Exploratory Qualitative Analysis of the Acceptability of HIV Prevention Methods Among Pregnant and Lactating Women Interviewed During the Randomized Blinded Phase of PURPOSE 1

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PURPOSE 1

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Conclusions

- A subsample of 13 pregnant and lactating participants from PURPOSE 1 emphasized the benefit of consistent HIV protection—showing that twice-yearly lenacapavir (LEN) injections offer peace of mind without the burden of daily adherence
- All participants emphasized the desire to protect their fetus or infant from acquiring HIV
- However, some participants shared concerns about using an investigational study drug while pregnant or lactating, especially when it was being administered to the abdomen
- There was a willingness amongst participants to continue injections, citing potential availability of an alternative injection site (thigh) as a motivating factor
- These findings underscore the value of education and counseling about the efficacy, safety, tolerability, and pharmacokinetics of twice-yearly LEN for successful pre-exposure prophylaxis (PrEP) implementation among pregnant and lactating participants

Summary

- HIV prevention medication, also known as “PrEP,” helps to lower the chances of someone getting HIV, including for people who are pregnant and lactating
- PrEP is mostly available as a pill, taken by mouth (orally); however, to work effectively, 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, young cisgender women (people who are assigned female at birth) received either a LEN injection two times a year or a pill every day; LEN was very effective in protecting them from getting HIV
- The goal of this substudy was to understand how people who were pregnant and lactating felt about taking pills every day and having an injection two times a year
- People who were pregnant and lactating were willing to take pills or receive an injection, but felt more protected from getting HIV with injections
- It was important to people who were pregnant and lactating that their baby was protected from getting HIV
- These results highlight how important it is to include pregnant and lactating people in studies looking at new medications, such as LEN, and ensure they receive proper education and counseling about how the drug works and behaves in the body to support successful use for HIV prevention

Introduction

- Pregnant and lactating people are disproportionately vulnerable to HIV acquisition[1,2]
- Daily oral PrEP is highly effective against HIV acquisition if taken as directed.[3,4] However, uptake of, adherence to, and persistence on PrEP among cisgender women, including pregnant and lactating people, remain suboptimal[5,6]
- Better understanding of the challenges, barriers, and facilitators associated with much-needed novel PrEP modalities may help to optimize adherence among pregnant and lactating people
- Historically, pregnant and lactating people have been excluded from Phase 3 clinical trials of HIV PrEP, due to safety concerns during pregnancy and lactation, and contraception has been a requirement of participation[5,7-9]
- PURPOSE 1 (NCT04994509) was the first Phase 3 PrEP trial to support the inclusion of pregnant and lactating participants and demonstrated efficacy and safety of twice-yearly subcutaneous (SC) LEN for PrEP among cisgender young women, including in pregnant and lactating participants[10]
  - PURPOSE 1 was implemented before the World Health Organization (WHO) and International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network toolkit guidelines for the inclusion of pregnant and lactating people, but follows all the recommendations[11]

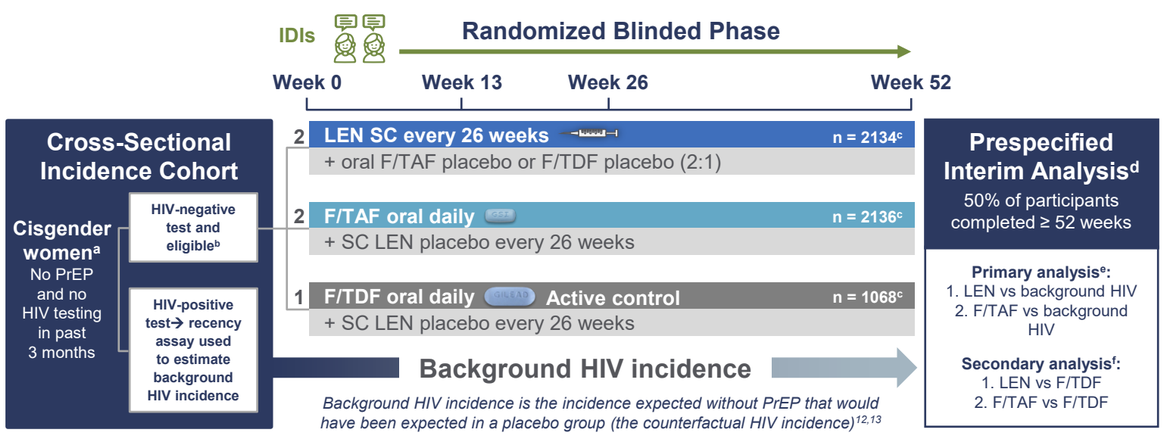
Objective

- To explore the acceptability of twice-yearly SC LEN injections and daily oral PrEP in pregnant and lactating participants during the randomized blinded phase of PURPOSE 1

Methods

- PURPOSE 1 was a Phase 3, double-blind, randomized controlled trial evaluating the efficacy and safety of twice-yearly SC LEN, administered primarily in the abdomen, or daily oral emtricitabine/tenofovir alafenamide (F/TAF) or emtricitabine/tenofovir disoproxil fumarate (F/TDF) for PrEP in adolescent girls and young women (**Figure 1**)
- Contraception was provided for free but was not required. Participants who became pregnant were counseled about the benefits and risks and reconsented either to continue on the study drug or to move to the pharmacokinetic tail phase to receive open-label F/TDF
- During the randomized blinded phase, 16 in-depth interviews (IDIs) with 13 pregnant and lactating participants were conducted at five South African substudy sites
  - The majority of interviews (n = 12) were conducted during pregnancy, with four interviews conducted during lactation
  - Three participants were interviewed twice, during both pregnancy and lactation
- Interviews followed a semistructured guide, were audio recorded, and were translated and/or transcribed in English by local qualitative research staff
- Analysis of key issues related to acceptability of twice-yearly subcutaneous LEN or daily oral PrEP during pregnancy and lactation included perceived benefits, barriers, and concerns and was conducted using protocol-defined objectives and IDI topics (**Table 1**). Data were coded in Dedoose™, analyzed thematically, and summarized. Analyses were restricted to IDIs captured prior to the release of data on efficacy and safety of LEN from PURPOSE 1

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]Because 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; IDI, in-depth interview; IRR, incidence rate ratio; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; SC, subcutaneous.

Table 1. Sample IDI Topics

IDI Topic Focus Areas	
• Previous experience of pregnancy prevention and HIV prevention • Motivation to join study • Attitude toward study products • Experience using products during study and while pregnant and lactating • Disclosure of study product use to others	• Community perspectives on pregnant/lactating people using HIV prevention products • Overall satisfaction with study products while pregnant/lactating • Willingness to use study products in the future while pregnant or lactating

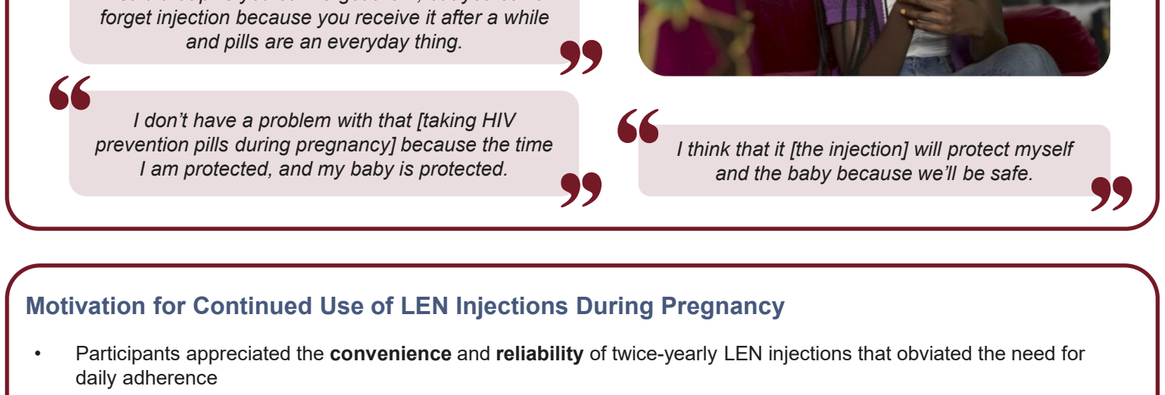
IDI, in-depth interview.

Results

Participants

- Although most PURPOSE 1 participants consented to stay on the blinded study drug after becoming pregnant (n/N = 398/487), most pregnant and lactating participants interviewed in this qualitative substudy opted to stop the use of active/placebo injections (n/N = 9/13; **Figure 2**)

Figure 2. Pregnancy Disposition



[a]510 pregnancies in 487 participants. [b]Participants who chose to stop active/placebo injections received daily oral PrEP.
PrEP, pre-exposure prophylaxis.

Participants Emphasized the Desire to Protect Themselves and Their Babies From Acquiring HIV

- Compared with twice-yearly LEN injections, participants cited barriers to effective daily oral PrEP, including adherence challenges, side effects, and pill fatigue when combined with prenatal medications
- Participants who preferred daily oral PrEP during pregnancy and lactation cited its established safety, their familiarity with oral PrEP, and the convenience of taking it with prenatal medications

> *If I am not taking the injection and then I am also stopping the pills… if I were to get infected with HIV that means even the baby will get infected, so I think continuing is the best to prevent me and my child.*

> *Pills satisfy me but not like injection. Just like I said that pills you can forget them, but you can’t forget injection because you receive it after a while and pills are an everyday thing.*

> *I don’t have a problem with that [taking HIV prevention pills during pregnancy] because the time I am protected, and my baby is protected.*

> *I think that it [the injection] will protect myself and the baby because we’ll be safe.*

Motivation for Continued Use of LEN Injections During Pregnancy

- Participants appreciated the **convenience** and **reliability** of twice-yearly LEN injections that obviated the need for daily adherence
- Despite the injection site–related pain and discomfort, participants felt **consistently protected**
- Participants who chose to continue LEN injections during pregnancy perceived the blinded injections as **safe and effective** for HIV protection

> *I’m very much satisfied with the injection, a lot too, just that you never know someone’s status. I can’t say I have slept with someone who is positive while I was receiving the injection and I never got sick. But I’m satisfied with it, and I don’t even doubt it.*

> *I said that if I will be taking the injection and it lasts for six months, it means I’ll be protected for that six months and then after six months I take another injection, I’ll be protected from HIV, rather than a condom or tablets.*

> *You even sometimes miss the time to drink it [PrEP pill], yet with the injection you know that it is something that is always in your blood [stream]. You get injected [every 6 months] yet with the pill you take it daily. So, I feel alright with the injection.*

> *It’s that the injection will not reach the child, the injection is only for me and there is no way that it can destroy the baby even though I get the injection, it’s safe.*

Participant Interest in Potential Alternative Injection Sites

- Some participants expressed a theoretical interest in future **availability of an alternative injection site (thigh)** as a motivating factor
- The potential use of the thigh as an alternative injection site was well received and seemed to address prior hypothetical concerns about how the use of abdominal injections might impact the infant

> *I’m okay with it [PrEP injection] if it won’t be in the stomach [and] will be in the thigh.*

> *Because I feel that it’s safe when I take the pills, for the baby though, compared to getting the injection. I feel that the injection goes directly to my stomach, which is around the area where the baby is.*

> *So, it’s okay I can carry on but I won’t allow to be injected on the stomach, I will inject it [PrEP injection] on the thigh until I give birth, only after I will carry on to be injected on the stomach.*

Acceptability and Concerns Around LEN Injections During Pregnancy and Lactation

- Participants who preferred daily oral PrEP to twice-yearly LEN injections noted:
  - Unknown safety of the injections during pregnancy and lactation
  - Previous injection-related pain
- Additionally, some participants raised concerns about potential exposure of the study drug to the infant during lactation

> *When the taxi moved from the speed humps, my stomach was painful. Even when I was laughing, my stomach was painful. I was like, no. I was in pain for the whole week. I said no more, so I thought that if I continued with the [PrEP] injection, maybe my baby would get hurt, and the baby would feel the pain I was also feeling.*

> *When I compare them is like injection is not okay for me when I’m breastfeeding... but pills I see them okay when I’m breastfeeding because injection I think that maybe it will go in the breast... when a baby feed, then will feed that injection.*

Limitations

- The study population included in the current analysis was small. Themes from IDIs from this subset of participants may not represent the attitudes or opinions of other pregnant and lactating participants involved in the PURPOSE 1 study

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