Injection Site Reactions with Subcutaneous Lenacapavir Administration at Alternate Injection Sites

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Conclusions

- The frequency of injection site reactions (ISRs) at alternate injection sites following subcutaneous (SC) lenacapavir (LEN) administration was generally similar when compared with the abdomen as reference
- ISRs were predominantly Grade 1/2, with only one Grade 3
- Safety data reported here, together with previously reported pharmacokinetic (PK) data, support further investigation of alternate injection sites for SC LEN administration
- More data on ISRs at alternate injection sites will be collected in future studies of LEN for pre-exposure prophylaxis

Plain Language Summary

- Lenacapavir is a medicine approved for the treatment of HIV infection in people who have already received many different HIV medicines but whose current medicines are not working
- Lenacapavir is usually given as an injection under the skin in the stomach area once every six months
  - — Side effects can occur where the injection is given, including pain, redness, swelling, lumps under and thickening of the skin
  - — Giving the injections in different locations of the body could help make these side effects less bothersome
- In this study, people without HIV were given lenacapavir injections in one of four different locations of the body: thigh, upper arm, buttocks, or stomach area
  - — We assessed the number and type of side effects between the different injection sites
- Overall, no one experienced any serious side effects
  - — Side effects were mostly mild-to-moderate, whether the injection was given in the thigh, upper arm, buttocks, or stomach area

Background

- LEN is a first-in-class, long-acting, HIV-1 capsid inhibitor approved for the treatment of multidrug-resistant HIV-1 infection, in combination with other antiretrovirals, in heavily treatment-experienced individuals[1,2]
- Following oral loading doses, LEN is administered as SC injections (927 mg given as 2 x 1.5 mL injections) in the abdomen every 6 months[1,2]
- ISRs are the most commonly reported adverse event (AE) following SC LEN administration
  - – Rotation of SC LEN injections between different anatomical sites could mitigate the impact of ISRs and facilitate long-term adherence
- We conducted a Phase 1 study in participants without HIV-1 to evaluate the PK and safety of SC LEN administration at alternate injection sites using the abdomen as a reference
  - – PK data were previously reported; LEN SC injection in the thigh, upper arm, and gluteal region achieved similar or slightly higher overall LEN exposures compared with the reference abdomen injection[3]

Objective

- To evaluate the safety of a single dose of SC LEN injection into the thigh, upper arm, and gluteal region compared with the abdomen

Methods

- This was a Phase 1, open-label, parallel design, randomized, single-dose study
- Participants were healthy males and nonpregnant, nonlactating females aged 18–55 years old with a body mass index of 19–30 kg/m^2
- Participants received a single dose of SC LEN (927 mg as two 1.5 mL injections) bilaterally, either in the thigh, upper arm, or gluteal region or in different quadrants of the abdomen
- Safety endpoints were incidence of AEs and laboratory abnormalities
- Injection site examinations were performed on Day 1, daily on Days 2–10, and at each subsequent visit through Day 270

Results

- Baseline characteristics were generally balanced between cohorts (**Table 1**)
  - – Overall median age was 46 years, and 50% of participants were male

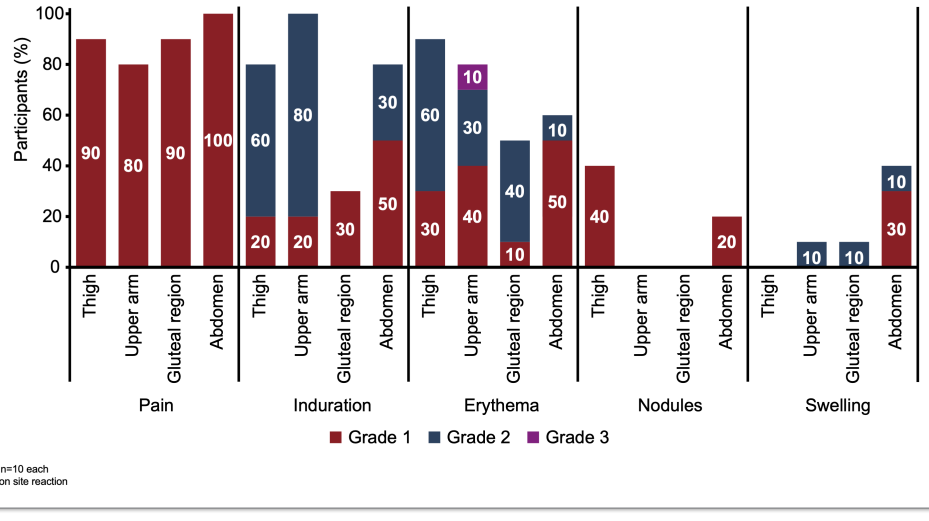
Table 1. Baseline Characteristics

	Thigh n=10	Upper arm n=10	Gluteal region n=10	Abdomen n=10
Median (IQR) age, years	48 (39–51)	43 (38–47)	44 (31–48)	49 (36–51)
Male, n (%)	5 (50)	6 (60)	4 (40)	5 (50)
Race, n (%) White Black or African American	 7 (70) 3 (30)	 8 (80) 2 (20)	 10 (100) 0	 7 (70) 3 (30)
Mean (SD) BMI, kg/m^2	27.0 (1.6)	27.2 (2.9)	26.9 (2.2)	27.0 (2.4)

BMI, body mass index

- Of the 40 participants enrolled, four discontinued the study: one due to a protocol violation (abdomen cohort), one due to consent withdrawal (gluteal region cohort), and two who were lost to follow-up (thigh cohort, abdomen cohort)
- There were no serious AEs, and no AEs led to study discontinuation
- Treatment-related AEs occurred in 38/40 (95%) participants
  - – Except for ISRs, all treatment-related AEs were Grade 1
- ISRs occurred in 38/40 (95%) participants
  - – Most ISRs were Grade 1 or 2; one Grade 3 (erythema, upper arm cohort) was observed (**Figure 1**)
  - – The most common ISRs were pain (90% of participants), induration (73%), erythema (70%), nodules (15%), and swelling (15%); incidence across injection site cohorts is shown in **Figure 1**

Figure 1. Most Common ISRs by Injection Site



All cohorts n=10 each
ISR, injection site reaction

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AK, EM, GS, and **GS** are all employees and shareholders of Gilead Sciences, Inc.

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