PURPOSE

Prevention with PURPOSE

HIV DRUG THERAPY GLASGOW 2026

Higher Persistence on Twice-yearly Lenacapavir Versus Daily F/TDF for PrEP in the UK and France in the PURPOSE 5 Study

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Presenter Disclosures

Disclosures

- Chloe Orkin has received research grants from Gilead Sciences, Inc., MSD, and ViiV Healthcare; consulting fees and payment for lectures from Gilead Sciences, Inc., GSK, MSD, Bavarian Nordic, and ViiV Healthcare; support for attending meetings from Gilead Sciences, Inc., ViiV Healthcare, Bavarian Nordic; and is on the board of Governing Council of the International AIDS Society
- Gilead Sciences, Inc. funded the study and designed the study with input from the PI and community advisory groups. The PIs and study staff gathered data; Gilead Sciences, Inc. monitored the conduct of the trial, received the data, and performed analyses
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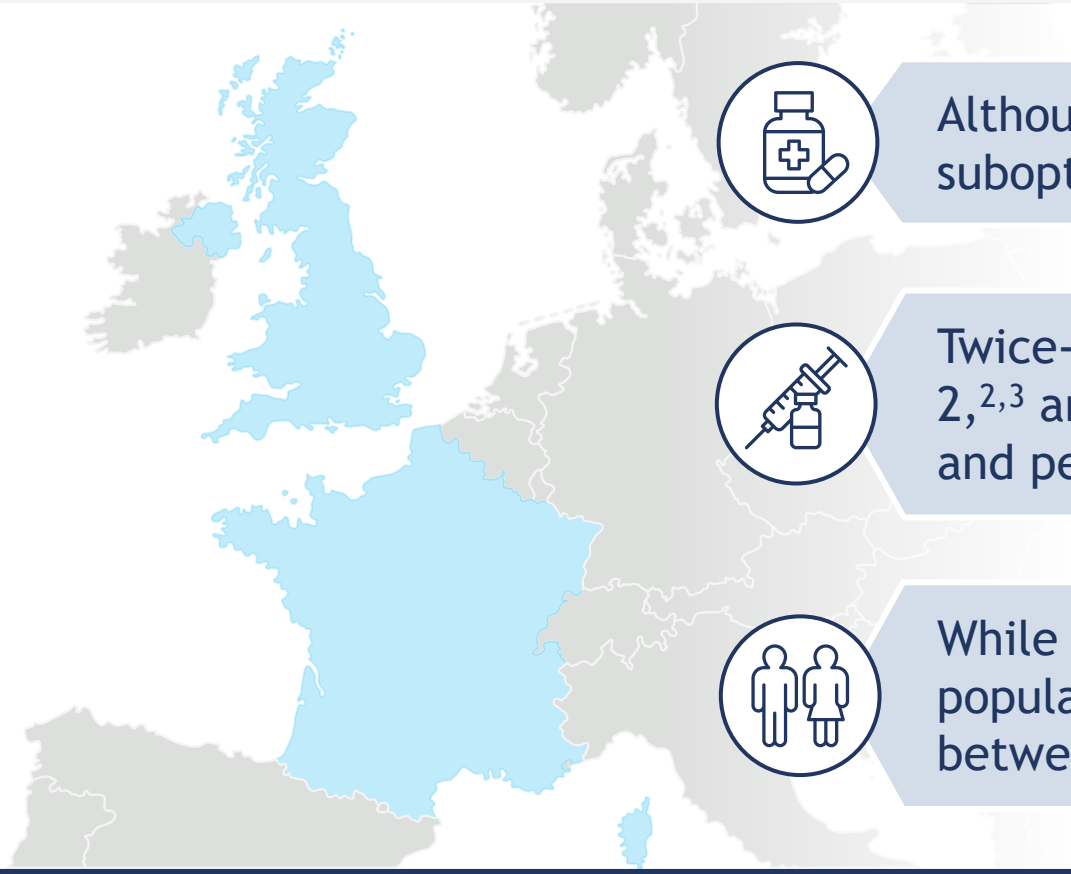
PI, principal investigator.

Twice-yearly SC LEN Demonstrated Favorable Safety and Superior Efficacy to F/TDF in PURPOSE 1 and PURPOSE 2



Although oral HIV PrEP is highly effective when taken daily, suboptimal adherence and discontinuations reduce effectiveness[1-3]

Twice-yearly SC LEN was highly efficacious in PURPOSE 1 and PURPOSE 2,[2,3] and has the potential to increase the uptake of, adherence to, and persistence on PrEP, thereby increasing effectiveness

While overall PrEP use is high in France and the UK, many key populations remain underserved by oral PrEP and inequities remain between PrEP availability and uptake[4-10]

PURPOSE 5 is a Phase 2 open-label study assessing persistence at 1 year, defined as sustained adherence over time, on LEN or F/TDF in PWBP disproportionately affected by HIV and not currently using PrEP in France and the UK

F/TDF, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **PWBP**, people who would benefit from PrEP; **SC**, subcutaneous.

1. Marrazzo J, et al. *JAMA*. 2024;331:930-37. 2. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. 3. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92. 4. UK Health Security Agency. HIV testing, PrEP, new HIV diagnoses and care outcomes for people accessing HIV services: 2025 report - GOV.UK (accessed Oct. 19, 2026). 5. Public Health England. https://assets.publishing.service.gov.uk/media/602166b08fa8f51474577bf7/hpr2020_hiv19.pdf (accessed Oct. 19, 2026). 6. Whelan I, et al. *Lancet HIV*. 2023;10:e472-81. 7. Shannon K, et al. *Lancet*. 2018;392:698-710. 8. Santé Publique France. https://www.santepubliquefrance.fr/maladies-et-traumatismes/infections-sexuellement-transmissibles/vih-sida/documents/bulletin-national/vih-et-ist-bacteriennes-en-france.-bilan-2023 (accessed Oct. 19, 2026). 9. Gosselin A, et al. *Sex Transm Infect*. 2020;96:227-31. 10. Billioti de Gage S, et al. *Lancet Reg Health Eur*. 2022;22:100486.

PURPOSE 5 Evaluated Persistence on Twice-yearly SC LEN vs Daily Oral F/TDF for PrEP in France and the UK

Open-Label Randomized Phase

Inclusion Criteria

Individuals who met UK and EU guidelines[1,2] for PrEP and were not currently taking PrEP (no use of PrEP for ≥ 4 weeks)[b,c]

Day 1[a] | Week 4 | Week 13 | **Week 26** | Week 39 | **Week 52**

2 **LEN SC every 26 weeks** n = 180[d]

1 **F/TDF oral daily** n = 87[d]

Primary Analysis

All participants completed ≥ 52 weeks of follow-up or prematurely discontinued

Primary analysis:
Persistence on LEN or F/TDF at Week 52

Secondary analysis:
Safety, acceptability, and PK of LEN vs F/TDF

Exploratory analysis:
Prevention of HIV-1 acquisition by LEN

Persistence was defined as sustained adherence to PrEP over 52 weeks

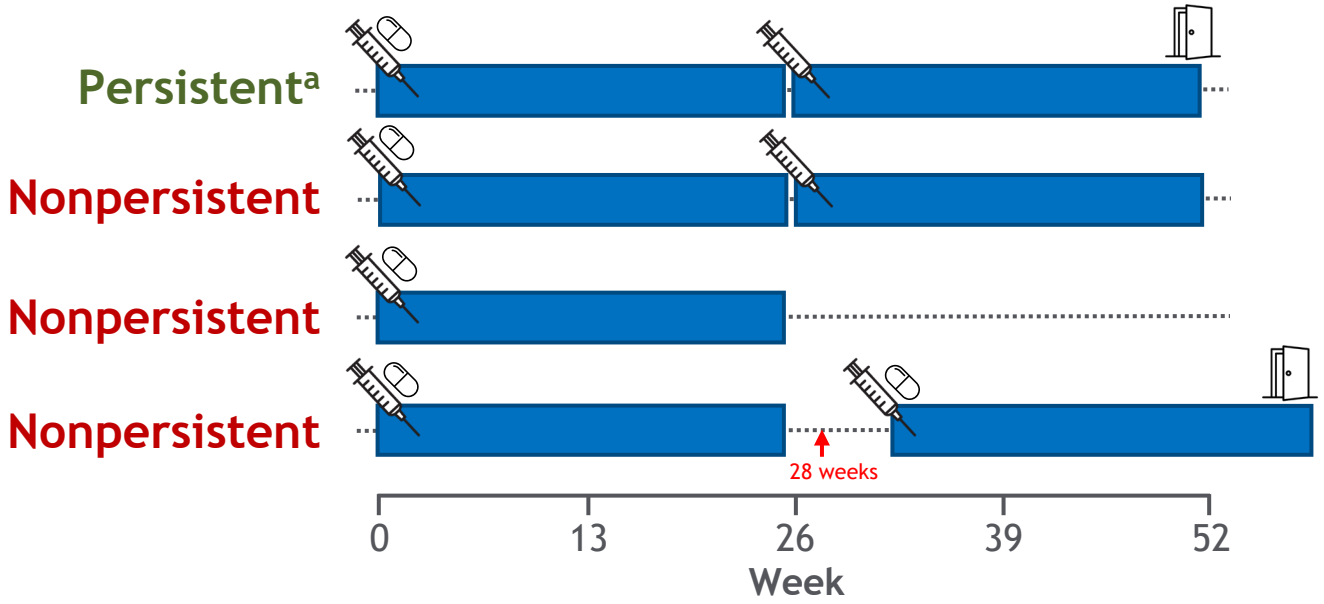
ClinicalTrials.gov: NCT06513312

[a]On Days 1 and 2, all participants receiving LEN received a pharmacologic loading dose of 600 mg oral LEN. [b]≥ 18 years of age, HIV-negative test, eGFR ≥ 60 mL/min. [c]HIV-negative status was confirmed by a local rapid HIV-1/2 antibody (Ab)/antigen (Ag) test, central HIV-1/2 Ab/Ag, and HIV-RNA NAAT at screening and on Day 1. [d]n numbers represent completed enrollment and received at least 1 dose of study drug. **eGFR**, estimated glomerular filtration rate; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **NAAT**, nucleic acid amplification testing; **PK**, pharmacokinetics; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous. 1. British Association for Sexual Health and HIV/British HIV Association. https://bhiva.org/wp-content/uploads/2025/07/2025-PrEP-guidelines.pdf (accessed Oct. 19, 2026). 2. EACS. https://eacs.sanfordguide.com/eacs-part1/art/eacs-pre-exposure-prophylaxis (accessed Oct. 19, 2026).

Defining Annual Persistence on PrEP:
Sustained adherence to study drug and follow-up visits over 52 weeks

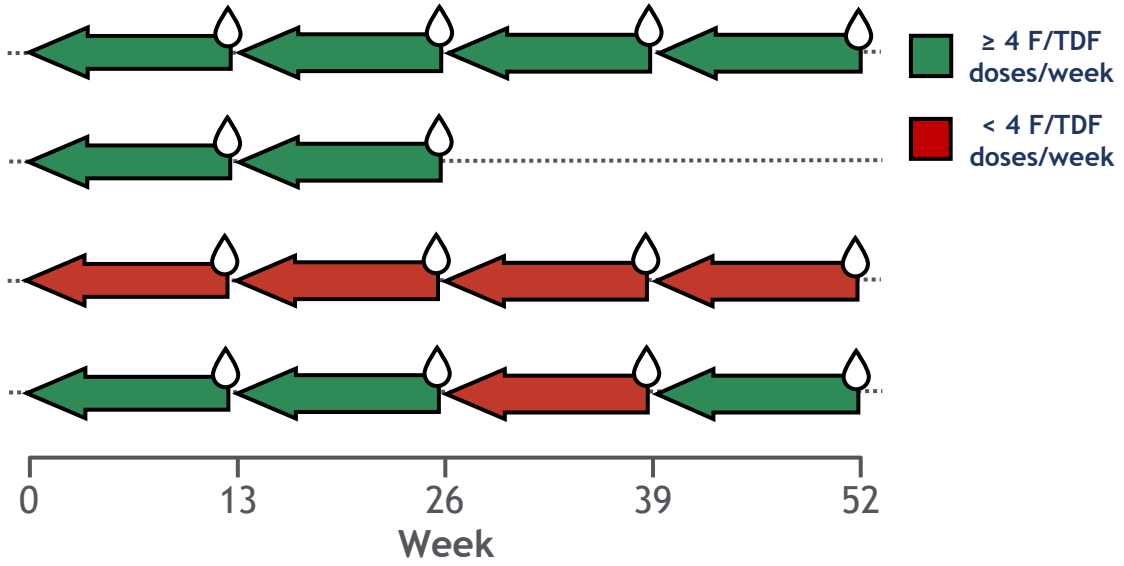
LEN

Injection at baseline, on-time injection at Week 26, and on-time follow-up visit attendance at Week 52[a]



F/TDF

On-time visits and DBS TFV-DP concentrations consistent with ≥ 4 doses/week at all of the following timepoints: Weeks 13, 26, 39, and 52[b]



Persistence was defined as <u>continued adherence to PrEP regimen and follow-up visits over 52 weeks</u>

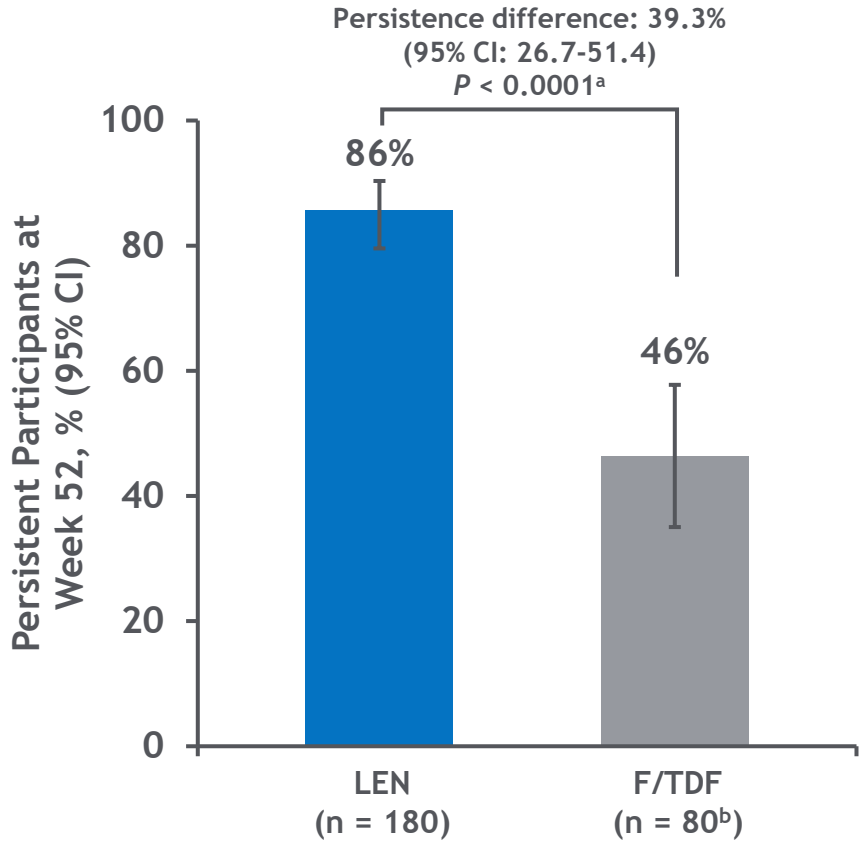
Nonpersistence on PrEP included participants who discontinued study drug for any reason. The proportion of participants with persistence through Week 52 was reported for each study group with 2-sided 95% exact CIs based on the Clopper-Pearson method.
[a]On-time injection at Week 26 and on-time follow-up visit at Week 52 were defined as 26 weeks (± 2 weeks) after the last injection. [b]One DBS concentration could be missing if that visit still occurred on-time and DBS concentrations at the three other timepoints were consistent with ≥ 4 doses/week. **CI**, confidence interval; **DBS**, dried blood spot; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **TFV-DP**, tenofovir diphosphate.

Baseline Characteristics Were Balanced Across Study Groups

Characteristic	LEN (n = 180)	F/TDF[a] (n = 87)	Overall (N = 267)
PrEP naïve, n (%)	68 (38)	33 (38)	101 (38)
Gender, n (%)[b]			
Cisgender men	130 (72)	63 (72)	193 (72)
Cisgender women	14 (8)	5 (6)	19 (7)
Transgender men	10 (6)	3 (3)	13 (5)
Transgender women	13 (7)	13 (15)	26 (10)
Gender nonbinary	12 (7)	3 (3)	15 (6)
Median age, years (IQR)	34 (28, 40)	34 (29, 43)	34 (28, 41)
Age ≤ 25 years, n (%)	30 (17)	15 (17)	45 (17)
Race or ethnic origin, n (%)			
White	110 (66)	62 (75)	172 (69)
Black	18 (11)	9 (11)	27 (11)
Asian	15 (9)	5 (6)	20 (8)
Other[c]	24 (14)	7 (8)	31 (12)
Not permitted[d]	13	4	17
Hispanic or Latino ethnicity, n (%)[e]	10 (6)	4 (5)	14 (6)
Born abroad, n (%)[f]	51 (29)	18 (21)	69 (26)
Diagnosis of bacterial STI in previous 12 months, n (%)	55 (31)	22 (25)	77 (29)
Engagement in sex work or transactional sex in previous 12 months, n (%)	17 (9)	10 (11)	27 (10)

[a]88 participants were randomized and one participant discontinued before receiving study drug. [b]One participant identified as androgenous. [c]This includes one American Indian or Alaska Native participant and one Native Hawaiian or Pacific Islander participant in the LEN group. [d]Not permitted entered if information cannot be collected due to regulations or if the participant declines to provide information. [e]Denominators excluded participants with missing or not permitted entered. [f]Those with country of birth other than France or the UK. The denominator excluded participants with missing or not permitted country of birth (three with LEN and two with F/TDF). **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **IQR**, interquartile range; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **STI**, sexually transmitted infection.

Significantly More Participants Persisted on LEN versus F/TDF at Week 52



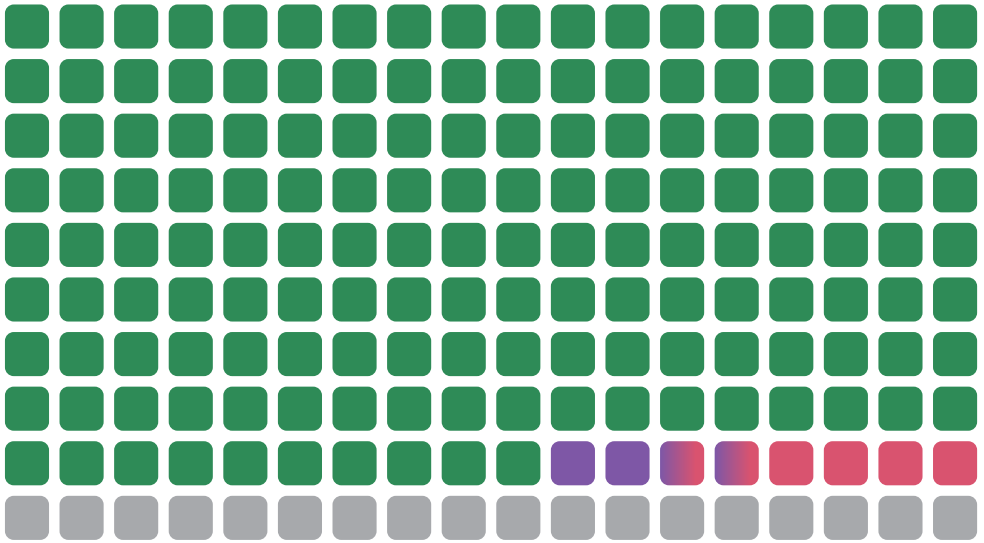
At Week 52, persistence on LEN was 39.3% higher than on F/TDF

[a]*P* value for persistence difference is based on Fisher's exact test. [b]Seven participants were excluded from the full analysis set due to no available DBS TFV-DP at any of the Week 13, 26, 39, or 52 visits.
CI, confidence interval; **DBS**, dried blood spot; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **SC,** subcutaneous; **TFV-DP**, tenofovir diphosphate.

Premature Discontinuation Was Similar Between Groups, While Nonadherence Was Higher with F/TDF

LEN (n = 180)[a,b]

154 of 180 persisted (86%)



- Persistent at Week 52 (n = 154, 86%)
- Out-of-window Week 26 LEN injection (n = 4, 2%)[e]
- Out-of-window Week 52 follow-up visit (n = 6, 3%)[e]
- Premature discontinuation of study drug or study before Week 52 (n = 18, 10%)

F/TDF (n = 80)[a,b,c,d]

37 of 80 persisted (46%)



- Persistent at Week 52 (n = 37, 46%)
- Lowest TFV-DP in DBS consistent with 2-3 doses/week (n = 5, 6%)
- Lowest TFV-DP in DBS consistent with < 2 doses/week (n = 25, 31%)
- Out-of-window visits (n = 6, 8%)
- Premature discontinuation of study or study drug before Week 52 (n = 7, 9%)

Nearly twice as many participants persisted on LEN at Week 52

[a]Percentages are of participants in each group. [b]Participants who were nonpersistent were categorized into early discontinuation versus nonadherence to the randomized PrEP regimen. If participants remained on study drug at 52 weeks, reasons for nonadherence were assessed. For participants in the F/TDF group, they were categorized by lowest TFV-DP concentration in DBS at Weeks 13, 26, 39, or 52, followed by out-of-window visits. If the six participants who were deemed nonpersistent due to out-of-window visits were considered persistent, 43 of 80 participants would be persistent on F/TDF at Week 52 (53.8%; $P < 0.0001$ vs LEN group). [c]Nonadherence in the F/TDF group was defined by TFV-DP concentrations in DBS and out-of-window visits. [d]Seven participants were excluded from the full analysis set due to no available DBS TFV-DP at any of the Week 13, 26, 39, or 52 visits. [e]Two participants had both out-of-window Week 26 LEN injection and Week 52 follow-up visit. **DBS**, dried blood spot; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **TFV-DP**, tenofovir diphosphate.

Premature Discontinuations Occurred in a Similar Proportion of Participants in the LEN and F/TDF Groups

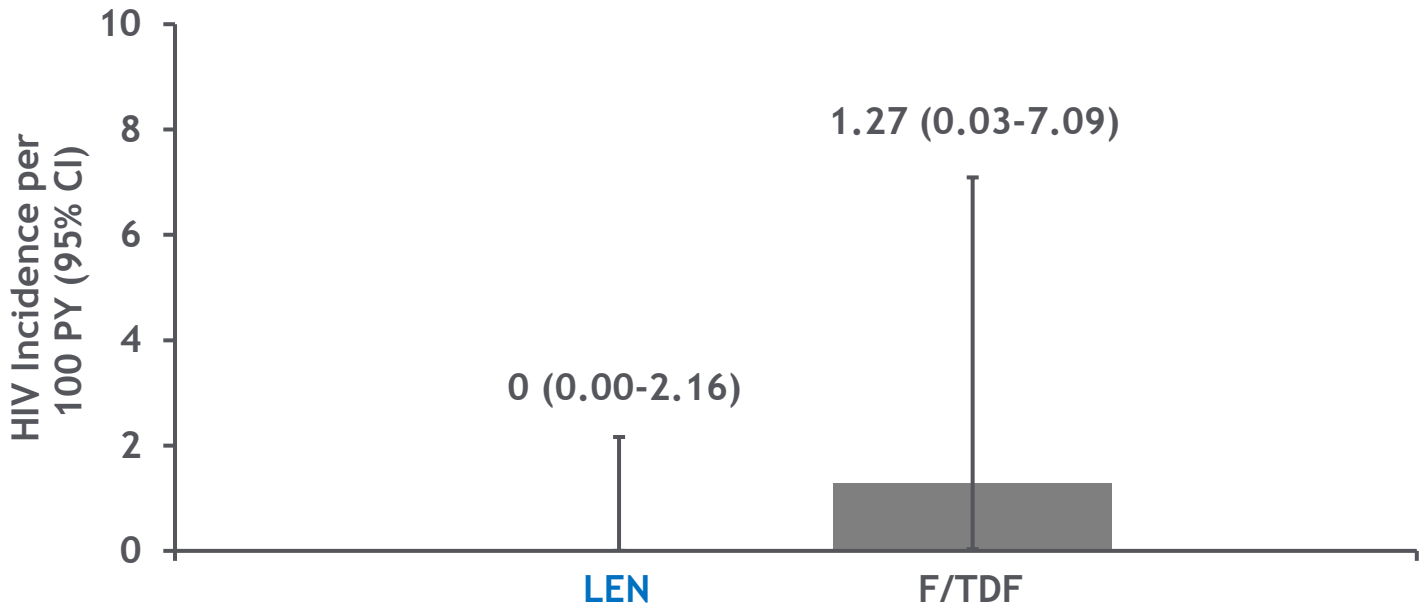
n (%)	LEN (n = 180)	F/TDF (n = 80[a])
Premature discontinuation of study drug or study prior to Week 52	18 (10)	7 (9)
Investigator's discretion	1 (< 1)[b]	0
Adverse events	0	0
Participant's decision or withdrawal of consent	13 (7)	2 (3)
Nonadherence to study drug	1 (< 1)	0
Lost to follow-up	2 (1)	4 (5)
HIV-1 acquisition	0	1 (1)
Missing	1(< 1)	0

Participant reasons for discontinuing LEN injections or withdrawing consent (n = 13) included:

- ISRs (n = 3)
- Did not like/did not want further injections (n = 3)
- Relocated (n = 3)
- Lifestyle changes (n = 1)
- No additional rationale documented (n = 3)

[a]Seven participants were excluded from the full analysis set due to no available DBS TFV-DP at any of the Week 13, 26, 39, or 52 visits; two of these seven participants discontinued prior to Week 13 due to AEs with F/TDF. [b]One participant was discontinued at the discretion of the investigator due to participant experiencing macular urticaria which was assessed as related to LEN. The investigator discontinued LEN but reported discontinuation as at their discretion rather than due to AE.
AE, adverse event; **DBS**, dried blood spot; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **ISR**, injection site reaction; **LEN**, lenacapavir; **TFV-DP**, tenofovir diphosphate.

No HIV Acquisitions Were Reported in Participants Receiving LEN



	LEN	F/TDF
No. of participants:	180	87
New HIV acquisitions:	0	1
PY of follow-up:	171	79

At diagnosis, the participant who acquired HIV in the F/TDF group had evidence of low adherence by TFV-DP concentrations in DBS (< 2 doses of F/TDF per week on average)

CI, confidence interval; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **PY**, person-years; **TFV-DP**, tenofovir diphosphate.

Adverse Events and STIs Were Similar Across Groups

n (%)	LEN (n = 180)	F/TDF (n = 87)
Any AE (excluding ISRs)	157 (87)	71 (82)
Grade ≥ 3	8 (4)	6 (7)
Serious AEs	7 (4)	3 (3)
AEs leading to discontinuation of study drug	0	2 (2)
Death	0	0
AEs occurring in ≥10% of participants in either group (excluding ISRs)		
Anal gonococcal infection	20 (11)	12 (14)
Anal chlamydia infection	19 (11)	9 (10)
Diarrhea	14 (8)	13 (15)
Oropharyngeal gonococcal infection	20 (11)	3 (3)
Nausea	7 (4)	9 (10)
Sexually transmitted infections (STIs)[a]		
Gonorrhea, chlamydia, or *Trichomonas vaginalis*	48 (27)	25 (29)
Gonorrhea	26 (15)	18 (21)
Chlamydia	30 (17)	11 (13)
Trichomonas vaginalis	2 (8)	0
Syphilis	9 (5)	4 (5)

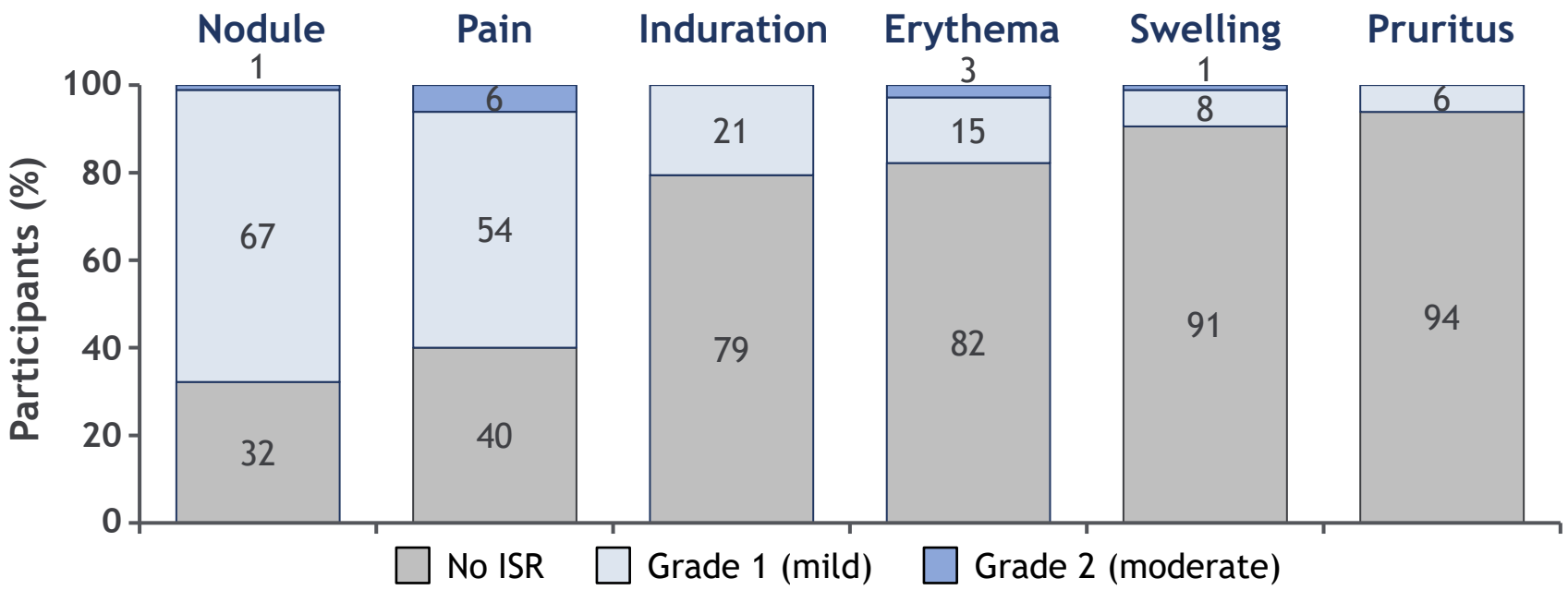
Twice-yearly SC LEN was generally safe and well tolerated. No new safety concerns were identified

AEs were coded according to MedDRA Version 29.0. Treatment-emergent AEs began on or after study drug first dose through last exposure date for the randomized phase, or the day prior to the initiation of study drug in the next study phase, whichever is earlier.
Death includes any death that occurred during the randomized phase. Severity grades were defined by Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1. [a]STI summary is from laboratory assessments or investigator diagnosis. For the STI analysis, there were 177 participants included in the LEN group and 85 participants included in the F/TDF group. **AE,** adverse event**; F/TDF**, emtricitabine/tenofovir disoproxil fumarate**; ISR**, injection site reaction; **LEN,** lenacapavir; **SC**, subcutaneous; **STI**, sexually transmitted infection.

Most ISRs with LEN Were Mild

LEN
(n = 180 participants with ≥ 1 injection)

ISRs occurring in ≥ 10 participants receiving LEN injections



- 169 (94%) participants had AEs of ISRs
- No severe (Grade 3 or 4) ISRs

ISR frequency and severity were similar to other LEN for PrEP studies[1,2]

Reported injection site reactions were to study drug-related injection only and were coded according to the Medical Dictionary for Regulatory Activities, Version 29.0. Severity grades were defined by Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1. Due to rounding, percentages may not total 100. Multiple ISRs were counted only once per participant for the highest severity grade for each preferred term.

AE, adverse event; **ISR**, injection site reaction; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous. 1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. 2. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92.

LEN Trough Concentrations at Week 26

Mean (90% CI) C_{trough} was above the target concentration of 15.5 ng/mL (IQ4)

	PURPOSE 5	PURPOSE 1 and PURPOSE 2[a]
Mean C_{trough} (ng/mL)	23.5	27.4
90% CI lower bound	22.0	26.2
5th percentile of C_{trough}	8.7	8.6

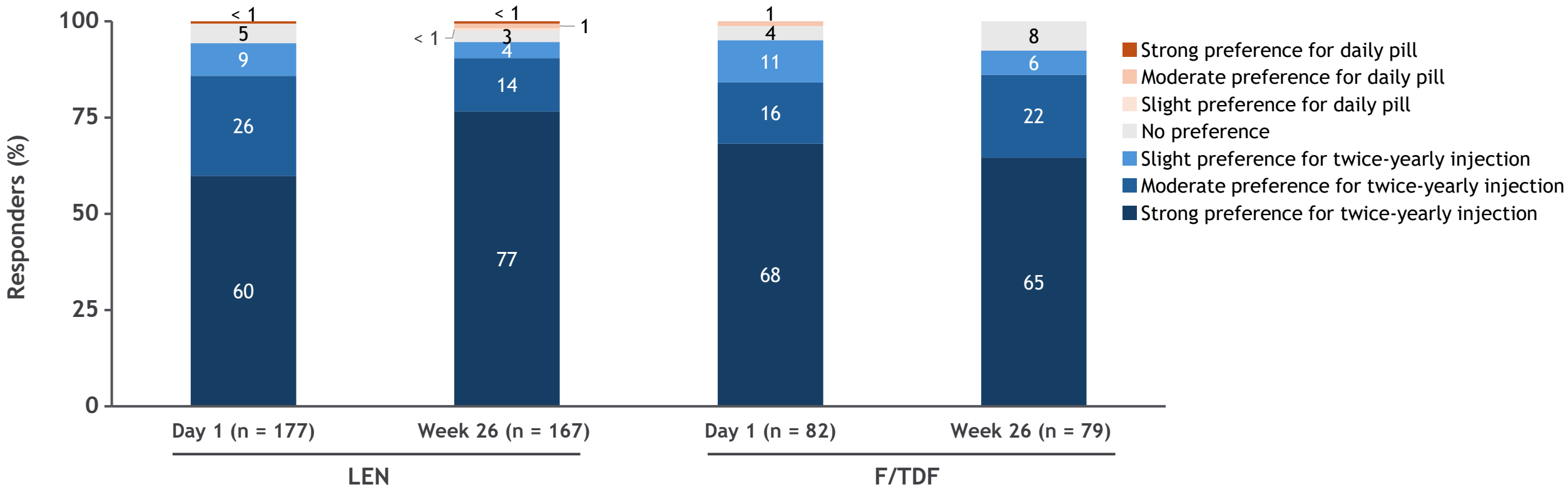
Observed LEN concentrations at Week 26 in PURPOSE 5 were similar to those in PURPOSE 1 and PURPOSE 2

IQ was defined as the protein-adjusted 95% effective concentration in MT-4 cells, and IQ4 as 4× the protein-adjusted 95% effective concentration, *in vitro*.[1]

[a]Data from PURPOSE 1 and PURPOSE 2 represent analysis of pooled data from a randomly preselected, representative sample of 10% of the participants chosen for PK evaluation.

CI, confidence interval; **C_{trough}**, trough concentration; **IQ4**, inhibitory quotient 4; **LEN**, lenacapavir; **PK**, pharmacokinetics. 1. Margot N, et al. Poster O-324 presented at: HIV Drug Therapy Glasgow; Oct. 5-8, 2020; Glasgow, UK.

Most Participants Preferred a Twice-Yearly LEN Injection Over a Once Daily Pill for PrEP



Strong preference for injection increased from Day 1 to Week 26 in participants receiving LEN

F/TDF, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir.

Persistence Was Higher With Twice-Yearly SC LEN than Daily Oral F/TDF in the UK and France



PURPOSE 5 demonstrated significantly higher PrEP persistence at Week 52 with twice-yearly SC LEN than daily oral F/TDF among PWBP in the UK and France, consistent with PURPOSE 1 and PURPOSE 2[1,2]

LEN was generally safe and well tolerated. There were no observed HIV acquisitions in participants receiving LEN

- Safety, including injection experience, was similar to that observed in PURPOSE 1 and PURPOSE 2[3,4]

Most participants expressed a strong preference for twice-yearly injection over a daily oral pill

Based on a rigorous, objective measure of persistence, PURPOSE 5 supports the potential public health impact of LEN in improving PrEP persistence, and consequently PrEP effectiveness, among PWBP not currently taking PrEP

F/TDF, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **PWBP**, people who would benefit from PrEP; **SC**, subcutaneous.

1. Bekker LG, et al. Oral 048 presented at: HIV Drug Therapy Glasgow; Nov. 10-13, 2024; Glasgow, UK. 2. Ogbuagu O, et al. Oral PS08.5 presented at: EACS; Oct. 15–18, 2025; Paris, France.
3. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. 4. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92.

Acknowledgments

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PURPOSE 5 Study Sites

- AP-HP - Hôpital Avicenne
- AP-HP - Hôpital Bichat - Claude Bernard
- AP-HP - Hôpital Lariboisière
- AP-HP - Hôpital Saint Antoine
- AP-HP - Hôpital Saint-Louis
- Axess Sexual Health
- Barts Health NHS Trust (Ambrose King Centre)
- Birmingham Heartlands Hospital
- Brighton and Sussex CRF
- Chelsea and Westminster Hospital
- CHU de Nice Archet 1
- The Hathersage Centre
- Homerton University Hospital
- Hôpital Européen Marseille
- King's College Hospital - Caldecot Road
- North Manchester General Hospital

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