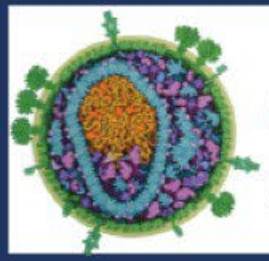

CROI
Conference on Retroviruses and Opportunistic Infections

Twice-Yearly Subcutaneous Lenacapavir for PrEP: Updated HIV-1 Incidence and Safety Data in PURPOSE 1 at the End of the Randomized Blinded Phase

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Disclosures

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- All authors contributed to and approved the presentation
- Gilead Sciences funded and designed the studies 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.

Adolescent Girls and Young Women in Sub-Saharan Africa Have a Critical Need for Effective HIV Prevention

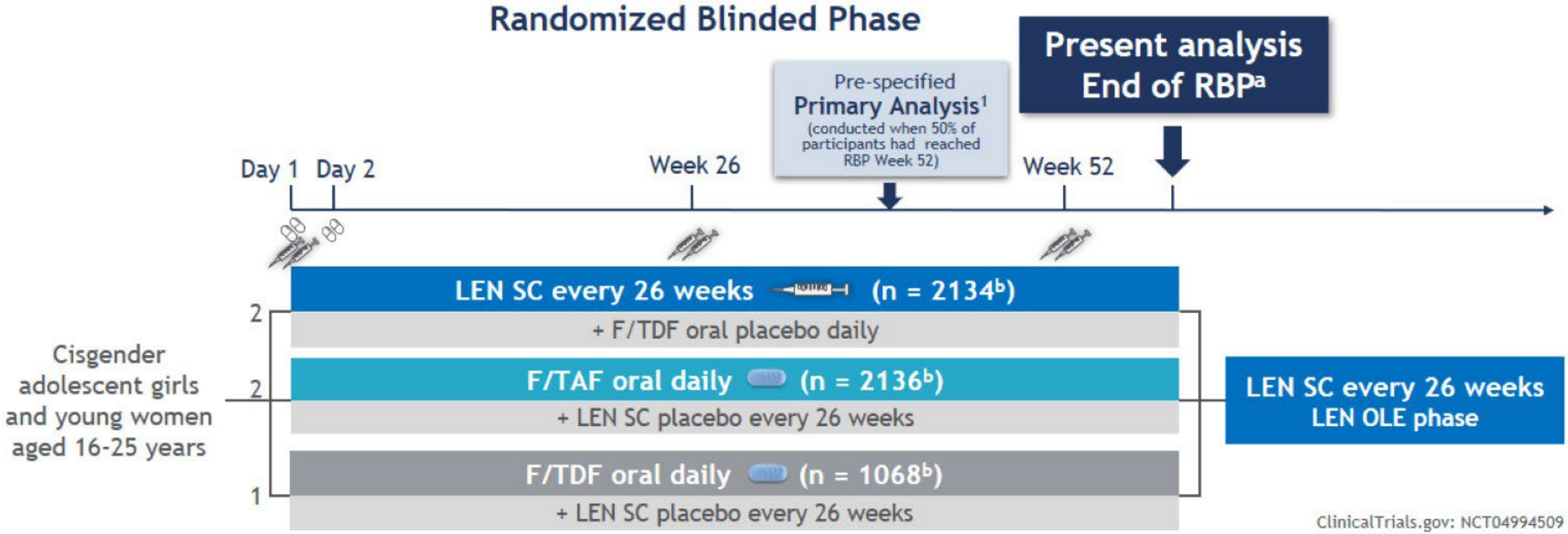
- Globally, 45% of all new HIV infections in 2024 were among girls and women[1]
- In sub-Saharan Africa, girls and women accounted for 63% of new HIV infections[1]
- Twice-yearly SC LEN for PrEP showed robust efficacy and a favorable safety profile in cisgender adolescents and young women in South Africa and Uganda in PURPOSE 1[2]

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 1

LEN, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous.

1. UNAIDS. Fact sheet - Latest global and regional statistics on the status of the AIDS epidemic (accessed Feb. 4, 2026). 2. Bekker LG, et al. *N Engl J Med.* 2024;391:1179-92.

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

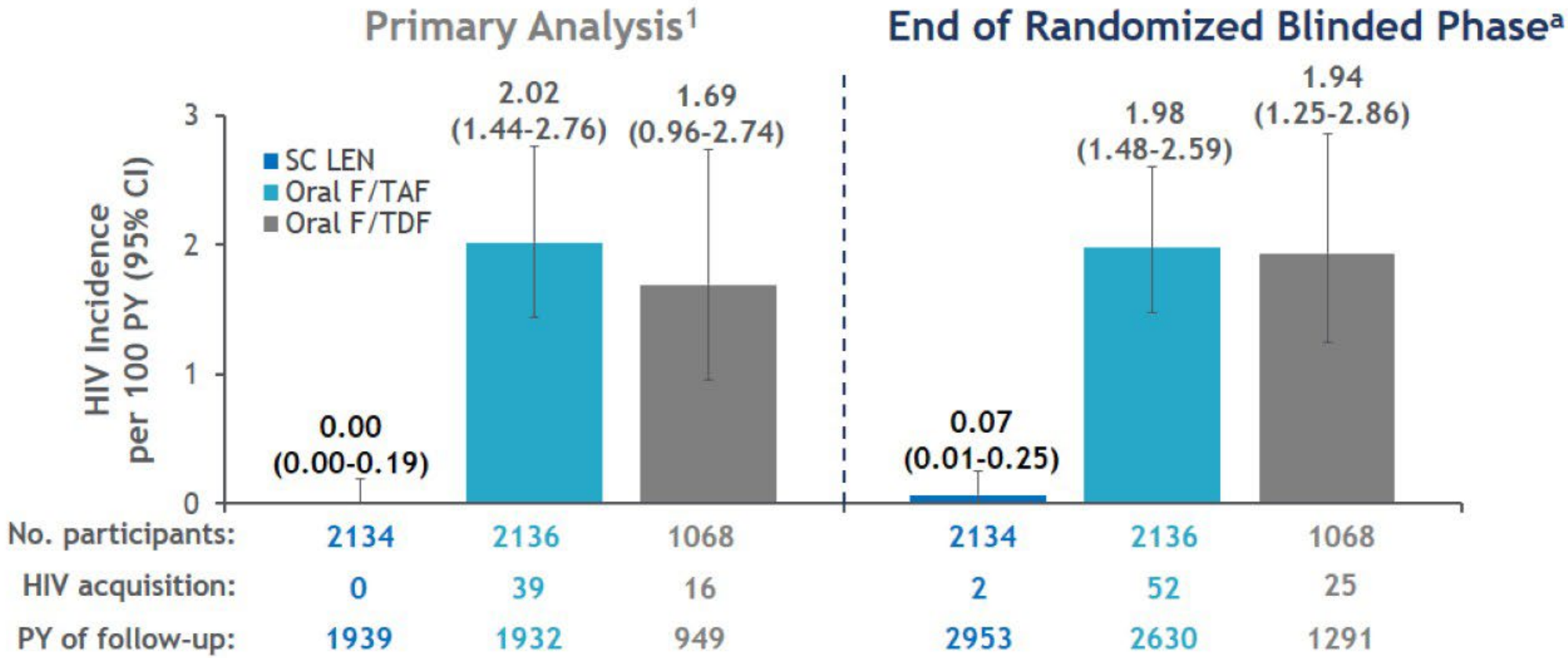


We report HIV incidence and safety data through the end of the randomized blinded phase, encompassing an additional 2054 PY of follow-up

[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]Full analysis set for efficacy analyses.
F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; OLE, open-label extension; PY, person years; RBP, randomized blinded phase; SC, subcutaneous.

1. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92.

LEN Efficacy Remained High Through the End of the Randomized Blinded Phase

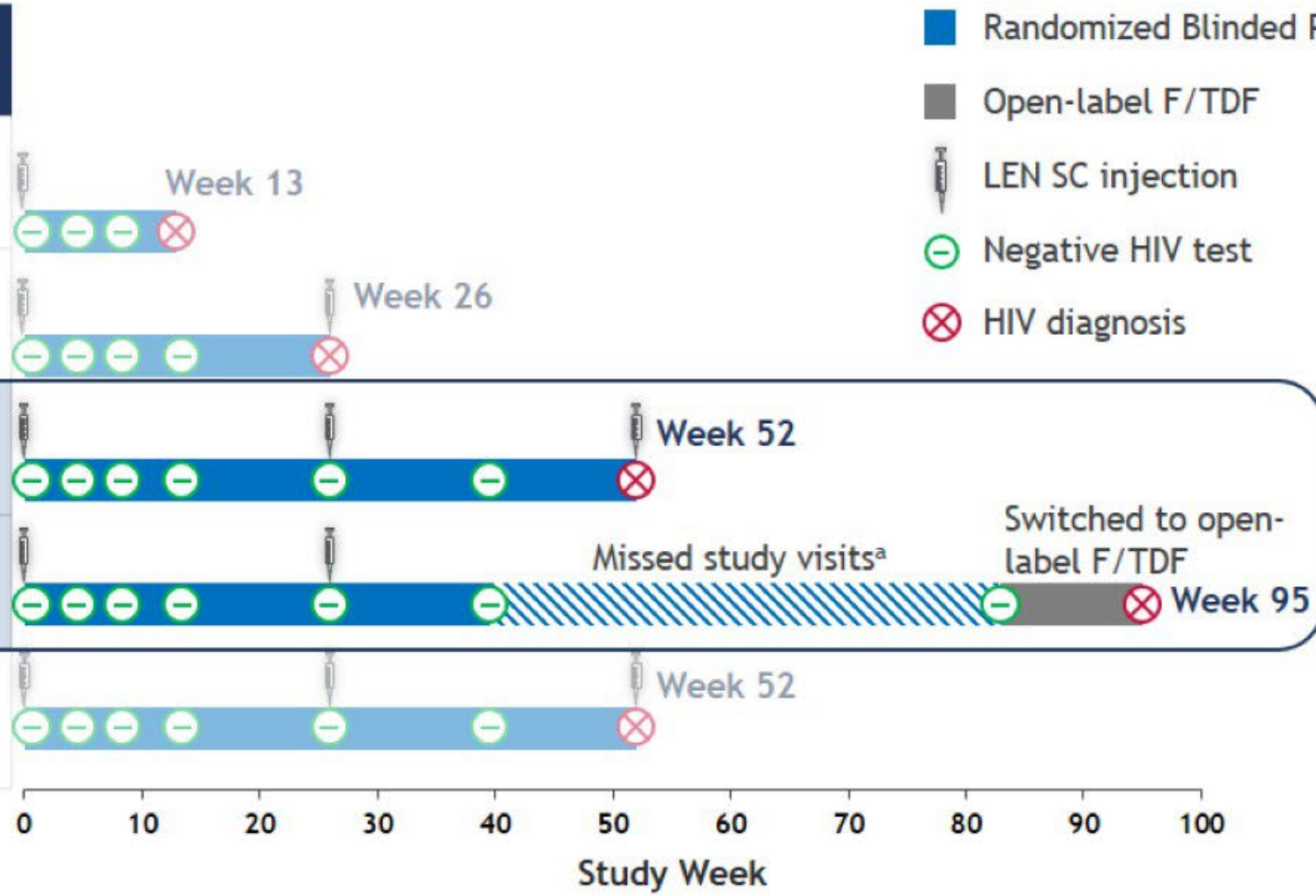


There were 77 incident HIV infections in the oral PrEP arms and 2 incident HIV infections in the LEN arm

[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/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; PY, person-years. 1. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92.

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	**This presentation**	**C (new)**
PURPOSE 1	**This presentation**	**D (new)**
PURPOSE 2	Next presentation	E (new)



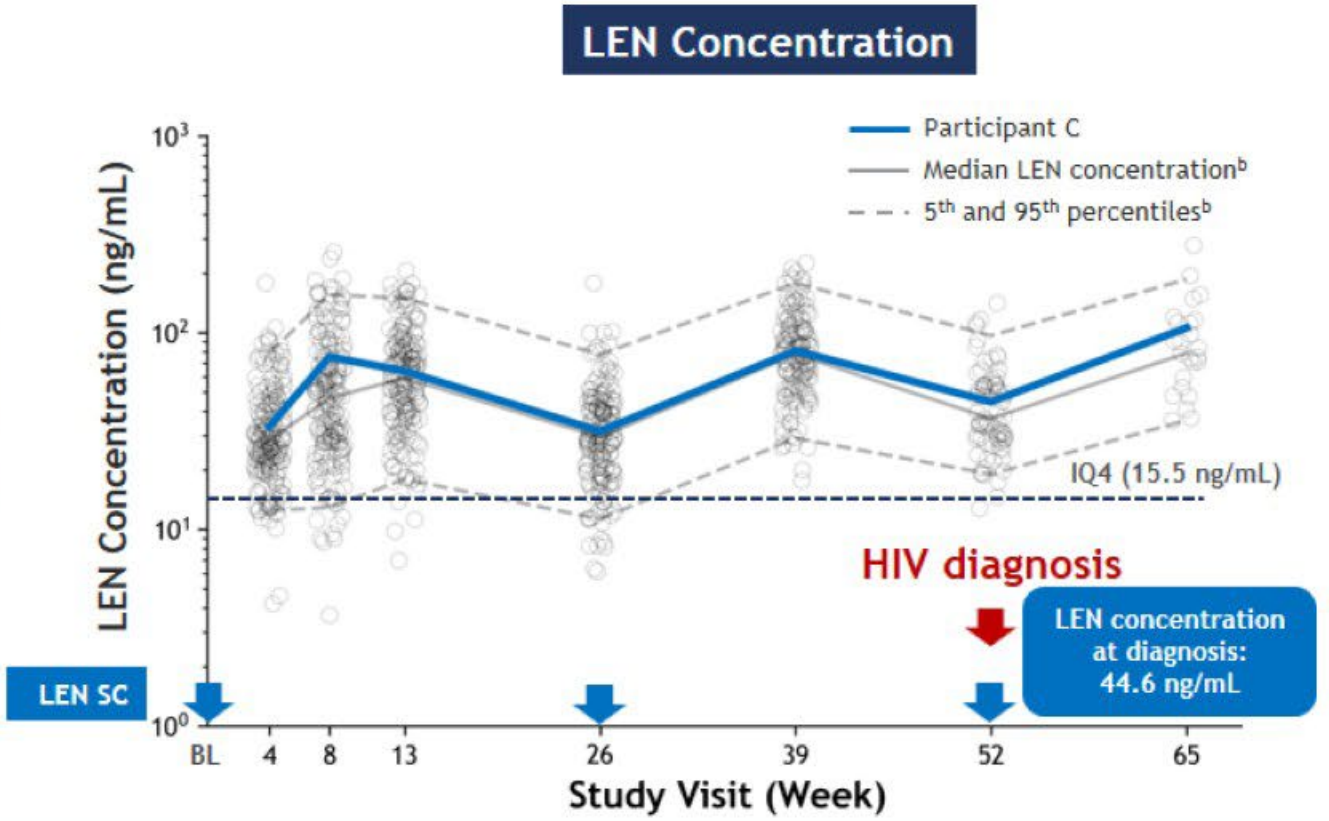
[a]Missed LEN injections.
F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; SC, subcutaneous.

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 C

- Young woman tested positive for chlamydia at Week 52
- HIV diagnosed clinically on-study at Week 65 by typical serologic testing; retrospective RNA test found to be positive at Week 52/OLE Day 1

HIV Diagnostics	LEN (Randomized Blinded Phase)							LEN (OLE)
Study visit week	BL	4	8	13	26	39	52/ OLE D1	65/ OLE W13
Study day	0	30	57	92	183	274	365	456
Rapid Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Central Ag/Ab	(-)	(-)				(-)	(-)	(+)
HIV-1/2 Ab diff								Ind.
Qualitative RNA								(+)
Quantitative RNA, c/mL	(-)					(-)	47[a]	78



Participant C received all LEN injections on time and was diagnosed with standard HIV serologic testing; LEN concentrations were 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 = 165), W8 (n = 158), W13 (n = 163), W26 (n = 156), W39 (n = 129), W52 (n = 73), W65 (n = 23), indicated as circles in the graph. 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]

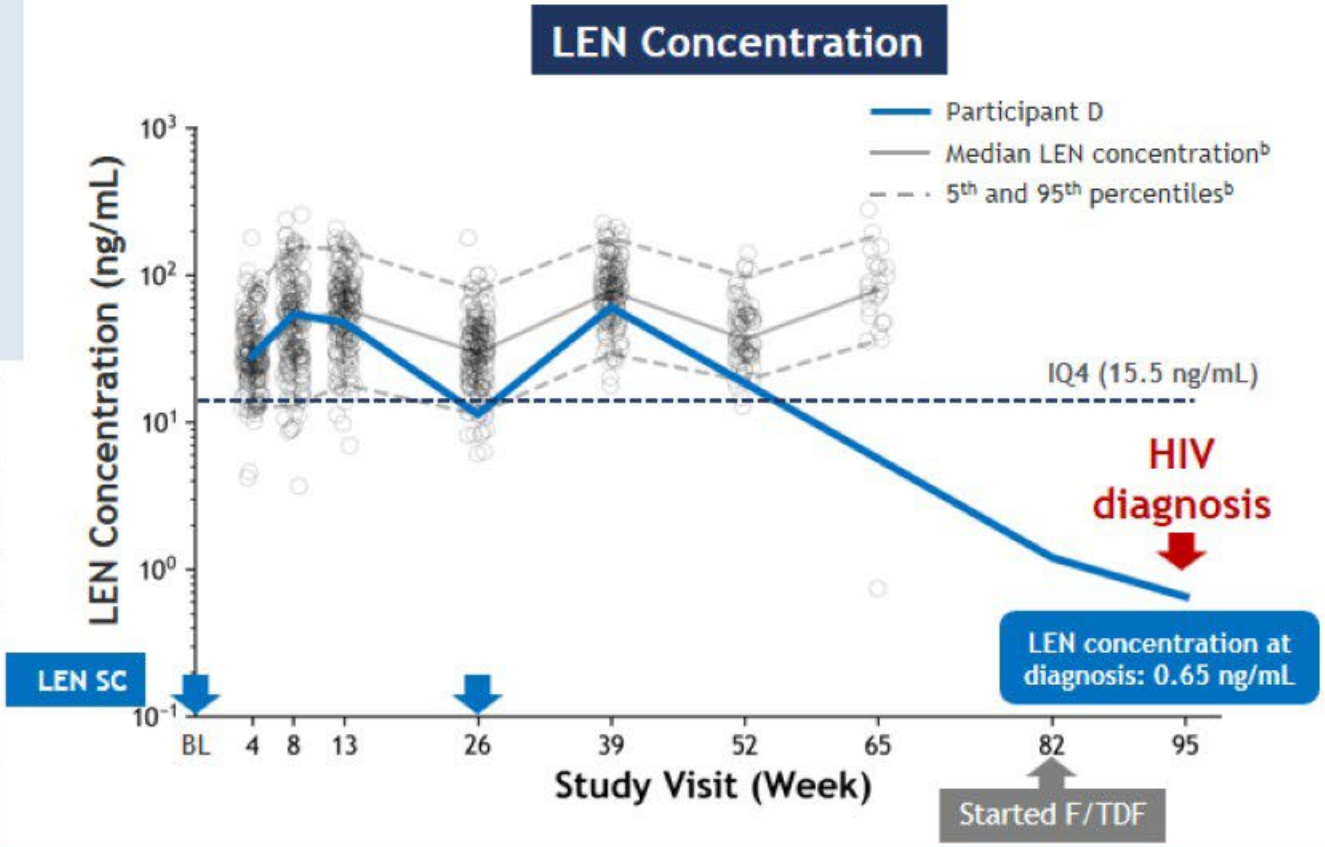
Ab, antibody; **Ag**, antigen; **BL**, baseline; **c**, copies; **diff**, differentiation; **Ind**, indeterminate; **IQ**, inhibitory quotient; **LEN**, lenacapavir; **OLE**, open-label extension; **PK**, pharmacokinetics; **SC**, subcutaneous; **W**, week.

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

LEN Plasma Concentrations in Participant D

- Young woman had last LEN injection at Week 26, then missed Week 52 injection
- Transitioned to open-label F/TDF at Week 82; HIV-negative at that time
- HIV diagnosed at Week 95, 487 days after last LEN injection

HIV Diagnostics	LEN (Randomized Blinded Phase)							Open-label F/TDF	
Study visit week	BL	4	8	13	26	39	52	82	95
Study day	0	30	57	92	183	271		579[a]	670
Rapid Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	Missed	(-)	(+)
Central Ag/Ab	(-)	(-)	(-)				Missed	(-)	(+)
HIV-1/2 Ab diff									(HIV-1+)
Qualitative RNA									
Quantitative RNA, c/mL	(-)							(-)	134,000



Participant D was diagnosed with HIV-1 after LEN discontinuation, while receiving open-label F/TDF, approximately 16 months after the last LEN injection

[a]Participant presented at W82 after missing all their protocol-specified visits following W39 and transitioned to open-label oral F/TDF. [b]In the prespecified subset of participants analyzed for LEN PK at W4 (n = 165), W8 (n = 158), W13 (n = 163), W26 (n = 156), W39 (n = 129), W52 (n = 73), W65 (n = 23), indicated as circles in the graph. 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] **Ab**, antibody; **Ag**, antigen; **BL**, baseline; **c**, copies; **diff**, differentiation; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **IQ**, inhibitory quotient; **LEN**, lenacapavir; **PK**, pharmacokinetics; **SC**, subcutaneous; **W**, week. 1. Margot N, et al. Poster O-324 presented at: HIV Glasgow; 5-8 October 2020; Glasgow, UK.

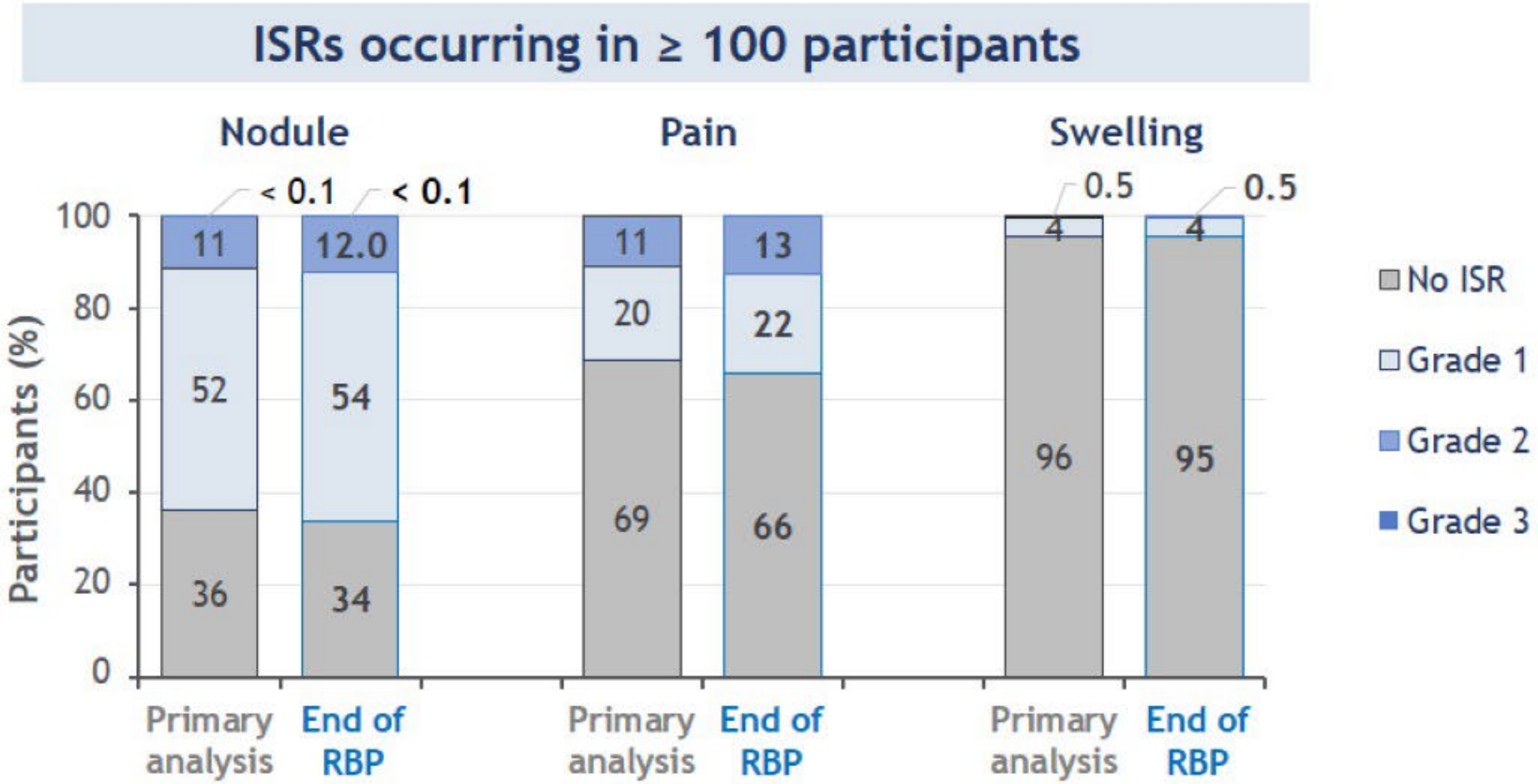
LEN Tolerability Profile Was Similar With Extended follow-up Through the End of the Randomized Blinded Phase

AE, n (%)	Primary Analysis[1] LEN (n = 2138)	End of Randomized Blinded Phase LEN (n = 2140)[a]
Any AE[b,c]	1631 (76)	1743 (81)
Grade ≥ 3	88 (4)	114 (5)
Serious AEs	59 (3)	81 (4)
AEs leading to discontinuation of study regimen	5 (<1)	9 (<1)
Injection-site reactions[c]	1470 (69)	1519 (71)
Grade 2	406 (19)	444 (21)
Grade 3[d]	4 (<1)	4 (<1)
Leading to discontinuation of study regimen	4 (<1)[e]	4 (<1)
AEs occurring in ≥ 10% of participants (excluding injection-site reactions)		
Headache	285 (13)	327 (15)
Urinary tract infection	307 (14)	344 (16)
Genitourinary chlamydia infection	300 (14)	352 (16)
Upper respiratory tract infection	271 (13)	344 (16)

No new safety concerns with LEN arose through the end of the RBP with additional follow-up

[a]End of RBP includes safety data from study start through end of RBP, inclusive of primary analysis event. N number differs from published primary analysis data[1] that were based on planned treatment; end of RBP analysis is based on actual treatment given. [b]AEs were treatment-emergent in participants who received at least one dose of study drug and exclude injection-site reactions. [c]Coded according to the Medical Dictionary for Regulatory Activities, Version 27.0 (primary analysis) and 28.0 (end of RBP analysis) and the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, version 2.1. [d]Highest grade. [e]All due to SC nodules (one participant discontinued due to both an SC nodule and injection-site pain). AE, adverse event; LEN, lenacapavir; RBP, randomized blinded phase; SC, subcutaneous. 1. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92.

ISR Incidence and Severity in the LEN Group Remained Consistent with the Primary Analysis[1]



The majority of participants did not report ISRs other than expected injection site nodules; there were no new discontinuations due to ISRs

ISR, injection-site reaction; LEN, lenacapavir; RBP, randomized blinded phase; SC, subcutaneous.

1. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92.

PURPOSE 1 Conclusions

- Twice-yearly SC LEN remains highly efficacious for HIV prevention among adolescent girls and young women
- Through the end of the RBP, 2 participants in the LEN arm acquired HIV-1, maintaining a low incidence of 0.07 per 100 PY with LEN
- LEN continued to be well-tolerated
  - Incidence of ISRs 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 young women through the end of the randomized blinded phase of PURPOSE 1

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

PURPOSE 1 Acknowledgments

- We would like to extend our thanks to all participants, their families and communities, the investigators and site staff, the global community advisors, and the members of the PURPOSE 1 study team for their insights and support
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