Integrating Gender-Affirming Hormone Therapy With Twice-Yearly Subcutaneous Lenacapavir for HIV Prevention: Longitudinal Qualitative Insights From Transgender and Nonbinary PURPOSE 2 Participants

THPED306

PURPOSE 2

Steven Meanley[1,2], Louis Listerud[1,2], Blake Kosciow[1,2], Alana Richards[1,2], Dovie L Watson[2,3], Ian Frank[2,3], Valeria D Cantos[4], Susanne Doblecki-Lewis[5], Lillian B Brown[6], J Carlo Hojilla[6], Christoph C Carter[6], José A Bauermeister[1,2]

[1]Department of Family and Community Health, University of Pennsylvania School of Nursing, Philadelphia, PA, USA; [2]Eidos LGBTQ+ Health Initiative, University of Pennsylvania School of Nursing, Philadelphia, PA, USA; [3]Division of Infectious Diseases, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA; [4]Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA; [5]Division of Infectious Diseases, University of Miami Miller School of Medicine, Miami, FL, USA; [6]Gilead Sciences, Inc., Foster City, CA, USA

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Conclusions

- Subcutaneous (SC) lenacapavir (LEN) was highly acceptable among transgender and nonbinary (TNB) participants, and was more acceptable than alternative pre-exposure prophylaxis (PrEP) modalities
- Familiarity with gender-affirming hormone therapy (GAHT) injections may help reduce needle- and pain-related concerns about long-acting injectable (LAI) PrEP
- Transparent, gender-inclusive communication from PURPOSE 2 staff cultivated trust and self-efficacy to use LEN and GAHT concurrently
- Providers should center affirming communication, recognize GAHT-related concerns, and support integration of LEN within gender-affirming care settings
- Findings should be interpreted cautiously; the study sample predominantly identified as nonbinary and may not reflect all TNB experiences, in contrast to the overall gender-diverse study population, which included a higher proportion of transfeminine participants

Plain Language Summary

- Pre-exposure prophylaxis (PrEP) is a medicine that lowers the chance of getting human immunodeficiency virus (HIV)
- Many transgender and nonbinary (TNB) people who use PrEP also receive gender-affirming care, such as gender-affirming hormone therapy (GAHT), to support their gender identity
- Some PrEP medicines, such as lenacapavir (LEN) or cabotegravir, are given as injections. It is important to understand and address concerns in the TNB community about the safety of these medicines and their use in combination with GAHT
- In this study, researchers conducted Zoom interviews with people before or after they received either LEN or placebo injections for HIV PrEP. The study took place at 14 clinical sites in the United States as part of a clinical trial called PURPOSE 2
- The interviews showed that many participants found LEN acceptable and supported its use for HIV PrEP. Previous experience with GAHT helped reduce fear of needles and made injections feel more normal. However, participants had questions about the number of injections needed when taking both GAHT and LEN, and about using the same injection sites, reinforcing the importance of counseling on the lack of drug interactions with GAHT and using alternative (non-abdomen) injection sites
- The interviews also showed that clear and gender-inclusive communication from clinical staff helped build trust and reassurance
- Healthcare providers should communicate in ways that affirm people's gender identity and address their concerns about taking LEN and GAHT together. They should also make sure that LEN fits well within each person's gender-affirming care

Introduction

- PURPOSE 2 (NCT04925752) is a randomized, placebo-controlled Phase 3 trial of the safety and efficacy of twice-yearly SC LEN for HIV PrEP in cisgender gay, bisexual, and other men who have sex with men, and gender-diverse populations[1]
- At the primary analysis, HIV incidence in the LEN arm was significantly lower than background incidence (96%), and LEN demonstrated superior efficacy to daily oral emtricitabine/tenofovir disoproxil fumarate (F/TDF) in preventing HIV infection (89%), with favorable safety and tolerability[1]
- Recognizing the critical importance of considering LAI PrEP alongside gender-affirming care,[2] the PURPOSE 2 study engaged with community and providers to incorporate gender-affirming care for TNB participants into the trial design and include PrEP clinical trial research sites with this expertise[3]
- Community feedback recommended emphasizing the safety of coadministration of LEN and GAHT, and conducting in-depth interviews to better understand the experience of TNB people who face disproportionate HIV burden and persistent unmet HIV prevention needs[4,5]

Objective

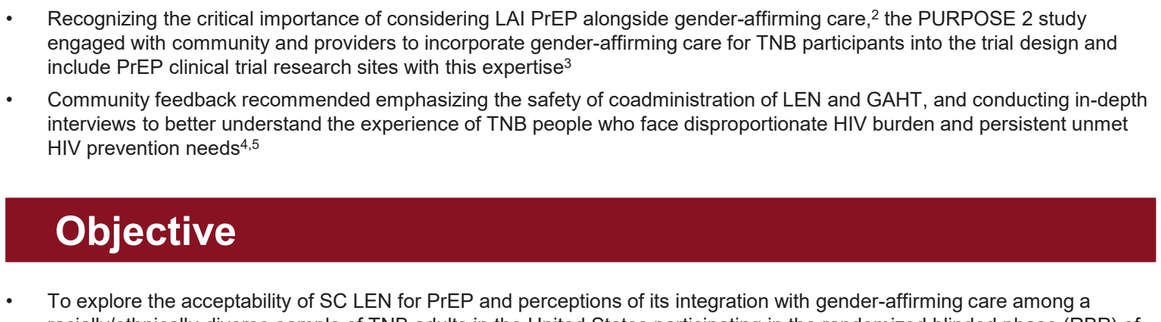
- To explore the acceptability of SC LEN for PrEP and perceptions of its integration with gender-affirming care among a racially/ethnically diverse sample of TNB adults in the United States participating in the randomized blinded phase (RBP) of PURPOSE 2

Methods

PURPOSE 2 Qualitative Study

- The objective of the PURPOSE 2 qualitative study was to understand the views and experiences of participants receiving LEN or F/TDF in a randomized, blinded, placebo-controlled study focusing on acceptability, tolerability, and preference
- Participants in the qualitative study completed serial interviews by Zoom throughout the RBP of the study (**Figure 1**)
  - The number of participants for interviews 1-3 varied due to recruitment challenges during the interview 1 timeframe. Five participants took part in interview 1, and were included in interviews 2 and 3; interviews 2 and 3 were subsequently expanded to include more TNB participants

Figure 1. PURPOSE 2 Serial Qualitative Descriptive Design



ClinicalTrials.gov: NCT04925752

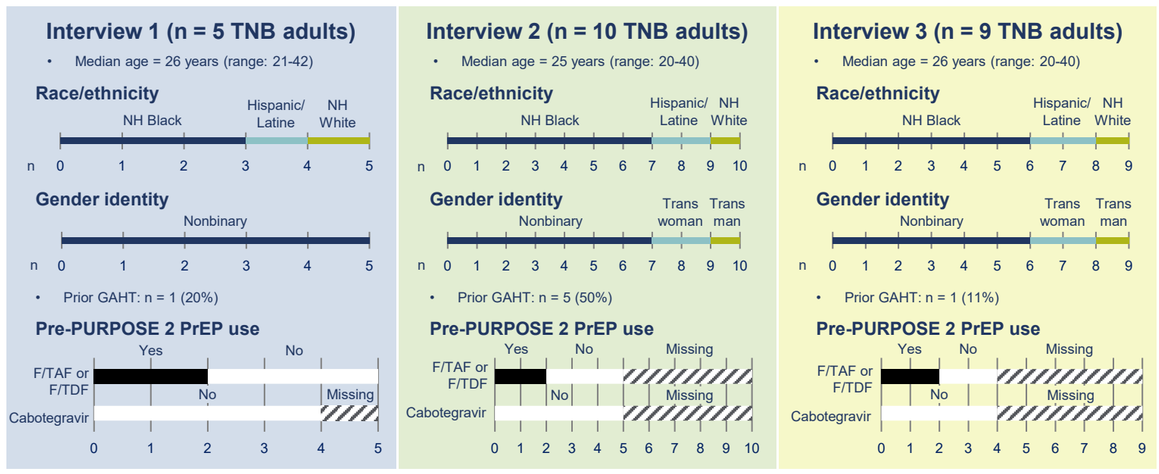
- **Interview topics:** Attitudes, trial experiences, anticipated challenges of taking LEN post-trial, and concerns about integrating LEN with GAHT
- **Codebook thematic analysis:** Transcripts analyzed cumulatively

[a]Participants who declined LEN OLE were offered up to 78 weeks of open-label F/TDF if they were on blinded LEN in RBP. [b]Cisgender men and gender-diverse people aged ≥ 16 years who have sex with men and are at risk of HIV acquisition. [c]Included in the full analysis set for primary efficacy analyses (additional participants are included in the safety analysis).
F/TDF, emtricitabine/tenofovir disoproxil fumarate; GAHT, gender-affirming hormone therapy; LEN, lenacapavir; OLE, open-label extension; RBP, randomized blinded phase; SC, subcutaneous.

Results

- The majority of participants in this qualitative study were Black or Hispanic and identified as nonbinary; use of PrEP before PURPOSE 2 among those with data was reported by 2/5 at interview 1, 2/5 at interview 2, and 2/4 at interview 3 (**Figure 2**). Of the 9 participants identifying as TNB, 5 took GAHT at some point during the study

Figure 2. Participant Characteristics by Interview Timepoint in PURPOSE 2



F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; GAHT, gender-affirming hormone therapy; NH, non-Hispanic; PrEP, pre-exposure prophylaxis; TNB, transgender and nonbinary.

- Participants across three interviews generally endorsed LEN but also raised questions about the number of injections, using the same anatomic injection site for LEN and GAHT, fear of needles, and potential GAHT/LEN interactions. Some participants also felt that prior experience with GAHT injections could help normalize LEN injections (**Figure 3**)
  - While these interviews were conducted prior to the presentation of observed data from PURPOSE supporting the absence of drug-drug interactions with GAHT, the study protocol described the absence of bidirectional interactions based on the clinical pharmacology of GAHT and LEN[6]

Figure 3. Thematic Patterns Across Three Interviews Demonstrated High Endorsement of LEN Despite Participant Questions About Injection Site Nodules and Interactions With GAHT

High acceptability and endorsement of LEN for HIV prevention

Non-Hispanic White nonbinary/ transmasculine individual, age 18-24

> **I think it's a bit more accessible than having the pill, or like the two-month, because not everyone can set aside the time to do that** cause it's like I know I have to like build my work schedule around my doctors and such because of chronic illness and such and that's very difficult, if it was for the two-month injectable, like having to build in, I have to get this shot every two months as well. It's a lot for people so I think doing **the once every six months is a bit more... accessible in general**.

Non-Hispanic Black transgender woman, age 35-44

> **I've actually been on the pills previously**… probably just for a couple of weeks then [I was] like **oh my God, this is so ridiculous, I can't keep up**.

Role of gender-affirming care on trust building with TNB people

Non-Hispanic White nonbinary/ transmasculine individual, age 18-24

> They were so excited and very like um informative and encouraging for me to do a study… and **it was a really great affirming experience as like a patient**.

Reassurance about GAHT/LEN interactions

Non-Hispanic White nonbinary individual, age 18-24

> I was [previously concerned about drug interactions], and that's one of the first things I asked about when I was consulted about this, if there would be any issues…**I was told there is no interactions with it.**

Non-Hispanic Black genderfluid individual, age 18-24

> **I think I would have to do more research on that to inform that taking HRT wouldn't really like um wouldn't really interact with each other**, I don't know that.

GAHT normalizing injections and reducing fear of needles

Non-Hispanic Black genderfluid individual, age 18-24

> I would say like the shot part and getting over like the mental barriers of like actually injecting yourself made me used to like just getting the check up shots or even the shots so **it's made me like less afraid of pain I guess**.

Reassurance about co-administration of LEN and GAHT injections[a]

Hispanic other/unknown transgender man, age 18-24

> Like if I have two nodules on one side and you know that's where I would take said T shot, **I just don't want to interfere** in terms of like you know if I already have something there like I don't want to add another nodule. I mean obviously it goes away, but **I'd rather just have like a clear zone to do my shot** than worrying about doing it in between the two that are already there.
>
> I mean I would say, yeah that's the only [thing] that hinders **but as long as it's like switched up like I don't mind as much.** I just need to be cautious where to inject myself

Role of gender-affirming discussions to mitigate TNB individuals' fears and concerns

Non-Hispanic Black genderfluid individual, age 18-24

> **It breaks down even a stigma for me about medical care**… I feel like kinda of like knowing from like my doctor's perspective and these doctors' perspectives on two totally different types of medications and what they're used for but kinda have the same – at the end of the day – **the same goal which is to be healthy and make sure that you're the best version of yourself** in whatever form that takes, so I'd say that that's it.

[a]Following the RBP, additional anatomic locations were allowed (thigh, arm, and buttock) and the USPI includes thigh as an injection location[7]

GAHT, gender-affirming hormone therapy; HRT, hormone replacement therapy; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; RBP, randomized blinded phase; TNB, transgender and nonbinary; USPI, US Prescribing Information.

- Further details around participants' concerns and thoughts on injections are shown in **Figure 4**

Figure 4. The Perceived Benefits of LEN Outweighed Participants' Concerns About Injections

> Advantages? Well just that you're used to it… and then **disadvantages… just the minor pain**, but I think it's all the same. It's more helpful than it is detrimental…
>
> *Hispanic transgender man, age 18-24*

> **Taking like an injectable form of hormones was like something I was really nervous about** when I first started because I was afraid of needles… and now I just will do a shot, like my T [testosterone] shot, very quickly right before we leave the house… **it's become way more normal for me**.
>
> *Non-Hispanic White nonbinary/transmasculine individual, age 18-24*

> Like **I'm getting the shot every 6 months… do I have to do this for the rest of my life** or will it eventually like plateau out? I'm on testosterone so I'm already kind of signed up [to do] this shot… once a week for the rest of my life, so this is just another one to add.
>
> *Non-Hispanic White nonbinary/transmasculine individual, age 18-24*

> **Advantages, I mean… you're already used to injections** so what's you know one more or two more in this case, right. Like you're already used to it… [so it] makes it bearable.
>
> *Hispanic other/unknown transgender man, age 18-24*

References: **1.** Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. **2.** Restar A, et al. *Sci Rep*. 2024;14:23482. **3.** Cespedes M, et al. *PLoS One*. 2022;17:e0267780. **4.** Gianella S, et al. *Clin Infect Dis*. 2018;66:1460-466. **5.** Fehrenbacher AE, et al. *AIDS Behav*. 2025;29:1136-57. **6.** Arora P, et al. Poster PII-100 presented at: ASCPT; March 4-6, 2026; Denver, CO. **7.** Yeztugo (lenacapavir) USPI, Gilead Sciences, Inc., June 2025.

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Correspondence: Lillian B Brown, Lillian.Brown6@gilead.com.