First Year of Lenacapavir Long-Acting Injectable Use in the OPERA Cohort

Poster #688

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Background

- Heavily treatment experienced (HTE) people with HIV require complex and highly tailored ART regimens
- Lenacapavir (LEN) :
  - 1st capsid inhibitor approved by the FDA (22DEC2022)
  - Indicated for HTE individuals with multidrug resistant HIV-1 infection who are failing their current ART regimen due to resistance, intolerance, or safety concerns
  - Twice yearly injections (2 injections every 26 ± 2 weeks)
  - Combined with an optimized background regimen (OBR), i.e., other ARVs selected based on each person's susceptibility and tolerability

Objective

To describe LEN use in the United States during its first year post-approval among people with HIV in the OPERA cohort

Methods

Study design

- OPERA cohort: prospectively captured, routine clinical data from EHRs in the US (260 clinics, 23 US states/territories)
  - Represents ~14% of people with HIV in the US
- Secondary data analysis of EHR data

Study population

- Inclusion criteria
  - People with HIV-1
  - Aged ≥18 years old
  - ART-experienced
  - Started LEN between 22DEC2022 and 31DEC2023
- Censoring criteria
  - Death
  - Loss to follow-up (12 months after last contact)
  - Study end (31DEC2023)
  - LEN discontinuation

ARV changes

- Continuation: all ARVs remained the same (excluding the addition of LEN)
- Simplification (not mutually exclusive):
  - Fewer ARV agents (including LEN)
  - Fewer ARV classes (including LEN)
  - Fewer pills/days (excluding oral LEN at initiation)
- Other change: changes resulting in the same or a larger number of ARV agents, ARV classes and pills/day

Analyses

- LEN uptake: number of individuals with a LEN prescription vs. any LEN injections
- Among LEN injection recipients
  - Baseline demographic and clinical characteristics
  - Comparison of ARVs in the LEN background regimen vs. prior regimen
- Among LEN injection recipients with ≥1 month of follow-up: changes in background regimen during LEN use

Results

Figure 1. LEN uptake between 22DEC2022 and 31DEC2023 in the OPERA cohort

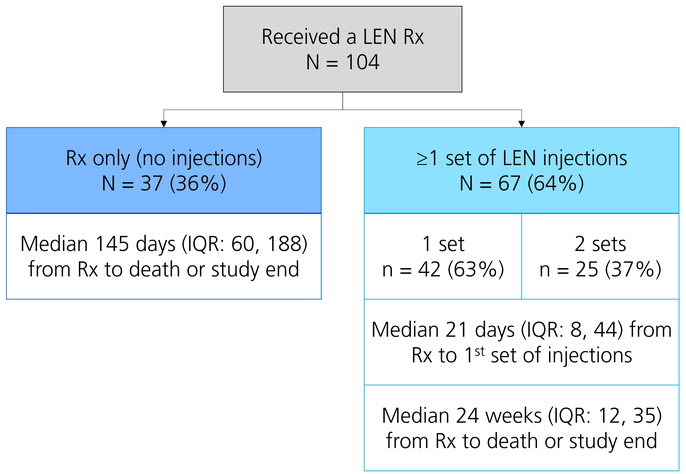


Table 2. Characteristics of the ART regimen prior to LEN start and of the background regimen at LEN start

	Rx only N=37	LEN injections N=67	
	Prior regimen[a]	Prior regimen[a]	Background regimen[b]
Duration of prior regimen, median months (IQR)	21 (8, 28)	7 (1, 24)	NA
# anchor agents[c] (excluding LEN), n (%)			
1	15 (40)	10 (15)	16 (24)
2	11 (30)	33 (49)	31 (46)
≥3	11 (30)	24 (36)	20 (30)
ARV classes (excluding LEN; not mutually exclusive), n (%)			
NRTI	26 (70)	40 (60)	39 (58)
INSTI	32 (86)	54 (81)	52 (78)
PI	11 (30)	33 (49)	29 (43)
NNRTI	11 (30)	32 (48)	29 (43)
Entry inhibitor	12 (32)	31 (46)	29 (43)
≥1 month of follow-up, n (%)	NA	NA	61 (91)
Any change in background regimen, n (%)	NA	NA	18 (30)
# background regimen changes, median (IQR)	NA	NA	2 (1, 2)

[a] Combination of ARVs used 16 days prior to LEN Rx or first set of LEN injections
[b] Combination of other ARVs on the day of the first set of LEN injections
[c] Agent from one of the following classes: INSTI, PI (except boosting agents), NNRTI or entry inhibitor

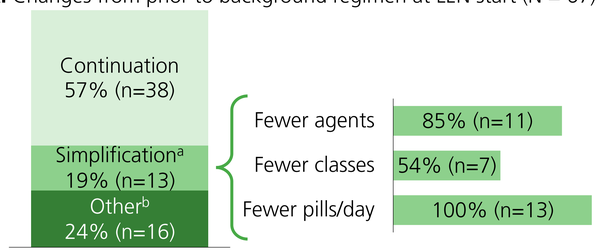
Abbreviations: ART, antiretroviral therapy; ARV, antiretroviral; EHR, electronic health records; HTE, heavily treatment experienced; IQR, interquartile range; LEN, lenacapavir; N, number; OBR, optimized background therapy; Rx, prescription

Table 1. Baseline characteristics among individuals with a LEN Rx only or ≥1 set of LEN injections

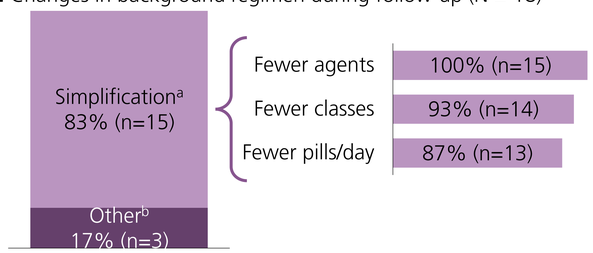
	Rx only N=37	LEN injections N=67
Age, median (IQR)	56 (40, 61)	55 (44, 62)
Women, n (%)	≤5 (≤14)	17 (25)
Black race, n (%)	12 (32)	32 (48)
Hispanic, n (%)	7 (19)	10 (15)
HIV viral load (copies/mL), n (%)		
<50	16 (43)	35 (52)
≥50 to <200	10 (27)	11 (16)
≥200	11 (30)	21 (31)
CD4 cell count (cells/μL), n (%)		
≥500	12 (32)	24 (36)
≥350 to <500	6 (16)	22 (33)
≥200 to <350	9 (24)	8 (12)
<200	10 (27)	13 (19)
Any comorbidity	33 (89)	61 (91)
AIDS-defining events history, n (%)	23 (62)	32 (48)
Payer (not mutually exclusive), n (%)		
Medicare	6 (16)	30 (45)
Medicaid	14 (38)	31 (46)
Commercial Insurance	24 (65)	38 (57)
Ryan White/ADAP	6 (16)	8 (12)

Figure 2. ARV changes (A) from prior regimen to background regimen at LEN start, and (B) in background regimens during follow-up

A. Changes from prior to background regimen at LEN start (N = 67)



B. Changes in background regimen during follow-up (N = 18)[c,d]



[a] Types of simplification are not mutually exclusive
[b] Changes resulting in the same or a larger number of ARV agents, ARV classes and pills/day
[c] Changes from prior to background regimen at LEN start: continuation, 50% (n = 9); simplification, 17% (n = 3); other, 33% (n = 6)
[d] Individuals with multiple changes are represented once, with all changes summarized as ever/never

Discussion

- Over the first year since LEN approval in the US, 104 individuals received a LEN prescription, although only 67 received any LEN injections (**Fig 1**)
  - Follow-up was sufficient to observe a first set of injection for most people with a prescription only (**Fig 1**)
  - People who received LEN injections were more likely to be women, Black or an have an undetectable viral load, and less likely to have a history of AIDS-defining events than people with a prescription only (**Table 1**)
  - People who received LEN injections had been on their prior regimen for longer and tended to receive more complex regimens with >1 anchor agent (**Table 2**)
- While LEN is indicated for individuals who are failing their current regimen (i.e., resistance, intolerance, safety), 68% of initiators had a viral load <200 copies/mL, suggesting that the switch may have been motivated by tolerability, safety or simplification concerns rather than virologic failure (**Table 1**)
- LEN was added to the prior regimen which was maintained unchanged in 57% (**Fig 2**)
- The prior regimen was simplified in 19% at LEN initiation; all received fewer pills/day, most received fewer ARV agents, counting LEN (**Fig 2**)
- 30% of individuals with ≥1 month of follow-up experienced some changes in background regimen during LEN use (**Table 2**), of whom 83% experienced a simplification (**Fig 2**)
- Study strengths
  - Large, diverse cohort representative of HIV care in the US
  - Assessed real-world use of LEN in the US through EHR data from routine clinical care
- Study limitations
  - Small sample size
  - No data on resistance
  - Reasons for LEN initiation and background regimen selection could not be assessed due to their incomplete documentation in the EHR
- Treatment outcomes will be assessed in a future analysis

Key Findings

- This overview of the first year of LEN use in a large US cohort showed a varied but small group of people with HIV receiving LEN injections
- Most had well-controlled HIV before LEN initiation
- A subset of LEN users were able to simplify their ART regimen at LEN initiation or during follow-up

Acknowledgements

This research would not be possible without the generosity of people living with HIV and their OPERA caregivers. Additionally, we are grateful for the following individuals: Kelly Oh (SAS programming), Kristine Ferguson (QA), Bernie Stooks (data management), Lisa Lutzi & Nicole Shaw (data management/quality), and Judy Johnson & Quateka Cochran (clinical data classification).

Support

This research was supported by Gilead Sciences

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