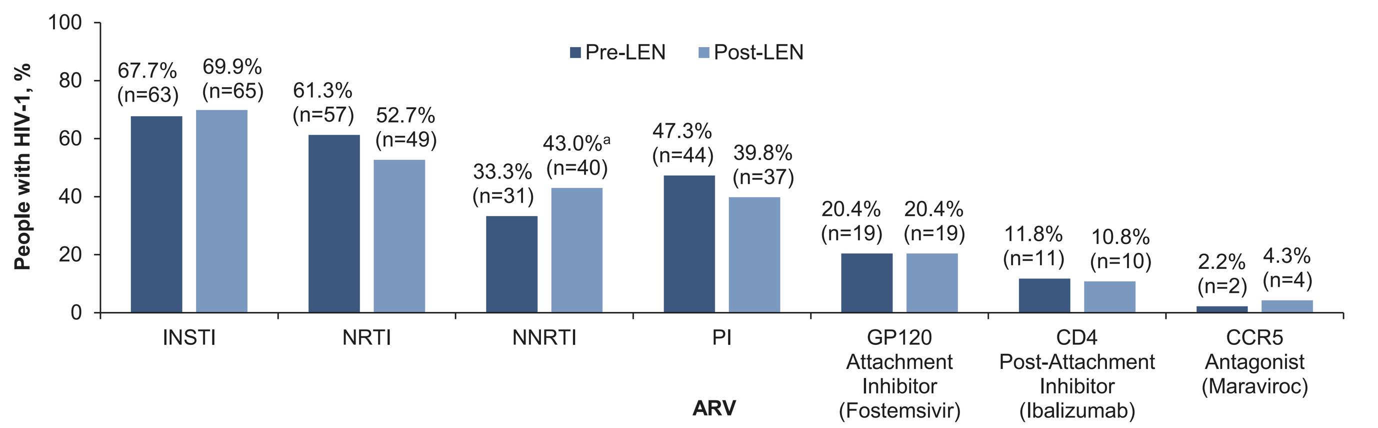


Missing=excluded analysis was used to derive the proportion of HTE people with HIV-1 with HIV-1 RNA <50 copies/mL and <200 copies/mL. N numbers only reflect people with HIV-1 with available data at each timepoint, and differ due to varying durations of study drug exposure.
HTE, heavily treatment-experienced.

OBR Patterns

- Two months before the first LEN injection, the median (IQR) number of core ARVs prescribed was 2 (1–3)
  - — The most common prior ARV classes were integrase strand transfer inhibitor (INSTI; 68%), NRTI (61%), and protease inhibitor (47%) (**Figure 3**)
  - — The median (IQR) duration of prior ARV regimen was 113 (59–392) days
- Two months after the first LEN injection, the median (IQR) number of core ARVs prescribed remained unchanged at 2 (1–3)
  - — The most common ARV classes post-LEN were INSTI (70%), NRTI (53%), and non-NRTI (43%) (**Figure 3**)
  - — The median (IQR) duration of current ARV regimen was 77 (30–264) days
- At LEN initiation, 47% of participants changed the ARVs they were on 2 months prior to LEN switch
- Overall, 22% of participants had fewer agents in their ARV regimen following LEN switch

Figure 3. Prior and Current ARV Use



[a]The most common NNRTI regimen people started taking was cabotegravir/rilpivirine, which increased from n=8 pre-LEN to n=15 post-LEN.
ARV, antiretroviral; CCR5, C-C chemokine receptor type 5; GP, glycoprotein; INSTI, integrase strand transfer inhibitor; LEN, lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

LEN Adherence and Discontinuation

- Median (IQR) adherence to LEN was 83.5 (52.4–100) (**Table 2**)

Table 2. LEN Adherence and Discontinuations

	LEN injection (n=93)
Percentage adherence to LEN, median (IQR)	83.5 (52.4–100)
Participants who received only one LEN injection, n (%)	45 (48.4)
Participants who received LEN maintenance injections, n (%)	48 (51.6)
All LEN maintenance injections within the expected time window[a]	21 (22.6)
At least one LEN maintenance injection within the expected time window[a]	28 (30.1)
All LEN maintenance injections outside the expected time window	20 (21.5)
LEN discontinuation (switched to another regimen, and no subsequent LEN injection), n/N (%)	13/92[b] (14.1)
Median (IQR) days to discontinuation	183 (183–183)

[a]Any injection in the window of 24 weeks to 28 weeks after the previous injection. [b]One patient had invalid drug data.
Adherence was calculated as 100% minus the proportion of days during the follow-up period that the participant was not considered "on treatment". Participants were considered on treatment for 182 days following any LEN injection.
IQR, interquartile range; LEN, lenacapavir.

- LEN was discontinued by 14.1% (13/92) of people with HIV-1 after their first injection (reasons for discontinuation were not available); one individual had invalid drug data
  - — Following discontinuation of LEN, these participants switched to the regimens listed in **Table 3**

Table 3. Regimens Switched to by People with HIV-1 Who Discontinued LEN

n (%)	People with HIV-1 who discontinued LEN injection (n=13)
ABC+DRV/c+F/TDF+FTR	1 (7.7)
B/F/TAF	1 (7.7)
B/F/TAF+DOR	1 (7.7)
CAB/RPV	1 (7.7)
DRV/c+FTR	1 (7.7)
DRV/c/FTC/TAF+CAB/RPV	1 (7.7)
DRV/c	1 (7.7)
DRV+DTG+F/TAF+FTR+RTV	1 (7.7)
DRV/c+DTG	1 (7.7)
DTG/3TC	1 (7.7)
DTG+FTR	1 (7.7)
DTG+MVC+RTV+TPV	1 (7.7)
IBA	1 (7.7)

3TC, lamivudine; ABC, abacavir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; DOR, doravirine; DRV/c, darunavir/cobicistat; DTG, dolutegravir; F or FTC, emtricitabine; FTR, fostemsavir; IBA, ibalizumab; LEN, lenacapavir; MVC, maraviroc; RPV, rilpivirine; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TPV, tipranavir.

Laboratory Measures

- Laboratory biomarkers remained stable through the 18-month follow-up period (**Table 4**)

Table 4: Laboratory Measures from Baseline Through the 18-Month Follow-Up Period

	LEN injection (n=93)			
	Baseline	**6 months**	**12 months**	**18 months**
eGFR, n	79	71	57	45
Median (IQR) eGFR	89 (78–105)	92 (76–106)	95 (74–105)	94 (71–104)
Creatinine, n	79	71	57	45
Median (IQR) creatinine, mg/dL	0.94 (0.76–1.12)	0.94 (0.82–1.09)	0.89 (0.80–1.08)	0.92 (0.83–1.21)
LDL cholesterol, n	58	38	40	28
Median (IQR) LDL cholesterol, mg/dL	100 (83–120)	92 (75–122)	100 (74–132)	93 (72–130)
Cholesterol/HDLC, n	12	14	8	5
Median (IQR) cholesterol/HDLC ratio	3.8 (3.2–4.5)	3.1 (2.4–4.5)	2.7 (2.2–3.3)	2.9 (2.6–3.6)
Triglycerides, n	58	39	40	28
Median (IQR) triglycerides, mg/dL	133.0 (92.0–204.0)	159.0 (94.0–233.0)	122.5 (79.0–176.5)	109.0 (74.5–185.5)
ALT, n	79	68	56	44
Median (IQR) ALT, U/L	19.0 (13.0–33.0)	20.5 (13.0–30.5)	23.5 (14.0–32.5)	19.5 (13.5–28.5)
AST, n	79	68	56	45
Median (IQR) AST, U/L	23.0 (18.0–33.0)	21.0 (17.0–31.5)	24.0 (18.0–35.5)	24.0 (18.0–30.0)
CD4 count, n	18	13	10	3
Median (IQR) CD4 cell count, cells/μL	261 (51–458)	263 (138–489)	180 (80–299)	245 (152–329)

Data are reported for participants with non-missing data for each laboratory measure.
ALT, alanine transaminase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; HDLC, high-density lipoprotein cholesterol; IQR, interquartile range; LDL, low-density lipoprotein; LEN, lenacapavir.

Limitations

- Reasons for ARV regimen switch and/or discontinuation are not collected in administrative data sources
- Missing mortality data and incomplete laboratory results (viral load, CD4/CD8, and resistance testing) within HealthVerity may impact the clinical evaluation of the data
- Viral suppression was evaluated using missing=excluded analysis; therefore, results should be interpreted with caution, as missing data could reflect treatment discontinuations
- Selection bias may be present as this analysis only includes people with HIV-1 who have access to a healthcare system and who have continuous commercial healthcare insurance coverage