Participant-Reported Outcomes With Long-Acting Lenacapavir-Based Regimens Among Heavily Treatment-Experienced People Living With HIV in the CAPELLA Clinical Trial

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Key Findings

- In the CAPELLA trial, fewer participants reported symptoms as bothersome at week 52 vs baseline, with decreases in HIV-SI scores ranging from 1% to 15%
- EQ-5D-5L index and VAS scores, SF-36 physical and mental component summary scores, and NPRS scores were stable through 52 weeks

Conclusions

- In the CAPELLA trial, these PRO results demonstrate high, stable HRQoL over time, supporting the tolerability of SC lenacapavir plus OBR
- The PRO results for HTE PLWH align with the favorable safety profile and low discontinuation rates of lenacapavir
- Previously reported high rates of virologic suppression and increases in CD4+ cell count with lenacapavir treatment may help explain how this population of HTE PLWH had decreased symptom severity while staying within adult US norms for EQ-5D-5L and SF-36 measures
- These data, reflecting the perspectives of the people treated, highlight the potential for lenacapavir plus OBR to decrease most HIV symptoms, without compromising HRQoL, for HTE PLWH

Introduction

- Heavily treatment-experienced (HTE) people living with HIV (PLWH) and multidrug resistance have limited treatment options and often have low CD4+ T-cell counts[1-4]
- Low CD4+ T-cell counts have significant negative impacts on health—increasing the risk of opportunistic infections, comorbidities, and death—and on health-related quality of life (HRQoL)[2,3]
- Lenacapavir is a first-in-class capsid inhibitor that can be administered subcutaneously (SC) twice a year[5,6]
  - Lenacapavir is approved in various regions for HTE PLWH with multidrug resistance when used in combination with an optimized background regimen (OBR)[7-11]
- In the ongoing Phase 2/3 CAPELLA study (NCT04150068), SC lenacapavir added to an OBR led to high rates of virologic suppression and was generally well tolerated by HTE PLWH[12]
  - At week 52, a viral load of <50 copies/mL was reported in 78% of participants, with a mean increase in the CD4+ cell count of 97 cells/mm^3
  - No serious adverse events related to lenacapavir were reported and only 1 participant discontinued at week 52 due to an injection site reaction (nodule; Grade 1)

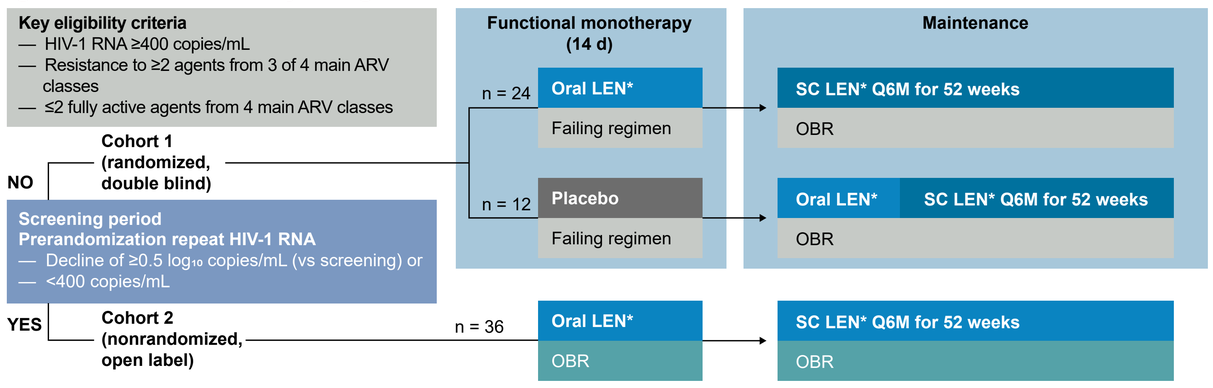
Objective

- To assess participant-reported outcomes (PROs) related to HIV symptoms, injection pain, and overall HRQoL in the CAPELLA study among HTE PLWH treated with lenacapavir in combination with an OBR

Methods

- The study design for CAPELLA was described previously[6]

Figure 1. CAPELLA study design



*Oral LEN administered as 600 mg on days 1 and 2 and 300 mg on day 8; SC LEN administered as 927 mg (2 × 1.5 mL) in the abdomen on day 15.
ARV, antiretroviral; ATV, atazanavir; d, day; LEN, lenacapavir; OBR, optimized background regimen (investigational agents, such as fostemsavir, were allowed; ATV, ATV/cobicistat, ATV/ritonavir, efavirenz, entecavir, nevirapine, and tipranavir were not allowed); Q6M, every 6 months; SC, subcutaneous.

- Scores from 4 validated PRO instruments were collected at baseline and through week 52

Table 1. Participant-reported outcome instruments

PRO instrument	Description	Scale range
EQ-5D-5L (index score and VAS)[13]	Provides insights into HRQoL and how health conditions may limit or worsen daily activities	Index score = 0–1; VAS = 0–100, where higher values indicate better health
SF-36[14]	Examines 8 dimensions of physical and mental health and function	0–100 with norm-based scoring (mean = 50, SD = 10), where higher scores indicate better health
HIV-SI[15]	Assesses 20 common symptoms associated with HIV treatment or disease	0–4 with higher scores indicating more bothersome symptoms; scores were dichotomized as not bothersome (0–1) and bothersome (2–4)
NPRS[16]	Assesses pain intensity at the time of the most recently received injection	0–10, where higher scores indicate worse pain

HIV-SI, HIV-Symptom Index; HRQoL, health-related quality of life; NPRS, numeric pain rating scale; PRO, participant-reported outcome; SF-36, Short Form-36; VAS, visual analogue scale.

Results

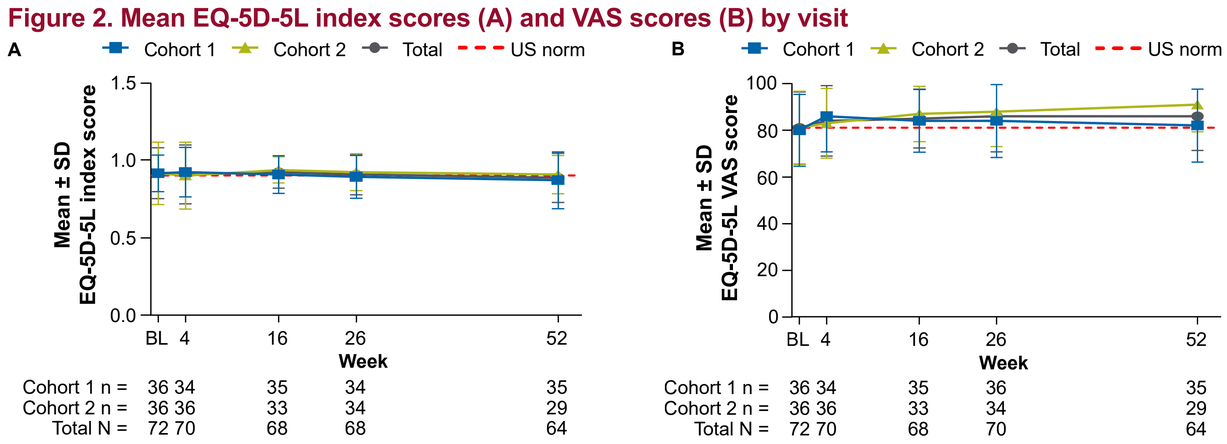
Table 2. Baseline characteristics

Characteristic	Cohort 1 LEN (n = 24)	Cohort 1 Placebo (n = 12)	Cohort 2 LEN (n = 36)	All participants (N = 72)
Age, median (range), years	55 (24–71)	54 (27–59)	49 (23–78)	52 (23–78)
Sex, female	7 (29)	3 (25)	8 (22)	18 (25)
Race				
Black	10 (42)	6 (55)	11 (31)	27 (38)
White	12 (50)	4 (36)	13 (36)	29 (41)
Asian	2 (8)	1 (9)	12 (33)	15 (21)
Data could not be collected	0	1 (9)	0	1 (1)
Viral load, median (range), log10 copies/mL	4.2 (2.3–5.4)	4.9 (4.3–5.3)	4.5 (1.3–5.7)	4.5 (1.3–5.7)
CD4+ count, median (range), cells/mm^3	172 (16–827)	85 (6–237)	195 (3–1296)	150 (3–1296)
<200 cells/mm^3	16 (67)	11 (92)	19 (53)	46 (64)
Resistance to ≥2 drugs in major class				
NRTI	23 (96)	12 (100)	36 (100)	71 (99)
NNRTI	22 (92)	12 (100)	36 (100)	70 (97)
Protease inhibitor	20 (83)	8 (67)	30 (83)	58 (81)
INSTI	20 (83)	7 (58)	23 (64)	50 (69)
All 4 major classes	14 (58)	3 (25)	16 (44)	33 (46)
Median overall susceptibility score of OBR[a]	2.0	1.3	2.0	2.0
Number of fully active agents in the OBR				
0	4 (17)	2 (17)	6 (17)	12 (17)
1	7 (29)	7 (58)	13 (36)	27 (38)
≥2	13 (54)	3 (25)	17 (47)	33 (46)

Data are n (%) unless otherwise specified.
[a]The drug susceptibility score to an individual antiretroviral medication was deemed according to a proprietary algorithm, with 1.0 = full susceptibility, 0.5 = partial susceptibility, and 0 = no susceptibility. The overall susceptibility score of the optimized background therapy was the sum of the individual scores. For historical resistance reports, the scores were derived from data provided by the investigators.
CD, cluster of differentiation; INSTI, integrase strand transfer inhibitor; LEN, lenacapavir; NNRTI, non–nucleoside reverse-transcriptase inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor; OBR, optimized background regimen.

- A total of 72 participants were enrolled, with each cohort consisting of 36 participants
- The median age (range) for all participants was 52 (23–78) years
- Among all participants, 64% had <200 CD4+ cells/mm^3
- Overall, 22% of participants had a baseline CD4+ count of <50 cells/mm^3

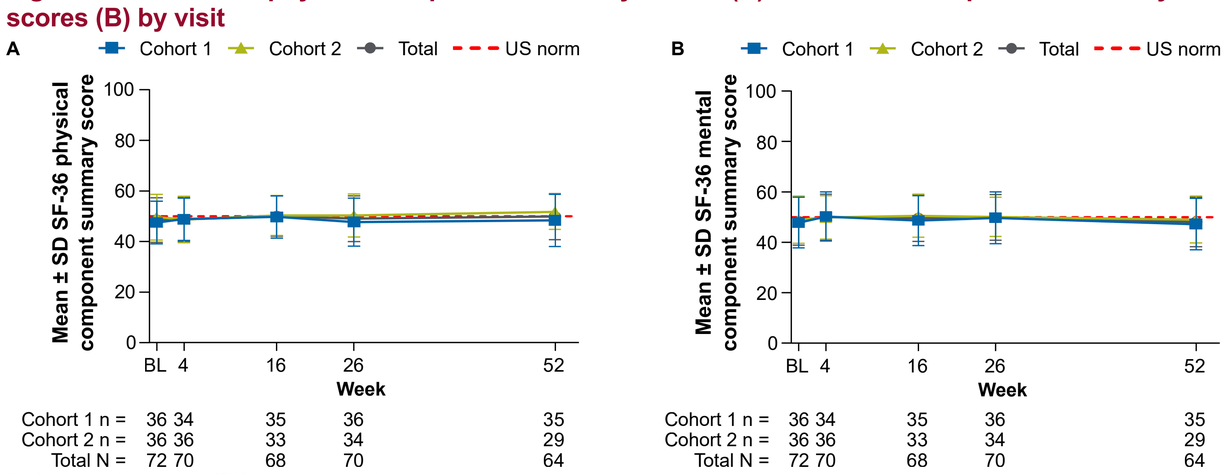
Figure 2. Mean EQ-5D-5L index scores (A) and VAS scores (B) by visit



BL refers to day 1 of the trial. Higher EQ-5D-5L scores indicate better quality of life. EQ-5D-5L index scores range from 0–1.
BL, baseline; VAS, visual analogue scale.

- The baseline mean EQ-5D-5L index and visual analogue scale (VAS) scores for all participants were 0.870 and 81.0, respectively (compared with US adult population norms of 0.851 and 80.4[7], respectively)
- For all participants at week 52, the mean change from baseline values for the index and VAS scores were −0.06 and 3, while the minimal important change (MIC) values are 0.063 and 7.0
- Both mean EQ-5D-5L scores remained stable over time; mean scores stayed within the MIC thresholds for improving or worsening

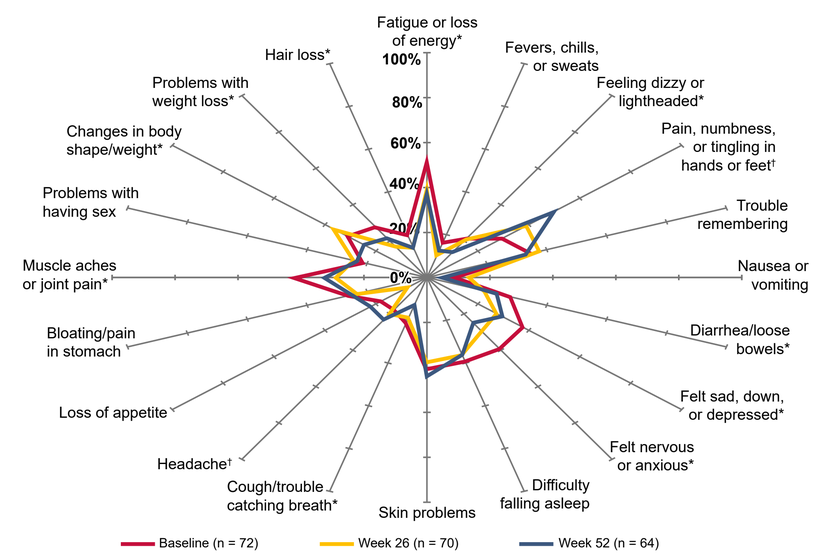
Figure 3. Mean SF-36 physical component summary scores (A) and mental component summary scores (B) by visit



BL refers to day 1 of the trial. Higher SF-36 scores indicate better functioning than lower scores.
BL, baseline; SF-36, Short Form 36.

- At baseline, the mean Short Form-36 (SF-36) physical component and mental component summary scores for all participants were 48.5 and 48.4, respectively, compared with US norms of 50 for each component score[14]
- Among all participants, the mean change from baseline values in SF-36 physical component and mental component summary scores were 1.0 and −0.9 at week 52, while the MIC values are 2.0 and 3.0, respectively
- Both SF-36 component summary scores were stable through 52 weeks; mean scores stayed within the MIC thresholds for improving or worsening

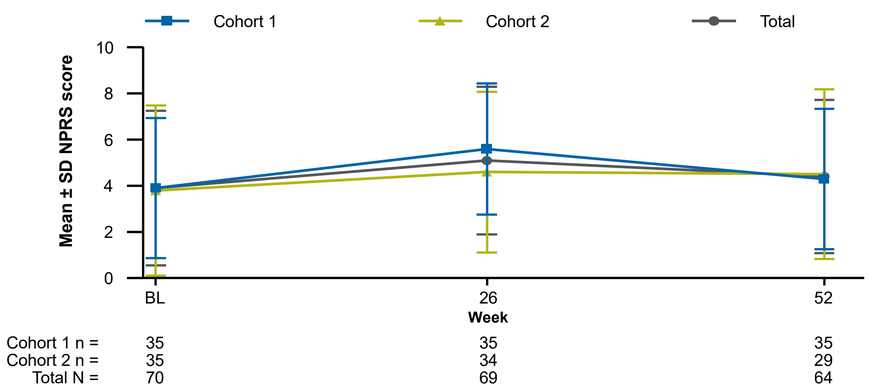
Figure 4. Proportion of individuals who reported each symptom as at least a little bothersome (HIV-SI ≥2) among all participants



- Fewer participants reported symptoms as bothersome at week 52 vs baseline (ranging from a 1% to 15% decrease), signifying stability or a decline in their HIV-related symptoms
- By week 52, the greatest decrease in symptoms reported as bothersome were fatigue or loss of energy (−15%), nervous or anxious (−14%), and muscle aches or joint pain (−10%)
- A few symptoms increased ≥5% by week 52, including headache and pain, numbness, or tingling in the hands or feet

Baseline refers to day 1 of the trial. Percentages in the plot are based on participants responding 2 ("it bothers me a little"), 3 ("it bothers me"), and 4 ("it bothers me a lot") on the HIV-SI response scale.
*≥5% decrease at week 52 vs baseline. †≥5% increase at week 52 vs baseline.
HIV-SI, HIV-Symptom Index.

Figure 5. Mean NPRS scores by visit



- Mean Numeric Pain Rating Scale (NPRS) score ranged from 3.9 to 5.1 through week 52 for all participants
- At week 52 among all participants, the mean change from baseline was less than the MIC of 2.0, and so did not represent a meaningful change
- While individual NPRS scores were highly variable over time with no clear trend, the mean score remained stable

BL refers to the day of the first SC injection. Higher NPRS scores indicate worse pain.
BL, baseline; N/A, not applicable; NPRS, Numeric Pain Rating Scale; SC, subcutaneous.

Limitations

- The number of study participants was small (N = 72)
- The general inherent limitations of participant-reported outcome instruments apply
  - Interpretation of scales may differ from participant to participant (ie, an HRQoL score signifying poor health to some may be considered as the best possible health for others)
- The EQ-5D-5L and SF-36 instruments—general measures of health—may not be specific or sensitive enough to detect differences between subgroups in this participant population
- Due to the heterogeneous nature of the OBR, which often contains antiretrovirals with varied safety profiles, it is difficult to infer causal association with LEN

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