PURPOSE

Prevention with PURPOSE

AIDS 2026
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High Efficacy of Twice-Yearly Subcutaneous Lenacapavir for PrEP Through 52 Weeks of Open-Label Extension in PURPOSE 2

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Acknowledgments and Presenter Disclosures

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Disclosures

- Marcelo H Losso has received research grants from Gilead Sciences, Inc. and ViiV Healthcare through Fundación IBIS and Hospital Ramos Mejía
- Gilead Sciences, Inc. funded the study and designed the study with input from the PI and Global Community Advisory and Accountability Group. The PIs and study staff gathered data; Gilead Sciences, Inc. monitored the conduct of the trial, received the data, and performed analyses
- Medical writing support was provided by Thierry Deltheil, PhD (Aspire Scientific Ltd, UK), and was funded by Gilead Sciences, Inc.

PI, principal investigator.

Summary

What is your main question?

- Does twice-yearly SC LEN for PrEP continue to be efficacious and well tolerated with longer-term follow-up in the open-label extension (OLE) of PURPOSE 2?

What did you find?

- LEN was highly efficacious through the first 52 weeks of the OLE
- One participant on open-label LEN acquired HIV during 52 weeks of the OLE
- The tolerability of LEN was similar through Week 52 of the OLE in participants who continued LEN or switched from oral F/TDF

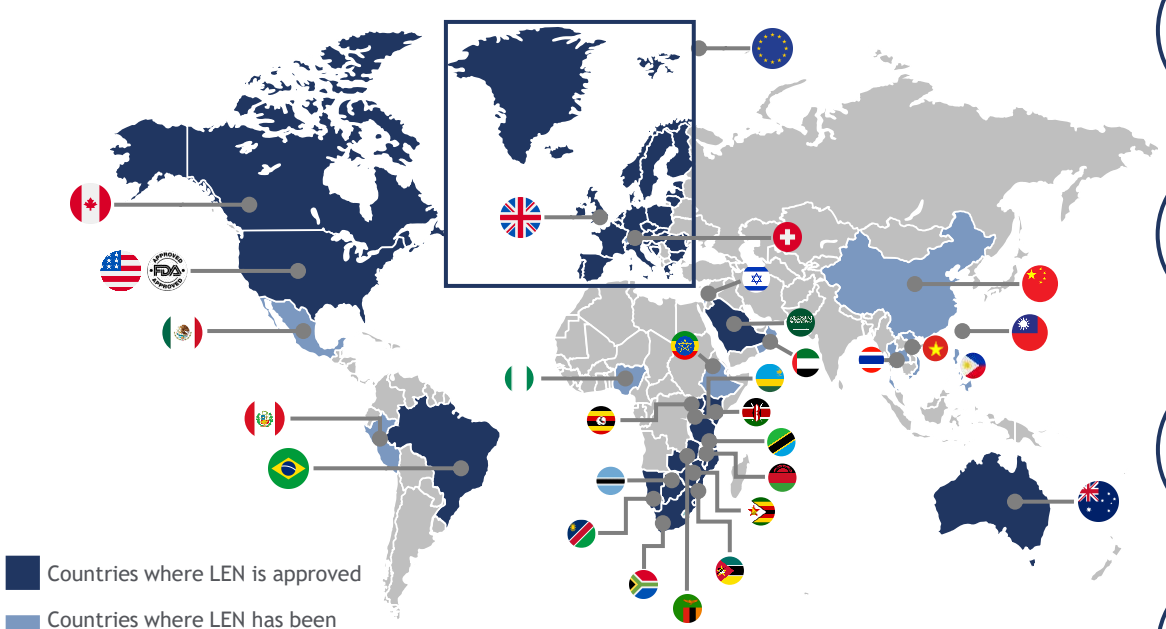
Why is it important?

- The high efficacy of twice-yearly SC LEN, in combination with a consistent safety profile, reinforces LEN as a transformative PrEP option for men and gender-diverse individuals who have sex with men

F/TDF, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous.

Twice-Yearly SC LEN for PrEP is Highly Efficacious in Men and Gender-Diverse Individuals in PURPOSE 2

LEN Regulatory Approvals and Submissions



In 2022, ~ 20% of new HIV diagnoses occurred in gay, bisexual, and other men who have sex with men aged 15–49 worldwide[1]

Compared with cisgender individuals, transmasculine and transfeminine individuals are 7 and 66 times more likely to acquire HIV, respectively[2]

At the primary analysis, twice-yearly SC LEN was highly efficacious for HIV prevention among cisgender men and gender-diverse individuals who have sex with men[3]

Following the primary analysis results, PURPOSE 2 participants chose to continue on LEN or switch to LEN in an open-label extension (OLE)

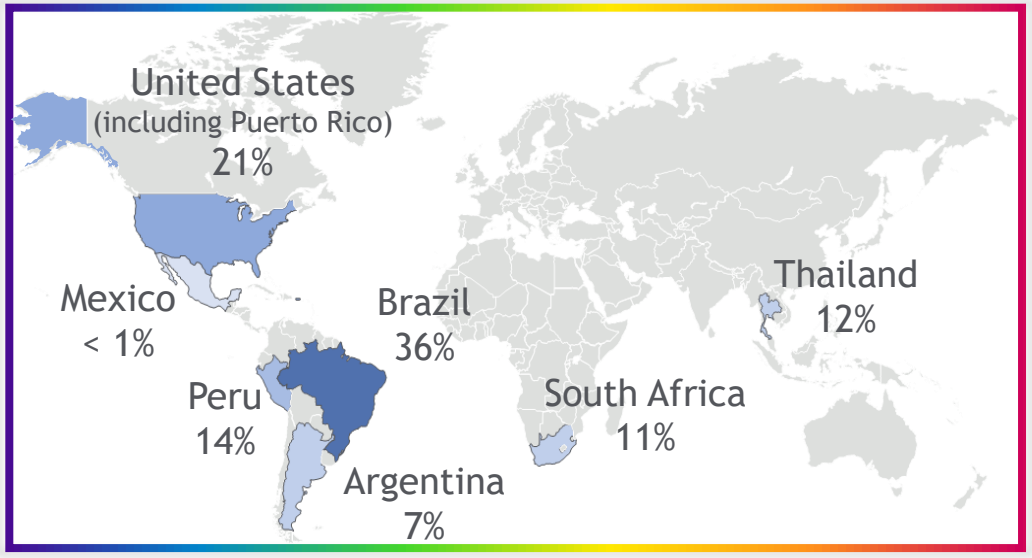
We present longer-term HIV incidence and safety outcomes through 52 weeks of the open-label extension (OLE), including the first switch data from oral F/TDF to SC LEN

F/TDF, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous.

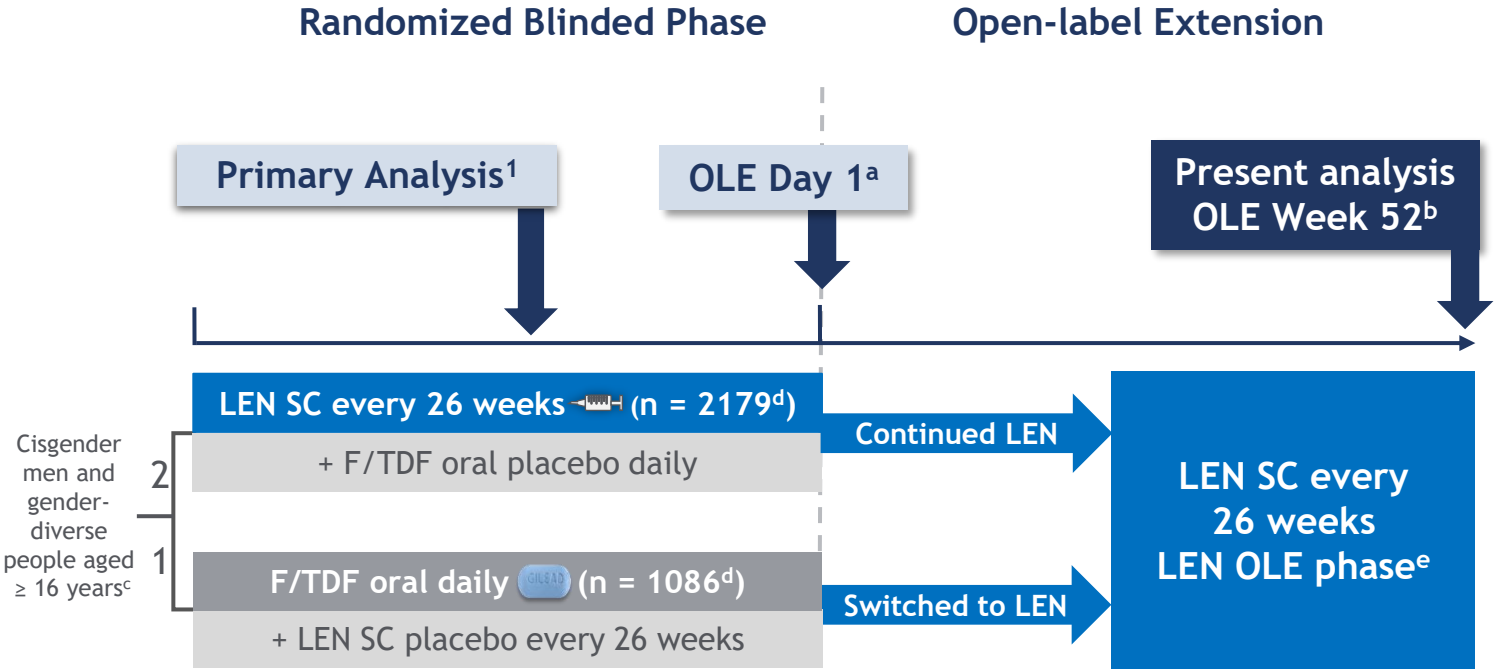
1. UNAIDS. https://www.unaids.org/sites/default/files/media_asset/2024-unaids-global-aids-update_en.pdf (accessed July 20, 2026). 2. Stutterheim SE, et al. *PLoS One*. 2021;16:e0260063.
3. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

PURPOSE 2 Longer-Term Follow-up Through OLE Week 52

PURPOSE 2 Enrolled Participants



Darker shading corresponds to a higher proportion of participants

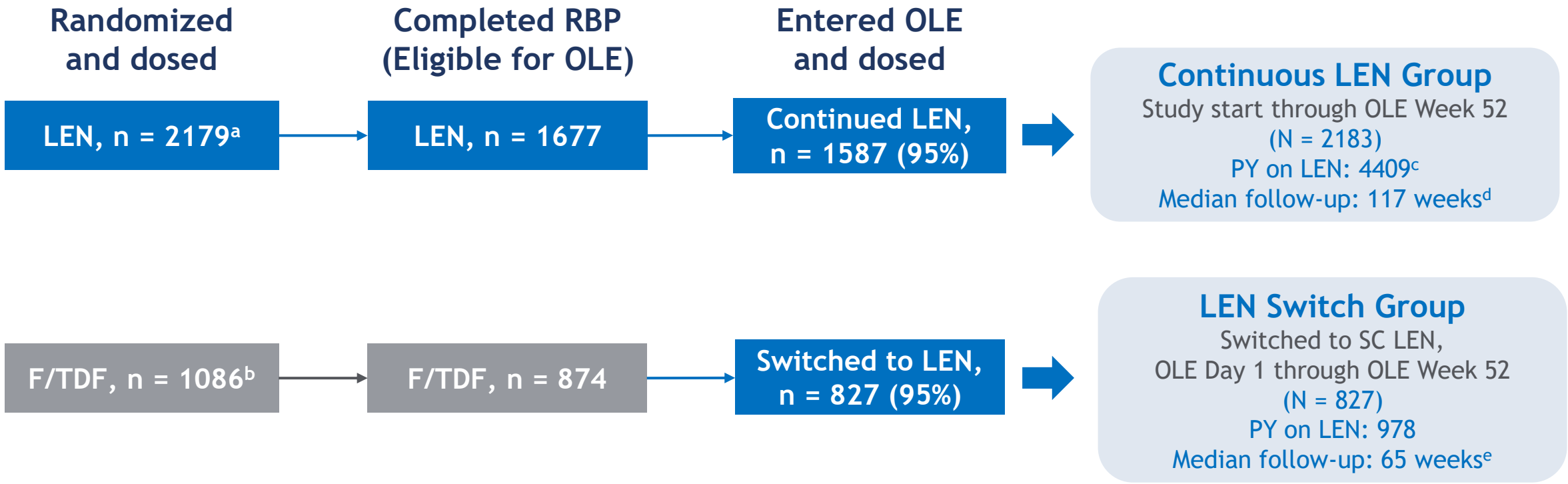


ClinicalTrials.gov: NCT04925752

The present analysis includes over 5000 person-years on LEN

[a]Participants who declined LEN OLE were offered up to 78 weeks of open-label F/TDF (or either open-label F/TDF or F/TAF in US participants) if they were on blinded LEN in RBP. [b]The present analysis was conducted when 99% of participants reached OLE Week 52. [c]Men and gender-diverse individuals who have sex with men and are at risk of HIV acquisition. [d]Included in the full analysis set for primary efficacy analyses (additional participants are included in the safety analysis). [e]In the optional OLE, participants received SC LEN every 26 weeks, including oral LEN loading if they had not received LEN in the prior 28 weeks. **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **PY**, person-years; **RBP**, randomized blinded phase; **SC**, subcutaneous. 1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

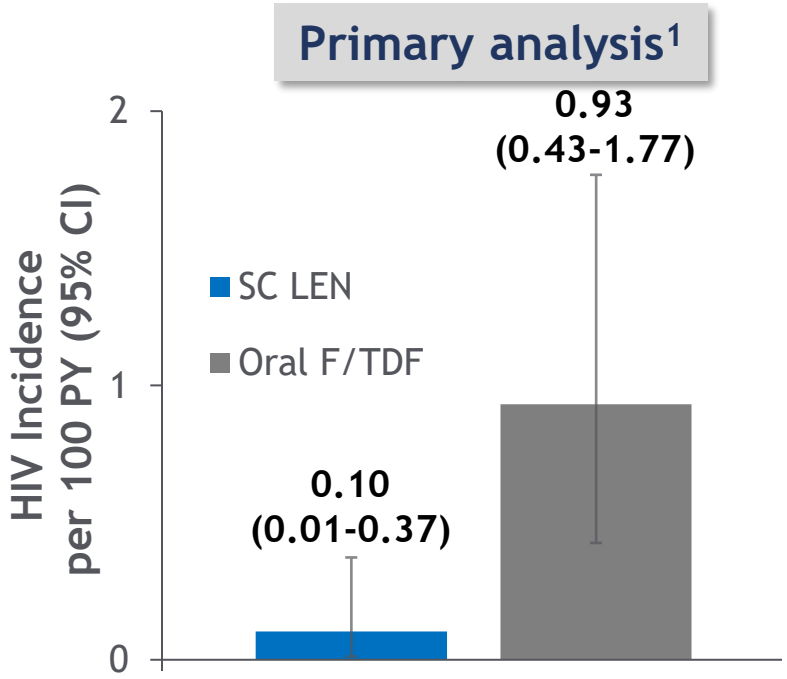
The Majority of Participants Chose Open-Label LEN



95% of participants who completed the RBP opted to continue or switch to LEN in the OLE

[a]Excludes four randomized participants who received a diagnosis of HIV-1 on or prior to first dose, after screening. [b]Excludes two participants who received a diagnosis of HIV-1 on or prior to first dose, after screening. [c]This does not include the PK tail. [d]Continuous LEN group median follow-up (min-max): 117 weeks (0.1-236.6). [e]LEN switch group median follow-up (min-max): 65 weeks (0.9-77.1)
F/TDF, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **PK**, pharmacokinetics; **PY**, person-years; **RBP**, randomized blinded phase; **SC**, subcutaneous.

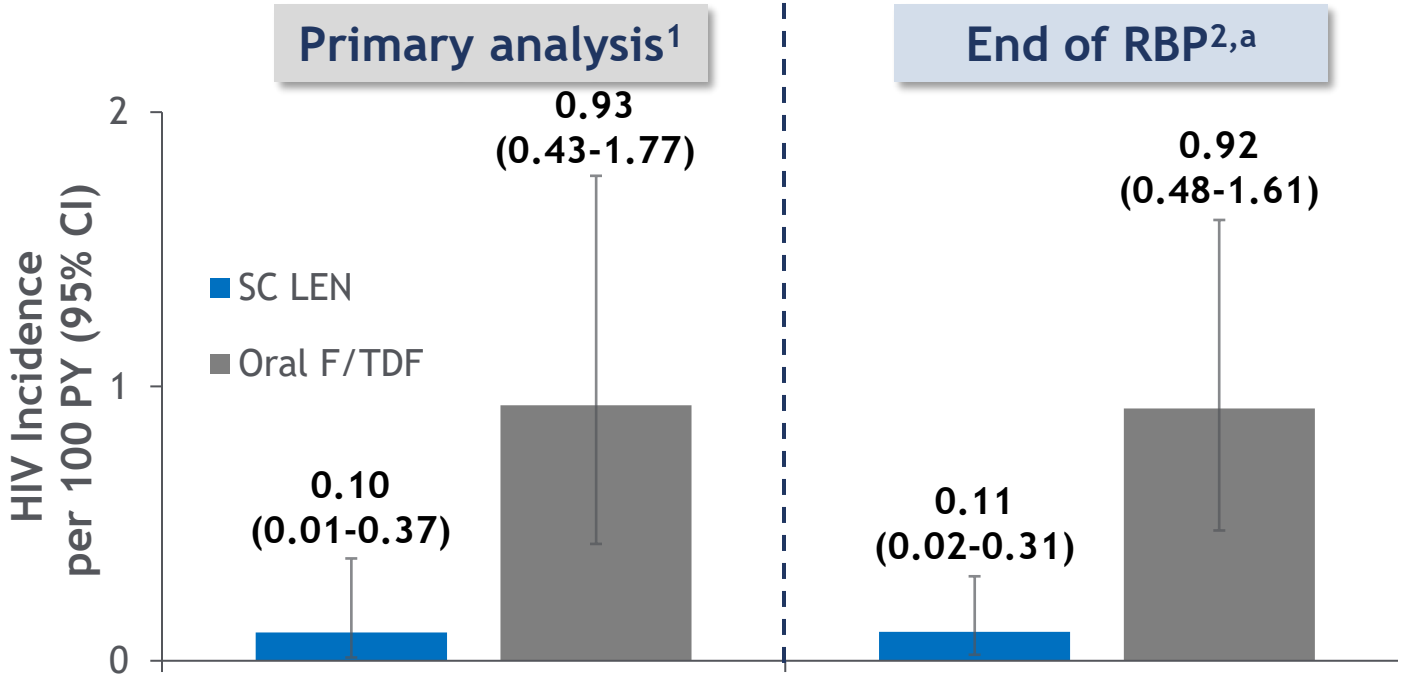
LEN Efficacy Remained High Through OLE Week 52



No. of participants:	2179	1086
New HIV acquisitions:	2	9
Cumulative HIV acquisitions:	2	9
PY of follow-up:	1938	967

The present analysis was conducted when 99% of participants reached OLE Week 52. [a]Includes all data observed during the RBP and follow-up time after the first dose of open-label oral PrEP administered after premature discontinuation of randomized study drug (if applicable) or after stopping any PrEP during the study (if applicable) and on or prior to the first dose of open-label LEN. [b]Includes all data observed during the LEN OLE and follow-up time after the first dose of open-label oral PrEP administered after premature discontinuation of LEN OLE study drug (if applicable) or after stopping any PrEP during the study (if applicable). [c]Continuous LEN group includes participants who received LEN in the RBP. [d]LEN switch group includes participants who switched from F/TDF to LEN in the OLE.
CI, confidence interval; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **PrEP**, pre-exposure prophylaxis; **PY**, person-years; **RBP**, randomized blinded phase; **SC**, subcutaneous.
1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. 2. Cantos V, et al. Oral 129 presented at: CROI; Feb. 22-25, 2026; Denver, CO, USA.

LEN Efficacy Remained High Through OLE Week 52



No. of participants:	2179	1086	2179	1086
New HIV acquisitions:	2	9	1	3
Cumulative HIV acquisitions:	2	9	3	12
PY of follow-up:	1938	967	2843	1305

The present analysis was conducted when 99% of participants reached OLE Week 52. [a]Includes all data observed during the RBP and follow-up time after the first dose of open-label oral PrEP administered after premature discontinuation of randomized study drug (if applicable) or after stopping any PrEP during the study (if applicable) and on or prior to the first dose of open-label LEN. [b]Includes all data observed during the LEN OLE and follow-up time after the first dose of open-label oral PrEP administered after premature discontinuation of LEN OLE study drug (if applicable) or after stopping any PrEP during the study (if applicable). [c]Continuous LEN group includes participants who received LEN in the RBP. [d]LEN switch group includes participants who switched from F/TDF to LEN in the OLE.

CI, confidence interval; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **PrEP**, pre-exposure prophylaxis; **PY**, person-years; **RBP**, randomized blinded phase; **SC**, subcutaneous.

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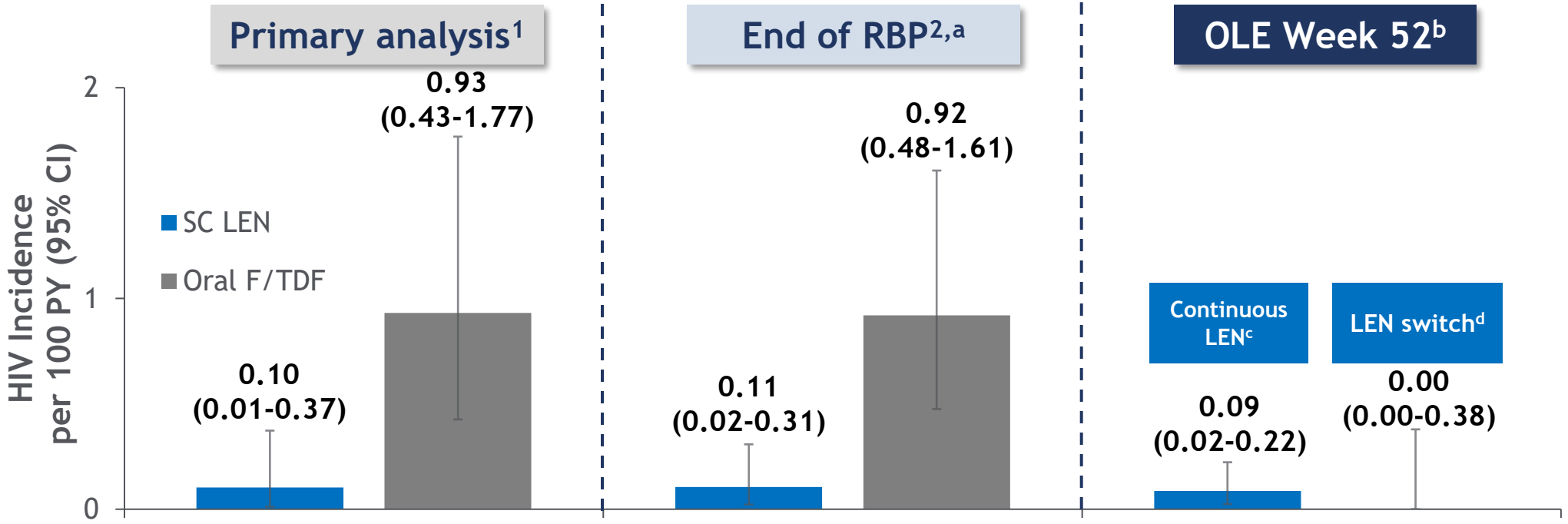
LEN Efficacy Remained High Through OLE Week 52



HIV incidence (95% CI) combining all LEN person-time was 0.07 (0.02-0.18) per 100 PY

No. of participants:	2179	1086	2179	1086	2179	825
New HIV acquisitions:	2	9	1	3	1	0
Cumulative HIV acquisitions:	2	9	3	12	4	0
PY of follow-up:	1938	967	2843	1305	4602	974

HIV incidence on LEN remained stable: only one new HIV acquisition occurred during OLE in a participant randomized to LEN who continued on LEN. There were no HIV acquisitions in participants who switched from oral PrEP to LEN

The present analysis was conducted when 99% of participants reached OLE Week 52. [a]Includes all data observed during the RBP and follow-up time after the first dose of open-label oral PrEP administered after premature discontinuation of randomized study drug (if applicable) or after stopping any PrEP during the study (if applicable) and on or prior to the first dose of open-label LEN. [b]Includes all data observed during the LEN OLE and follow-up time after the first dose of open-label oral PrEP administered after premature discontinuation of LEN OLE study drug (if applicable) or after stopping any PrEP during the study (if applicable). [c]Continuous LEN group includes participants who received LEN in the RBP. [d]LEN switch group includes participants who switched from F/TDF to LEN in the OLE.

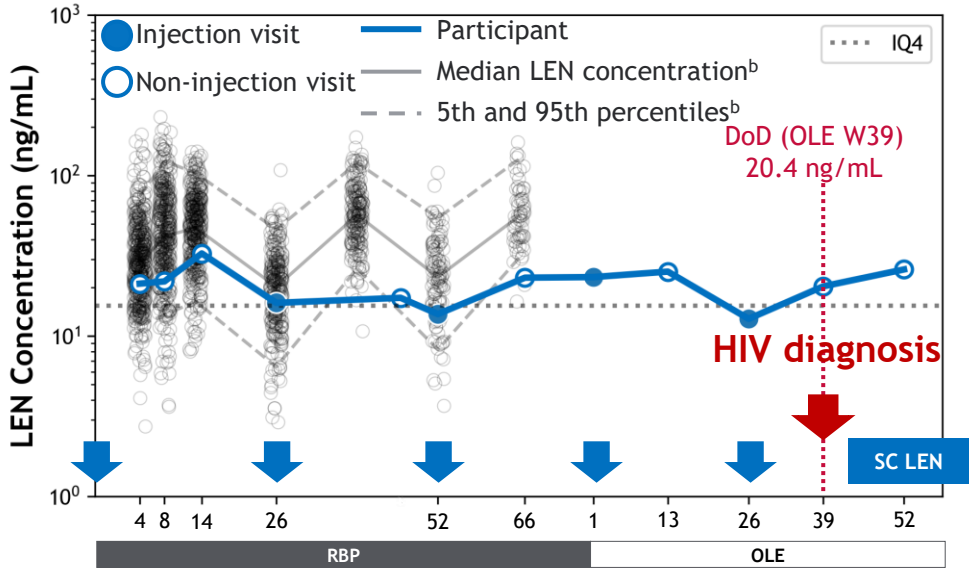
CI, confidence interval; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **PrEP**, pre-exposure prophylaxis; **PY**, person-years; **RBP**, randomized blinded phase; **SC**, subcutaneous.

1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. 2. Cantos V, et al. Oral 129 presented at: CROI; Feb. 22-25, 2026; Denver, CO, USA.

HIV Serology, Viral Load, and LEN Plasma Concentrations in Participant with HIV Acquisition During OLE

- Gender-diverse person with history of syphilis, rectal chlamydia (RBP Week 39), and rectal gonorrhea (RBP Week 52 and OLE Week 39)
- Diagnosed with HIV at OLE Week 39

Diagnostics	LEN (Randomized Blinded Phase)									LEN (OLE)			
Study visit week	BL	W4	W8	W13	W26	W39	W52	W65	W78/ OLE D1	OLE W13	OLE W26	OLE W39	OLE W52
Rapid Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(+)
Central Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(+)
HIV-1/2 Ab diff													Ab(+)
Quantitative RNA, c/mL	ND						ND			ND	ND	243,000[a]	9410



This participant received all injections on time and was diagnosed with standard HIV testing; LEN concentrations were generally within the overall range observed in the prespecified subset. Capsid mutation Q67H was present at OLE Week 39

[a]Retrospective. [b]In the prespecified subset of participants analyzed for LEN PK at W4 (n = 374), W8 (n = 340), W13 (n = 362), W26 (n = 267), W39 (n = 154), W52 (n = 111), and W65 (n = 50). 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] The circles in the figure depict LEN concentrations in individual participants included in the prespecified subset. **Ab**, antibody; **Ag**, antigen; **BL**, baseline; **c**, copies; **D**, day; **diff**, differentiation; **DoD**, date of diagnosis; **IQ**, inhibitory quotient; **LEN**, lenacapavir; **ND**, not detected; **OLE**, open-label extension; **PK**, pharmacokinetics; **RBP**, randomized blinded phase; **SC**, subcutaneous; **W**, week.

1. Margot N, et al. Poster O-324 presented at: HIV Glasgow; Oct. 5-8, 2020; Glasgow, UK.

LEN Safety and Tolerability Was Similar in Participants Initially Randomized to LEN and Those Who Switched to LEN From Oral PrEP

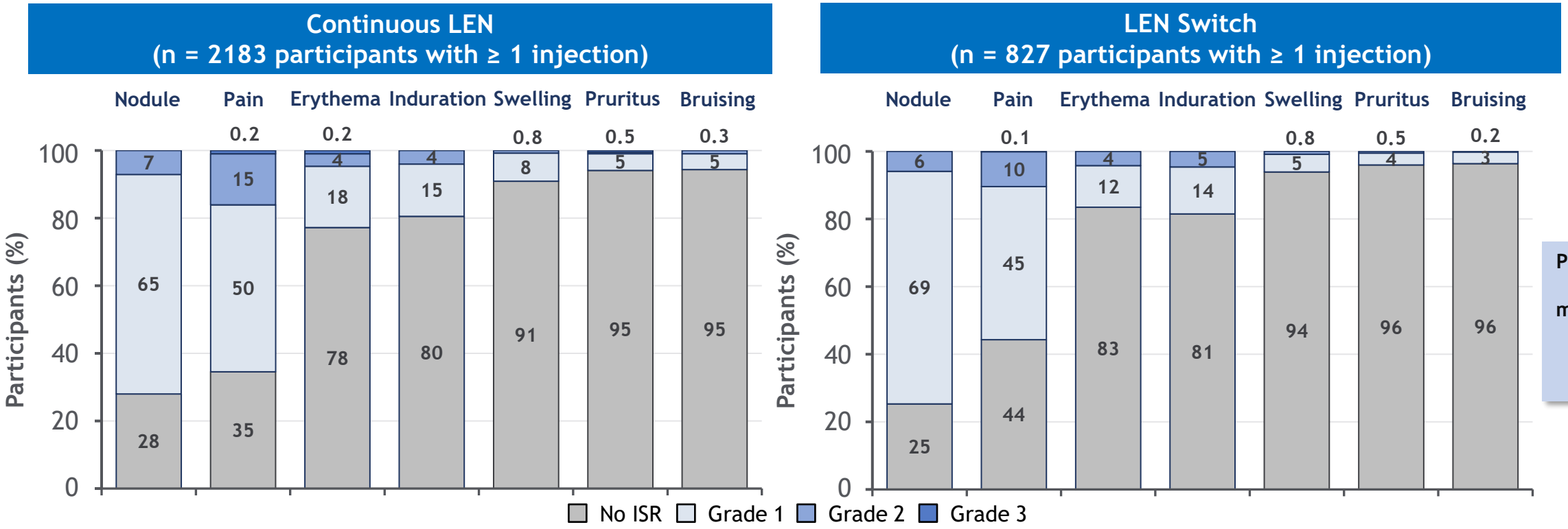
AE, n (%)	Continuous LEN Group (n = 2183)	LEN Switch Group (n = 827)
Cumulative duration of exposure to LEN, PY	**4409**	**978**
Any AE[a,b]	1869 (86)	658 (80)
Grade ≥ 3	183 (8)	36 (4)
Serious AEs	148 (7)	27 (3)
AEs leading to discontinuation of study regimen	8 (< 1)	0
ISRs (participants receiving active LEN injections)	1922 (88)	745 (90)
Grade 2	524 (24)	172 (21)
Grade 3[c]	17 (1)	4 (< 1)
Leading to discontinuation of study regimen	27 (1)	0
AEs occurring in ≥ 15% of participants (excluding ISRs)		
Oropharyngeal gonococcal infection	551 (25)	146 (18)
Anal chlamydia infection	551 (25)	137 (17)
Anal gonococcal infection	465 (21)	124 (15)

No new safety concerns with LEN arose through Week 52 of the OLE

Continuous LEN group includes participants who received LEN in either the RBP or LEN OLE through study discontinuation and excludes PK Tail Phase. LEN switch group includes participants who switched from F/TDF to LEN in the OLE through study discontinuation, excluding PK Tail Phase. The present analysis was conducted when 99% of participants reached OLE Week 52. [a]AEs were treatment-emergent in participants who received at least one dose of study drug and exclude injection site reactions. [b]Coded according to the Medical Dictionary for Regulatory Activities, Version 28.0 and the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1. [c]Highest grade. **AE**, adverse event; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **ISR**, injection site reaction; **LEN**, lenacapavir; **OLE**, open-label extension; **PK**, pharmacokinetics; **PrEP**, pre-exposure prophylaxis; **PY**, person-years; **RBP**, randomized blinded phase.

ISR Incidence and Severity Were Similar in Continuous LEN and LEN Switch Groups

ISRs occurring in ≥ 100 participants receiving active LEN injections through OLE Week 52



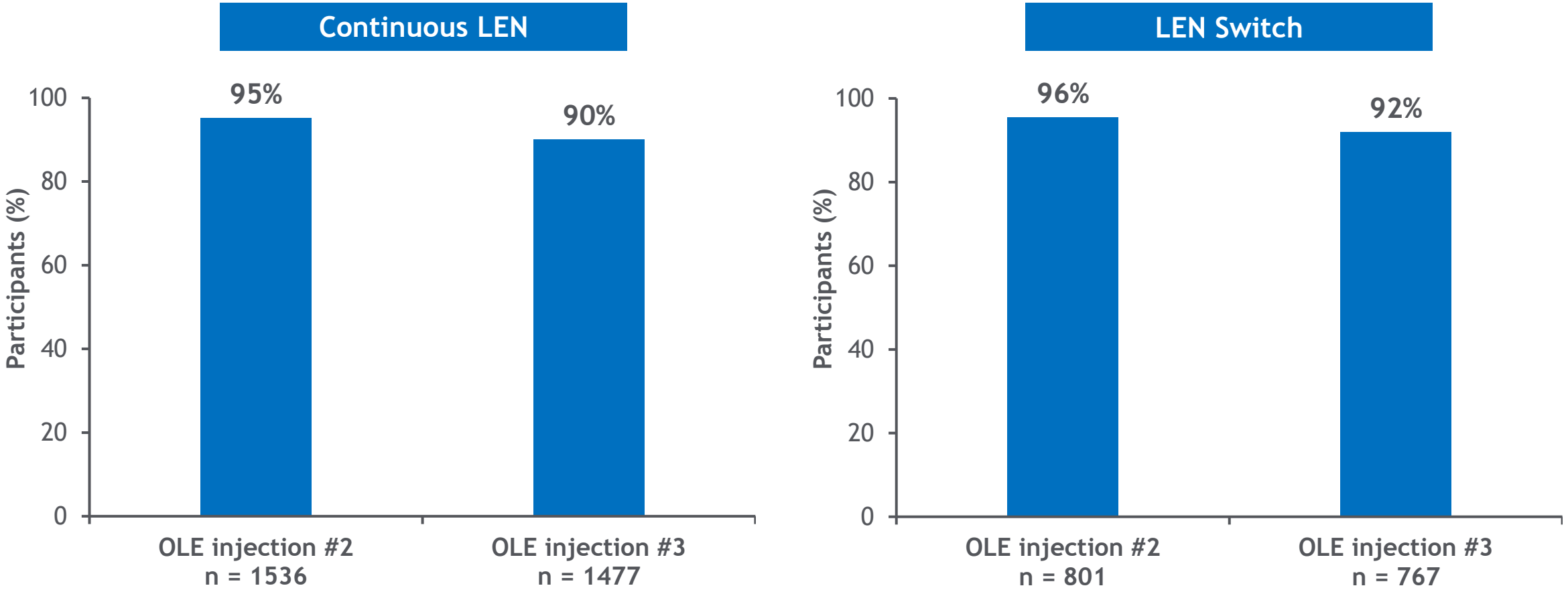
Please see Poster TUPEC184 for more information on alternative injection site tolerability

The majority of participants did not report ISRs other than expected injection site nodules and pain

ISRs that are reported here were to study drug-related injection only and were coded according to the Medical Dictionary for Regulatory Activities, Version 28.0. Continuous LEN group includes participants who received LEN in the RBP. LEN switch group includes participants who switched from F/TDF to LEN in the OLE. Due to rounding, percentages may not total 100. The present analysis was conducted when 99% of participants reached OLE Week 52.

F/TDF, emtricitabine/tenofovir disoproxil fumarate; **ISR**, injection site reaction; **LEN**, lenacapavir; **OLE**, open-label extension; **RBP**, randomized blinded phase.

On-Time Injection Adherence to Open-Label LEN Injections Was High



Adherence to open-label LEN injections in both groups was high

The total number of participants used as denominators for each time point were the number of participants expected to receive an injection (participants with the potential to be followed up on or beyond the injection visit window without discontinuing LEN before the injection visit window). On-time adherence was defined as injection within ≤ 28 weeks after the previous injection at Weeks 26 or 52 after first OLE LEN injection. Continuous LEN group includes participants who received LEN in the RBP. LEN switch group includes participants who switched from F/TDF to LEN in the OLE. The present analysis was conducted when 99% of participants reached OLE Week 52. **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **PY**, patient-years; **RBP**, randomized blinded phase.

Twice-yearly SC LEN Continues to Demonstrate High Efficacy and Is Well Tolerated Through Longer-Term Follow-up (Week 52 of OLE)

The majority of participants chose to switch (95%) or continue (95%) to open-label LEN

With longer-term follow-up, LEN remained highly efficacious and well tolerated, which confirms primary analysis and data through the end of RBP[1,2]

- There were zero HIV acquisitions in people who switched and one in a participant who continued LEN
- Safety, including injection experience, was similar among those who switched from oral PrEP and those who continued on LEN

Adherence to open-label LEN remained high over time in participants who switched from oral PrEP to LEN and in participants who continued LEN

These extended data through 52 weeks of OLE in PURPOSE 2 and > 5000 PY of follow-up reinforce twice-yearly SC LEN as a transformative PrEP option for gay, bisexual, and other men who have sex with men

LEN, lenacapavir; **OLE**, open-label extension; **PrEP**, pre-exposure prophylaxis; **PY**, person-years; **RBP**, randomized blinded phase; **SC**, subcutaneous.

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