GILEAD | Medical Information

Sunlenca® (lenacapavir) Injection Site Reactions

This document is in response to your request for information regarding the use of subcutaneous (SUBQ) Sunlenca® (lenacapavir [LEN]) for the treatment of HIV-1 and injection site reactions (ISRs).

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.

Summary

Product Labeling[1]

Administration of LEN may result in local ISRs. If clinically significant ISRs occur, evaluate and institute appropriate therapy and follow-up.

Improper administration (intradermal injection) has been associated with serious ISR reactions, including necrosis and ulcer. Ensure LEN is only administered SUBQ in the abdomen.

The most common adverse reactions (all grades) reported in ≥3% of participants in CAPELLA were nausea and ISRs.

Please refer to the LEN USPI for complete product information.

Clinical Data on SUBQ LEN and ISRs

In a pooled analysis of the CAPELLA and CALIBRATE studies (median exposure, 125 weeks and 88 weeks, respectively), ISRs were reported in 63%, 46%, and 55% of participants in CAPELLA and in 42%, 52%, and 43% of participants in CALIBRATE after the first, second, and third SUBQ LEN injections, respectively. A majority of ISRs were mild to moderate in severity, and no Grade 4 ISRs were reported. Five participants discontinued SUBQ LEN due to ISRs.[2]

Clinical Data on SUBQ LEN and ISRs

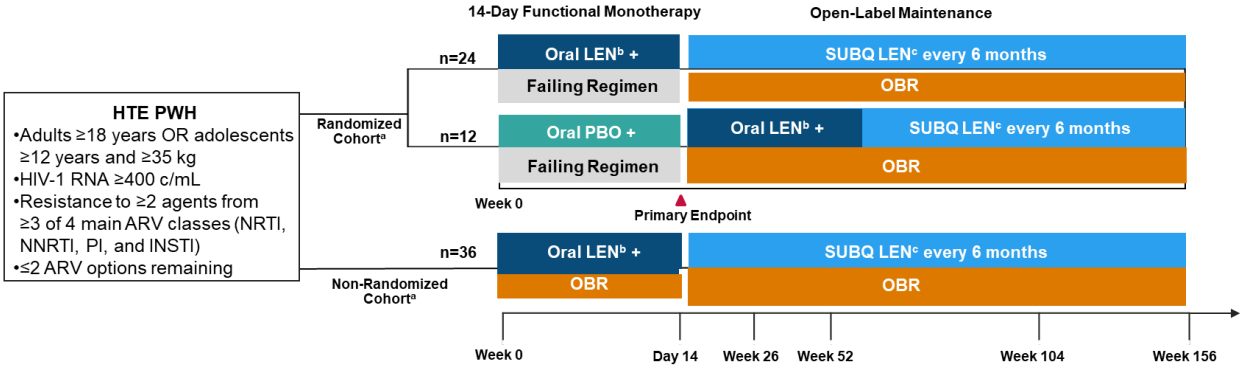
CAPELLA: LEN in HTE PWH

Study design

CAPELLA (NCT04150068) is an ongoing, phase 2/3, randomized, PBO-controlled clinical study designed to evaluate LEN as add-on therapy to a failing regimen in HTE PWH with multidrug resistance. Participants in both cohorts receive either oral LEN or PBO for 14 days in addition to their failing regimen or OBR. Both cohorts then enter the maintenance phase,

which is evaluating the safety and efficacy of SUBQ LEN administered every 6 months in combination with an OBR (Figure 1).[3]

Figure 1. CAPELLA: Study Design[3-6]



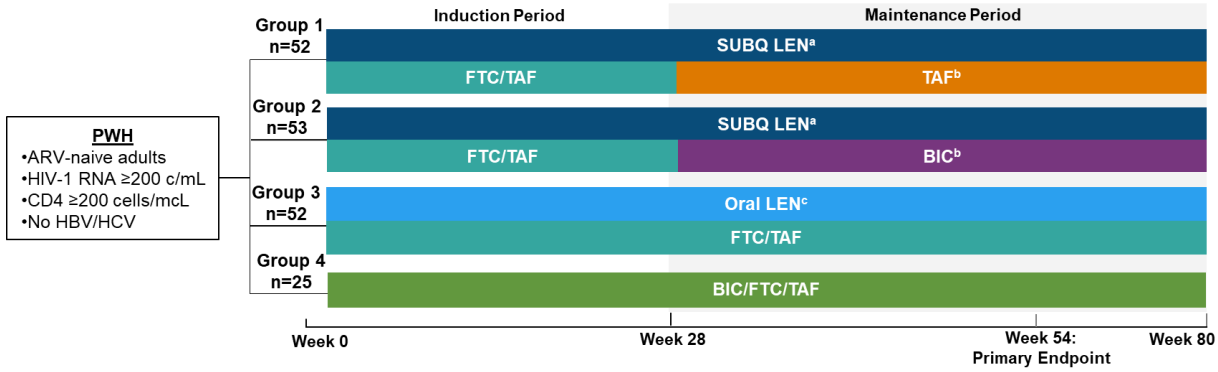
Abbreviations: ATV=atazanavir; COBI=cobicistat; INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleoside reverse transcriptase inhibitor; NRTI=nucleoside reverse transcriptase inhibitor; PI=protease inhibitor; RTV=ritonavir.
[a]Participants with <0.5 $\log_{10}$ decline in HIV-1 RNA and HIV-1 RNA ≥400 c/mL were enrolled in the randomized cohort. Participants were enrolled in the non-randomized cohort if they had ≥0.5 $\log_{10}$ decline in HIV-1 RNA and/or had HIV-1 RNA <400 c/mL or were enrolled after the randomized cohort was fully recruited.
[b]Oral LEN dosing schedule: Day 1, 600 mg; Day 2, 600 mg; and Day 8, 300 mg.
[c]SUBQ LEN dosing schedule: 927 mg (2 × 1.5 mL) on Day 15 and then every 6 months.
Note: ATV, ATV/COBI, ATV/RTV, efavirenz, etravirine, nevirapine, and tipranavir were not permitted for use in OBR.

CALIBRATE: LEN in ARV-Naive PWH

Study design

CALIBRATE (NCT04143594) was a phase 2, randomized, open-label, active-controlled clinical study that evaluated the safety and efficacy of LEN in ARV-naive PWH. Participants received SUBQ or oral LEN in combination with other oral ARV agents or BIC/FTC/TAF alone (Figure 2).[7,8]

Figure 2. CALIBRATE: Study Design[7,8]



Abbreviation: CD4=cluster of differentiation 4.
[a]The LEN dosing schedule included an oral lead-in phase (Day 1: 600 mg; Day 2: 600 mg; Day 8: 300 mg) followed by SUBQ LEN 927 mg (2 × 1.5 mL) on Day 15 and every 6 months (26 weeks) thereafter.
[b]Participants were required to have HIV-1 RNA <50 c/mL at Weeks 16 and 22 to initiate treatment with a two-agent regimen at Week 28. Those with HIV-1 RNA ≥50 c/mL discontinued the study at Week 28.
[c]The oral LEN dosing schedule was the following: 600 mg on Day 1, 600 mg on Day 2, and 50 mg on Day 3 and onwards.

Note: FTC/TAF (200/25 mg), TAF (25 mg), BIC (75 mg), and BIC/FTC/TAF (50/200/25 mg) were administered as daily oral doses.

CAPELLA and CALIBRATE ISR Data

An analysis of ISRs occurring after each of the first 3 SUBQ LEN injections was conducted among the 175 participants who received ≥1 dose of SUBQ LEN in the CAPELLA (N=72) and CALIBRATE (n=103) studies.[2]

Table 1. CAPELLA and CALIBRATE: Baseline Demographics and Characteristics[9a]

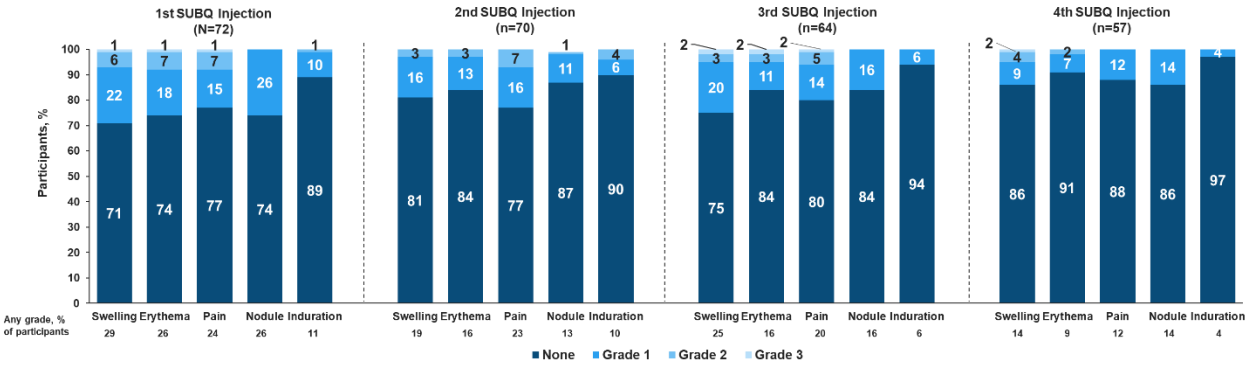
Key Demographics and Characteristics	CAPELLA (N=72)	CALIBRATE (N=105)[b]
Age, median (range), years	52 (23–78)	30 (19–61)
Female at birth, %	25	6
Black, %	38	46
Hispanic/Latinx, %	21	44
Weight, median (range), kg	70.5 (41.4–126)	77.1 (47.6–163.8)
BMI, median (range), kg/m^2	25 (14.9–42.6)	25.2 (17.5–51.1)

[a]Included all participants from CAPELLA and participants in treatment Groups 1 and 2 from CALIBRATE.
[b]Two participants in CALIBRATE were randomly assigned but never received a dose of SUBQ LEN.

Participants in CAPELLA received a median (IQR) of 10 (8–10) injections with a median (IQR) duration of exposure of 125 (111–140) weeks, and participants in CALIBRATE had a median (IQR) of 6 (6–8) injections with a median (IQR) duration of exposure of 88 (83–107) weeks. In both studies, SUBQ LEN 927 mg (2 × 1.5 mL) was administered into the abdomen every 6 months.[2]

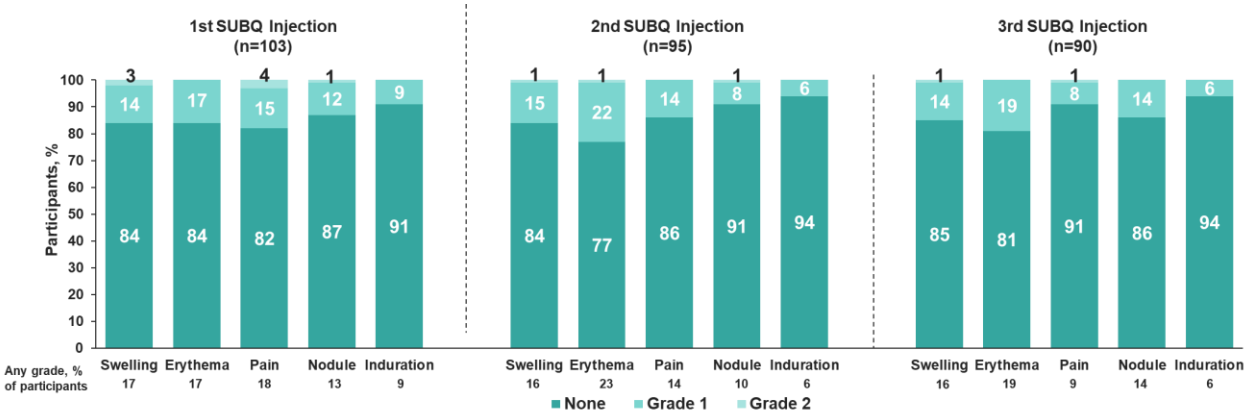
ISRs were reported in 63%, 46%, and 55% of participants in CAPELLA and in 42%, 52%, and 43% of participants in CALIBRATE after the first, second, and third SUBQ LEN injections, respectively (Figure 3 and Figure 4). The majority of ISRs were Grade 1 or 2 in severity, and no Grade 4 ISRs were reported.[2]

Figure 3. CAPELLA Study: ISRs Related to SUBQ LEN After First Four Injections[2,3,6a]



[a]Percentage denominators are the number of participants who received an injection at that visit. Percentages may not total 100% due to rounding.

Figure 4. CALIBRATE Study: ISRs Related to SUBQ LEN After First Three Injections[2a]



[a]Percentage denominators are the number of participants who received an injection at that visit. Percentages may not total 100% due to rounding.

In both studies combined, the mean duration of swelling, erythema, and pain was 10, 5, and 3 days, respectively. Nodules and indurations resolved after a median duration of 245 days and 194 days, respectively. The durations of the most common ISRs in each study are presented in Table 2.[2]

Table 2. CAPELLA and CALIBRATE Studies: Durations of ISRs Related to SUBQ LEN[2]

Duration, Median (IQR), Days	CAPELLA (N=72)	CALIBRATE (n=103)
Swelling	8 (4–15)	11 (6–15)
Erythema	5 (3–8)	5 (2–11)
Pain	3 (1–4)	2 (1–6)
Nodule	252 (113–524)	250 (100–369)
Induration	183 (63–498)	215 (144–415)

One participant in CAPELLA and 4 participants in CALIBRATE discontinued SUBQ LEN due to ISRs (Grade 1 induration, n=3; Grade 1 nodule(s), n=1; Grade 1 erythema and swelling, n=1), and only 1 discontinuation occurred after the first year of follow-up.[2]

In CAPELLA, after the fourth SUBQ LEN injection at Week 78, 8 participants had new nodules. Two participants had new indurations; 1 of these participants had ongoing indurations from the first through third injections, and 1 of these participants had an ongoing induration from the third injection.[3]

From CAPELLA and CALIBRATE, dermatology evaluations and/or skin biopsies were performed for 6 participants who had nodules or indurations that lasted for ≥6 months (Table 3). The nodules and indurations were not visible to participants or clinicians, but they were palpable. Chronic granulomatous inflammation consistent with a foreign body reaction to drug depot was noted and was consistent with pre-clinical findings.[2]

Table 3. CAPELLA and CALIBRATE Studies: Dermatology and Biopsy Evaluations[2]

ISR	Day	Summary of Findings
CAPELLA		
Grade 1 nodule	15	Granulomatis foreign body reaction in adipose panicle and fatty tissue necrosis, compatible with foreign body panniculitis
Grade 1 nodule	15, 215	Abdominal injection scars present; 4 SUBQ indurations found, 2 on each side of the abdomen. No biopsy was performed.

ISR	Day	Summary of Findings
CAPELLA		
Grade 2 nodule	204	Area palpable; no erythema or swelling. No biopsy was performed.
CALIBRATE		
Grade 1 nodule	380	SUBQ periumbilical nodules apparent upon deep palpation; no tenderness upon palpation; no overlying skin changes Biopsy results: minimal chronic inflammation; no granulomatous inflammation of foreign body reaction; no evidence of panniculitis
Grade 1 nodule	463	Fibrosis and giant cell reaction, compatible with ISR
Grade 1 swelling	561	Focal dermal fibrosis, possibly representing edge of old rupture cyst or folliculitis. Focal areas of granulomatous inflammation surrounding small collections of amorphous material, consistent with a granulomatous reaction to injected medication

References

1. SUNLENCA, Gilead Sciences Inc. SUNLENCA® (lenacapavir) tablets, for oral use. SUNLENCA® (lenacapavir) injection, for subcutaneous use. US Prescribing Information. Foster City, CA.
2. Castagna A, Arevalo JLB, Jean-Michel M, et al. Follow-Up of Injection Site Reactions in Clinical Studies of People Using Lenacapavir Every 6 Months for HIV Treatment.[Poster: eP.A.104]. Paper presented at: The 19th European AIDS Conference; October,18–21, 2023,; Warsaw, Poland.
3. Segal-Maurer S, DeJesus E, Stellbrink HJ, et al. Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection. *N Engl J Med.* 2022;386(19):1793-1803.
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5. Ogbuagu O, Segal-Maurer S, Ratanasuwan W, et al. Efficacy and safety of the novel capsid inhibitor lenacapavir to treat multidrug-resistant HIV: week 52 results of a phase 2/3 trial. *The lancet. HIV.* 2023;10(8):e497-e505.
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Abbreviations

ARV=antiretroviral
BIC=bictegravir
c/mL=copies per milliliter
FTC=emtricitabine
HTE=heavily treatment-experienced
ISR=injection site reaction
LEN=lenacapavir
OBR=optimized background regimen
PBO=placebo
PWH=people with HIV
SUBQ=subcutaneous
TAF=tenofovir alafenamide

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Sunlenca US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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