Adherence to F/TAF in Cisgender Women Prevents HIV With Low Risk of Resistance or Diagnostic Delay

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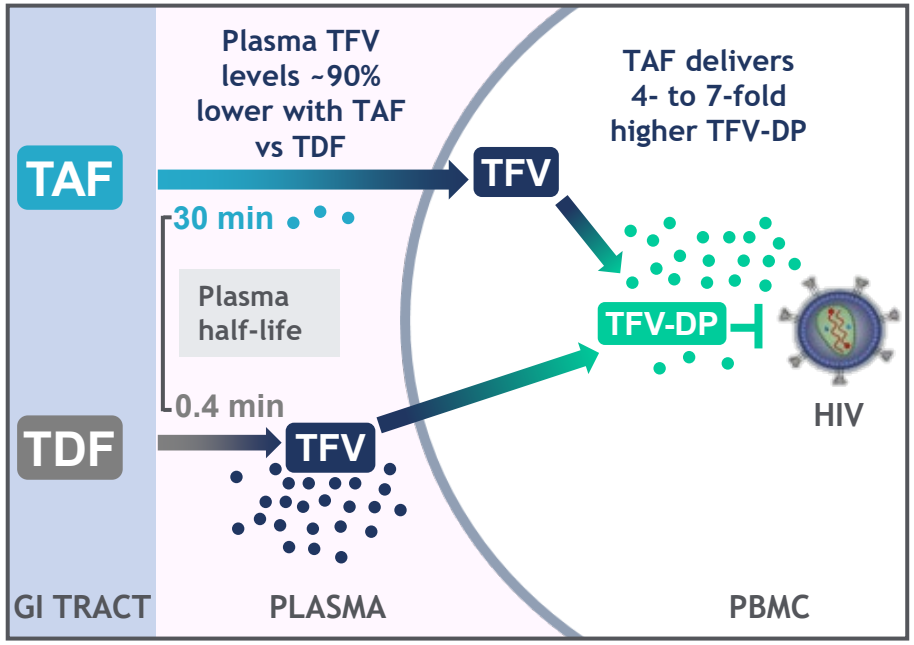
G-CAG, Global Community Advisory Group; **PI**, principal investigator.

Cisgender Women Need New HIV Prevention Choices

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



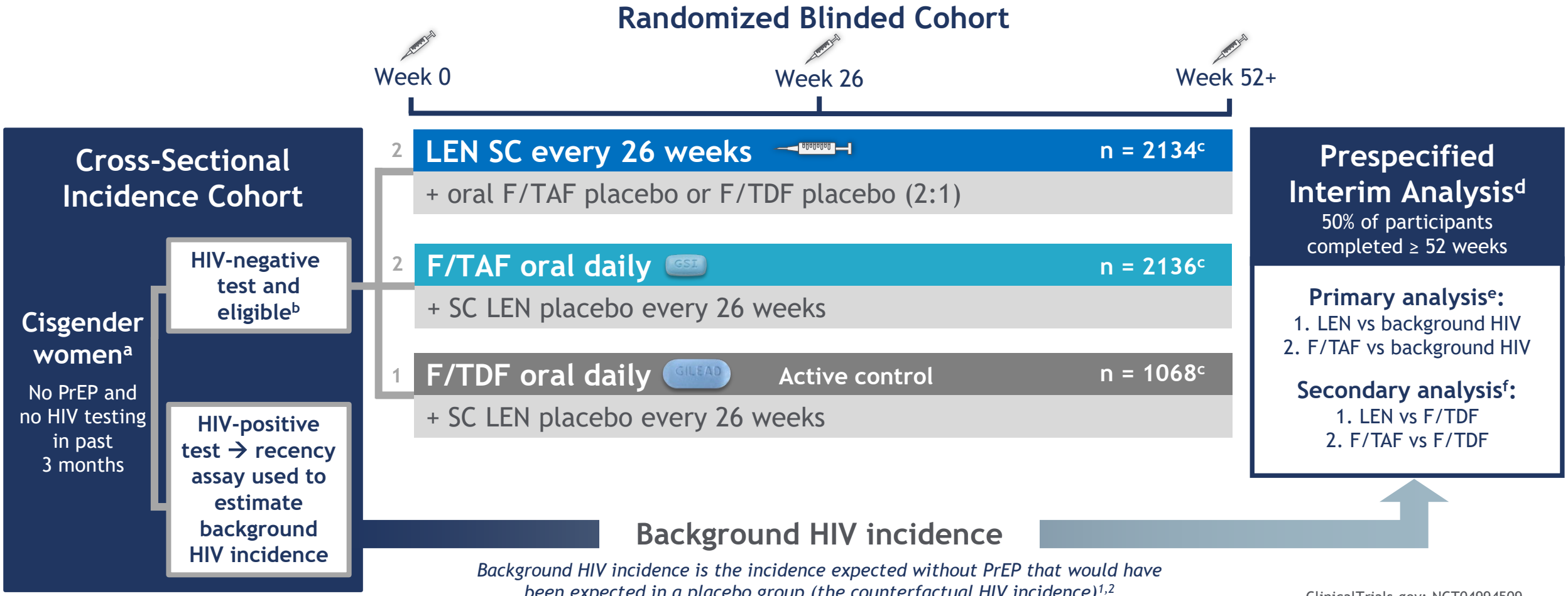
- **Cisgender women** account for **approximately half** of the annual **1.3 million** new cases of HIV globally[2]
- Only **~17%** of the UNAIDS 2025 target of **21.2 million people** were on PrEP in 2023[2]

- Oral tenofovir-based PrEP efficacy is highly correlated with adherence,[3] with >90% efficacy with 4 or more doses/week in RCTs and RWE[4,5]
- **F/TAF** is a smaller tablet than F/TDF. **TAF** is an orally bioavailable HIV NRTI with increased plasma stability and more rapid PBMC uptake compared with TDF[6]
- **F/TAF** has demonstrated efficacy and safety as PrEP in cisgender men and transgender women[5]

The aim of this analysis was to characterize incident HIV cases in the F/TAF group, including adherence, resistance, and timing of seroconversion

F/TAF, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **GI**, gastrointestinal; **LEN**, lenacapavir; **NRTI**, nucleotide reverse transcriptase inhibitor; **PrEP**, pre-exposure prophylaxis; **PBMC**, peripheral blood mononuclear cells; **RCT**, randomized controlled trial; **RWE**, real-world evidence; **SC**, subcutaneous; **TAF**, tenofovir alafenamide; **TDF**, tenofovir disoproxil fumarate; **TFV**, tenofovir; **TFV-DP**, tenofovir diphosphate; **UNAIDS**, Joint United Nations Programme on HIV/AIDS. 1. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 2. UNAIDS. https://aidsinfo.unaids.org (accessed Feb 24, 2025). 3. Baeten et al, *NEJM* 2012;367:399-410; 4. Marrazzo J, et al. *JAMA*. 2024;331:930-937; 5. Mayer KH, et al. *Lancet* 2020;396:239-54. 6. Lee WA, et al. *Antivir Ther*. 2022;27:13596535211067600.

PURPOSE 1 Study Design



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]Since the randomized blinded phase was stopped early due to an efficacy outcome, the interim analysis served as the primary analysis. [e]IRR was assessed using a Wald test or likelihood ratio test if there were zero infections.[1,2] [f]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; **IRR**, incidence rate ratio; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous. 1. Gao F, et al. *Stat Commun Infect Dis.* 2021;13:20200009. 2. Shao Y, Gao F. *Stat Commun Infect Dis.* 2024;16:20230004.

HIV Testing During the Randomized Blinded Phase

Screening/Baseline HIV Testing

- Rapid point-of-care fourth-generation Ag/Ab test and central laboratory fourth-generation Ag/Ab test, which, if positive, was confirmed by an HIV-1/2 Ab differentiation assay. If results were discrepant, qualitative HIV RNA NAAT test was conducted
- Quantitative HIV-1 RNA NAAT test also performed during screening and baseline

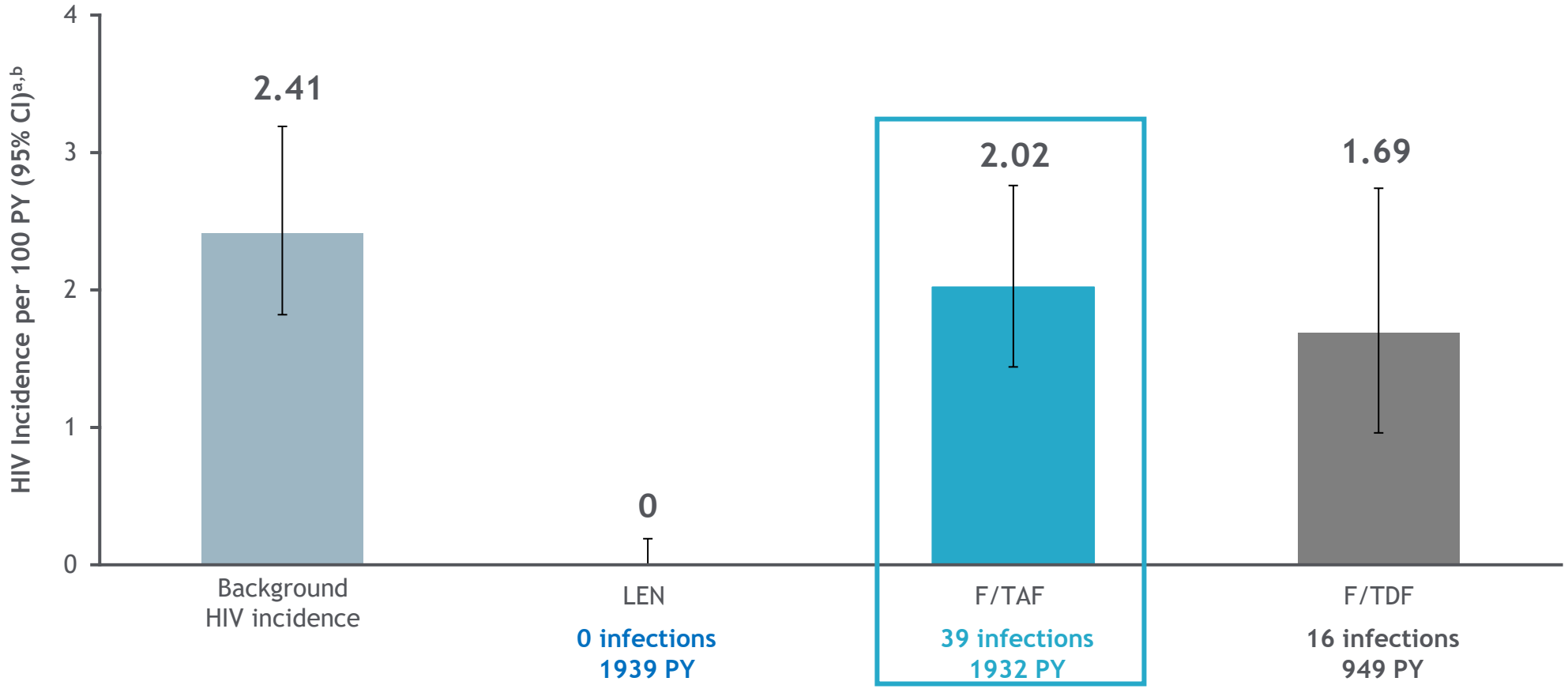
Follow-Up Visit HIV Testing (W4, 8, 13, Then Q13W)

- Rapid point-of-care and central laboratory fourth-generation Ag/Ab tests with same confirmation procedures

Retrospective HIV-1 RNA quantitative NAAT testing was done for all participants with incident HIV infection

Ab, antibody; **Ag**, antigen; **BL**, baseline; **NAAT**, nucleic acid amplification tests, **Q13W**, every 13 weeks; **Scr**, screening; **W**, weeks.

PURPOSE 1 Primary Analysis

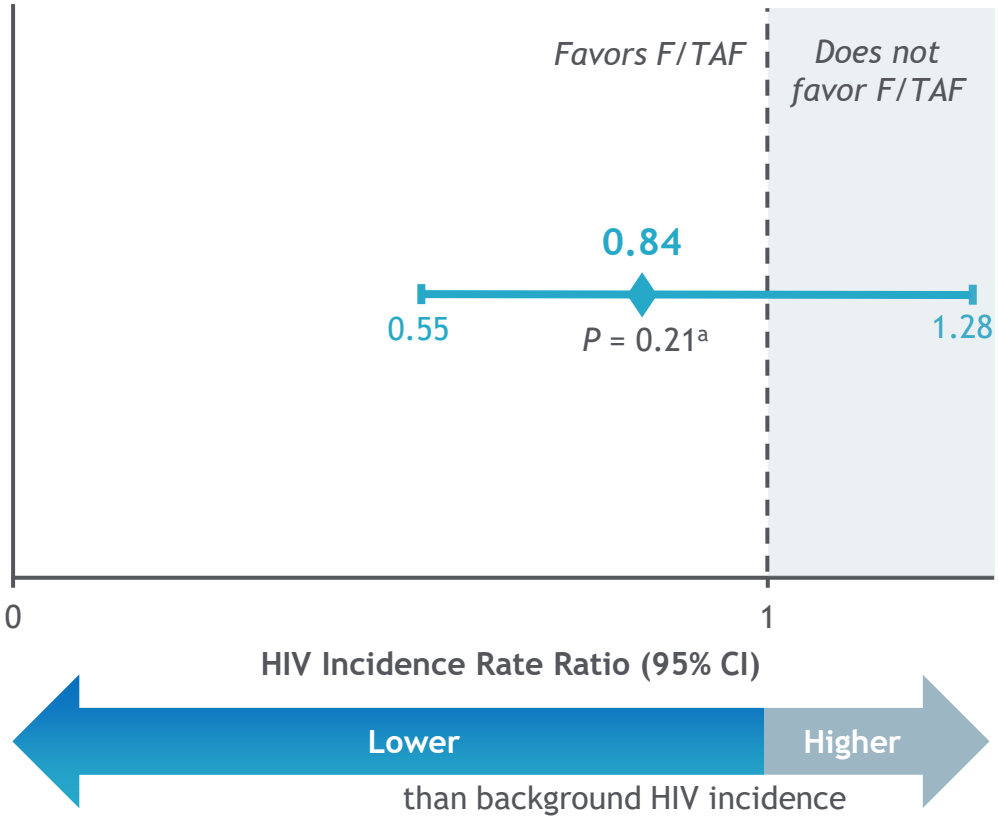


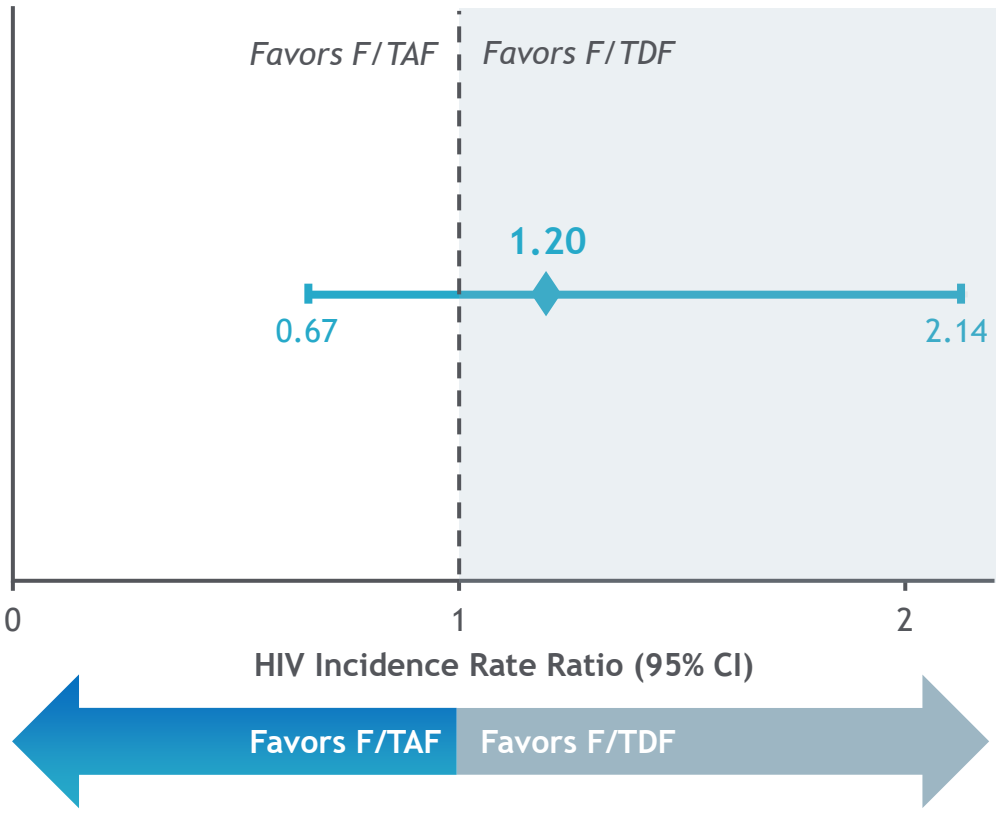
39 HIV infections occurred in the F/TAF group[1,2]

[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.
F/TAF, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **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 presented at: 25th International AIDS Conference; July 22–26, 2024; Munich, Germany.

F/TAF Primary and Secondary Endpoints





HIV incidence in the F/TAF group was not statistically different from background HIV incidence; F/TAF incidence was not statistically different from F/TDF[1,2]

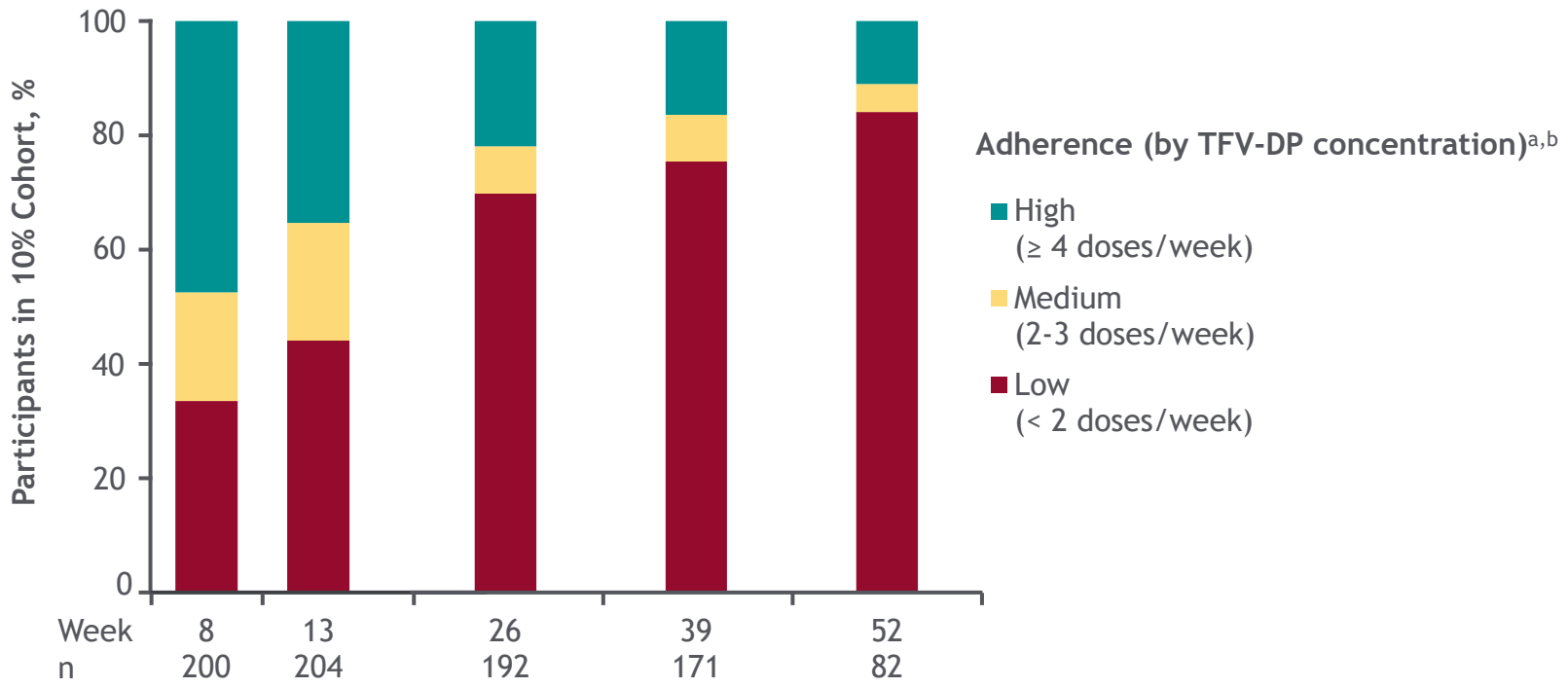
[a]HIV IRR versus background HIV was assessed using a Wald test.[3]

F/TAF, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **IRR**, incidence rate ratio.

1. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 2. Bekker L-G, et al. Oral presented at: 25th International AIDS Conference; July 22–26, 2024; Munich, Germany. 3. Gao F, et al. *Stat Commun Infect Dis*. 2021;13:20200009.

Adherence to Oral F/TAF Was Low

Adherence by Post-Baseline Visit

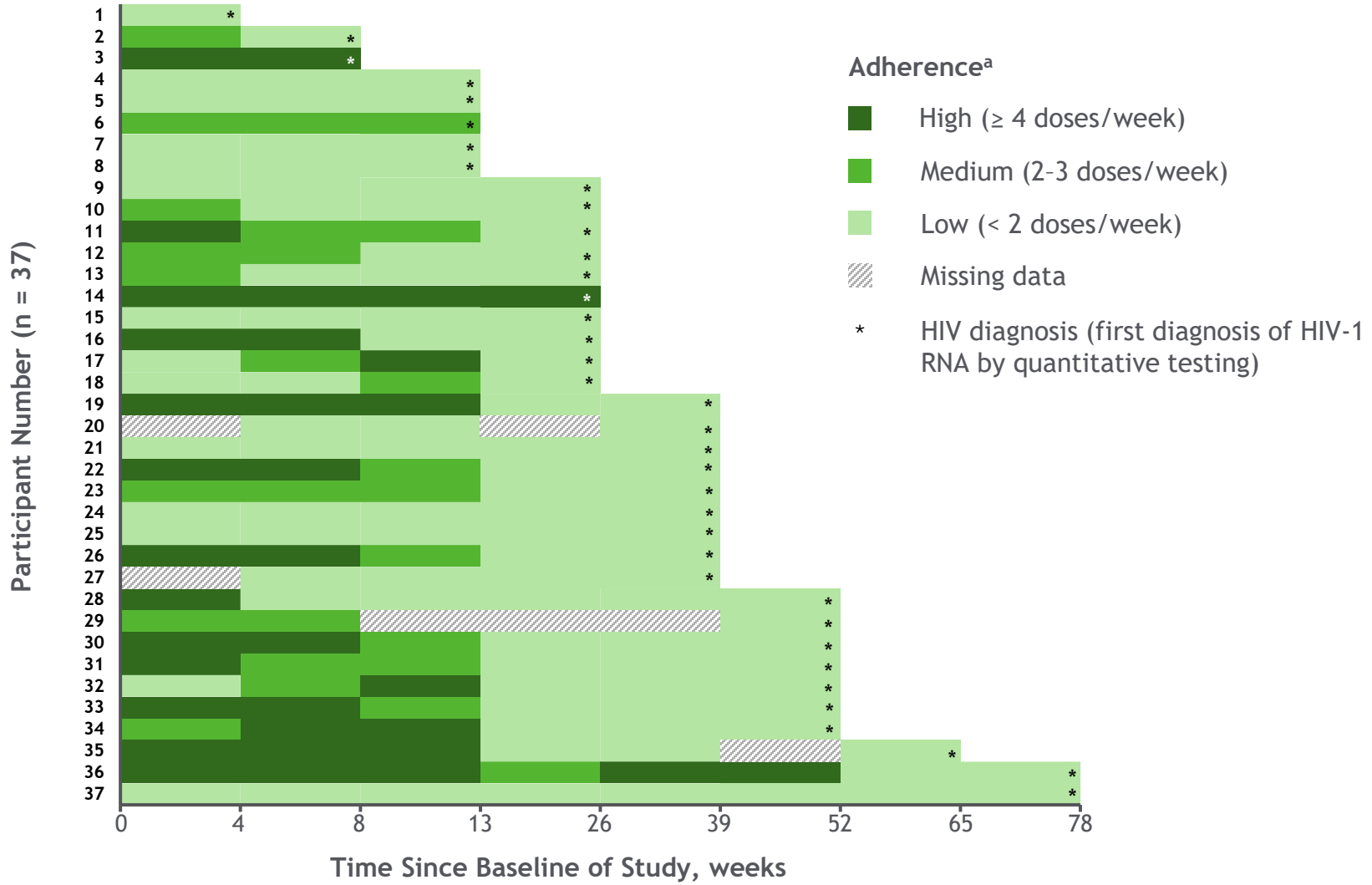


Most participants in the F/TAF group had low adherence to oral tablets, and adherence declined over time[1,2]

[a]Randomly preselected 10% sample of participants assessed for TFV-DP concentrations in DBS. [b]Adherence cutoffs for F/TAF: low < 450, medium ≥ 450 to < 950, high ≥ 950 fmol/punch.
DBS, dried blood spot; **F/TAF**, emtricitabine/tenofovir alafenamide; **TFV-DP**, tenofovir diphosphate.

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

Longitudinal Adherence Patterns

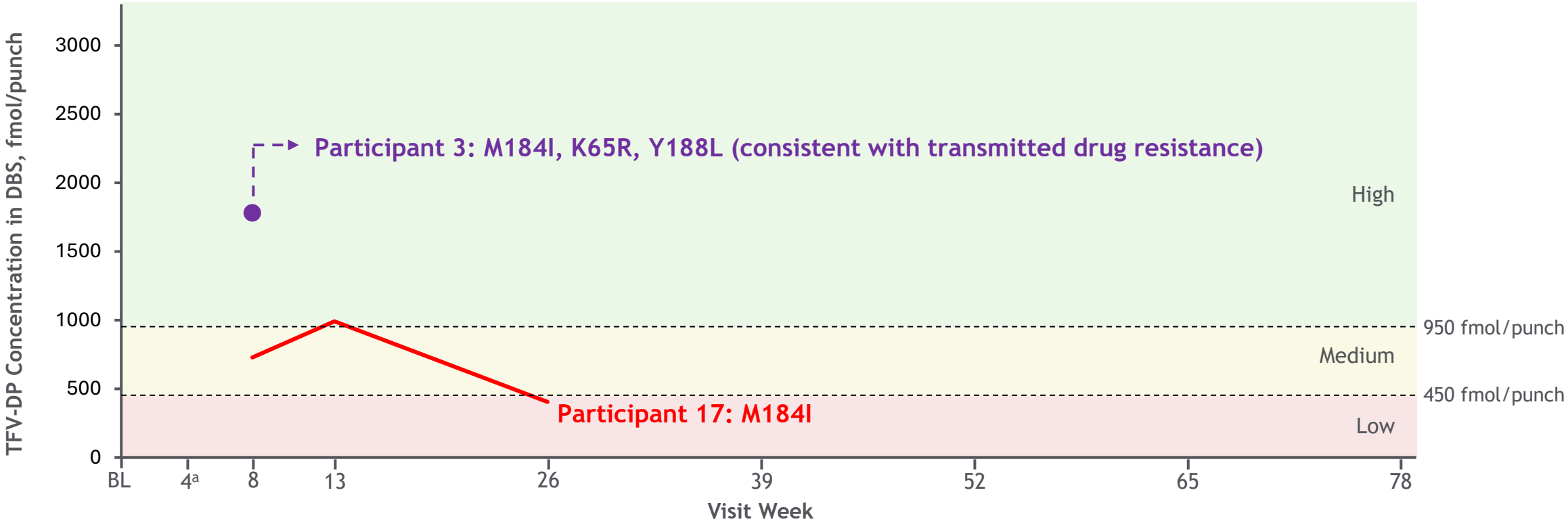


Almost all participants in the F/TAF group who were diagnosed with HIV had evidence of low adherence or a decrease in adherence over time

Each row represents a single participant. Each box represents DBS-based adherence for the corresponding time period. DBS data were unavailable for two participants receiving F/TAF.

[a]By TFV-DP DBS levels (adherence cutoffs: low < 450, medium ≥ 450 to < 950, high ≥ 950 fmol/punch). **DBS**, dried blood spot; **F/TAF**, emtricitabine/tenofovir alafenamide; **TFV-DP**, tenofovir diphosphate.

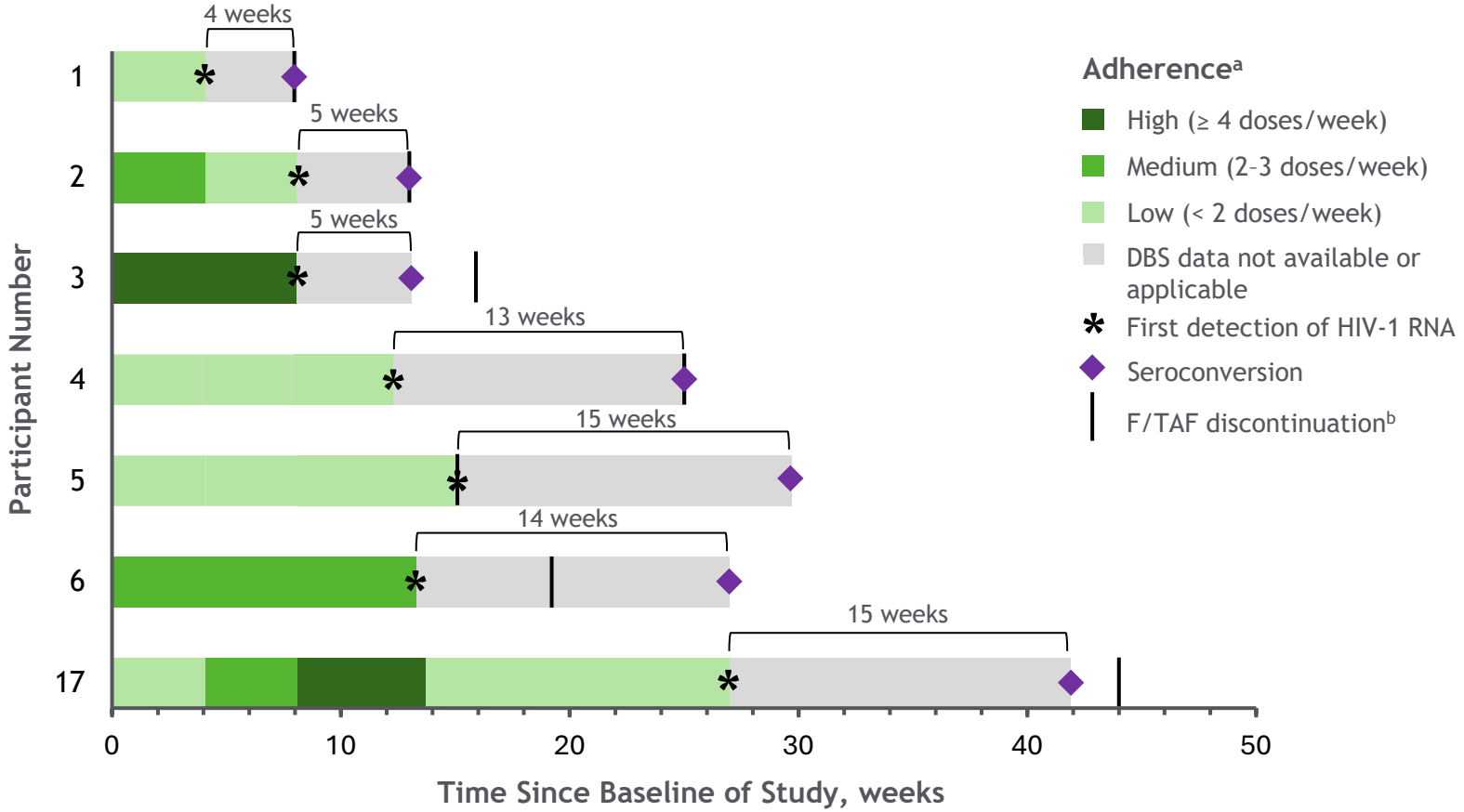
Adherence Patterns in Participants with Resistance-Associated Mutations



Emergence of antiretroviral resistance was rare in participants on F/TAF

Each line represents a single participant. [a]Week 4 data are not plotted as they were not at steady state.
BL, baseline; **DBS**, dried blood spot; **F/TAF**, emtricitabine/tenofovir alafenamide; **TFV-DP**, tenofovir diphosphate.

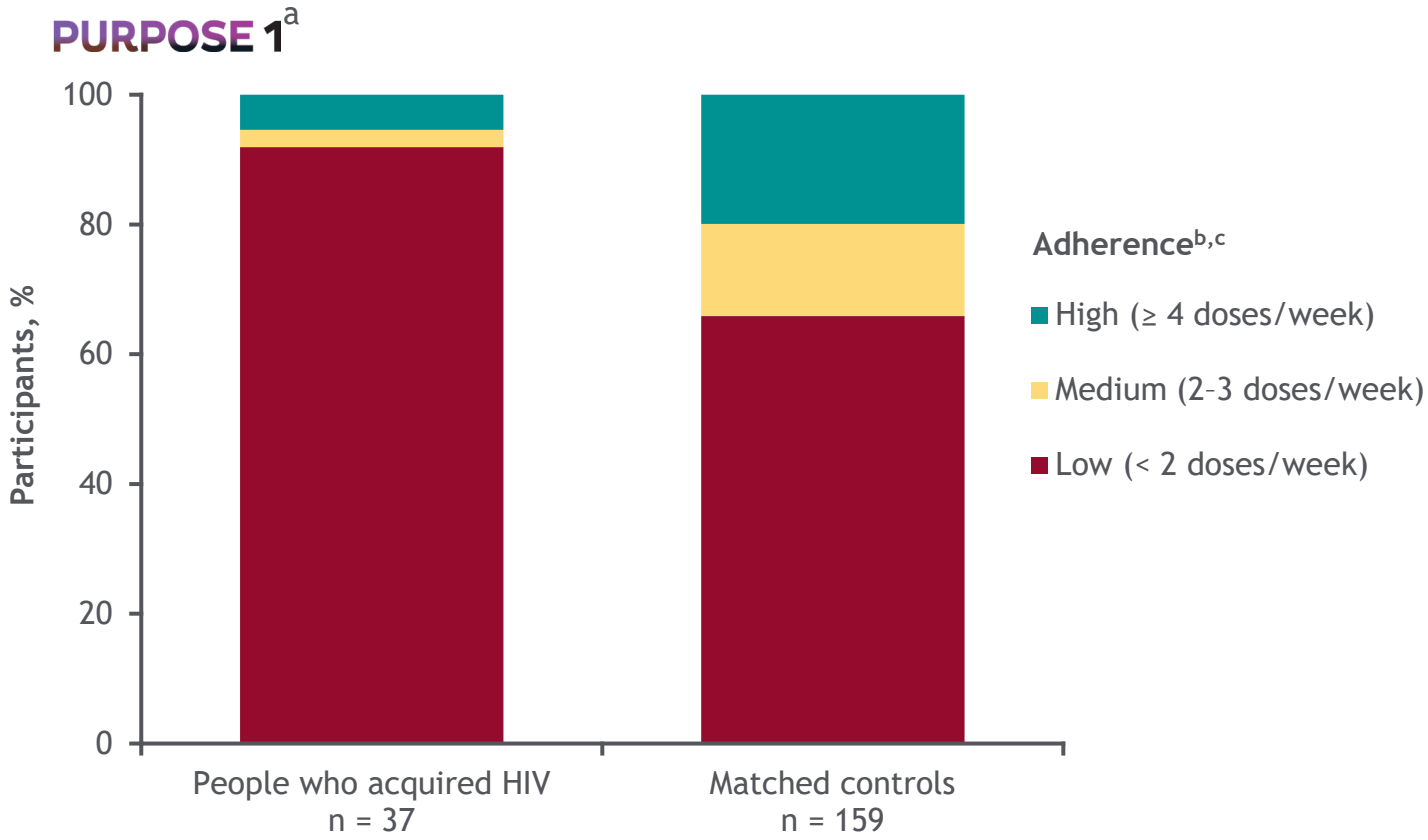
Adherence and Retrospective HIV-1 Testing Data in Participants With Detectable HIV-1 RNA Before Seroconversion

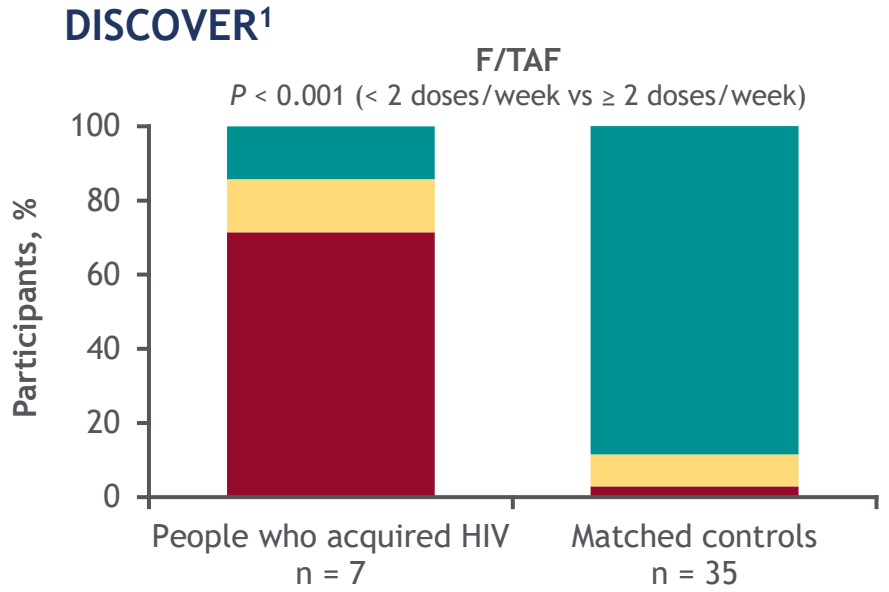


No evidence of significant delays in HIV diagnosis in participants who acquired HIV

[a]By TFV-DP DBS levels (adherence cutoffs: low < 450, medium ≥ 450 to < 950, high ≥ 950 fmol/punch).
[b]For participants 6 and 17, F/TAF discontinuation is the imputed last dose date for completely or partially missing last dose date.
DBS, dried blood spot; **F/TAF**, emtricitabine/tenofovir alafenamide; **TFV-DP**, tenofovir diphosphate.

Lower Chance of HIV Infection Associated With Medium or High Adherence to F/TAF: Consistent Results in Phase 3 PrEP Trials





F/TDF adherence-efficacy analyses from post-approval studies in women also show increased efficacy with increased doses/week[2]

Odds of HIV acquisition were 89% lower among cisgender women in PURPOSE 1 who took ≥ 2 pills per week (odds ratio: 0.11; 95% CI: 0.012-0.49; *P* = 0.0006)[3,4]

[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 < 950, high ≥ 950 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. **DBS**, dried blood spot; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **TFV-DP**, tenofovir diphosphate. 1. Mayer KH, et al. *Lancet* 2020; 396: 239-542. 2. Marrazzo J, et al. *JAMA*. 2024;331:930-937. 3. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 4. Bekker L-G, et al. Oral presentation at the 25th International AIDS Conference, July 22-26, 2024; Munich, Germany.

Conclusions

- Nearly all incident HIV cases in participants receiving F/TAF in PURPOSE 1 were attributable to low oral PrEP adherence
  - One case, with both TFV and FTC resistance, was likely explained by transmitted drug resistance
- Emergence of antiretroviral resistance was rare
- A minority of participants had detectable HIV RNA prior to serological diagnosis
  - Most had real-world or low adherence, suggesting that F/TAF did not cause a delay in diagnosis
- Case-control analysis indicates that F/TAF was efficacious in participants who took it with medium or high adherence consistent with prior clinical trials and real-world experience for oral tenofovir-based PrEP regimens

Consistent with prior studies of oral PrEP,[1,2] F/TAF is efficacious for HIV PrEP in cisgender women with adequate adherence

F/TAF, emtricitabine/tenofovir alafenamide; **FTC**, emtracitabine; **PrEP**, pre-exposure prophylaxis; **TFV**, tenofovir.

1. Landovitz RJ, et al. *Clin Infect Dis*. 2024;79:1197-1207. 2. Marrazzo J, et al. *JAMA*. 2024;331:930-7.

PURPOSE 1 Acknowledgments

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