Favorable Tolerability of Lenacapavir for PrEP Administered at Participant-Chosen Anatomic Sites in PURPOSE 1 and PURPOSE 2

TUPEC184

PURPOSE 1
PURPOSE 2

Carlos Brites[1], Marcelo H Losso[2], Jorge Gallardo-Cartagena[3], Pedro Cahn[4], Jesse Clark[5], Olivia Van Gerwen[6], Ishana Harkoo[7], Cheryl Louw[8], Noah Kiwanuka[9], Jenna Yager[10], Pamela Wong[10], Christoph C Carter[10], Moupali Das[10], Flavia Matovu Kiweewa[11]

[1]Complexo Hospitalar Universitário Professor Edgard Santos, Salvador, Brazil; [2]Hospital General de Agudos José María Ramos Mejía, Buenos Aires, Argentina; [3]Centro de Investigaciones Tecnológicas, Biomédicas y Medioambientales, Universidad Nacional Mayor de San Marcos, Lima, Peru; [4]Fundación Huésped, Buenos Aires, Argentina; [5]Department of Medicine, UCLA, Los Angeles, CA, USA; [6]Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, AL, USA; [7]Centre for the AIDS Programme of Research in South Africa, University of KwaZulu-Natal, Durban, South Africa; [8]Madibeng Centre for Research, Brits, South Africa; [9]Department of Epidemiology and Biostatistics, Makerere University School of Public Health, Kampala, Uganda; [10]Gilead Sciences, Inc., Foster City, CA, USA; [11]Makerere University–Johns Hopkins University Research Collaboration, Kampala, Uganda

To download this poster, the infographic summary, and other Gilead lenacapavir for PrEP presentations, scan the QR code

Conclusions

- After the PURPOSE 1 and PURPOSE 2 primary analyses, participants could choose to have subsequent lenacapavir (LEN) doses administered subcutaneously (SC) in the thigh, upper arm, or upper buttocks, or to continue to receive injections in the abdomen
- LEN was well tolerated across all SC injection sites
- Injection site reactions (ISRs) were less frequent with LEN injections administered in the thigh, upper arm, and upper buttocks compared with the abdomen
- Nodules and indurations occurring after thigh, upper arm, or upper buttock injections resolved more quickly than those occurring after abdomen administration
- Our findings support the safety and tolerability of LEN administration at participant-chosen anatomic sites, allowing greater flexibility and injection individualization

Plain Language Summary

- Lenacapavir injections given beneath the skin can help prevent people getting human immunodeficiency virus (HIV) when given every 6 months
- Initially, lenacapavir was studied as injections in the abdomen only
- In a later phase of the research studies, participants and their study doctors together could choose the injection site: abdomen, thigh, upper arm, or upper buttocks
- Participants who got injections in the thigh, upper arm, or upper buttocks had fewer injection site reactions (like bumps, swelling, or redness) than those who got injections in the abdomen
- When reactions occurred, they usually resolved sooner after injections in the thigh, upper arm, or upper buttocks than after injections in the abdomen
- Injections in all of these sites were considered safe, and most participants tolerated them well

Introduction

- Twice-yearly LEN for pre-exposure prophylaxis (PrEP) administered as SC injections in the abdomen was highly efficacious and well tolerated in the PURPOSE 1 and PURPOSE 2 studies[1,2]
- LEN is currently approved for abdomen or thigh injection in several geographies, including the US, Europe, and Brazil; abdomen or upper buttocks in South Africa; and abdomen, thigh, upper arm, or upper buttocks in Australia
- Offering participants choice of additional anatomic injection sites could improve injection experience

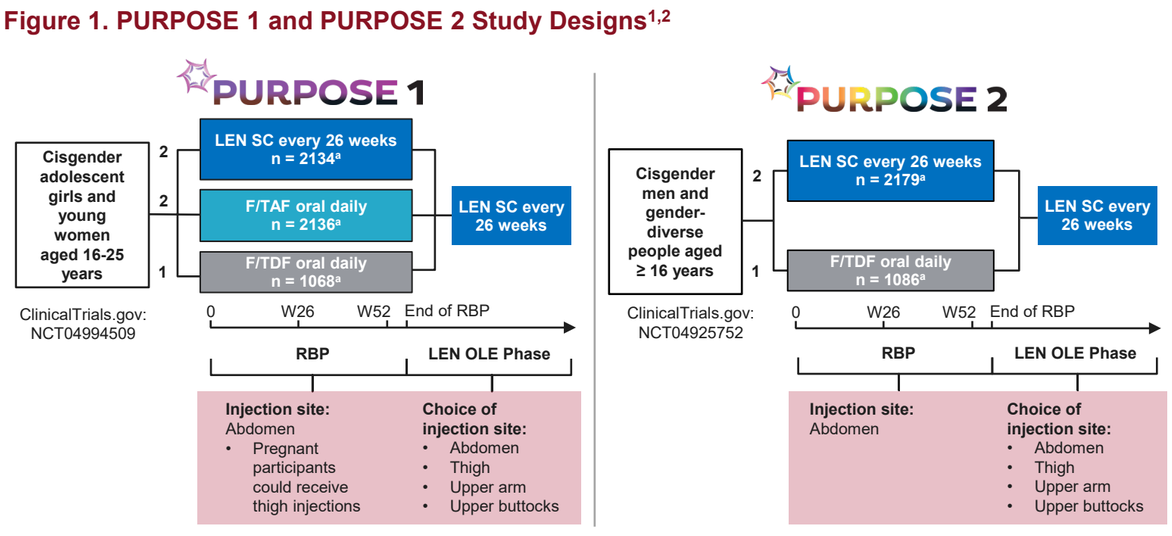
Objective

- To describe the tolerability of LEN SC administered in the thigh, upper arm, and upper buttocks compared with the abdomen

Methods

- PURPOSE 1 enrolled cisgender women aged 16-25 years; those who became pregnant could remain on study after reconsent (**Figure 1**)[1]
- PURPOSE 2 enrolled cisgender men, transgender women, transgender men, and gender-nonbinary individuals aged ≥ 16 years who have sex with partners assigned male at birth (**Figure 1**)[2]
- Participants in both studies received LEN SC injections in the abdomen during the randomized blinded phase (RBP) and pregnant participants in PURPOSE 1 could choose to receive thigh injections
- An optional open-label extension (OLE) following the RBP allowed for longer-term LEN follow-up. During the OLE, participants could choose injection in the abdomen, thigh, upper arm, or upper buttocks

Figure 1. PURPOSE 1 and PURPOSE 2 Study Designs[1,2]



[a]Full analysis set for efficacy analyses.

- Assessment of tolerability was based on investigator-reported adverse events (AEs) of ISRs
- ISR AEs were assessed across injection locations in two subgroups of participants in the studies:
  - **All LEN:** all participants who received active LEN injections in the RBP or OLE phase of the study
  - **LEN switch group:** participants who were randomized to daily emtricitabine/tenofovir alafenamide (F/TAF) or emtricitabine/tenofovir disoproxil fumarate (F/TDF) and received their first active LEN injection in the OLE phase of the study (with similar follow-up time across injection locations)

Results

- Approximately 95% of participants chose to participate in the OLE phase
- Median baseline weight and body mass index (BMI) were similar in participants choosing each injection site in PURPOSE 1 and PURPOSE 2 (**Table 1**)

Table 1. Baseline Characteristics of Participants Included in This Analysis

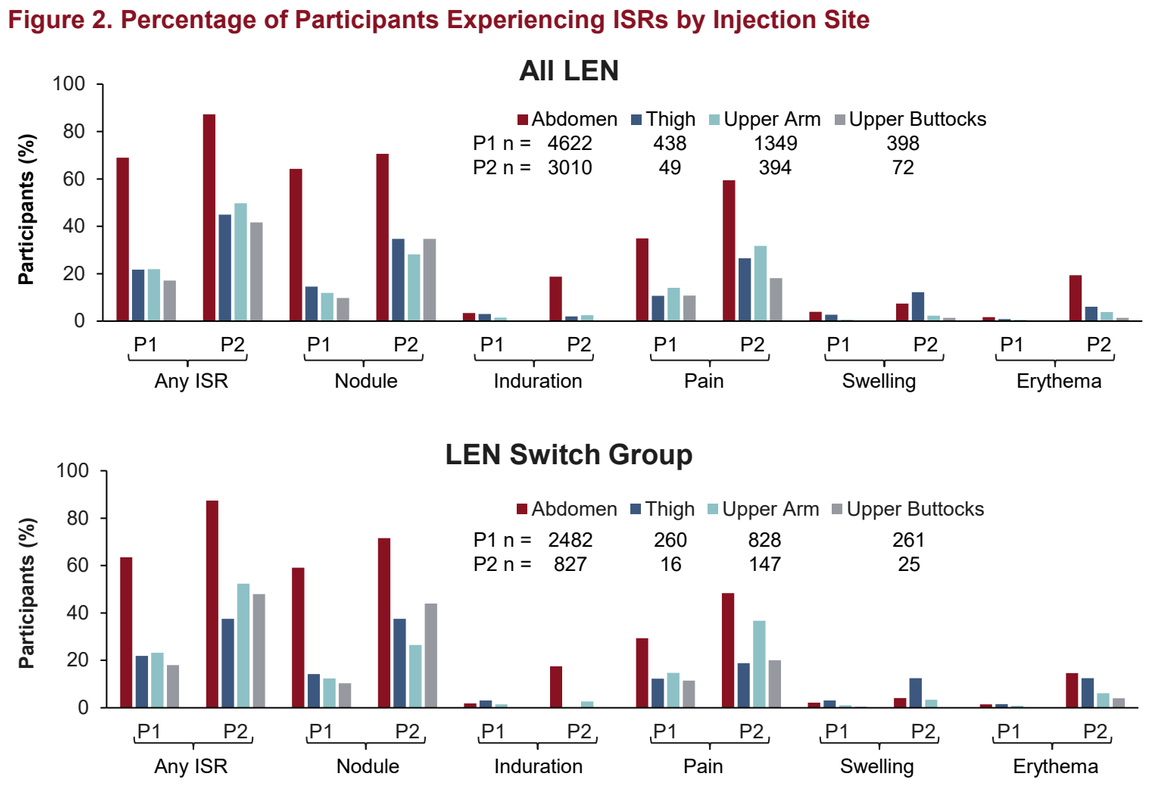
PURPOSE 1	Abdomen (n = 4622)	Thigh (n = 438)	Upper Arm (n = 1349)	Upper Buttocks (n = 398)
Female sex at birth, n (%)	4622 (100)	438 (100)	1349 (100)	398 (100)
Body weight,[a] kg, median (Q1, Q3)	65.2 (55.9, 79.5)	63.5 (55.8, 75.0)	69.8 (59.0, 84.0)	66.8 (56.6, 81.6)
BMI,[a] kg/m^2, median (Q1, Q3)	26.0 (22.3, 31.5)	25.6 (22.6, 30.0)	27.8 (23.6, 33.3)	26.8 (23.0, 32.0)
Pregnant or postpartum[b] at time of injection, n (%)	384 (8.3)	225 (51.4)	126 (9.3)	25 (6.3)
PURPOSE 2	**Abdomen (n = 3010)**	**Thigh (n = 49)**	**Upper Arm (n = 394)**	**Upper Buttocks (n = 72)**
Male sex at birth, n (%)	2953 (98.1)	46 (93.9)	390 (99.0)	72 (100)
Body weight,[a] kg, median (Q1, Q3)	75.7 (65.0, 89.0)	77.9 (65.6, 88.4)	81.7 (70.5, 97.1)	76.5 (68.9, 88.2)
BMI,[a] kg/m^2, median (Q1, Q3)	25.3 (22.1, 29.1)	24.5 (22.7, 28.9)	26.9 (23.6, 31.0)	25.4 (22.7, 28.8)

n-values include participants with at least one active LEN SC injection at the injection site location (received in either the RBP or LEN OLE phase for LEN randomized participants or received in the LEN OLE phase for F/TAF or F/TDF randomized participants).
[a]Body weight and BMI are at the time of the first active LEN SC injection at that anatomical location.
[b]Injection location occurring during pregnant/postpartum period defined as last menstrual period date through 6 weeks after the pregnancy outcome date.

- Through time of analysis, no participants receiving LEN injections in the thigh, upper arm, or upper buttocks had acquired HIV in PURPOSE 1 or PURPOSE 2

- Fewer participants reported ISRs when injections were given in nonabdominal injection sites (thigh, upper arm, or upper buttocks) compared to abdomen (**Figure 2**)

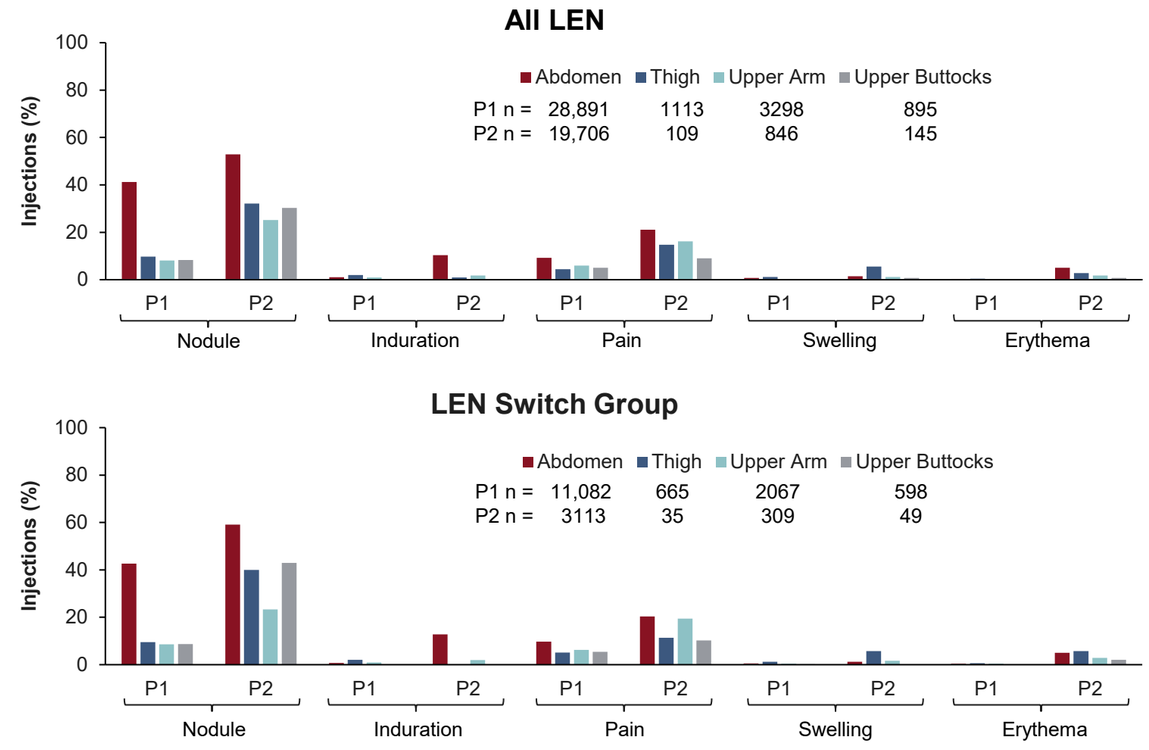
Figure 2. Percentage of Participants Experiencing ISRs by Injection Site



Includes the five most commonly reported ISR AEs.

- There were fewer AEs of injection site nodules and pain in the thigh, upper arm, or upper buttocks compared with the abdomen (**Figure 3**)

Figure 3. Percentage of Injections Resulting in ISRs by Injection Site



Includes the five most commonly reported ISR AEs. Each LEN dose was 927 mg by SC injection given as 2 × 1.5-mL injections. For nodules/indurations, bilateral events from the same injection visit were counted as separate AEs. For other ISRs, bilateral events were not counted separately and events with the same AE Preferred Term/ onset date were counted as one event.

- Injection site nodules and indurations generally resolved more quickly in nonabdominal sites than in the abdomen, although there was longer follow-up for abdominal injections administered during RBP (**Table 2**)
- LEN was well tolerated in participants who received injections at nonabdominal injection sites, with no reported serious ISRs or ISRs leading to study drug or study discontinuation (**Table 3**)

Table 2. Duration and Resolution of ISRs

PURPOSE 1	Abdomen		Thigh	Upper Arm	Upper Buttocks
	All LEN (n = 4622)	LEN Switch Group (n = 2482)	All LEN (n = 438)	All LEN (n = 1349)	All LEN (n = 398)
Total injections	28,891	11,082	1113	3298	895
Nodules, n (%)	11,899 (41.2)	4723 (42.6)	108 (9.7)	268 (8.1)	74 (8.3)
Resolved, n (%)[a]	7326 (61.6)	2275 (48.2)	57 (52.8)	80 (29.9)	19 (25.7)
Median (Q1, Q3) days to resolution[b]	260 (151, 364)	182 (91, 275)	90 (80, 174)	91 (72, 142)	90 (86, 97)
Indurations, n (%)	276 (1.0)	79 (0.7)	22 (2.0)	30 (0.9)	2 (0.2)
Resolved, n (%)[a]	213 (77.2)	47 (59.5)	13 (59.1)	25 (83.3)	1 (50.0)
Median (Q1, Q3) days to resolution[b]	87 (15, 262)	53 (17, 233)	15 (11, 49)	29 (10, 55)	95
PURPOSE 2	**Abdomen**		**Thigh**	**Upper Arm**	**Upper Buttocks**
	All LEN (n = 3010)	LEN Switch Group (n = 827)	All LEN (n = 49)	All LEN (n = 394)	All LEN (n = 72)
Total injections	19,706	3113	109	846	145
Nodules, n (%)	10,430 (52.9)	1839 (59.1)	35 (32.1)	213 (25.2)	44 (30.3)
Resolved, n (%)[a]	6201 (59.5)	597 (32.5)	10 (28.6)	98 (46.0)	11 (25.0)
Median (Q1, Q3) days to resolution[b]	270 (176, 367)	183 (106, 273)	116 (82, 178)	85 (32, 96)	182 (168, 184)
Indurations, n (%)	2025 (10.3)	398 (12.8)	1 (0.9)	15 (1.8)	0
Resolved, n (%)[a]	1641 (81.0)	288 (72.4)	1 (100)	12 (80.0)	N/A
Median (Q1, Q3) days to resolution[b]	85 (7, 191)	11 (6, 115)	93	22 (3, 95)	N/A

Each LEN dose was 927 mg by SC injection given as 2 × 1.5-mL injections. For nodules/indurations, bilateral events from the same injection visit were counted as separate AEs. [a]Percent resolved is out of the number of nodules or indurations. [b]Duration (days) = stop date minus onset date + 1.

Table 3. Safety and Tolerability by Injection Site

PURPOSE 1 Number of participants (%)	Abdomen		Thigh	Upper Arm	Upper Buttocks
	All LEN (n = 4622)	LEN Switch Group (n = 2482)	All LEN (n = 438)	All LEN (n = 1349)	All LEN (n = 398)
Any ISR	3188 (69.0)	1575 (63.5)	95 (21.7)	295 (21.9)	68 (17.1)
Any Grade 3 or 4 ISR	8 (0.2)	3 (0.1)	3 (0.7)	0	1 (0.3)
Any serious ISR	0	0	0	0	0
ISR leading to premature discontinuation of study drug	6 (0.1)	2 (< 0.1)	0	0	0
ISR leading to premature discontinuation of study	1 (< 0.1)	1 (< 0.1)	0	0	0
PURPOSE 2 Number of participants (%)	**Abdomen**		**Thigh**	**Upper Arm**	**Upper Buttocks**
	All LEN (n = 3010)	LEN Switch Group (n = 827)	All LEN (n = 49)	All LEN (n = 394)	All LEN (n = 72)
Any ISR	2628 (87.3)	723 (87.4)	22 (44.9)	196 (49.7)	30 (41.7)
Any Grade 3 or 4 ISR	18 (0.6)	3 (0.4)	0	0	0
Any serious ISR	1 (< 0.1)	1 (0.1)	0	0	0
ISR leading to premature discontinuation of study drug	27 (0.9)	0	0	0	0
ISR leading to premature discontinuation of study	3 (< 0.1)	0	0	0	0

References: **1.** Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92. **2.** Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

Acknowledgments: These studies were sponsored by Gilead Sciences, Inc. We thank all study participants and all participating study investigators and staff. Medical writing support was provided by Jessica Adams, PharmD, AAHIVE, of Gilead Sciences, Inc. Production assistance was provided by Aspire Scientific Ltd (UK) and was funded by Gilead Sciences, Inc. Medical writing funding support was provided by Gilead Sciences, Inc.

Abbreviations: AE, adverse event; BMI, body mass index; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; ISR, injection site reaction; LEN, lenacapavir; n, number of participants; OLE, open-label extension; P, PURPOSE; PrEP, pre-exposure prophylaxis; Q, quartile; RBP, randomized blinded phase; SC, subcutaneous(ly); W, Week.

Disclosures: **CB** has received research grants from the AIDS Malignancy Consortium and ViiV Healthcare; honoraria for speakers' bureaus and advisory boards for Gilead Sciences, Inc., Merck, and ViiV Healthcare; and is on the advisory committee of the Brazilian Society of Infectious Diseases. **MHL** has received research grants from Janssen and ViiV Healthcare, and has participated in advisory boards for ViiV Healthcare. **JG-C** has received research grants from UW/Fred Hutch CFAR, honoraria from Merck and ViiV Healthcare, and travel support from the HIV Vaccine Trials Network and the HIV Prevention Trials Network. **PC** reports honoraria for advisory boards, lectures, and educational events from Gilead Sciences, Inc. and ViiV Healthcare, and participates in the Moderna DSMB. **JC** has received research grants, travel support, and consulting fees from Gilead Sciences, Inc. and honoraria for educational events from Northridge Hospital Medical Center. **OVG** has received research grants from BioNTech, Gilead Sciences, Inc., and the National Institute for Allergy and Infectious Diseases; and consulting fees from Abbott, bioMerieux, and GSK. **IH**, **CL**, **NK**, and **FMK** do not have any disclosures to report. **JY**, **PW**, **CCC**, and **MD** are employees of Gilead Sciences, Inc., and may own stock in Gilead Sciences, Inc.

Correspondence: Jenna Yager, jenna.yager@gilead.com.