Factors Impacting Women's Choice of PrEP Product After the Randomized Blinded Phase of PURPOSE 1

WEPED077

PURPOSE 1

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Conclusions

- Consistent with findings at the conclusion of the randomized blinded phase of PURPOSE 1, in which 95% of participants opted into the open-label extension (OLE), most substudy participants also elected to use lenacapavir (LEN) in the OLE
- Participants expressed enthusiasm about future rollout of LEN and indicated a preference for LEN over daily pre-exposure prophylaxis (PrEP)
- The choice to use twice-yearly LEN for PrEP was largely shaped by extended duration of protection over 6 months, including freedom from the burden associated with daily adherence to pills
- These findings underscore the potential of twice-yearly subcutaneous LEN to improve PrEP uptake and adherence among adolescent girls and young women, and the importance of offering a choice of HIV prevention options to meet varying needs and preferences

Summary

- HIV prevention medication, also known as "PrEP," helps to lower the chances of someone getting HIV
- PrEP is mostly available as a pill, taken by mouth (orally); however, to work, oral PrEP should be taken every day, which many people find hard to do consistently
- LEN is a long-acting type of PrEP that is given as an injection two times a year (every 6 months)
- In a large clinical study called PURPOSE 1, in which young women either received LEN two times a year or a pill every day, LEN was very effective in protecting them from getting HIV. During the main study, the young women did not know whether they were receiving PrEP as a daily pill or as an injection
- When the main study was complete, participants could choose to stay in the study and continue to receive LEN
- The goal of this substudy was to explore young women's opinions on the study findings, how they felt about the PrEP they had been taking, and their decision to continue receiving a LEN injection twice a year or not, in in-depth interviews
- A majority of participants chose the twice-yearly injection because of the long period of protection and the lack of need to take daily pills

Introduction

- Cisgender women account for approximately half of the 1.3 million new HIV infections globally each year[1]
- Daily oral PrEP is highly effective against HIV if taken as directed.[2,3] However, uptake of, adherence to, and persistence on PrEP remain suboptimal among cisgender women,[4,5] with multiple factors attributable to inconsistent use and nonadherence, including sociostructural barriers, community-level stigma, health delivery access, privacy, and clinical experiences of side effects[6,7]
- LEN is a first-in-class, multistage HIV-1 capsid inhibitor that can be administered as a twice-yearly subcutaneous (SC) injection[8] and is currently being studied for the prevention of sexually acquired HIV-1 in people who want or need PrEP[9-11]
- The Phase 3 PURPOSE 1 trial, which evaluated the efficacy and safety of LEN for PrEP among cisgender adolescent girls and young women in South Africa and Uganda, found that twice-yearly LEN was 100% efficacious in preventing HIV infection, with no safety concerns[9]
- After the 52-week randomized blinded period, participants were given the option to continue receiving LEN for PrEP in an OLE
- In a previously reported qualitative substudy conducted during the randomized blinded phase of PURPOSE 1, both twice-yearly LEN injections and daily oral PrEP were widely perceived as helpful and protective. However, participants valued the sustained duration of protection from HIV associated with LEN and often preferred the fit within their daily lives, while viewing pain and injection-site reactions as an acceptable trade-off for those benefits[12]

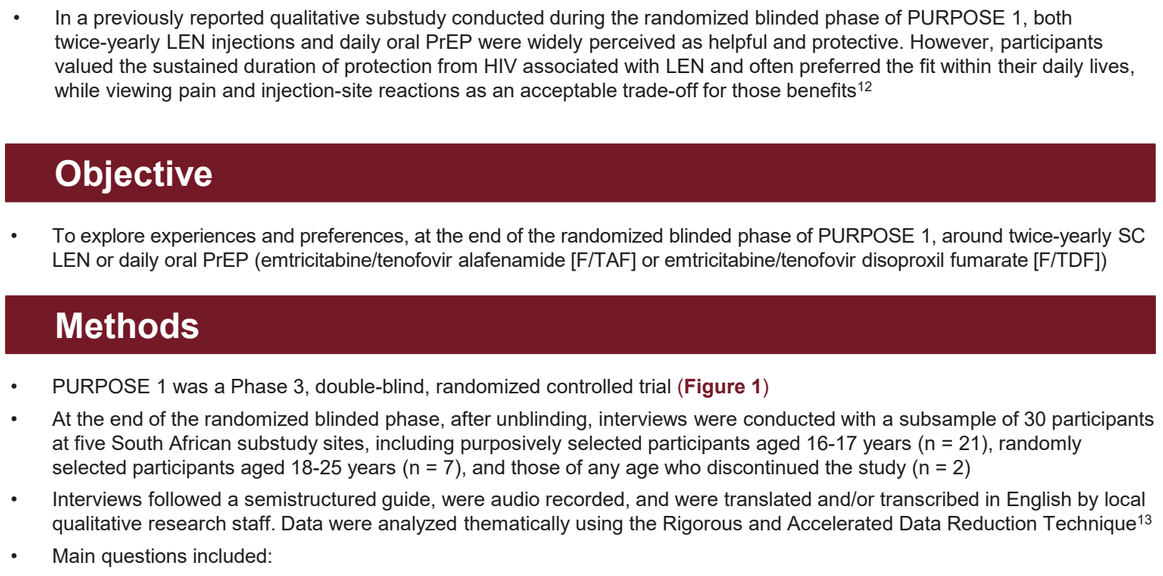
Objective

- To explore experiences and preferences, at the end of the randomized blinded phase of PURPOSE 1, around twice-yearly SC LEN or daily oral PrEP (emtricitabine/tenofovir alafenamide [F/TAF] or emtricitabine/tenofovir disoproxil fumarate [F/TDF])

Methods

- PURPOSE 1 was a Phase 3, double-blind, randomized controlled trial (**Figure 1**)
- At the end of the randomized blinded phase, after unblinding, interviews were conducted with a subsample of 30 participants at five South African substudy sites, including purposively selected participants aged 16-17 years (n = 21), randomly selected participants aged 18-25 years (n = 7), and those of any age who discontinued the study (n = 2)
- Interviews followed a semistructured guide, were audio recorded, and were translated and/or transcribed in English by local qualitative research staff. Data were analyzed thematically using the Rigorous and Accelerated Data Reduction Technique[13]
- Main questions included:
  - The PURPOSE 1 study has some important new results for HIV prevention. Tell me how you first heard about them
  - In this study, you now have the option to join the OLE or not. Let's talk about your choice—what have you decided?
  - For the first part of PURPOSE 1, all participants were receiving both an injection and daily oral tablets. Tell me what you knew about the way the two products were used and how they worked
  - Prior to your most recent study visit, which product did you believe was preventing HIV and why?
  - Looking forward, what expectations do you have for your next phase of product use in PURPOSE 1?

Figure 1. PURPOSE 1 Study Design



PURPOSE 1 ClinicalTrials.gov: NCT04994509. [a]Participants had the option to move to the OLE at their next visit following the primary analysis, which was at least 52 weeks of follow-up for most participants. [b]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. [c]Eligibility criteria included: weight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant. [d]n numbers represent the full analysis set for efficacy analyses. [e]Because the randomized blinded phase was stopped early due to an efficacy outcome, the interim analysis served as the primary analysis, and participants had the option to proceed to the LEN OLE phase. [f]Participants who prematurely discontinued the study drug during the randomized blinded phase or LEN OLE phase, or those randomized to LEN in the randomized blinded phase who declined to participate in the LEN OLE phase upon unblinding, transitioned to the PK tail phase. Participants received oral F/TDF once daily for 78 weeks beginning 26 weeks after the last LEN injection.
eGFR, estimated glomerular filtration rate; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; IDI, in-depth interview; LEN, lenacapavir; OLE, open-label extension; PK, pharmacokinetic; PrEP, pre-exposure prophylaxis; SC, subcutaneous.

Results

Participants Expressed Varied Emotions and Reactions to Study Group Unblinding

- At the time of unblinding, participants reflected on behaviors associated with likelihood of acquiring HIV and product (injection or daily pills) experience. Some expressed disappointment/regret in how they adhered to products, whereas others were not surprised by their product assignment, thinking they already knew which product (injection or pills) was active versus placebo, based on experiences during the study
- Participants' perceptions of the efficacy of active products were based on:
  - Dosing frequency (daily use of pills or long-acting nature of injections)
  - Severity of side effects
  - HIV status at the time of unblinding and reflection on adherence

> *I thought the [PrEP] injection was working. Injection… 'cause sometimes I would miss them [PrEP pills]. So even if I missed them, when I have sex I wouldn't have any problems.*

> *Ahhhh, I believe that pills are the one that are working because I take them every day, so injection I didn't believe that like it's the one that prevents HIV because like I want something that I see… it's happening every day, so I take my pills every day orally, seeing them I feel like the pills are the one that protects me… I was surprised that when I was telling myself that the pills, but it was injection [that was active]. Yah I was surprised, shame I was surprised.*

Decision-Making Process

- Overall, of the 30 participants interviewed, 27 chose to receive injections, 2 chose daily oral pills and 1 discontinued the study. Most participants chose independently, drawing on their own agency, motivations, and experiences during the randomized blinded phase
- Some participants consulted friends, family members, or healthcare providers, many of whom viewed the twice-yearly injections as acceptable or preferable

> *Eeh, I sat down and thought about it thoroughly at home yesterday morning, and I realized that the injection is something that will work for me because even my aunty said, "You don't take your pills accordingly… how is something going to help you if you don't take it accordingly?" Then I realized that, even if I don't want to, but I have to choose the injection.*

> *We were talking, debating. Isn't it, she got the injection. She is in the research, and she got the injection. I then said, it's better if I took the pills. Then she said, "The pills, instead of taking them every day, it's better to inject." I thought about this thing, and I changed my mind when I was here and thought, "No, let me take the injection because with the injection, you inject once, you inject twice a year," isn't it?*

> *I told [my mom] about the pains I was experiencing… and she said if it is something that you really want to do you can continue getting it but… if it turns out that what you are using is the real one there is no need for you change. Continue with the one that your heart says you must use.*

> *[Family and community] were happy. They said, "You will no longer be drinking pills... or coming back with pills." They [at home] said it is better because I was now going to be protected by the injection.*

SC LEN Injections Were Preferred Over Pills by Most Interviewed Participants, Largely Due to Long-Acting Protection and Convenience

- Participants who preferred SC LEN over daily oral PrEP in the OLE noted reasons for their preference:
  - Long-acting protection
  - Adherence challenges associated with pills
- The main challenges with daily pills included:
  - Difficulty with daily adherence
  - Side effects
  - Family dynamics (such as avoiding pills at home)
- While some participants noted injection-related pain, they generally considered it an acceptable trade-off, given the benefits of long-acting protection

> *I prefer the injection… because you inject once. Isn't it, you come back after 6 months? You don't need to, you know, like with the pills, to keep on taking them every single day, you see, the injection is better… you get it once, and I heard that works.*

> *The reason why I chose the injection is because I was forgetting to take the tablets, that's why I chose the injection.*

> *For me to choose injection…it's because I don't inject everyday just like the pills, I would forget that I forgot them. Injection stays in me…after 6 months I will go and inject again. There is no way I would forget.*

> *The choice of taking the injection is because I know I will not be getting it as the pills, but I will be getting it every 6 months… this will not be something I have to think about daily but rather after 6 months... I did have some thoughts of choosing the pills because the injection is painful. But I would think again that the pill is easy to forget so I must stick to the injection.*

A minority of participants did not choose to join the OLE phase

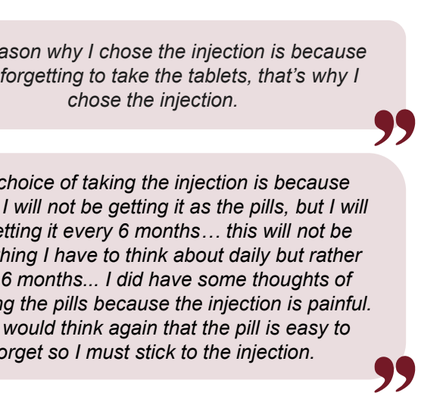
- Some preferred daily oral PrEP, citing familiarity with pills or discomfort from injection-site pain
- Other discontinued study participation due to life commitments or the discomfort of study procedures

> *The pills…there is no way that I can leave them and stay a month without taking them. It's a daily thing, you understand. What I mean is it's taken every day, when those pills are about to get finished, I will go and take another one just like and take them every day 'til my body adjusts and gets used to it.*

> *What made me stop, deciding to stop right now is that the bottles they use to draw blood are a lot… and after I have just received the [PrEP] injection, I feel pain here. So, I decided to stop 'cause even my boyfriend told me that I complain every day about blood draws and receiving injection.*

Participants Anticipated Lower Stress and Continued Efficacy in Transition to OLE Use of LEN

- Most participants were eager to stop using pills and switch to only injections, predicting lower stress and burden compared with pill use
- Many participants believed that continued use of LEN would help them maintain an HIV-negative status, offering a sense of safety and peace of mind



> *I feel so happy. I am happy because I don't have to worry about missing my [PrEP] pills anymore… especially if I am not home and I had forgotten to bring my pills with me, so I will not be stressing about that anymore.*

> *I am expecting that in my life I will not get the disease, any other disease, I will not get any diseases because I have now been educated. It would just be me not listening because there isn't anything that I don't know of concerning protecting myself from getting diseases.*

Limitations

- The small number of participants who preferred daily oral PrEP limited deeper analysis of factors influencing this preference
- Variability of participants' understanding of the clinical study design may have affected the depth and accuracy of some responses. For example, follow-up was required in some cases to clarify aspects of the study, such as use of one active product and one placebo during the randomized blinded phase

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