PURPOSE 1: Preference for Twice-Yearly Injection vs Daily Oral Pills for HIV PrEP in Cisgender Women

1230

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Conclusions

- This analysis reports PrEP administration preference data among cisgender women in a clinical trial of twice-yearly SC injections of LEN
- The majority of participants reported a preference for twice-yearly injectable PrEP
- Some participants indicated a preference for daily pills, highlighting the importance of choice
  - Understanding preferences may help inform discussions with individuals about PrEP options, once LEN becomes available
- Among participants with the potential to be followed up until Week 52, approximately three-quarters of participants maintained their baseline preference for twice-yearly injection at Week 52, whereas almost half who reported a preference for daily pills or no preference at baseline changed their preference to twice-yearly injection at Week 52
- Many participants reported greater confidence in their ability to remain adherent to PrEP and that they would feel more protected from HIV if PrEP were administered as twice-yearly injections versus as daily pills
- Participant preference, in combination with previously published clinical data demonstrating high efficacy and a favorable safety profile,[1] strongly suggests twice-yearly LEN could increase the uptake of, adherence to, and persistence on PrEP among cisgender women, thereby contributing to the overarching goal of ending the HIV epidemic

Background

- Oral pre-exposure prophylaxis (PrEP) is effective in preventing new HIV infection[2,3]; however, effectiveness is reliant on individuals' high adherence to the daily dosing regimen[3]
  - Many people cite the challenge of taking daily pills as a barrier to the uptake of and adherence to daily oral PrEP[4,5]
- Cisgender women make up more than half of people with HIV worldwide,[6] yet routine use of PrEP in this population remains low[3,7]
- New PrEP modalities that meet the needs, routines, and preferences of more individuals can increase uptake of and adherence to PrEP and reduce barriers that lead to early discontinuation
- Lenacapavir (LEN) is a first-in-class, multistage HIV-1 capsid inhibitor that can be administered by subcutaneous (SC) injection twice yearly,[8] and is currently being studied for the prevention of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg[1,9,10]
- The Phase 3 PURPOSE 1 trial evaluated the efficacy and safety of LEN for PrEP in cisgender women in South Africa and Uganda[1]
  - The trial found that twice-yearly SC LEN was well tolerated and 100% efficacious in preventing HIV infection[1]

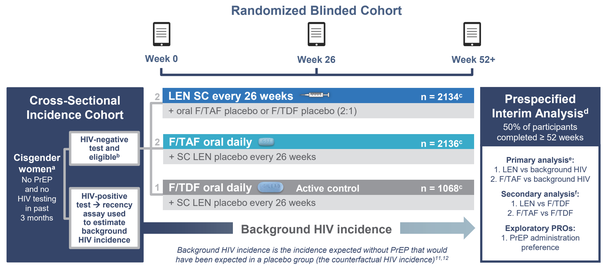
Objective

- To examine the PrEP administration preferences of PURPOSE 1 participants and how different methods of administration may impact their confidence about PrEP adherence and feelings about HIV risk

Methods

- PURPOSE 1 (NCT04994509) was a Phase 3, double-blind, randomized controlled trial (**Figure 1**)
  - Cisgender women aged 16-25 years were randomized 2:2:1 to receive SC LEN every 26 weeks, oral emtricitabine/tenofovir alafenamide (F/TAF) daily, or oral emtricitabine/tenofovir disoproxil fumarate (F/TDF) daily, along with the alternate SC or oral placebo
- Participants completed an electronic questionnaire (via a website or an app) on their PrEP administration feelings and preferences during injection visits (baseline, Week 26, and Week 52) (**Figure 2**)
  - Responses were submitted privately (except for participants who required assistance to complete the questionnaires)
- Results were pooled across the treatment arms and categorical responses were analyzed descriptively

Figure 1. PURPOSE 1 Study Design



PURPOSE 1 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.[11,12] [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; PRO, participant-reported outcome; SC, subcutaneous.

Figure 2. Questions and Possible Responses From the Electronic Questionnaire

Q	**If I could take just one kind of PrEP medication, knowing they both worked equally well, I would prefer to take PrEP medication:**		
A	By injection every 6 months	I have no preference one way or the other	By a daily pill
Q	**I would rate my preference for the PrEP medication I prefer as[a]:**		
A	Slight preference	Moderate preference	Strong preference
Q	**Thinking about the future, I would expect to be more able to take my PrEP medication without missing a dose if I received the medication:**		
A	By injection every 6 months	No difference; either by injection every 6 months or by a daily pill	By a daily pill
Q	**Thinking about the future, I would expect to feel more protected from HIV if my PrEP medication was given to me:**		
A	By injection every 6 months	No difference; either by injection every 6 months or by a daily pill	By a daily pill

Participants marked one response option per question. [a]Participants who reported no preference for PrEP administration type did not answer this question.
PrEP, pre-exposure prophylaxis.

Results

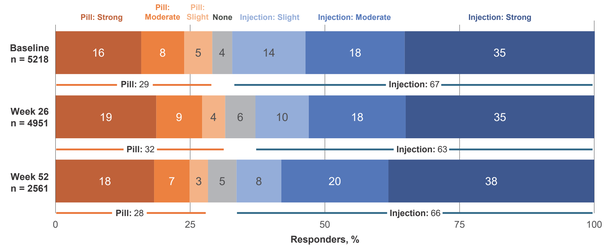
Participants

- Of 5345 participants randomized and dosed, 5218 completed the questionnaire at baseline
  - At the time of the primary analysis, 4951 participants had completed the Week 26 questionnaire and 2561 participants had completed the Week 52 questionnaire (the number of participants was lower at Week 52 due to the early termination of the randomized blinded phase of the study)

Overall Preferences

- Approximately two-thirds of participants preferred twice-yearly injections over daily pills, few had no preference, and less than one-third preferred daily pills (**Figure 3**)
  - Among those with a preference for either injection or pills, slightly more than half reported their preference as "strong"
- Results were similar across the different treatment arms

Figure 3. PrEP Administration Preferences (Daily Oral Pill vs Twice-Yearly Injection)



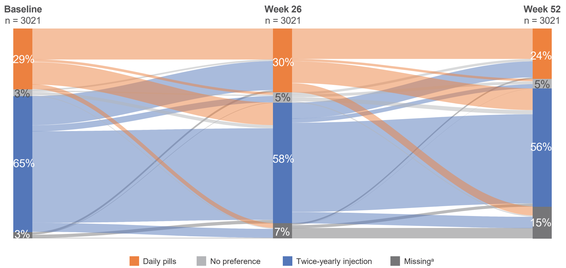
Approximately two-thirds of participants preferred twice-yearly injections versus daily pills

The population presented is based on all observed non-missing responses at each visit. Question: If I could take just one kind of PrEP medication, knowing they both worked equally well, I would prefer to take PrEP medication: 1) by injection every 6 months; 2) I have no preference one way or the other; 3) by a daily pill. Follow-up question for participants who reported a preference for pills or injections: I would rate my preference for the PrEP medication I prefer as: 1) slight preference; 2) moderate preference; 3) strong preference. Percentages may not sum to 100% due to rounding.
PrEP, pre-exposure prophylaxis.

Change in Preferences Over 52 Weeks

- At Week 52, among participants who received a dose and completed the questionnaire at baseline and Week 52:
  - 53% (44/83) who reported no preference at baseline and 47% (327/703) who reported a preference for daily pills at baseline shifted their preference to twice-yearly injections
  - 75% (1283/1707) maintained their baseline preference for twice-yearly injections, whereas 49% (341/703) maintained their baseline preference for daily pills

Figure 4. Shifts in Preference Through 52 Weeks of Follow-Up Among Participants With the Potential to Reach Week 52

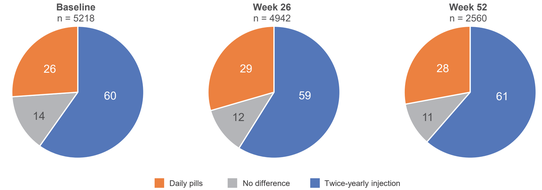


The majority of participants maintained their baseline preference for twice-yearly injection at Week 52

The population presented is limited to participants with the potential to reach Week 52 at the time of the interim/primary analysis. *The missing category includes participants who had either reached Week 52 of the trial but did not complete the questionnaire at the respective timepoints or who had discontinued the trial prior to Week 52.

Feelings About PrEP Administration Type

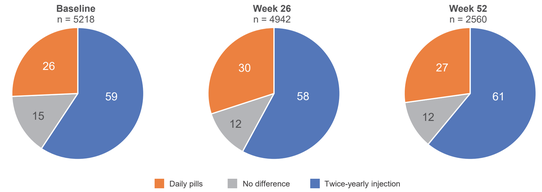
Figure 5. Participants Who Would Expect to Be More Adherent to PrEP in the Future if PrEP Were Received as a Twice-Yearly Injection Versus as Daily Oral Pills



More than half of participants reported greater confidence in their ability to remain adherent to PrEP with twice-yearly injections versus daily pills

The population presented is based on all observed non-missing responses at each visit. Question: Thinking about the future, I would expect to be more able to take my PrEP medication without missing a dose if I received the medication: 1) by injection every 6 months; 2) no difference; either by injection every 6 months or by a daily pill; or 3) by a daily pill.
PrEP, pre-exposure prophylaxis.

Figure 6. Participants Who Would Expect to Feel More Protected From HIV if PrEP Were Received as a Twice-Yearly Injection Versus as Daily Oral Pills



More than half of participants reported that they would feel more protected from HIV with twice-yearly PrEP injections versus daily pills

The population presented is based on all observed non-missing responses at each visit. Question: Thinking about the future, I would expect to feel more protected from HIV if my PrEP medication was given to me: 1) by injection every 6 months; 2) no difference; either by injection every 6 months or by a daily pill; or 3) by a daily pill.
PrEP, pre-exposure prophylaxis.

Limitations

- As is common with all survey-based data, cognitive biases may have influenced the questionnaire responses
- Preference for twice-yearly injection may be overrepresented
  - Participants who volunteered and consented to participate in PURPOSE 1 may have had a disproportionately favorable opinion of twice-yearly injection and of PrEP overall, prior to the start of the trial
- Self-reported responses are specific to the trial participants, and generalization of the results to broader populations may be limited
- Assistance with completing the questionnaires was provided to participants who requested it; however, despite this, there may have been differences in the interpretation of the questions between participants
- PrEP administration preference data were only collected for PrEP products available in the PURPOSE 1 trial. Participants were not asked about other modes of administration such as intramuscular injections or vaginal rings

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