PURPOSE
Prevention with PURPOSE

HIV DRUG THERAPY GLASGOW 2024

Annual Persistence in Use of Twice-Yearly Lenacapavir Versus Daily Oral PrEP in the PURPOSE 1 Phase 3 Trial

Linda-Gail Bekker[1], Noah Kiwanuka[2], Pearl Selepe[3], Amy Ward[4], Ramin Ebrahimi[5], Yang Zhao[5], Christoph Carter[5], Alexander Kintu[5], Jenna Yager[5], Moupali Das[5], Quarraisha Abdool Karim[6], for the PURPOSE 1 Study Team

[1]The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa; [2]Department of Epidemiology and Biostatistics, Makerere University School of Public Health, Kampala, Uganda; [3]Clinical Research Division, The Aurum Institute - Klerksdorp Clinical Research Site, South Africa; [4]Department of Medicine, Vuka Research Clinic, University of Cape Town, Cape Town, South Africa; [5]Gilead Sciences, Inc., Foster City, CA, USA; [6]Department of Epidemiology and Prevention, Centre for the AIDS Programme of Research in South Africa, Durban, South Africa, and Department of Epidemiology, Mailman School of Public Health, New York, NY, USA

HIV Drug Therapy Glasgow; November 10–13, 2024; Glasgow, UK

Disclosures

- Honoraria for advisories from Gilead Sciences, Merck (Pty) Ltd, ViiV Healthcare
- Research grants to the Desmond Tutu Health Foundation to conduct implementation science obtained from Johnson & Johnson, ViiV Healthcare
- Served on the Data Safety Monitoring Board for the PrEPVACC HIV Vaccine trial
- Gilead Sciences funded the study 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
- Copyediting and graphics support was provided by Aimee Sherlock, MSc, of Aspire Scientific (Bollington, UK), and was funded by Gilead Sciences, Inc.

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

Suboptimal PrEP Uptake, Adherence, and Persistence Globally

PURPOSE 1 evaluated the safety and efficacy of twice-yearly SC LEN or daily oral F/TAF for HIV prevention in cisgender women

LEN is a **first-in-class**, multistage HIV-1 capsid inhibitor with **high potency** and a **long half-life**, supporting **twice-yearly SC injection**[1,2]

Consistent adherence to PrEP over time is an important predictor of effectiveness. Daily oral PrEP is highly efficacious, but **daily adherence is challenging** and may lead to decreased adherence and persistence and, therefore, decreased effectiveness[3,4]

An efficacious, **long-acting agent** could eliminate the need for daily oral adherence and increase persistence, thereby increasing PrEP effectiveness

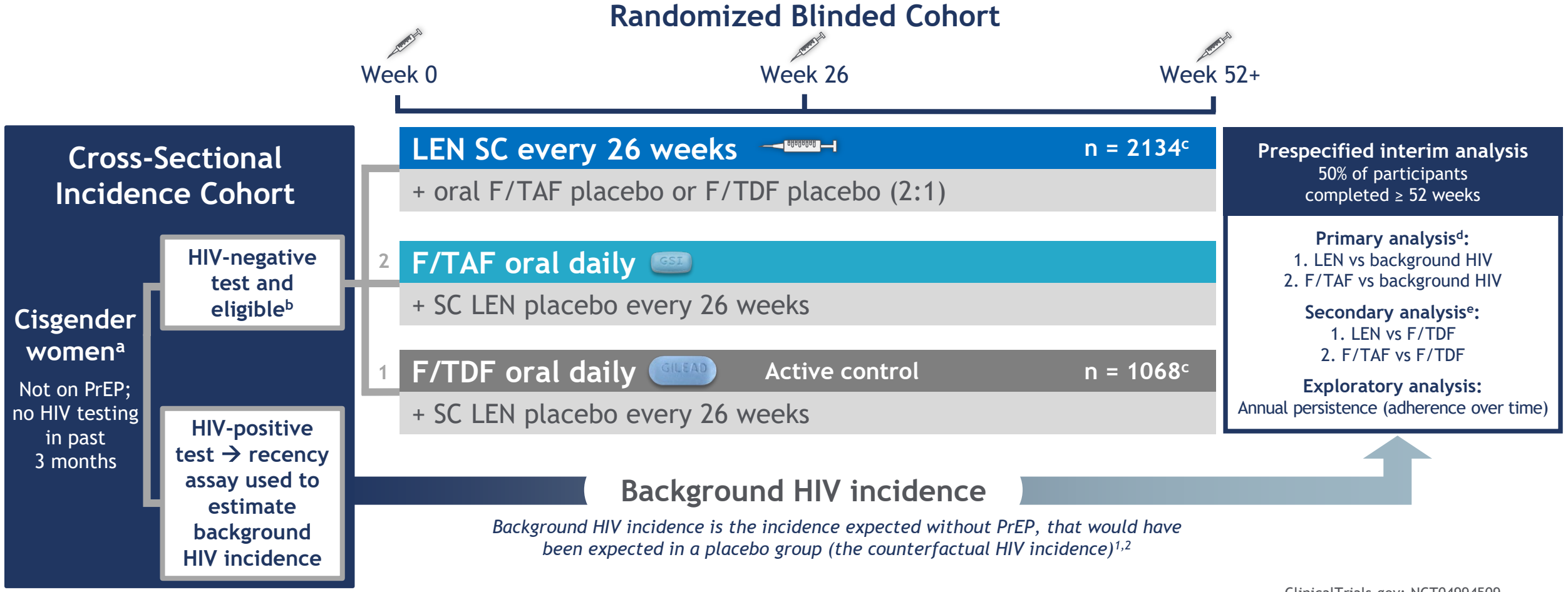
The aim of this PURPOSE 1 sub-analysis was to characterize annual persistence, defined as consistent adherence over 1 year, to LEN and daily oral F/TAF or F/TDF

F/TAF, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **HIV**, human immunodeficiency virus; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous.

1. Link JO, et al. *Nature*. 2020;584(7822):614-18. 2. Segal-Maurer S, et al. *N Engl J Med*. 2022;386(19):1793-803. 3. Landovitz RJ, et al. *Clin Infect Dis*. 2024;Epub ahead of print. 4. Marrazzo J, et al. *JAMA*. 2024;331(11):930-7.

PURPOSE 1 Study Design

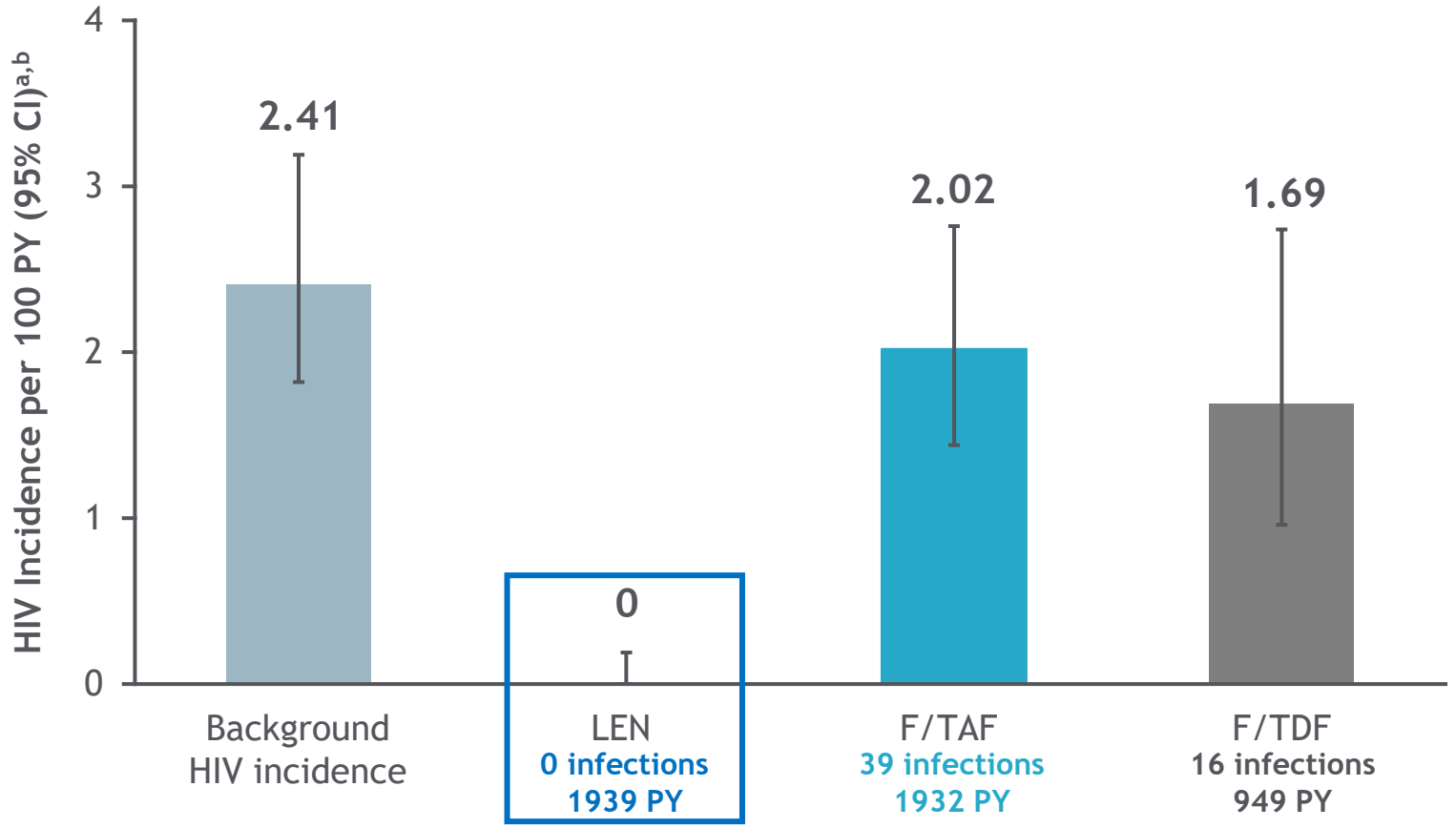
LEN and F/TAF for PrEP among Cisgender Women



ClinicalTrials.gov: NCT04994509

[a]The first participant was screened in August 2021, the 50th percentile participant was randomized in May 2023, and the last participant was randomized in September 2023. [b]Eligibility criteria included: weight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant. [c]n numbers represent the full analysis set for efficacy analyses. [d]IRR was assessed using a Wald test or likelihood ratio test if there were zero infections.[1,2] [e]IRR was assessed using Poisson regression or an exact conditional Poisson regression model in case of zero infections. **eGFR**, estimated glomerular filtration rate; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **HIV**, human immunodeficiency virus; **IRR**, Incidence rate ratio; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous. 1. Gao F, et al. *Stat Commun Infect Dis*. 2021;13(1):20200009. 2. Shao Y, Gao F. *Stat Commun Infect Dis*. 2024;16(1):20230004.

Zero HIV Infections in Cisgender Women receiving LEN



LEN demonstrated 100% HIV prevention efficacy compared with background HIV incidence and was superior to F/TDF[1,2]

LEN demonstrated 100% efficacy for HIV prevention in cisgender women[1,2]

[a]Overall n: background HIV incidence group, 8094; LEN, 2134; F/TAF, 2136; F/TDF, 1068. [b]95% CIs: background HIV incidence group, 1.82-3.19; LEN, 0-0.19; F/TAF, 1.44-2.76; F/TDF, 0.96-2.74.
CI, confidence interval; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **HIV**, human immunodeficiency virus; **LEN**, lenacapavir; **PY**, person-years.
1. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 2. Bekker L-G, et al. Oral presentation at the 25th International AIDS Conference, July 22–26, 2024; Munich, Germany.

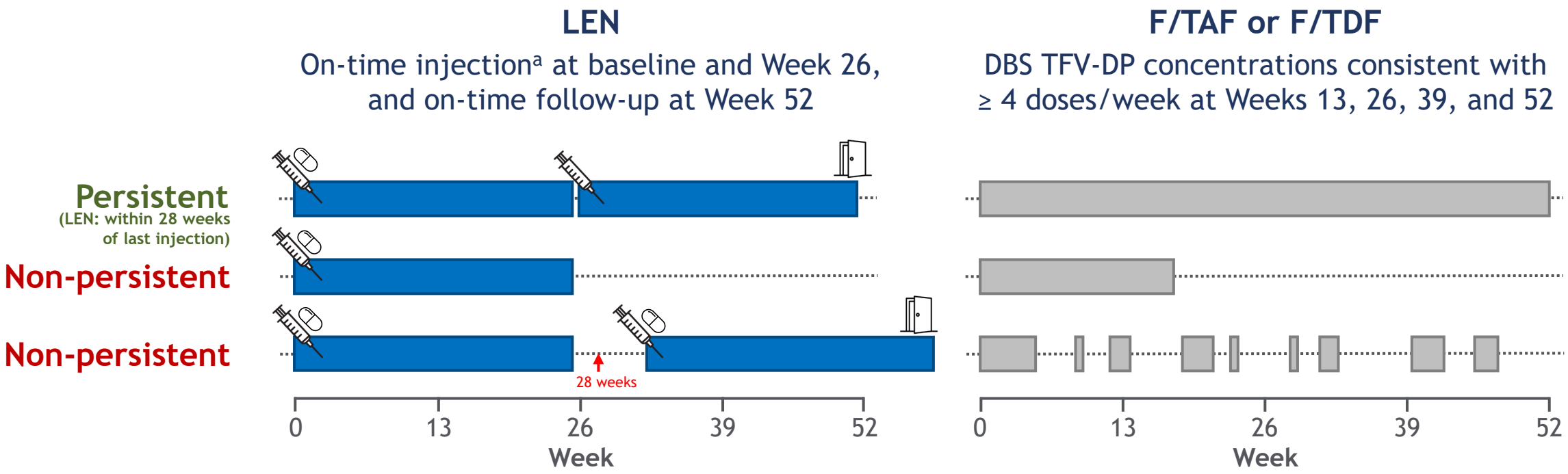
The PURPOSE Program

PURPOSE 1 and PURPOSE 2 demonstrated that twice-yearly LEN is highly efficacious, safe and well tolerated for HIV prevention in the most globally, racially, ethnically, and gender-diverse Phase 3 program conducted to date[1-4]

PURPOSE 1 NCT identifier: NCT04994509; PURPOSE 2: NCT04925752; PURPOSE 3: NCT06101329; PURPOSE 4: NCT06101342. PURPOSE studies available at: https://www.purposestudies.com/ (accessed November 11, 2024). Access statements: https://www.gilead.com/company/company-statements/2024/updated-statement-on-access-planning-in-high-incidence-resource-limited-countries-for-lenacapavir-for-hiv-prevention (accessed November 11, 2024); https://www.gilead.com/news/news-details/2024/gilead-signs-royalty-free-voluntary-licensing-agreements-with-six-generic-manufacturers-to-increase-access-to-lenacapavir-for-hiv-prevention-in-high-incidence-resource-limited-countries (accessed November 11, 2024). **CGBMSM**, cisgender gay and bisexual men who have sex with men; **FR**, France; **GNB**, gender nonbinary individuals; **HIV**, human immunodeficiency virus; **LEN**, lenacapavir; **NCT**, National Clinical Trial; **PWID**, people who inject drugs; **TGM**, transgender men; **TGW**, transgender women; **UK**, United Kingdom; **US**, United States. 1. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 2. Bekker L-G, et al. Oral presentation at the 25th International AIDS Conference, July 22-26, 2024; Munich, Germany. 3. Kelley CF, et al. Oral presentation at the 5th HIV Research for Prevention Conference, October 6-10, 2024; Lima, Peru. 4. Kelley CF et al. Oral presentation at IDWeek, October 16-19, 2024; Los Angeles, CA, USA.

Defining Annual PrEP Persistence

Annual persistence was characterized in a random, preselected 10% sample of participants
(limited to those who could have had ≥ 1 year of study follow-up at the time of the interim analysis)



Annual persistence to injections defined as on-time injection at baseline and Week 26, and on-time follow up visit at Week 52

[a]On-time injection at Week 26 and Week 52 was defined as within 28 weeks after the last injection.

DBS, dried blood spot; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **TFV-DP**, tenofovir-disphosphate.

Adherence to Injections Was High While Adherence to Oral F/TAF and F/TDF Was Poor

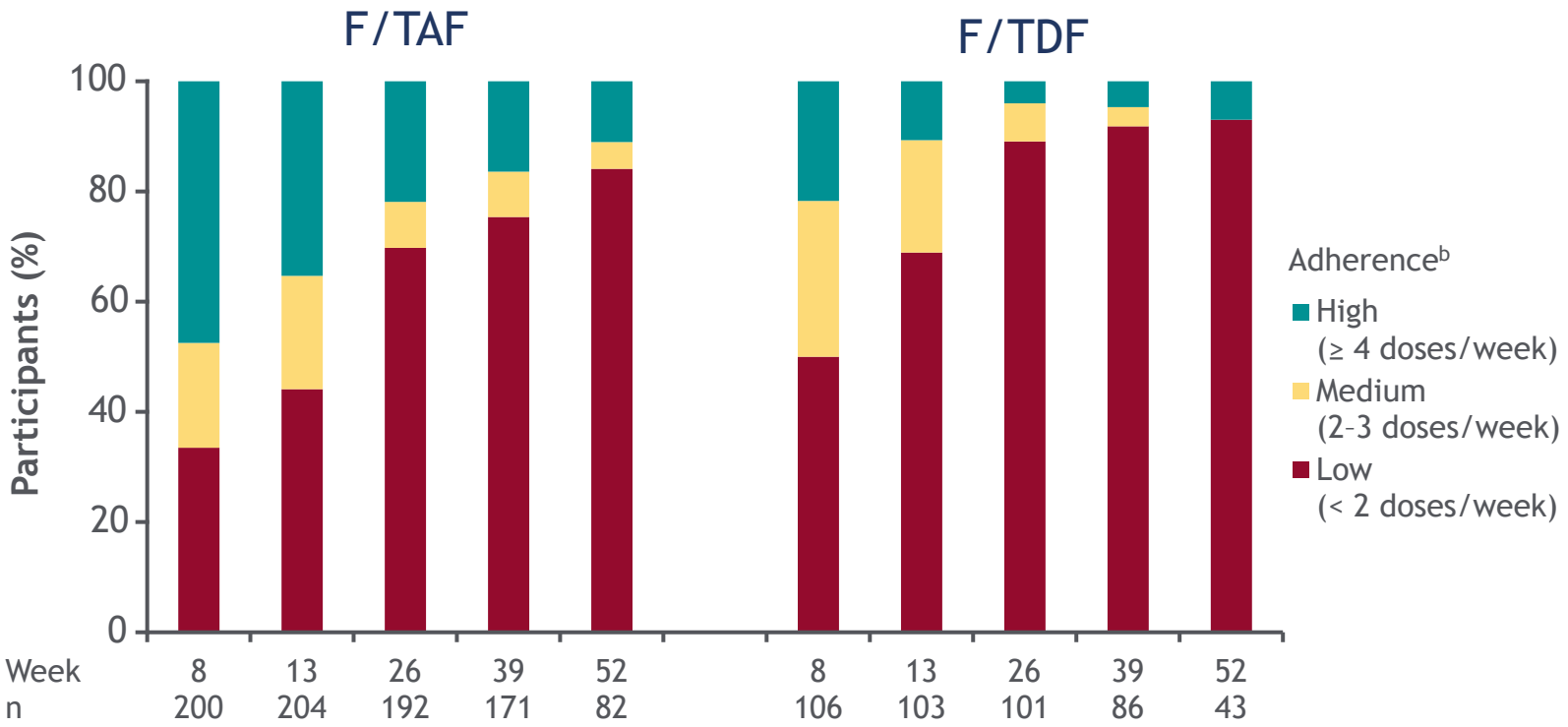
Injection Adherence

LEN injections were on time (< 28 weeks from last injection)[a] for:

- **91% (1832/2012) at Week 26**
- **94% (836/894) at Week 52**

On-time injection rate was similar for LEN and placebo (F/TAF and F/TDF) injections

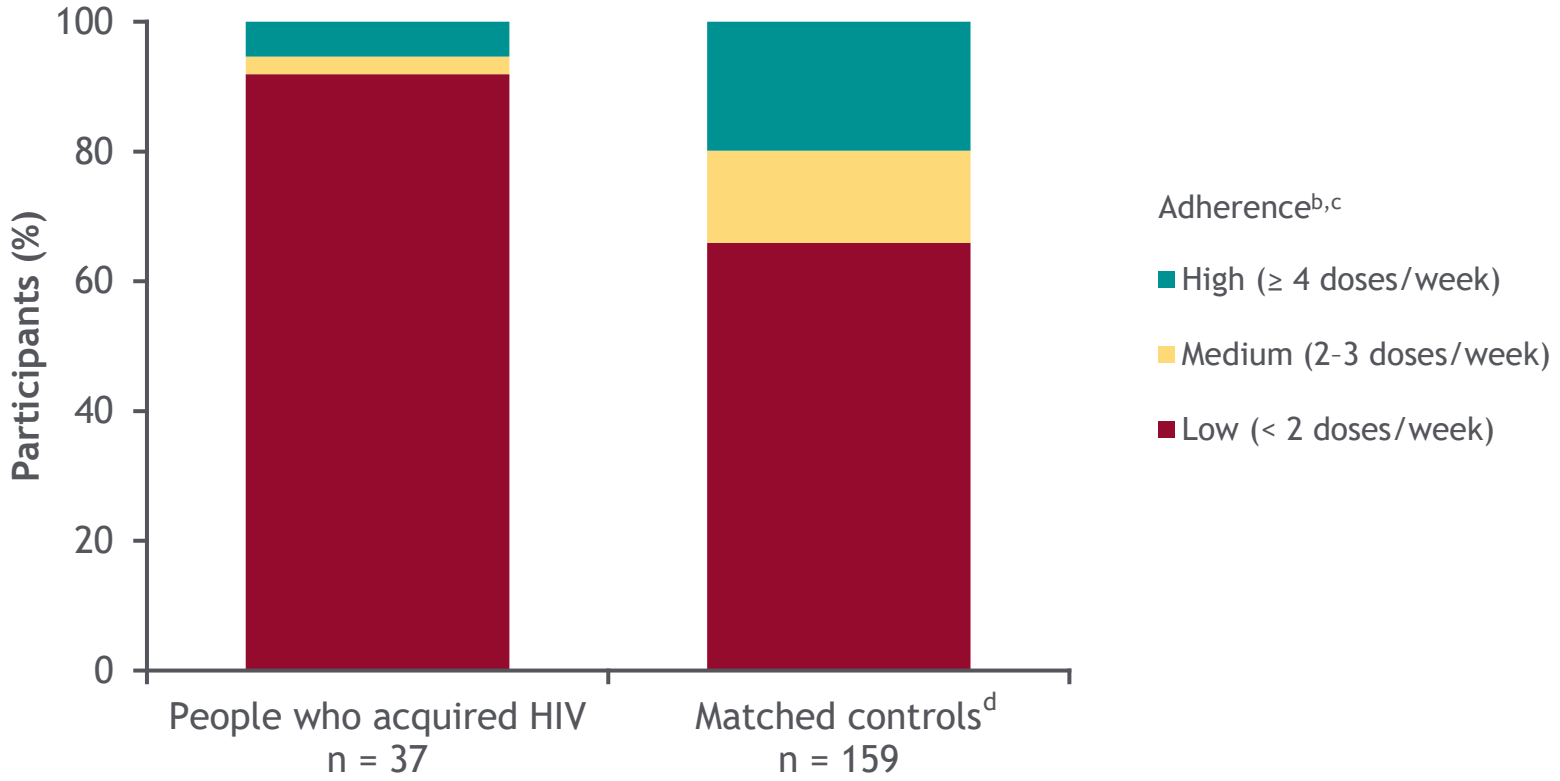
Adherence by TFV-DP Concentration in 10% Cohort



On-time adherence to injections was high
Most participants in both the F/TAF and F/TDF groups had low adherence to oral tablets, and adherence declined over time[1,2]

[a]Participants who presented late required negative HIV testing to reinitiate study product, which included reloading with oral LEN or placebo. [b]Preselected 10% sample of participants assessed for TFV-DP concentrations in DBS (adherence cutoffs for F/TAF: low < 450, medium ≥ 450 to < 900, high ≥ 900 fmol/punch; and for F/TDF: low < 350, medium ≥ 350 to < 700, high ≥ 700 fmol/punch). **DBS**, dried blood spot; **TFV-DP**, tenofovir diphosphate; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **HIV**, human immunodeficiency virus; **LEN**, lenacapavir. 1. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 2. Bekker L-G, et al. Oral presentation at the 25th International AIDS Conference, July 22-26, 2024; Munich, Germany.

Lower Chance of HIV Infection Associated With Medium or High Adherence to F/TAF: A Matched Case-Control Analysis[a]

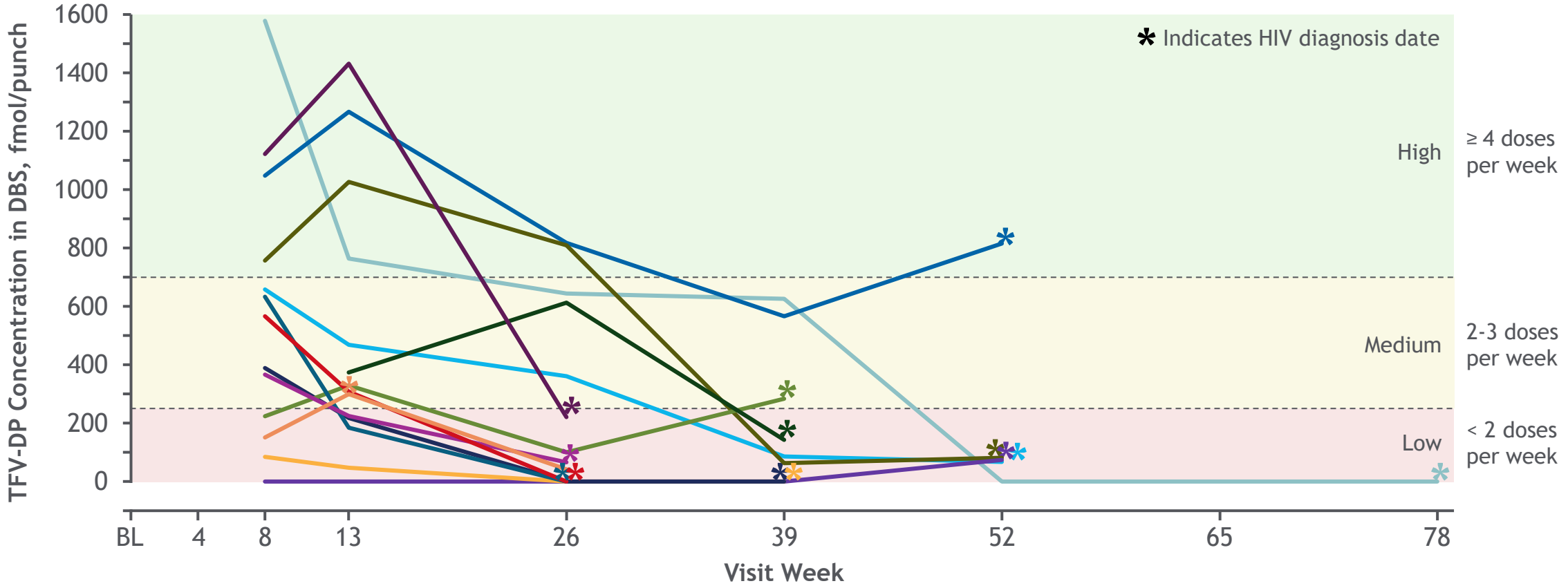


A significantly lower likelihood of HIV infection is associated with medium or high adherence compared with low adherence (odds ratio: 0.11; 95% CI 0.012-0.485; *P* = 0.0006)[1,2]

[a]Conditional logistic regression. Controls matched on site and baseline VOICE score from the same visit as the HIV diagnosis visit of each case. Each of 37 case participants contributed one sample. A trial participant could serve as a control for more than one case participant; 159 participants contributed 176 samples to be used as matched controls. [b]By TFV-DP DBS levels (adherence cutoffs for F/TAF: low < 450, medium ≥ 450 to < 900, high ≥ 900 fmol/punch). [c]Missing DBS concentrations imputed for participants with HIV infection based on last concentration prior to HIV diagnosis, and decay rate based on the median half-life. [d]Available data shown in stacked bar. **CI**, confidence interval; **DBS**, dried blood spot; **TFV-DP**, tenofovir diphosphate; **F/TAF**, emtricitabine/tenofovir alafenamide; **HIV**, human immunodeficiency virus.

1. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 2. Bekker L-G, et al. Oral presentation at the 25th International AIDS Conference, July 22-26, 2024; Munich, Germany.

Participants Who Acquired HIV on F/TDF Had Declining Adherence



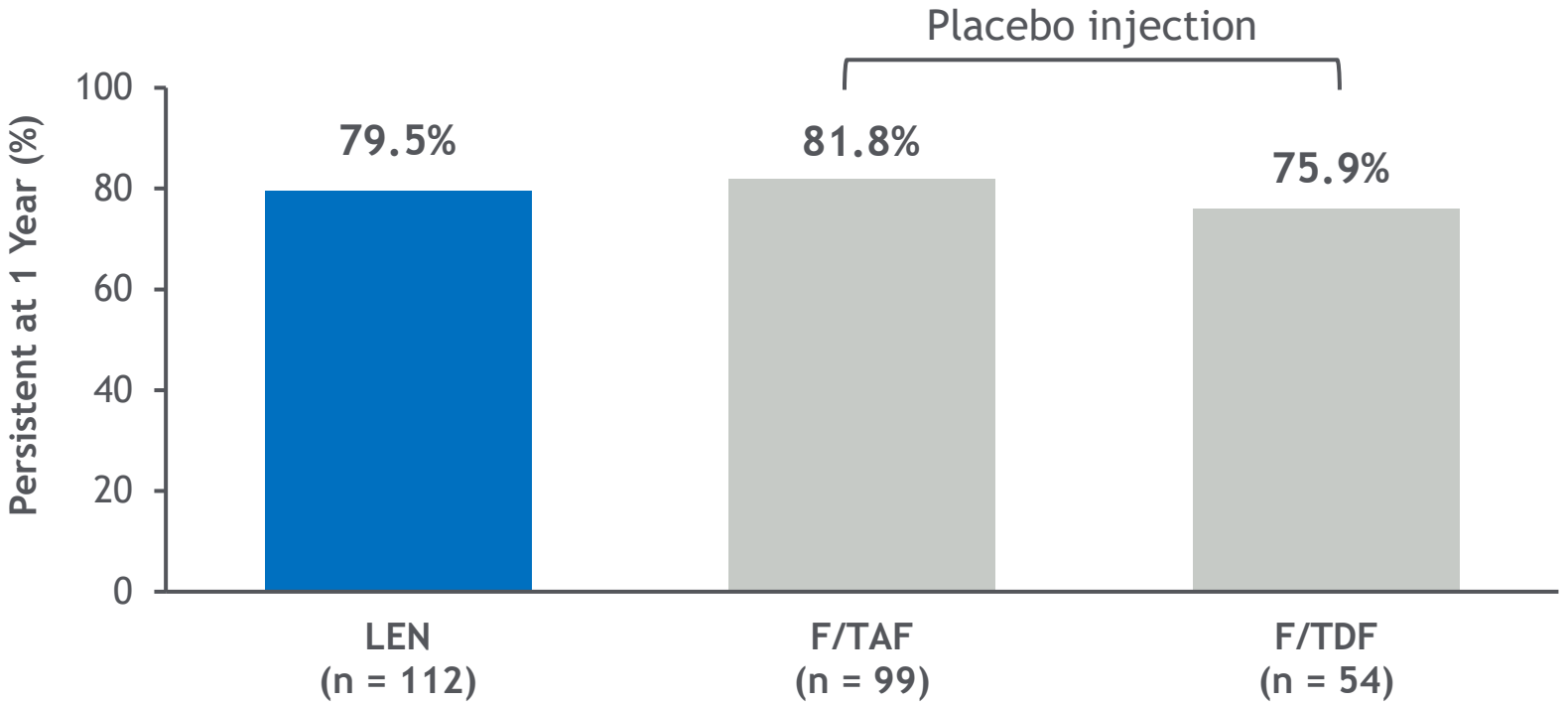
All participants in the F/TDF group who were diagnosed with HIV had evidence of low adherence or a decrease in adherence over time

Adherence cutoffs for F/TDF: low < 350, medium ≥ 350 to < 700, high ≥ 700 fmol/punch. Each line represents a single participant who acquired HIV in the F/TDF group. Week 4 data are not plotted as these data were not at steady state. Measurements below the limit of quantification (defined as 25 fmol/punch) are plotted as 0. DBS data were not available for two participants who acquired HIV in the F/TDF group.

BL, baseline; **DBS**, dried blood spot; **HIV**, human immunodeficiency virus; **TFV-DP**, tenofovir diphosphate; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate.

Annual Persistence on LEN Injections or Placebo Injections Was High

Annual persistence on LEN was assessed by on-time injections at Week 26 and Week 52 (within 28 weeks of the last injection)

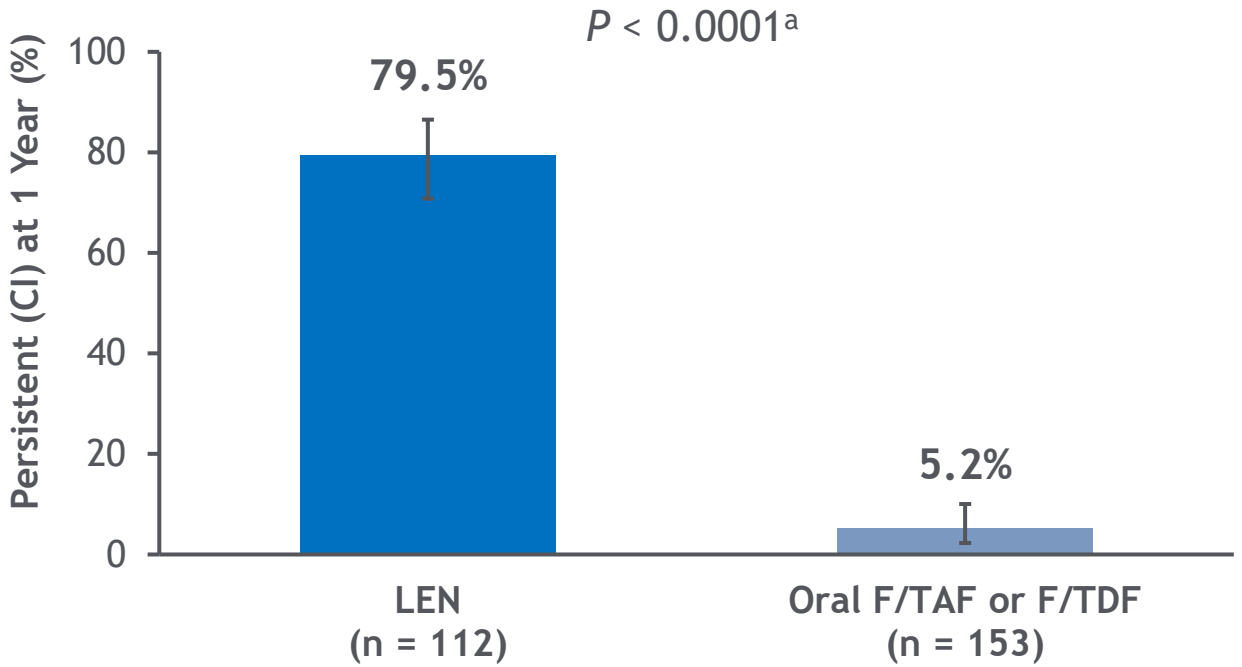


Annual persistence on LEN injections was not different compared with persistence on placebo injections in the F/TAF or F/TDF groups

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

Higher Annual Persistence on Twice-Yearly LEN Versus Daily Oral F/TAF or F/TDF

Annual persistence on LEN was assessed by on-time injections at Week 26 and Week 52 (within 28 weeks of the last injection).
Annual persistence on oral F/TAF or F/TDF was assessed by TFV-DP concentration in DBS



Annual persistence was significantly higher on twice-yearly LEN than on daily oral F/TAF or F/TDF, which helps elucidate the LEN efficacy findings in PURPOSE 1

[a]*P* value was calculated based on Fisher's exact test.

CI, confidence interval; **DBS**, dried blood spot; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **TFV-DP**, tenofovir-diphosphate.

Conclusions

- Annual persistence was assessed in PURPOSE 1 by evaluating on-time injections and by measuring DBS drug levels during the blinded, randomized phase of the study
  - Decreased PrEP adherence and persistence is associated with decreased prevention effectiveness[1–3]
- Significantly higher annual persistence was observed with twice-yearly LEN vs daily oral F/TAF or F/TDF
- The same approach to evaluate annual persistence and assess the potential benefit of twice-yearly LEN vs daily oral F/TDF will be used in PURPOSE 5 in France and the UK

Persistence on twice-yearly LEN was very high over 1 year in contrast to suboptimal oral F/TAF and F/TDF persistence, supporting the potential for LEN to have greater HIV prevention benefits beyond those of currently available PrEP options

DBS, dried blood spot; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **HIV**, human immunodeficiency virus; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **UK**, United Kingdom.

1. Landovitz RJ, et al. *Clin Infect Dis*. 2024;Epub ahead of print. 2. Marrazzo J, et al. *JAMA*. 2024;331(11):930-7. 3. Jourdain H, et al. *Lancet Public Health*. 2022;7(6):e529-36.

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

Graphical and copyediting support was provided by Aimee Sherlock, MSc, of Aspire Scientific (Bollington, UK), and was funded by Gilead Sciences, Inc.

PURPOSE 1

To access a copy of this presentation and other supplemental information, please scan the QR code

SCAN ME