

High Incidence of Sexually Transmitted Infections and Sexual Behaviors Associated with HIV Acquisition Among Cisgender Men and Gender-Diverse Individuals in PURPOSE 2

Meredith Clement¹, Allison L Agwu², Anchalee Avihingsanon³, Jill Blumenthal⁴, Susan Buchbinder⁵, Valeria D Cantos⁶, Jorge A Gallardo-Cartagena⁷, Nittaya Phanuphak⁸, Ricardo P Vasconcelos⁹, Pamela Wong¹⁰, Lillian B Brown¹⁰, Christoph C Carter¹⁰, Kenneth H Mayer¹¹

¹Louisiana State University Health Sciences Center – New Orleans, New Orleans, LA, USA; ²The Johns Hopkins University School of Medicine, Baltimore, MD, USA; ³HIVNAT, Thai Red Cross AIDS and Infectious Diseases Research Centre and Center of Excellence in Tuberculosis; Chulalongkorn University, Bangkok, Thailand; ⁴University of California San Diego, San Diego, CA, USA; ⁵San Francisco Department of Public Health, San Francisco, CA, USA; ⁶Emory University School of Medicine, Atlanta, GA, USA; ⁷Universidad Nacional Mayor de San Marcos, Lima, Peru; ⁸Institute of HIV Research and Innovation – Pribta Tangerine Clinic, Bangkok, Thailand; ⁹Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; ¹⁰Gilead Sciences, Inc., Foster City, CA, USA; ¹¹The Fenway Institute, Fenway Health and Harvard Medical School, Boston, MA, USA

Copies of this poster obtained through QR (Quick Response) code are for personal use only and may not be reproduced without written permission of the authors



Conclusions

- PURPOSE 2 participants had high levels of diagnosed sexually transmitted infections (STIs) and reported sexual behaviors associated with increased likelihood of HIV acquisition at baseline and throughout the study, with no evidence of risk compensation
- Despite this ongoing vulnerability, HIV acquisition was rare in the lenacapavir (LEN) group, further supporting the high efficacy of twice-yearly subcutaneous (SC) LEN for HIV pre-exposure prophylaxis (PrEP)

Plain Language Summary

- Human immunodeficiency virus (HIV) prevention medicine, called pre-exposure prophylaxis (PrEP), lowers the chance of someone getting HIV
- Lenacapavir (LEN) is approved to help prevent HIV. It is given as an injection under the skin twice a year (every 6 months)
- In a large clinical study called PURPOSE 2, LEN worked very well at preventing HIV in cisgender men, transgender women, transgender men, and gender-diverse individuals who have sex with men
- At the start of the study and during the study, participants were tested for sexually transmitted infections (STIs) and answered questions about their sexual behaviors
- The researchers looked at how many participants had STIs and the sexual behaviors they reported during the study
- Even though many participants had STIs and engaged in behaviors linked to a higher chance of acquiring HIV, LEN continued to work very well at preventing HIV

Introduction

- The Phase 3 PURPOSE 2 trial, conducted in the USA, Brazil, Thailand, South Africa, Peru, Argentina, and Mexico, demonstrated high efficacy of twice-yearly SC LEN for PrEP in cisgender men and gender-diverse individuals¹
- The presence of STIs, including rectal gonorrhea, rectal chlamydia, and syphilis, is a marker for condomless sexual activity, and is associated with higher rates of HIV acquisition²⁻⁷
- Chemsex is the use of psychoactive drugs before or during sexual activity. The prevalence of chemsex ranges globally from 8-32% of men who have sex with men and is associated with increased rates of acquisition of both HIV and STIs⁸⁻¹⁶

Objective

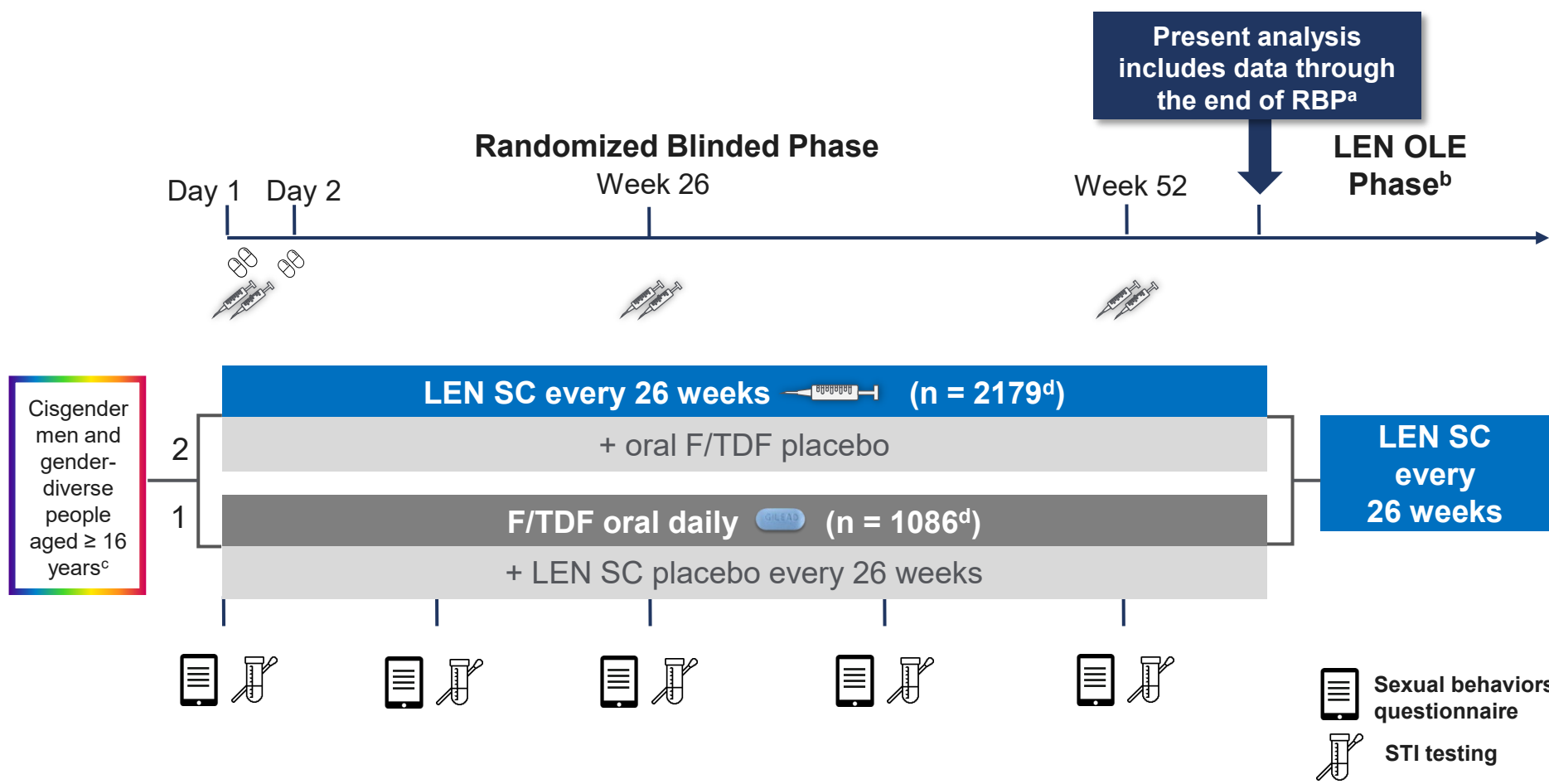
- To describe self-reported sexual behaviors and the incidence of STIs associated with HIV acquisition at baseline and through the end of the randomized blinded phase (RBP) of PURPOSE 2

Methods

Study Design and Procedures

- PURPOSE 2 (NCT04925752) is a Phase 3, double-blind, active-controlled randomized trial in individuals aged ≥ 16 years who have sex with men and were at risk of HIV acquisition. Participants were randomized 2:1 to receive SC LEN every 26 weeks or oral emtricitabine/tenofovir disoproxil fumarate (F/TDF) daily (**Figure 1**)
- Participants were regularly tested for STIs
 - At baseline and every 13 weeks thereafter, oropharyngeal and rectal swabs and urine specimens were collected for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* testing
 - Participants were tested for syphilis at baseline and every 13 weeks thereafter according to each site's standard algorithm. Investigators determined syphilis stage based on clinical findings, history, and laboratory results
 - Participants were treated or referred for treatment for new positive results for any incident STI
 - STI outcomes were summarized using descriptive statistics
- Sexual behaviors in the prior 3 months, including number of partners, receptive anal sex acts, and chemsex acts, were self-reported by questionnaire at baseline and every 13 weeks thereafter

Figure 1. **PURPOSE 2 Study Design**¹



ClinicalTrials.gov: NCT04925752

¹Includes 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 while at risk of HIV. ²Participants who declined LEN OLE were offered up to 78 weeks of open-label F/TDF if they were on blinded LEN in the RBP. ³Cisgender men and gender-diverse people aged ≥ 16 years who have sex with men and are at risk of HIV acquisition. ⁴Included in the full analysis set for primary efficacy analyses (additional participants are included in the safety analysis). ⁵F/TDF: emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; OLE, open-label extension; PrEP, pre-exposure prophylaxis; RBP, randomized blinded phase; SC, subcutaneous; STI, sexually transmitted infection.

Sexual Behaviors Questionnaire

- A sexual behaviors questionnaire was administered at baseline and every visit (every 13 weeks) throughout the study, in which participants self-reported numbers of partners or specific sex acts within the prior 3 months (**Figure 2**)

Figure 2. Selected Questions From the Sexual Behaviors Questionnaire

Figure 2 displays three sample questions from the Sexual Behaviors Questionnaire, each with a response box for 'Number of Partners' and a 'Prefer not to answer' option.

Question 1: In the past 3 months, approximately how many sex partners have you had? If you have not had any sex partners in the past 3 months, please enter '0':

Question 2: In the past 3 months, how many times have you had receptive anal sex? By receptive anal sex, we mean when your partner puts their penis into your anus. If you have not had receptive anal sex in the past 3 months, please enter '0':

Question 3: In the past 3 months, how many times have you taken drugs before or during sex? If you have not taken drugs before or during sex in the past 3 months, please enter '0':

Results

Participants

- At baseline, rectal gonorrhea or chlamydia was diagnosed in 12% (242/2084) of participants in the LEN group and 12% (123/1034) in the F/TDF group. Syphilis was reported in 4% (84/2183) of participants in the LEN group and 4% (43/1088) in the F/TDF group (**Table 1**)

Table 1. PURPOSE 2 Baseline Characteristics

Characteristic, n (%)	LEN, N = 2183	F/TDF, N = 1088
Age, years, median (range)	28 (17-74)	29 (17-73)
Age 16 to ≤ 25, years	752 (34)	344 (32)
Non-White race*	1453 (67)	742 (68)
Hispanic/Latine ethnicity*	1378 (63)	675 (62)
Gender identity		
Cisgender man	1697 (78)	846 (78)
Gender diverse	486 (22)	242 (22)
STIs		
Chlamydia trachomatis or Neisseria gonorrhoeae*	391 (18)	217 (20)
Rectal Neisseria gonorrhoeae or Chlamydia trachomatis	242 (12)*	123 (12)*
Syphilis	84 (4)	43 (4)
No prior HIV test	597 (27)	306 (28)
Any prior lifetime use of PrEP	515 (24)	249 (23)
Self-reported use of stimulants with sex in the last 12 weeks	491 (22)	271 (25)

Participants



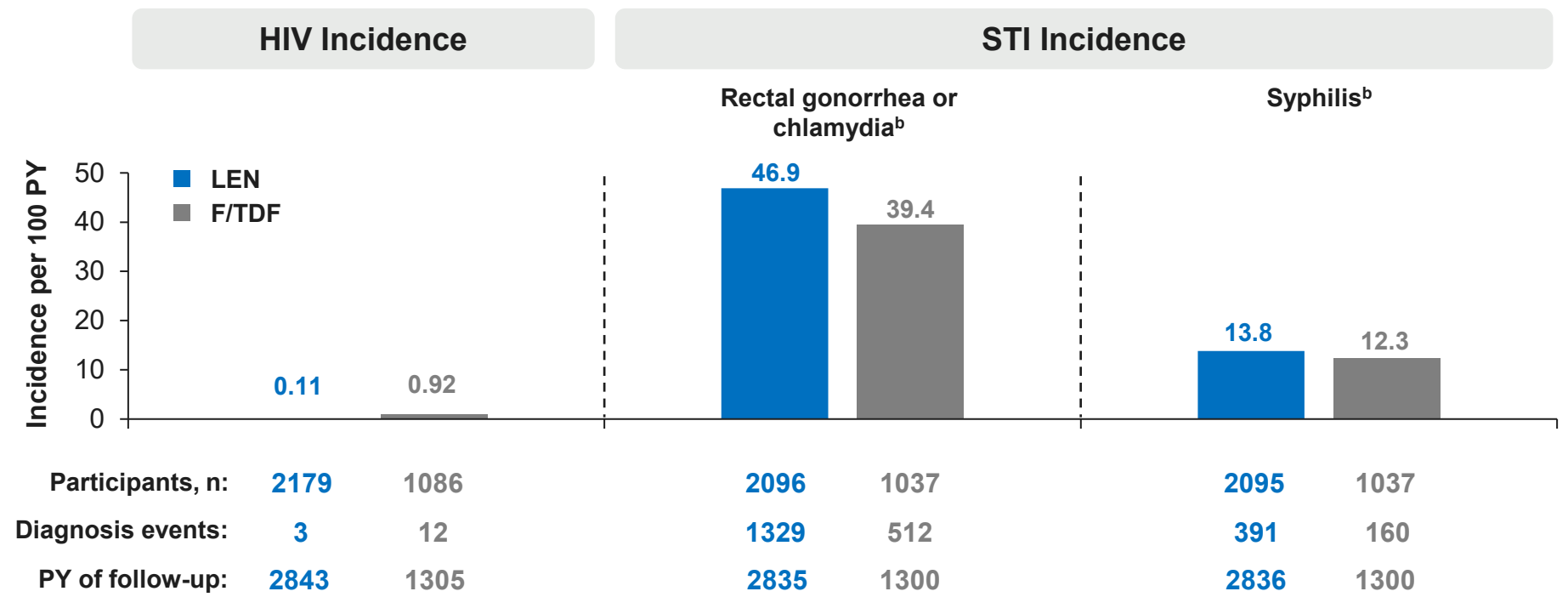
Brazil 36%
USA 21%
Peru 14%
Thailand 12%
South Africa 11%
Argentina 7%
Mexico <1%

Six participants were subsequently determined to have had HIV acquisition at the time of randomization, and thus 3265 were included in the modified ITT efficacy analysis. Unavailable or missing data were excluded from the calculations of percentages. ^aRace data were unavailable for eight participants in the LEN group and two participants in the F/TDF group. ^bEthnicity data were unavailable for one participant in the LEN group. ^cTesting for *T. vaginalis* was also performed at investigator discretion for participants assigned female at birth (1 case of *T. vaginalis* diagnosed at baseline in the LEN group). ^dDiagnoses of chlamydia or gonorrhea were based on rectal, oropharyngeal, and urine testing at a central laboratory. ^eThe denominator is 2084. ^fThe denominator is 1034. F/TDF, emtricitabine/tenofovir disoproxil fumarate; ITT, intention-to-treat; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

Sexually Transmitted Infections

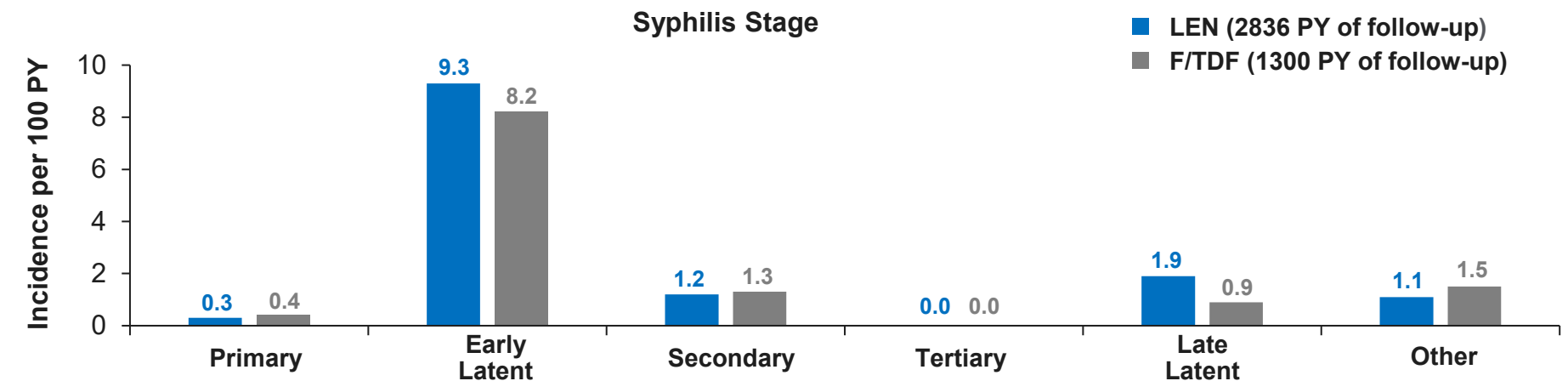
- Through the end of the RBP (**Figure 3**)
 - In the LEN group, 1329 episodes of rectal gonorrhea or chlamydia (incidence rate [IR]: 46.9 per 100 person-years [PY]) and 391 episodes of syphilis (IR: 13.8 per 100 PY) were diagnosed
 - In the F/TDF group, 512 episodes of rectal gonorrhea or chlamydia (IR: 39.4 per 100 PY) and 160 episodes of syphilis (IR: 12.3 per 100 PY) were diagnosed
 - The HIV IR was 0.11 per 100 PY in the LEN group and 0.92 per 100 PY in the F/TDF group
- The greatest incidence of syphilis was in the early latent stage (**Figure 4**)
- Incidence of rectal STIs remained stable over time (**Figure 5**)

Figure 3. Incidence of HIV, Rectal STIs, and Syphilis Through the End of RBP^a



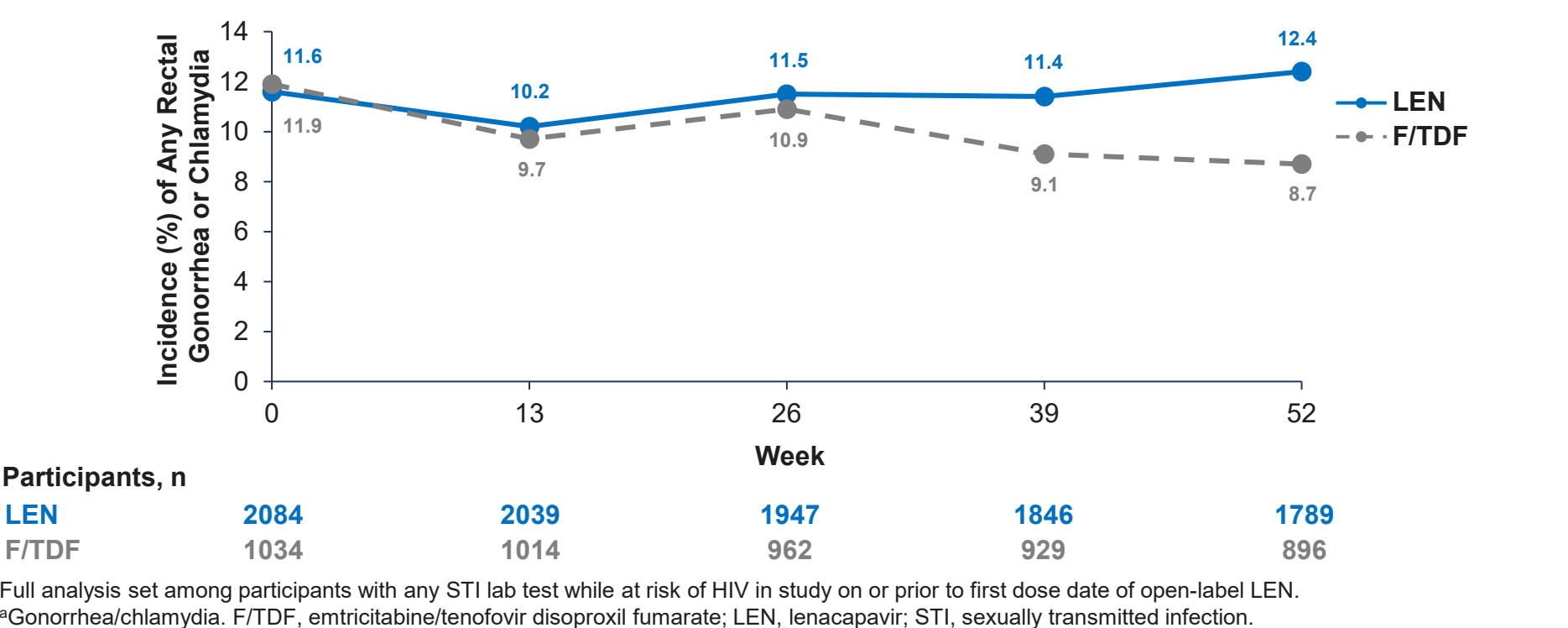
^aSee footnote a in Figure 1. ^bRectal gonorrhea and chlamydia are based on lab data and syphilis is investigator reported. F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; PY, person-years; RBP, randomized blinded phase; STI, sexually transmitted infection.

Figure 4. Syphilis by Stage Through the End of RBP^a



Number of reported events = number of unique participants and diagnosis dates (after first dose date) for each disease stage. ^aSee footnote a in Figure 1. F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; PY, person-years; RBP, randomized blinded phase.

Figure 5. Incidence of Rectal STIs^a Through Week 52



Sexual Behaviors Through Week 52

- Self-reported sexual behaviors remained consistent and comparable between groups, with a median of 3 to 5 partners per 3 months (**Figure 6**). The proportions of participants reporting ≥ 10 partners (22-32%) (**Figure 6**), ≥ 10 receptive anal sex acts (22-31%), and chemsex acts (21-29%) (**Figure 7**) also remained stable and comparable over time

Figure 6. Self-Reported Number of Sex Partners in Past 3 Months at Baseline and Weeks 13, 26, 39, and 52 by Study Group

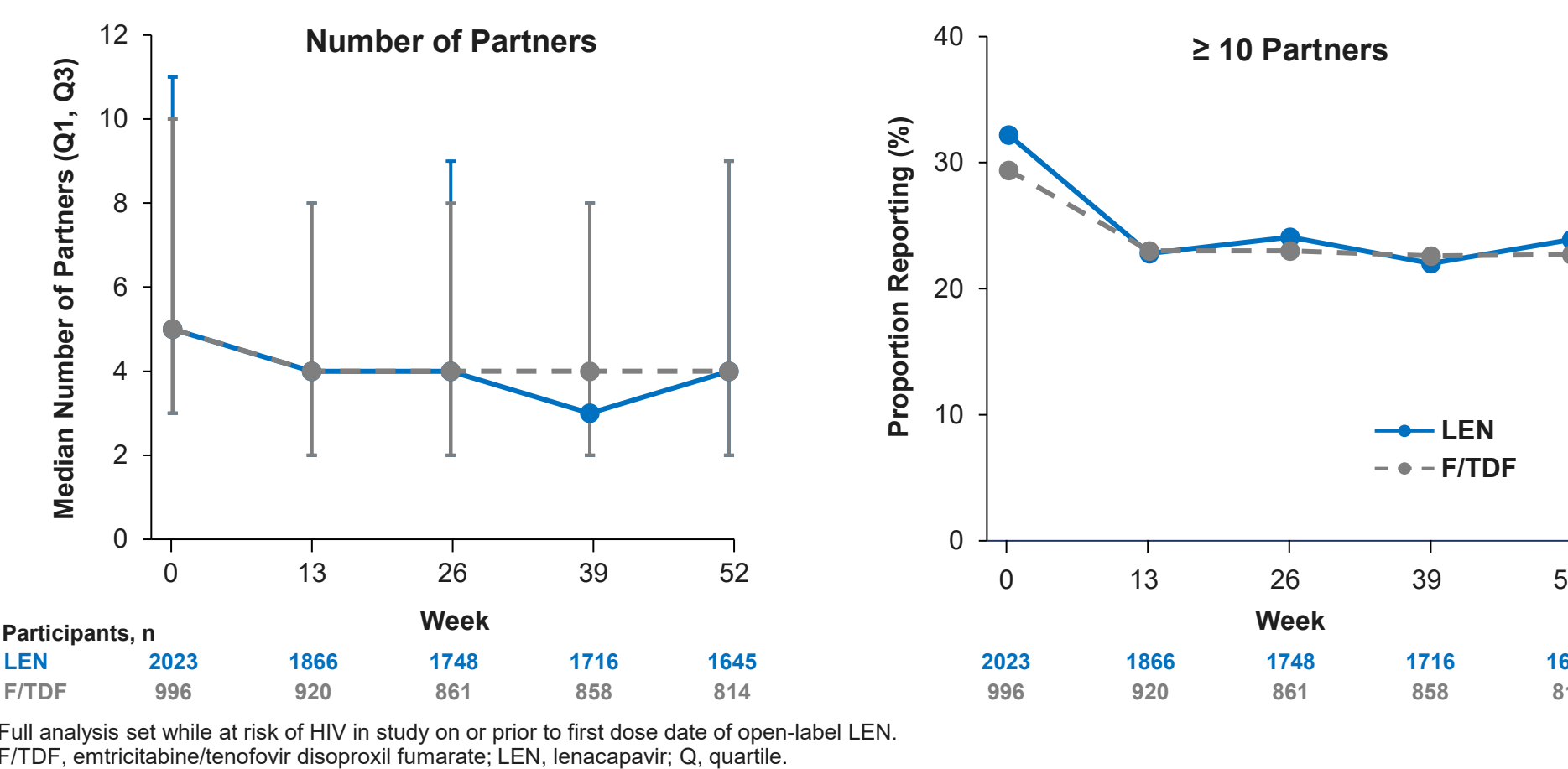
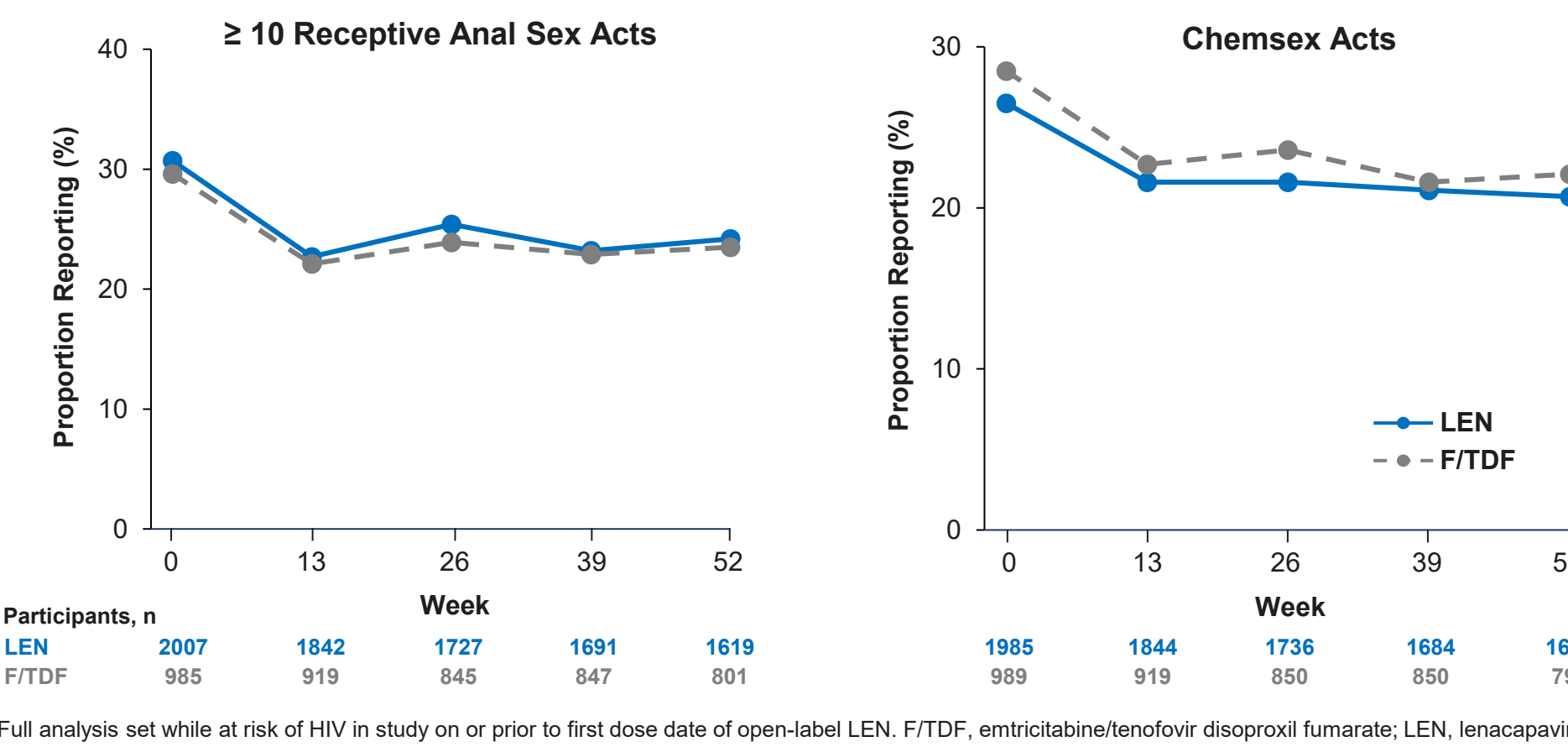


Figure 7. Self-Reported Number of Receptive Anal Sex Acts and Chemsex Acts in Past 3 Months at Baseline and Weeks 13, 26, 39, and 52 by Study Group



References: 1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. 2. Flannagan J, et al. *Transfus Med*. 2024;34:466-77. 3. WHO. https://www.who.int/health-topics/sexually-transmitted-infections#tab=tab_1 (accessed Oct. 8, 2026). 4. WHO. <https://www.who.int/news-room/fact-sheets/detail/hiv-aids> (accessed Oct. 8, 2026). 5. Mullick C, Murray J. *J Infect Dis*. 2020;221:214-21. 6. Wu MY, et al. *Sex Transm Infect*. 2021;97:525-33. 7. Malekinejad M, et al. *Sex Transm Dis*. 2021;48:e138-48. 8. Coronado-Munoz M, et al. *J Clin Med*. 2024;13:1812. 9. Baldry G, et al. *Int J STD AIDS*. 2026;37:884-91. 10. Maviglio F, et al. *Int J Environ Res Public Health*. 2022;20:294. 11. Georgiadis N, et al. *Drug Alcohol Depend*. 2025;275:112800. 12. Eustaquio PC, et al. *AIDS Behav*. 2024;28:3060-79. 13. Franklin J, et al. *Sex Health*. 2018;15:144-50. 14. Maxwell S, et al. *Int J Drug Policy*. 2019;63:74-89. 15. Whittington DD, et al. *J Sex Med*. 2026;23:qdag174. 16. Pastor I, et al. *AIDS Behav*. 2026;30:2101-8.

Acknowledgments: We extend our thanks to the PURPOSE 2 participants, their families, and all participating investigators. This study was funded by Gilead Sciences, Inc. Medical writing support was provided by Jenna Steere, PhD (Aspire Scientific Ltd, UK), and was funded by Gilead Sciences, Inc.

Disclosures: MC has received support from Gilead Sciences, Inc., ViV Healthcare, and Merck & Co. ALA has received support from Gilead Sciences, Inc. and ViV Healthcare. AA has received travel support from Gilead Sciences, Inc. and reports research grants to her institute from Gilead Sciences, Inc., ViV Healthcare, and MSD. JB has received support from and reports research grants to her institute from Gilead Sciences, Inc., SB has received support from Gilead Sciences, Inc., ViV Healthcare, and MSD. VDC has received support from Gilead Sciences, Inc., JAG-C has received support from Gilead Sciences, Inc., ViV Healthcare, and Merck & Co. NP has received support from Gilead Sciences, Inc., ViV Healthcare, and MSD. RPY has no financial relationship to disclose. PW, LBB, and CCC are employees and shareholders of Gilead Sciences, Inc., KHM has received support from Gilead Sciences, Inc., and ViV Healthcare.