Lenacapavir for PrEP: HIV-1 Incidence and Safety from PURPOSE 2 at the End of Randomized Blinded Phase

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Disclosures

- Dr Cantos has received institutional funding from Gilead Sciences, Inc. (Foster City, CA, USA)
- All authors contributed to and approved the presentation
- Gilead Sciences funded and designed the study with input from the PIs and G-CAG. The PIs and study staff gathered data; Gilead Sciences monitored the conduct of the trial, received the data, and performed analyses

G-CAG, Global Community Advisory Group; PI, principal investigator.

Men and Gender-Diverse Individuals Who Have Sex with Men Have a Critical Need for Effective HIV Prevention

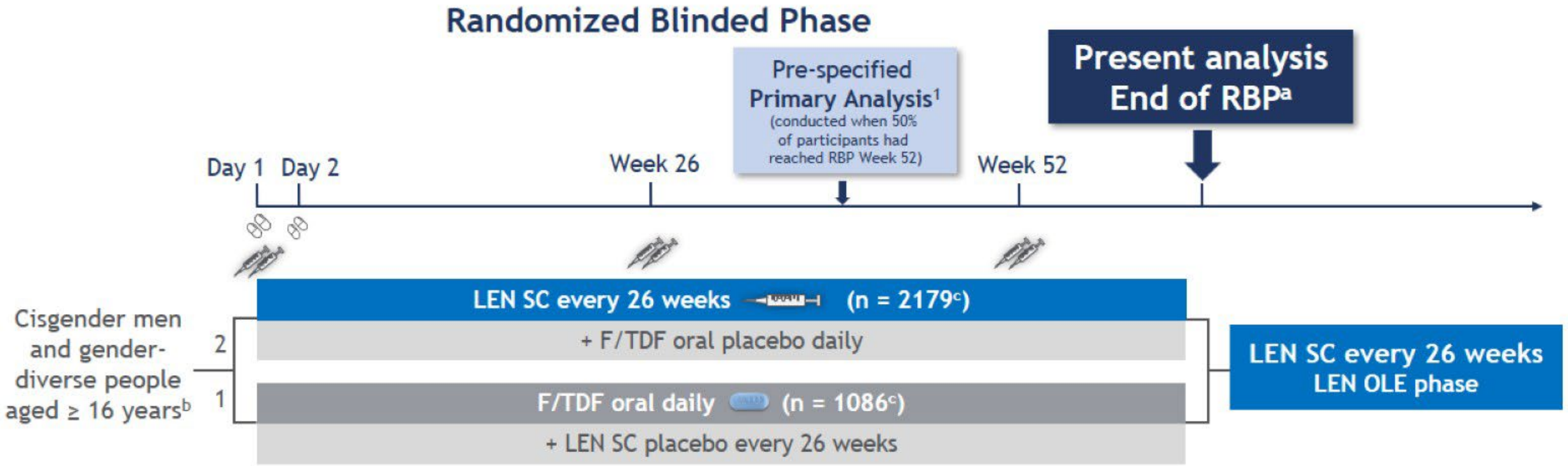
- Men who have sex with men remain disproportionately affected by HIV, with 20% of new HIV diagnoses occurring in this population aged 15-49 worldwide[1]
- Daily oral PrEP uptake and adherence remain low among populations most affected by HIV, highlighting the need for new, longer-acting options that avoid daily pills or frequent injections[2,3]
- PURPOSE 2 demonstrated high efficacy and safety of twice-yearly SC LEN for PrEP in cisgender men and gender-diverse individuals who have sex with men and who are disproportionately affected by HIV[4]

We present longer-term follow-up data on HIV incidence and safety of twice-yearly SC LEN for PrEP through the end of the randomized blinded phase of PURPOSE 2

LEN, lenacapavir; **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 Feb. 6, 2026). 2. Sullivan PS, et al. *J Int AIDS Soc*. 2020;23:e25461. 3. Grov C, et al. *Prev Sci*. 2019;20:168-77. 4. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

PURPOSE 2 is an Ongoing Phase 3, Double-Blind, Active-Controlled Randomized Trial[1]



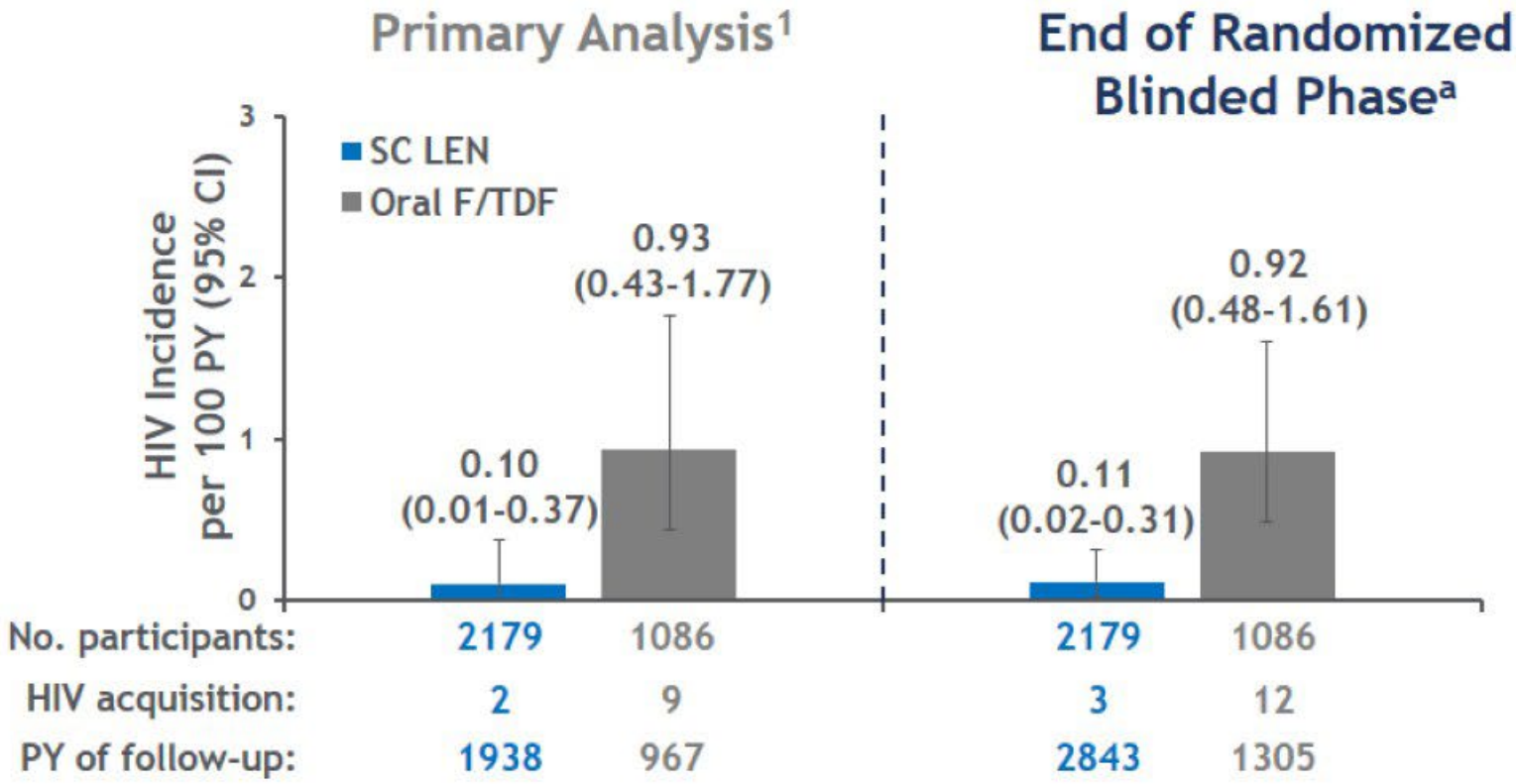
ClinicalTrials.gov: NCT04925752

We report HIV incidence and safety data[b] from study start through the end of the randomized blinded phase encompassing an additional 1243 PY of follow-up

[a]Participants who declined LEN OLE were offered up to 78 weeks of open-label F/TDF if they were on blinded LEN in RBP. [b]Cisgender men and gender-diverse people aged ≥ 16 years who have sex with men and are at risk of HIV acquisition. [c]Included in the full analysis set for primary efficacy analyses (additional participants are included in the safety analysis).
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.

LEN Remained Highly Efficacious Through the End of the Randomized Blinded Phase

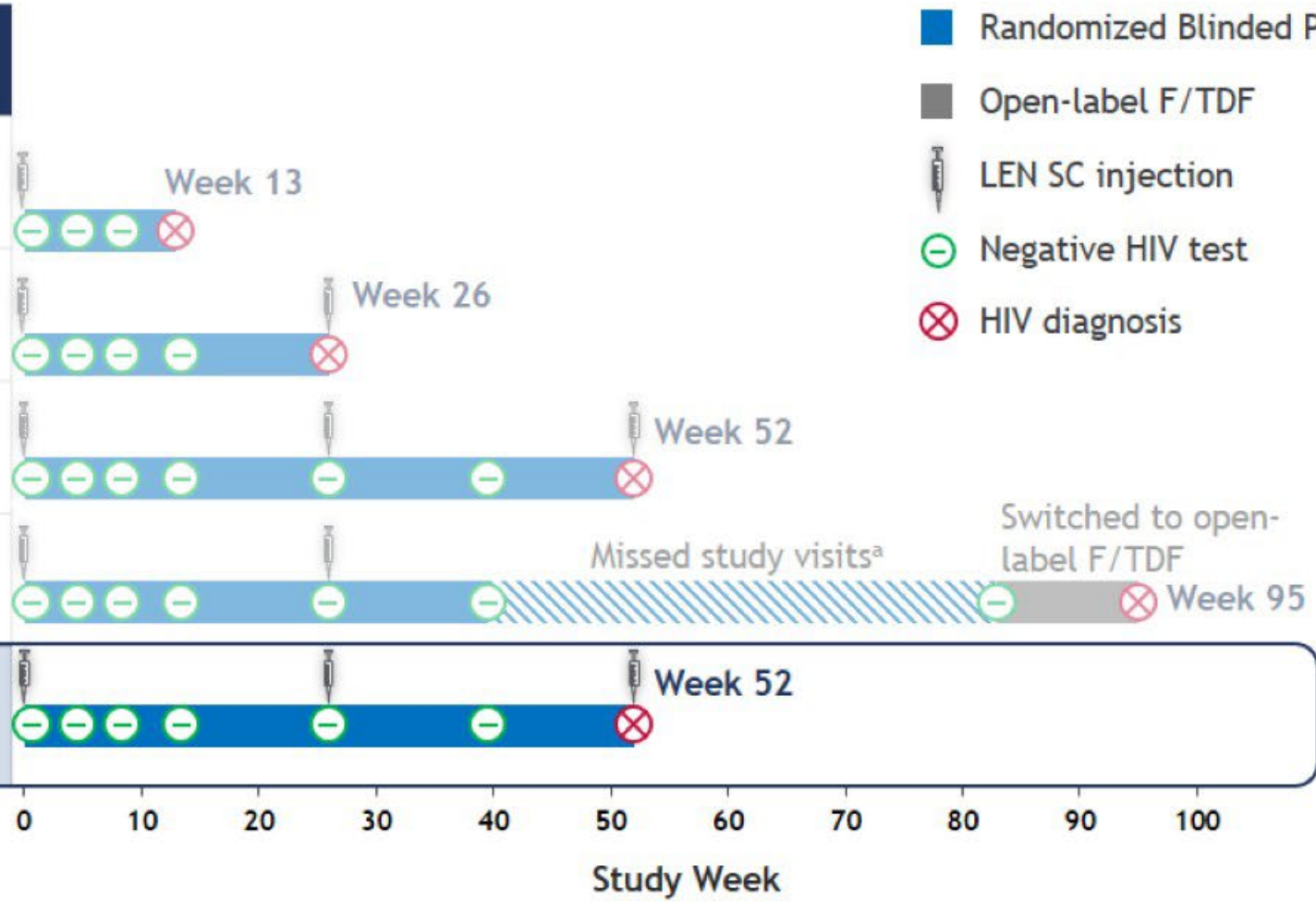


There were 12 incident infections among participants randomized to F/TDF and 3 incident infections among participants randomized to LEN

[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. CI, confidence interval; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; 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.

HIV Acquisition in LEN-Randomized Participants During PURPOSE 1 and PURPOSE 2

Study	Presented	Participant
PURPOSE 2	Previously presented[1,2]	A
PURPOSE 2	Previously presented[1,2]	B
PURPOSE 1	Prior presentation	C (new)
PURPOSE 1	Prior presentation	D (new)
PURPOSE 2	**This presentation**	**E (new)**



[a]Missed LEN injections.
F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; SC, subcutaneous.

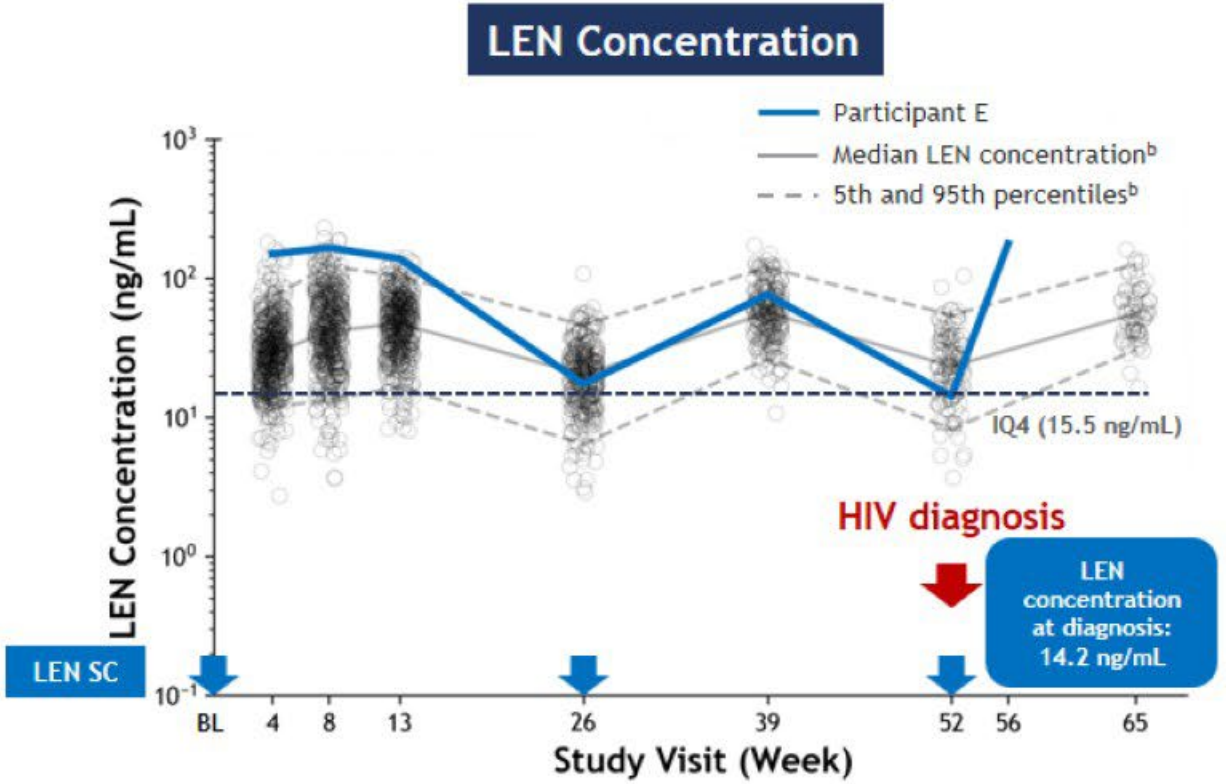
1. Ogbuagu O, et al. Oral O49 presented at: HIV Glasgow; November 10-13, 2024; Glasgow, UK. 2. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

LEN Plasma Concentrations in Participant E with Seroconversion

- Young gender-diverse person with history of rectal chlamydia at screening and Week 26 (Day 176), and rectal gonorrhea at Week 26 (Day 176)
- Diagnosed with HIV at Week 52 (Day 352)

HIV Diagnostics	LEN (Randomized Blinded Phase)						
Study visit week	BL	W4	W8	W13	W26	W39	W52/ OLE D1
Rapid Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Central Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(+)
HIV-1/2 Ab diff							Ab (-)
Quantitative RNA, c/mL	ND					ND[a]	2,020,000

HIV diagnosis



Participant E was diagnosed with standard HIV testing at Week 52. This participant received all injections on time and LEN concentrations were generally within the range of the prespecified subset of participants analyzed for PK[b]

[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), 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; IQ, inhibitory quotient; LEN, lenacapavir; ND, not detected; OLE, open-label extension; PK, pharmacokinetics; SC, subcutaneous; W, week.

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

LEN Tolerability Profile Was Similar With Extended follow-up Through the End of the Randomized Blinded Phase

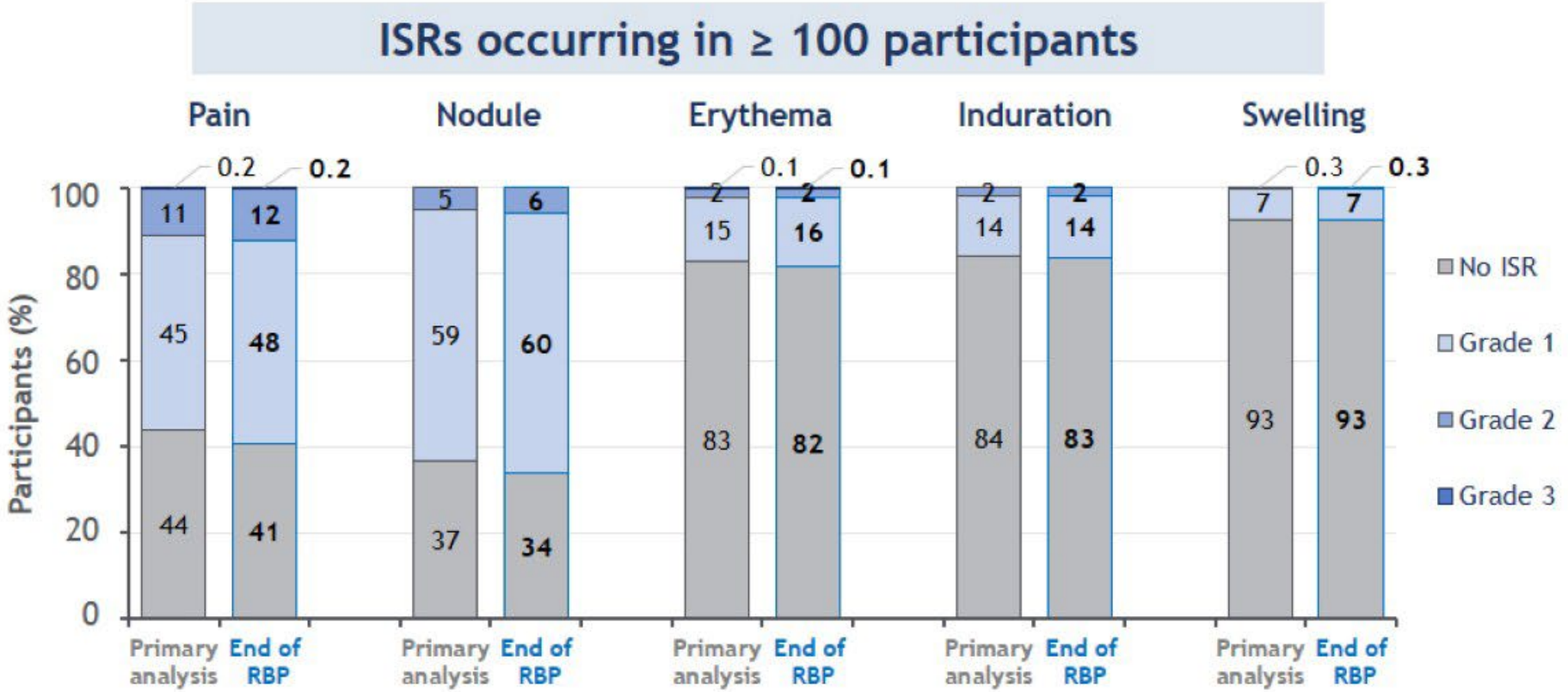
AE, n (%)	Primary Analysis[1] LEN (n = 2183)	End of Randomized Blinded Phase LEN (n = 2183)
Any AE[a,b]	1607 (74)	1721 (79)
Grade ≥ 3	91 (4)	119 (5)
Serious AEs	71 (3)	96 (4)
AEs leading to discontinuation of study regimen	7 (<1)	7 (<1)
Injection-site reactions[b]	1816 (83)	1851 (85)
Grade 2	361 (17)	390 (18)
Grade 3	14 (1)	14 (1)
Leading to discontinuation of study regimen	26 (1)	26 (1)
AEs occurring in ≥ 10% of participants (excluding injection-site reactions)[c]		
Anal chlamydia infection	289 (13)	351 (16)
Oropharyngeal gonococcal infection	283 (13)	344 (16)
Anal gonococcal infection	233 (11)	288 (13)

No new safety concerns with LEN arose through the end of the randomized blinded phase with additional follow up

[a]AEs were treatment-emergent in participants who received at least one dose of study drug and exclude injection-site reactions to study drug. [b]At primary analysis AEs were coded according to Medical Dictionary for Regulatory Activities 27.0 and at end of randomized blinded phase they were coded according to Medical Dictionary for Regulatory Activities 28.0. [c]AEs are ordered by frequency at end of randomized blinded phase.

AE, adverse event; LEN, lenacapavir. 1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

ISR Incidence Was Consistent with the Primary Analysis[1] and Most Were Low-Grade



After the primary analysis, there were no new discontinuations due to ISRs through the end of the RBP

ISR, injection-site reaction; RBP, randomized blinded phase. 1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

PURPOSE 2 Conclusions

In this analysis through the end of the randomized blinded phase, twice-yearly SC LEN remained highly efficacious for HIV prevention among cisgender men and gender-diverse individuals who have sex with men

Through the end of the randomized blinded phase, one additional participant on LEN acquired HIV-1 compared with two reported at primary analysis, maintaining a low incidence of 0.11 per 100 PY on twice-yearly SC LEN

LEN continued to be well-tolerated

- Incidence of ISRs in the LEN group was similar to the primary analysis, with no new discontinuations due to ISRs

Twice-yearly SC LEN for PrEP remained highly efficacious and well tolerated among cisgender men and gender-diverse individuals who have sex with men, through the end of the randomized blinded phase of PURPOSE 2

ISR, injection-site reaction; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; PY, person-years; SC, subcutaneous.

PURPOSE 2 Acknowledgments

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