

Dainielle Fox,<sup>1</sup> Justine Boles,<sup>2</sup> Emilie Elliot,<sup>3</sup> Apinya Vutikulird,<sup>4</sup> Amber Mottola,<sup>4</sup> Kim Fletcher,<sup>5</sup> Kehui Wang,<sup>6</sup> Suryakant Somvanshi,<sup>7</sup> Richard Grove,<sup>5</sup> Katherine L. Nelson,<sup>1</sup> Laure Dupont-Benjamin,<sup>8</sup> Piotr Budnik,<sup>2</sup> Jean van Wyk,<sup>2</sup> Harmony P. Garges,<sup>6</sup> Kimberley Brown<sup>1</sup>

<sup>1</sup>ViiV Healthcare, Durham, NC, USA; <sup>2</sup>ViiV Healthcare, London, UK; <sup>3</sup>ViiV Healthcare, Madrid, Spain; <sup>4</sup>Ark Clinical Research, Long Beach, CA, USA; <sup>5</sup>GSK, London, UK; <sup>6</sup>GSK, Durham, NC, USA; <sup>7</sup>GSK, GCC, Bengaluru, India; <sup>8</sup>ViiV Healthcare, Rueil-Malmaison, France

## Plain Language Summary

- CLARITY used a crossover study design, meaning each person received 1 dose of long-acting cabotegravir and 1 dose of long-acting lenacapavir at different times so that their injection experiences could be directly compared
- Long-acting cabotegravir injections were found to be more acceptable and caused fewer, less visible, and shorter lasting injection site reactions than long-acting lenacapavir injections

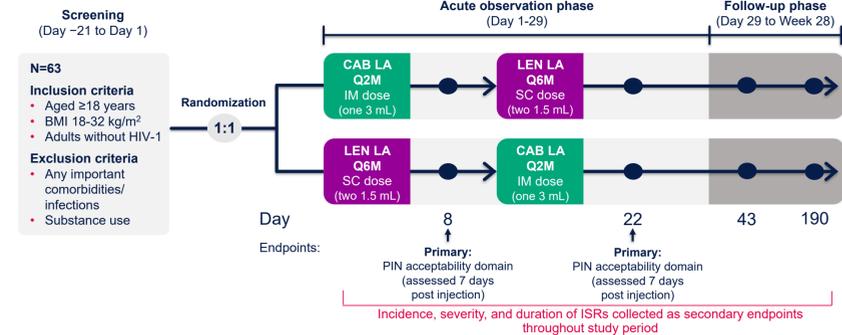
## Introduction

- Long-acting injectable (LAI) regimens provide improved adherence, confidentiality, and convenience over daily oral regimens<sup>1</sup>
- Injection-site reactions (ISRs) are common with LAI regimens and may cause long-lasting inflammatory effects, inadvertent disclosure, or lead to discontinuation of therapy and treatment<sup>2-5</sup>
- ISR profiles are important for individuals when selecting an LAI regimen for pre-exposure prophylaxis (PrEP), and the initial injection experience may determine an individual's willingness to continue therapy
- Despite the importance of ISRs, data on the characteristics associated with different LAI regimens are currently lacking
- The CLARITY study (NCT06970223) is a randomized crossover study that evaluates ISRs after a single dose each of long-acting cabotegravir intramuscular (CAB LA) and long-acting lenacapavir subcutaneous (LEN LA) injections<sup>6</sup>
- We have previously shown that a single dose of CAB LA had higher ISR acceptability\* and was preferred by participants compared with LEN LA after receiving a single dose each of CAB LA and LEN LA<sup>6,1</sup>
- Here we report detailed visible and palpable ISR events up to 190 days after administration of each study drug

## Methods

- CLARITY is an open-label, randomized crossover study comparing a single dose each of CAB LA and LEN LA in 63 people without HIV-1 (Figure 1)
- A single dose of CAB LA consists of 1 intramuscular gluteal injection, and a single dose of LEN LA consists of 2 subcutaneous abdominal injections

Figure 1. CLARITY Study Design



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

- Healthcare providers assessed ISRs at every study visit after dosing using Division of AIDS criteria
  - Assessed ISRs included pain, erythema, swelling, induration, pigmentation changes, pruritis, warmth, cellulitis, rash, and nodules
- The primary endpoint was defined as the proportion of participants reporting "very acceptable or totally acceptable" local reactions and pain at Day 8 and Day 22 (ie, 7 days after each injection) using the Perception of Injection (PIN) questionnaire, adapted from the validated Vaccinees' Perception of Injection questionnaire<sup>7,8</sup>
- Secondary endpoints included ISR incidence, severity, and duration through 6 months of follow-up
  - As part of the secondary endpoint, the PIN participant-reported outcomes are presented in terms of domain scores (bother, movement, sleep, acceptability) and individual item scores (anxiety before injection, pain during injection, satisfaction, anxiety after injection, willingness to continue) through Day 190
- Exploratory ISR assessments included a combination of 2-D photography and ultrasound scanning
- Qualitative interviews were conducted with a subset of participants at Day 8, Day 22, and at study discontinuation, if applicable

\*At Day 22, a higher proportion of participants reported that local reactions and pain were "very acceptable or totally acceptable" after CAB LA vs LEN LA injections (69% vs 48%;  $P=0.019$  in a post-hoc analysis). The mean (standard deviation [SD]) acceptability domain score in the Perception of Injection questionnaire was 1.9 (1.1) for CAB LA and 2.4 (1.2) for LEN LA, with lower scores indicating higher acceptability. \*After receiving both regimens, 90% ( $P<0.001$  in a post-hoc analysis) of participants reported that they preferred CAB LA over LEN LA.

In the CLARITY crossover study, results up to 6 months show that injection-site reactions were more frequent, visible, long-lasting, and bothersome after a single dose of long-acting lenacapavir compared with long-acting cabotegravir injections.

## Results

### Participant Baseline Demographics

- A diverse group of 63 participants (33% female, 38% Hispanic or Latine, and 29% Black or African American) were enrolled

### Frequency of ISR Events Among Participants

- Participants experienced fewer ISR events after CAB LA compared with LEN LA injections (Table 1)
  - The median (range) number of ISRs per participant was 2 (0-8) after CAB LA and 10 (3-20) after LEN LA

Table 1. Participant-Level Summary of ISR Frequency Through Day 190<sup>a</sup>

Variable, n (%)	CAB LA (n=61) <sup>b</sup>	LEN LA (n=62) <sup>b</sup>
Participants who experienced any ISR event	55 (90)	62 (100)
Number of ISR events <sup>c</sup>		
0	6 (10)	0
1	18 (30)	0
2	14 (23)	0
3 to 5	18 (30)	7 (11)
≥6	5 (8)	55 (89)

<sup>a</sup>In participants who received ≥1 injection. <sup>b</sup>One participant received CAB LA on Day 1 but did not receive LEN LA on Day 15. <sup>c</sup>Participants could experience more than 1 type of ISR event in response to injection.

### Summary of Overall ISR Events

- The total number of ISRs (CAB LA, n=150; LEN LA, n=642) was lower with CAB LA compared with LEN LA injections (Table 2)
- ISRs experienced after CAB LA injections resolved faster than those experienced after LEN LA injections (3% vs 22% not recovered/not resolved at Day 190)

Table 2. Summary of Overall ISRs Through Day 190<sup>a</sup>

Variable, n <sup>b</sup>	CAB LA (n=61) <sup>c</sup>	LEN LA (n=62) <sup>c</sup>
Total injections <sup>d</sup>	61	124
ISR events	150	642
Visible ISR events, n (%) of all events <sup>e</sup>	43 (29)	331 (52)
Maximum grade, n (%) of all injections		
Grade 1	37 (61)	59 (48)
Grade 2	13 (21)	59 (48)
Grade 3	5 (8)	6 (5)
Outcome, n (%) of all events <sup>f</sup>		
Recovered/Resolved	146 (97)	504 (79)
Not recovered/not resolved	4 (3)	138 (22)

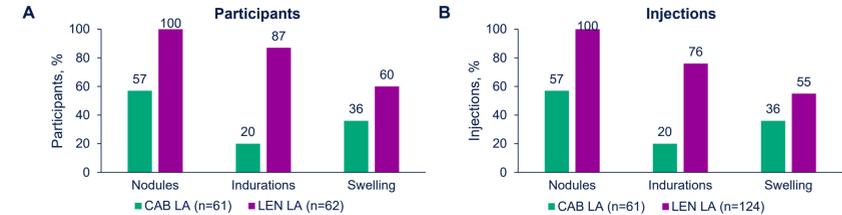
<sup>a</sup>In participants who received ≥1 injection. <sup>b</sup>Unless otherwise noted. <sup>c</sup>One participant received CAB LA on Day 1 but did not receive LEN LA on Day 15. <sup>d</sup>A single dose of CAB LA requires 1 injection; a single dose of LEN LA requires 2 injections. <sup>e</sup>Defined as having any erythema, hyperpigmentation, and/or visible nodules, indurations, or swelling. <sup>f</sup>Percentages may total >100% due to rounding.

### Summary of Nodule, Induration, and Swelling Events

- Fewer participants experienced nodules (CAB LA, 57%; LEN LA, 100%), indurations (CAB LA, 20%; LEN LA, 87%), and swelling (CAB LA, 36%; LEN LA, 60%) after CAB LA vs LEN LA injections (Figure 2)

- The proportions of nodules (14% vs 63%), indurations (83% vs 89%), and swelling events (77% vs 87%) that were visible were lower after CAB LA than LEN LA injections (Table 3)

Figure 2. (A) Proportions of Participants With ISRs and (B) Proportions of Injections Resulting in ISRs<sup>a</sup>



<sup>a</sup>A single dose of CAB LA consists of 1 injection; a single dose of LEN LA consists of 2 injections.

- The duration of nodules was shorter after CAB LA vs LEN LA injection, with 2 (6%) nodules with CAB LA persisting >180 days vs 101 (82%) nodules with LEN LA (Table 3)

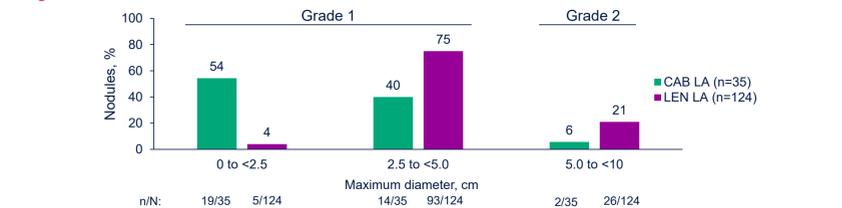
Table 3. Summary of Nodules, Indurations, and Swelling<sup>a</sup>

Characteristic	CAB LA (n=61) <sup>b</sup>	LEN LA (n=62) <sup>b</sup>
Nodules, n	35	124
Nodules unresolved by Day 190, n (%)	4 (11)	120 (97)
Duration of nodules, median (range), days <sup>c</sup>	64.0 (7-182)	196.5 (2-224)
Nodules visible at any time, n (%)	5 (14)	78 (63)
Indurations, n	12	94
Indurations unresolved by Day 190, n (%)	0 (0)	0 (0)
Duration of indurations, median (range), days <sup>c</sup>	12.0 (2-42)	14.0 (2-59)
Indurations visible at any time, n (%)	10 (83)	84 (89)
Swelling, n	22	68
Swelling unresolved by Day 190, n (%)	0 (0)	0 (0)
Duration of swelling, median (range), days <sup>c</sup>	5.0 (2-36)	7.0 (2-202)
Swelling visible at any time, n (%)	17 (77)	59 (87)

<sup>a</sup>In participants who received ≥1 injection. <sup>b</sup>One participant received CAB LA on Day 1 but did not receive LEN LA on Day 15. <sup>c</sup>Includes both resolved and unresolved ISRs (up to data cut-off date of Dec 29, 2025).

- Nodules were smaller in diameter after CAB LA vs LEN LA injections (Figures 3 and 4)

Figure 3. Maximum Size of Nodules<sup>a-d</sup>



<sup>a</sup>The median diameter of nodules was 2.0 cm for CAB LA and 4.1 cm for LEN LA. Most (54%) CAB LA nodules were <2.5 cm in diameter, while approximately 95% of LEN LA nodules were >2.5 cm in diameter. <sup>b</sup>Includes both resolved and unresolved ISRs (up to data cut-off date of Dec 29, 2025). <sup>c</sup>Modified DAIDS grading criteria for indurations/swelling (in which ISRs <2.5 cm in diameter or <6.25 cm<sup>2</sup> in surface area are also categorized as Grade 1) were extrapolated for nodules. By these criteria, 33/35 of CAB LA and 98/124 of LEN LA nodules were Grade 1, and 2/35 of CAB LA and 26/124 of LEN LA nodules were Grade 2. <sup>d</sup>By modified DAIDS grading criteria, indurations were 83% Grade 1 and 17% Grade 2 after CAB LA, and 96% Grade 1 and 2% Grade 2 after LEN LA. After CAB LA, 55% of swelling events were Grade 1 and 46% were Grade 2; after LEN LA, 34% of swelling events were Grade 1, 57% were Grade 2, and 9% were Grade 3.

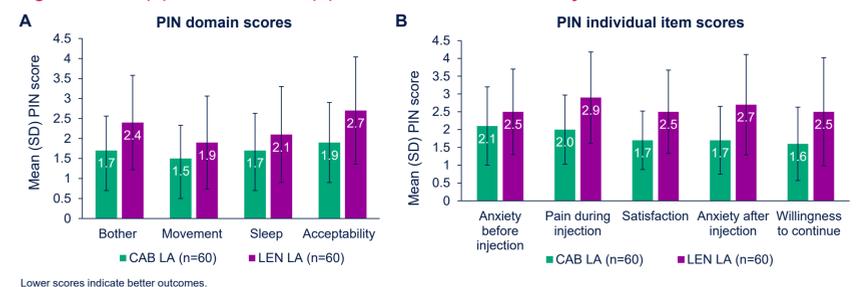
Figure 4. Representative Images of ISRs After CAB LA and LEN LA Injections



### Participant-Reported PIN Scores

- Across all PIN domains and individual items of assessment, participants consistently reported better results (indicated by lower scores) for CAB LA compared with LEN LA (Figure 5)
  - At Day 190, the proportions of participants reporting "very or totally acceptable" local reactions and pain were 70% for CAB LA and 37% for LEN LA
  - Most (85%) participants indicated a preference for CAB LA over LEN LA at Day 190

Figure 5. Mean (A) PIN Domain and (B) Individual Item Scores At Day 190



### Participant Experiences With ISRs

- Among participants who completed qualitative interviews at Days 8 and 22 (n=22), 91% expressed that their experiences with ISRs differed between CAB LA and LEN LA injections, primarily due to differences in severity of physical responses such as nodules and swelling

*"The nodules that I got in my abdomen were slightly larger and have been longer lasting than the one in the buttock" – Participant referencing LEN LA vs CAB LA, respectively*  
*"More redness, obviously the swelling, the tenderness, the pain when you put pressure on it and the nodules all were more severe or noticeable with these injections compared to the first" – Participant referencing LEN LA*

## Conclusions

- In CLARITY, ISRs after a single dose of LEN LA were more frequent, visible, severe, bothersome, and slower to resolve compared with those after a single dose of CAB LA, resulting in lower acceptability of local reactions and pain with LEN LA
  - In particular, nodules were larger, longer lasting, and more frequently visible after LEN LA vs CAB LA
- ISR profiles differentiate participant experiences with LAIs and can inform patient-provider discussions regarding optimal regimen choice

**Acknowledgments:** This study was funded by ViiV Healthcare. Editorial assistance and graphic design support for this poster were provided under the direction of the authors by Fingerpaint Medical and funded by ViiV Healthcare.

**References:** 1. Thouelle et al. *J Antimicrob Chemother.* 2022;77:290-302. 2. Maggi et al. *J Antimicrob Chemother.* 2004;53:678-681. 3. van 't Klooster et al. *Antimicrob Agents Chemother.* 2010;54:2042-2050. 4. Kelley et al. *N Engl J Med.* 2025;392:1261-1276. 5. Landovitz et al. *N Engl J Med.* 2021;385:595-608. 6. Boles et al. *EACS 2025*; Paris, France. Poster MeP20.4.LB. 7. Chevat et al. *Health Qual Life Outcomes.* 2009;7:21. 8. Chounta et al. *Adv Ther.* 2023;40:5300-5314.

## Disclaimer

**This content was acquired following an unsolicited medical information enquiry by a healthcare professional. Always consult the product information for your country, before prescribing a ViiV medicine. ViiV does not recommend the use of our medicines outside the terms of their license. In some cases, the scientific Information requested and downloaded may relate to the use of our medicine(s) outside of their license.**