Qualitative Assessment of Acceptability and Preferences for Injectable and Oral PrEP in PURPOSE 1

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PURPOSE 1

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Conclusions

- In this nested, qualitative substudy of PURPOSE 1, twice-yearly LEN injections and daily oral PrEP were widely perceived as helpful and protective
- LEN afforded both freedom from daily dosing and the ability to enjoy and not worry about sexual encounters—compared with oral PrEP—without barriers of concealing or remembering medication, or being judged for its use
- PURPOSE 1 participants valued sustained protection from HIV, often preferred the lifestyle fit of a twice-yearly injectable versus daily oral PrEP, and considered any pain or injection site reactions acceptable because of these benefits
- When considering oral PrEP, participants appreciated the smaller F/TAF (vs F/TDF) tablets and their comparative ease in swallowing
- These data suggest acceptability and preference for twice-yearly injections, while reinforcing the value of product choice

Background

- Cisgender women account for approximately half of the 1.3 million annual HIV infections globally[1]
- Daily oral pre-exposure prophylaxis (PrEP) is highly effective if taken as directed.[2,3] However, uptake of, adherence to, and persistence on PrEP among cisgender women—particularly adolescent girls and young women—remain suboptimal,[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]
- Better understanding of the challenges, barriers, and facilitators associated with much-needed novel PrEP modalities may help to optimize adherence within ongoing research studies and in the real world
- Lenacapavir (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 would benefit from PrEP[9-11]
- The Phase 3 PURPOSE 1 trial evaluated the efficacy and safety of LEN for PrEP in cisgender adolescent girls and young women in South Africa and Uganda[9]
- The trial found that twice-yearly LEN was 100% efficacious in preventing HIV infection, with no safety concerns[9]

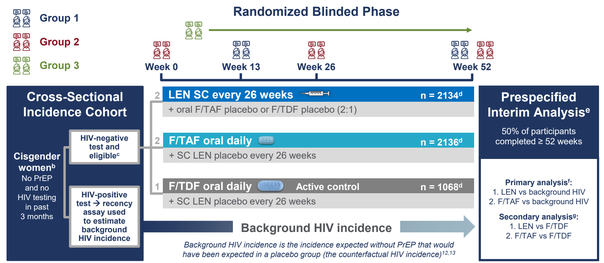
Objective

- To explore the acceptability, experiences, and preferences with twice-yearly SC LEN and daily oral PrEP (emtricitabine/tenofovir alafenamide [F/TAF] or emtricitabine/tenofovir disoproxil fumarate [F/TDF]), in a qualitative substudy of PURPOSE 1

Methods

- PURPOSE 1 (NCT04994509) was a Phase 3, double-blind, randomized controlled trial (**Figure 1**)
- During the randomized blinded phase, in-depth interviews (IDIs) were conducted at five geographically diverse South African trial sites (**Figure 2**), with:
  - A randomly selected subset of participants aged 18-25 years who received a single IDI at Week 13 or 52 (Group 1)
  - Purposively selected participants aged 16-17 years who completed serial IDIs at Weeks 0 (baseline data not included here), 26, and 52 (Group 2)
  - Participants aged 16-25 years who discontinued study/product, were pregnant or breastfeeding (P/BF), or acquired HIV and completed a single IDI (Group 3)
- IDIs were administered in English and/or local languages; interviewers administered a semistructured IDI guide with key questions and suggested probes (**Table 1**)
- An analytic codebook was developed using protocol-defined objectives and IDI topics (**Table 1**), emergent themes, and a socioecological framework. Data were coded in Dedoose™, analyzed thematically, and summarized. Analyses were restricted to IDIs captured before PURPOSE 1 interim results

Figure 1. PURPOSE 1 Study Design and Time Points for Single or Serial IDIs[a]



PURPOSE 1 ClinicalTrials.gov: NCT04994509. [a]A visit window of ± 30 days applied for IDIs that did not occur on the same day as study procedures. [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]Since the randomized blinded phase was stopped early due to an efficacy outcome, the interim analysis served as the primary analysis. [f]IRR was assessed using a Wald test or likelihood ratio test if there were zero infections.[12,13] [g]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
• Product characteristics
• Delivery mechanism
• Dosing regimen
• Effects on sexual encounter
• Partner's attitudes about product
• Product-associated norms
• Social harms
• Reactions and side effects
• Perceived safety
• Injection site preferences/reactions
• Positive/negative preferences
• Expectations of real-world implementation

IDI, in-depth interview.

Figure 2. Ancillary Site Locations

CAPRISA, Centre for the AIDS Programme of Research in South Africa; DTHF, Desmond Tutu Health Foundation; MatCH, Maternal, Adolescent and Child Heath Research; MM, Metropolitan Municipality; RHI, Reproductive Health and HIV Institute.

Results

Table 2. Participant Baseline Demographics

	Group 1 (n = 47)	Group 2 (n = 25)	Group 3, Discont. PrEP (n = 16)	Group 3, P/BF (n = 13)	Group 3, Acquired HIV (n = 8)	All Groups (n = 108)	All Others at Qual Sites (n = 831)	All Others at P1 Sites (n = 5237)
Age, years, median (range)	21 (18-25)	17 (16-18)	22 (18-25)	22 (19-24)	21 (18-24)	20 (16-25)	21 (16-26)	21 (16-26)
Highest education level, n (%)								
Did not attend primary school	0	0	0	0	0	0	0	39 (0.7)[a]
Primary school[b]	0	2 (8.0)	0	1 (7.7)	0	3 (2.8)	21 (2.5)	561 (10.7)[a]
Secondary school[b]	42 (89.4)	23 (92.0)	12 (75.0)	10 (76.9)	7 (87.5)	93 (86.1)	716 (86.2)	4153 (79.4)[a]
Some college or university	5 (10.6)	0	4 (25.0)	2 (15.4)	1 (12.5)	12 (11.1)	94 (11.3)	478 (9.1)[a]
Living with husband/partner, n (%)	3 (6.4)	0	1 (6.3)	2 (15.4)	0	6 (5.6)	40 (4.8)	347 (6.6)[a]
Any STI, n (%)[c]	18 (38.3)	8 (32.0)	4 (25.0)	6 (46.2)	5 (62.5)	40 (37.0)	288 (34.7)	1835 (35.0)
Any previous PrEP use, n (%)	10 (21.3)	2 (8.0)	2 (12.5)	5 (38.5)	1 (12.5)	19 (17.6)	98 (11.8)	316 (6.0)

One participant participated in both Group 1 and Group 3 P/BF IDIs. [a]Denominator = 5231. [b]Sum of "some" primary (or secondary) school education and primary (or secondary) school "complete" responses. [c]Laboratory results based on central laboratory or local laboratories for gonorrhea, chlamydia, and trichomonas vaginalis, and local laboratories only for syphilis. Discont., discontinued; IDI, in-depth interview; P/BF, pregnant or breastfeeding; P1, PURPOSE 1; PrEP, pre-exposure prophylaxis; qual, qualitative; STI, sexually transmitted infection.

Participants

- Overall, participant demographics at baseline were similar between Groups 1, 2, and 3 (**Table 2**). The median age of participants was 20 (range: 16-25) years, 19 (17.6%) participants reported any prior PrEP use, and baseline laboratory diagnoses of any sexually transmitted infections were high (40 [37.0%] participants)
- Demographics were also similar between the subset of PURPOSE 1 participants included in this analysis and all other participants enrolled at the five qualitative PURPOSE 1 sites, with some differences between the qualitative subgroups and all others at PURPOSE 1 sites

Findings

LEN Injection Duration Was Highly Favored for Convenience

- The **discreet** nature of SC LEN was favorable, especially for participants who preferred not to disclose their PrEP use to others in their life
- Participants felt that SC LEN offers more logistical **freedom**, especially compared with oral PrEP
- Many valued the **worry-free protection** over 6 months, eliminating the need for a daily reminder, which made adherence **easier** compared with daily doses

> *I will be injected because I am taking pills every day, you must forget everyday sometime there is that one day you will forget. So, the 6 month is not a problem because I will only go to the clinic after 6 months injected that's it… Just think I will only go twice in a year [for the PrEP injection] and after that I will be free than keeping myself busy with pills every day… This is* ***an easy option*** *for me*

Short-Lived Side Effects Were Worth the Trade-Off of Long-Term Protection

- Participants reported injection-related **pain** that generally resolved within 1-2 days and was mitigated by analgesics
- Some participants reported lumps at the injection site (SC nodules arising from the drug depot), which they disliked
- Most participants felt that any side effects of SC LEN were worth it for the protection afforded

> *I prefer the injection; though it is painful, it is better because it's the pain that you feel during that period of two days and the swelling for that week. Then you would relax for 5 months without any pain and without any stress, which is stress-free because you know that you are HIV protected. Then you go back there. But tablets are daily*

LEN Injections Suited Lifestyles, Particularly for Young Women

- Participants appreciated that injections **did not interfere** with their regular daily routines and did not necessitate anything of them during the period of protection
- Participants, particularly those aged 16-17 years, noted that injections suited their lifestyles, as they are "multitasking" and "juggling" along with "going out" and having "nice times", making pill use inconvenient

> *I would tell them to come join the study because we are not safe out there. I'd [tell] them to come join the study to help prevent themselves from getting HIV… I'd tell them that the injection is better compared to taking the pills every day. The injection is better because you take it once… Because we forget. Young people are always busy, so the injection is better*

Consideration for Alternative Injection Sites

- The location of the injection in the **abdomen** was unfamiliar and raised concerns for some participants, particularly when considering **pregnancy**
- Participants suggested alternative injection sites, such as the arms or buttocks

> *My concern was that you have to be injected, and you have to be injected on the stomach. I asked myself, why on the stomach? I didn't understand why the injection had to be injected in the stomach. Those were the concerns I had. The rest I didn't have a problem with because PrEP was pill used to protect ourselves but the injection on the stomach was concerning me, and I was scared that I might have a problem [side effects] if I am injected on the stomach*

Pills Are Familiar and Trusted, but Are "Boring" and Forgettable

- Participants found pills **comfortable** and **reliable**, with **smaller forms (F/TAF vs F/TDF) being easy to swallow**
- However, many participants also found persistently taking daily pills tedious and "boring" (ie, tiring and annoying)
- Participants reported that the **daily routine** of taking pills was often challenging for **adherence**

> *It's time, and travelling, sometimes I will go somewhere to my father, sometimes to my mother and stay there and sometimes I wouldn't think about taking along my medication. I would forget that's my experience, that I can forgot to take my tablets, and I missed them a lot because I travel a lot, and I will always forget to take them*

Perceptions of PrEP Mechanisms of Action and Protection Varied Among Participants

> *I would prefer the [PrEP] pills. Because they say the [PrEP] injection works, but I prefer to take the [PrEP] pills every day so that I can see that they are in fact working in my bloodstream. Even though I won't be able to see physically that they work; but I am sure that they are in my bloodstream because I am protected, and I am still negative*

> *I prefer the [PrEP] injection… I sometimes take [PrEP] tablets late but the [PrEP] injection [is] in my system for 6 months*

Limitations

- The main limitation is that 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 all (> 5300) participants involved in the PURPOSE 1 study

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