Cabotegravir Injections Are More Acceptable Than Lenacapavir Injections Following a Single Dose: Results From CLARITY, a Randomized Crossover Study of Long-Acting Injectable Antiretrovirals

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Key Takeaways

- **CLARITY describes injection site reactions (ISRs), tolerability, and preferences between long-acting cabotegravir (CAB) and long-acting lenacapavir (LEN) to enhance understanding of individuals who use long-acting injectable (LAI) antiretrovirals (ARVs) and provider experiences with LAI ARVs**
- **CAB injections were significantly more frequently accepted and preferred by participants than LEN injections**
- **By Day 22, ISRs were more frequent and visibly pronounced with LEN injections compared with CAB injections, underscoring key differences in tolerability profiles**

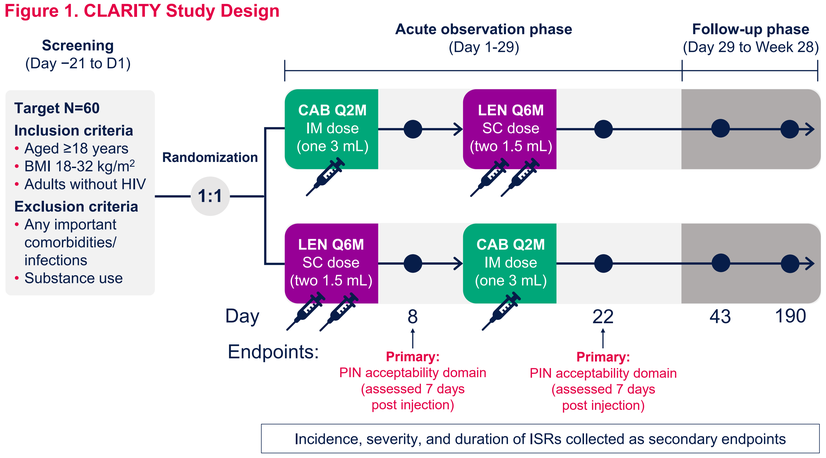
Purpose

- Studies show that the tolerability profile of long-acting injectable (LAI) antiretrovirals (ARVs) is an important factor influencing the treatment experiences and preferences of individuals who use LAI ARVs[1]
  - Currently, no data exist on differences in injection site reaction (ISR) profiles or ISR acceptability and tolerability between LAI ARVs and their administration route
- Understanding the experiences of healthcare providers (HCPs) administering different LAI ARV options is also important for recognizing differences in product preparation, administration, and ISR management
- The CLARITY study (NCT06970223) was designed to provide detailed insights into ISRs and the acceptability, tolerability, and preference of single doses of long-acting cabotegravir (CAB) intramuscular (IM) and long-acting lenacapavir (LEN) subcutaneous (SC) injections

Methods

- CLARITY is an open-label, randomized crossover study comparing CAB IM and LEN SC (1 dose each) in healthy adults without HIV-1, conducted at 1 site in the United States; each participant received both interventions during the study (Figure 1)
  - Single doses of CAB were administered as 1 injection and single doses of LEN as 2 injections, per product labeling
- The primary endpoint was local reaction acceptability 7 days after injection, measured using the 21-item Perception of Injection (PIN, adapted from the Sanofi Pasteur Vaccinees' Perception of Injection[2,3]) questionnaire as assessed by participants

Figure 1. CLARITY Study Design



BMI, body mass index; Q2M, every 2 months; Q6M, every 6 months.

- Participant and HCP preferences between CAB and LEN and the rationale for their preferences were assessed through a 2-item Study Medication Preference Questionnaire administered at Day 22 (7 days after the second injection)
- HCPs conducted ISR examinations at every study visit after dosing using Division of AIDS criteria; ISR pain, erythema, swelling, induration, nodule, pigmentation changes, and pruritus were assessed
- Here, we report the primary endpoint and ISR data up to 21 days after administration of each drug

Disposition and Baseline

Demographics and Baseline Characteristics

- CLARITY enrolled a diverse participant population; 29% were Black or African American, 38% were Hispanic or Latine, and 33% were female
- Mean (SD) age was 48 (14) years and median (SD) body mass index was 27 (3) kg/m²

Participant Disposition

- 64 participants entered the study; 1 participant was randomized but never received treatment (withdrawn by participant for "other" reason)
- 61 CAB doses (61 injections) and 62 LEN doses (124 injections) were administered in a total of 63 participants

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References: 1. Ramgopal et al. *Lancet HIV*. 2023;10:e566-e577. **2.** Chevat et al. *Health Qual Life Outcomes*. 2009;7:21. **3.** Chounta et al. *Adv Ther*. 2023;40:5300-5314.

Acceptability and Preference

CAB Injections Were More Acceptable Than LEN Injections

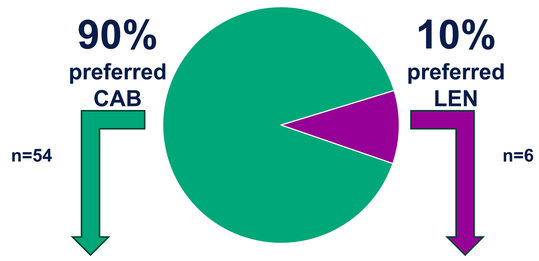
Figure 2. Proportion of Participants Reporting Local Reactions as "Totally or Very Acceptable" (PIN)[a] 7 Days Post Injection

[a]The questions "How acceptable was/were your local reactions?" and "How acceptable was your pain associated with your local reactions?" were used to assess acceptability (very/totally) from the PIN questionnaire. [b]7 days post injection (data from Days 8 and 22 are combined). 7 days post injection (data from Days 8 and 22 are combined). [c]Participants with available data.

- More participants found CAB injections "totally or very acceptable" compared with LEN; 69% CAB vs 48% LEN (Figure 2), which was statistically significant in a post-hoc analysis (*P*=0.019)

The Majority of Participants Preferred CAB Injections Over LEN Injections

Figure 3. Participant-Reported Preference at Day 22[a,b]



Rationale for preferring CAB (n=54/60)	n
Less pain during injection administration[c]	40
Less pain or soreness after injection administration	33
How long the injection nodules or swelling last	31
The size of the injection nodules or swelling	30
Number of injections received at each visit[d]	29

Rationale for preferring LEN (n=6/60)	n
Less pain or soreness after injection administration	5
How long the injection nodules or swelling last	3
The size of the injection nodules or swelling	3
Fewer number of side effects	3
Less severe side effects	2

[a]The question "Which medication regimen do you prefer" from the Study Medication Preference Questionnaire was used to assess preference on Day 22. [b]Participant preferences were assessed only at Day 22, after all participants had received both CAB and LEN injections. Participants were allowed to select multiple reasons for their stated preference. The top 5 reasons for preferring CAB or LEN are listed. [c]1/6 participants reported less pain during injection administration as the rationale for preferring LEN. [d]0/6 participants reported number of injections received at each visit as the rationale for preferring LEN.

- After receiving both ARVs, participants were significantly more likely to prefer CAB versus LEN (0.9; 95% CI 0.79, 0.96; *P*<0.001 post hoc; Figure 3)
- After both ARVs were administered, more HCPs at this study site preferred CAB (n=6 HCPs) versus LEN (n=1 HCP)
  - The 3 most common reasons HCPs preferred CAB included fewer number of reported side effects (5/6), less severe side effects (4/6), and less pain during injection (4/6); 1 HCP preferred LEN due to ease of injection preparation (note: HCPs could select more than 1 reason for their preference)

Conclusions

- **The CLARITY randomized crossover study found clinically and statistically relevant differences in ISR acceptability and tolerability, with more participants and HCPs favoring CAB over LEN injections after 1 dose of each ARV**
- **LEN LA injections led to more frequent and more visible ISRs**

Injection Site Reactions

Pain Was Lower With CAB on Day 1 but Similar Between Groups Thereafter

- 82% (51/62) of participants reported injection site pain for LEN vs 80% (49/61) for CAB
- Using the pain numerical rating scale (NRS), participants reported higher (more severe) pain scores on Day 1 of injection with LEN (mean [SD] 3.3/10 [2.6]) vs CAB (1.0/10 [1.6]); scores were similar on Days 3, 5, and 8
- Overall, peak pain was higher with LEN (mean 3.3/10) vs CAB (mean 2.4/10)

Fewer Visible/Palpable ISRs Were Reported With CAB Up to Day 22

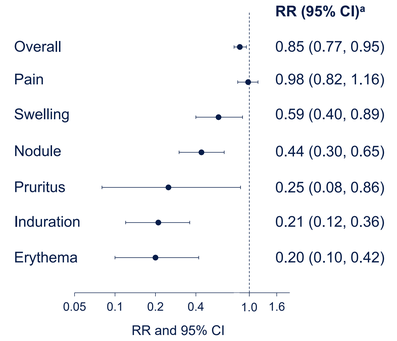
ISRs by Participant:

- There were lower relative risks of all non-pain ISRs while receiving CAB compared with LEN (Figure 4)
- 49% of participants receiving CAB and 100% of participants receiving LEN experienced a physical non-pain ISR event (Figure 5)
  - 30% (18/61) and 57% (35/62) experienced a Grade ≥2 ISR while receiving CAB and LEN, respectively
- Participants experienced a mean (range) of 2.4 (1-6) unique ISR events per CAB dose vs 8.7 (1-18) unique ISR events per LEN dose

ISRs by Injection Type:

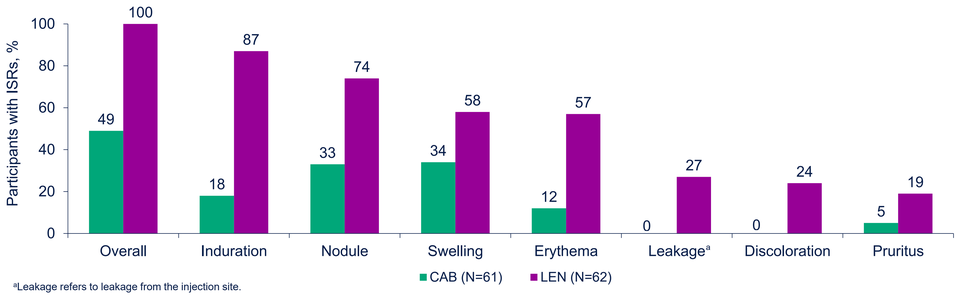
- ISRs were more frequent with LEN (n=538 ISRs in 62 participants) vs CAB injections (n=123 ISRs in 52 participants)
- Visible ISR events (defined as having any visible nodule, induration, swelling, erythema, or hyperpigmentation) were higher with LEN (n=221) vs CAB (n=36; Figure 6)
- No serious adverse events or discontinuations due to drug-related adverse events were reported across CAB and LEN

Figure 4. Relative Risk of ISRs With CAB



RR, relative risk. [a]Relative risk was calculated for ISR events that occurred across both treatment groups; RR was calculated as the ratio of the participant-level risk of ISRs with CAB to the participant-level risk with LEN. RR = 1 indicates no difference in risk, RR < 1 indicates lower risk in CAB participants.

Figure 5. Percentages of Participants With Non-Pain ISRs



[a]Leakage refers to leakage from the injection site.

Figure 6. Representative Images of CAB and LEN Injection Sites in One Participant

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