PURPOSE

A summary of PURPOSE 2, a study looking at how well lenacapavir works for HIV prevention in cisgender gay, bisexual, and other men, transgender people, and gender nonbinary people who have sex with partners assigned male at birth

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This is a summary of a scientific presentation that was originally presented by Dr Onyema Ogbuagu at HIV Glasgow 2024 (Twice-Yearly Lenacapavir PrEP in Cisgender Gay, Bisexual and Other Men, Transgender Women and Men, and Gender-Diverse People [PURPOSE 2]). This summary only presents selected data and is not intended to replace the full presentation. The intended audience for this summary is registered conference attendees.

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See **www.purposestudies.com** for more information on the PURPOSE studies

Background

Taking PrEP (pre-exposure prophylaxis) medications can reduce the chances of a person getting HIV.

Standard-of-care oral PrEP is a once-daily emtricitabine and tenofovir disoproxil fumarate (F/TDF) tablet. However, some people are unable to take F/TDF as prescribed, which can make the medication less effective. New PrEP options are needed, particularly for people who are disproportionately affected by HIV, including people of color and gender-diverse people.

Lenacapavir is an investigational medication for HIV prevention that works by targeting the capsid protein, which is needed for the HIV virus to replicate. Lenacapavir is given as an injection under the skin every 6 months.

In the PURPOSE 2 study, researchers looked at cisgender gay, bisexual, and other men, transgender people, and gender nonbinary individuals who have sex with partners assigned male at birth and who received lenacapavir, to see how well it worked at preventing HIV. They also looked at how well lenacapavir worked compared with F/TDF.

Why did researchers do this analysis?

Researchers wanted to know how well lenacapavir works to prevent HIV in cisgender gay, bisexual, and other men, transgender women, transgender men, and gender nonbinary individuals who have sex with male partners.

Who took part in the study and how were the medications studied?

4634 people were tested for HIV at the start of the study. The results of this testing were used to calculate **the background HIV rate**.

Participants

- Brazil (36%)
- US (21%)
- Peru (14%)
- Thailand (12%)
- South Africa (11%)
- Argentina (7%)
- Mexico (0.4%)

Because effective PrEP options exist, a true placebo group (with no active drug) was not used in this innovative study design. Researchers compared medications against the "background HIV rate," which was calculated by testing people for HIV at a screening visit. Positive samples were tested with a recency test, which determined if people had acquired HIV recently. Researchers then used that information to calculate the expected rate of new HIV infections in people not on PrEP

3271 people tested negative for HIV and received one of the study drugs (lenacapavir or F/TDF). Neither the doctors nor the study participants knew which group participants were assigned to. **Six** people were diagnosed with HIV on Day 1 of the study and therefore were not included in the analyses.

People randomized in the study

At least 16 years of age

67% non-White

22% identified as gender diverse

- 15% transgender women
- 6% gender nonbinary
- 1% transgender men

Study design

4634 people tested for HIV

3271 people HIV negative and received study drug

Group 1 (2183 people) → **Lenacapavir injections every 6 months** (and F/TDF placebo† tablet daily)

Group 2 (1088 people) → **F/TDF tablet once daily** (and lenacapavir placebo† injection every 6 months)

†Placebo tablets and injections contain an inactive substance and are not a medicine. They were used so that doctors and participants did not know which group they were in.

Week 0 — **12 months**

If diagnosed with HIV, people were referred to HIV care to start treatment for HIV.
The samples were tested with a recency test to calculate the background HIV rate.

What was measured?

Researchers measured the **incidence of HIV in each study group** and the background HIV incidence as the number of new HIV infections per "person-year." A person-year is equal to one person studied for 1 year.

Researchers measured how many people had **injections on time** or **took the number of tablets as directed.**

Researchers also looked at **whether the drugs were safe**, including assessment of injection-site reactions.

PURPOSE 2 enrolled the most diverse population of people of different races, ethnicities, and genders, across a broad age range, including people aged 17 to 74 years

A summary of PURPOSE 2, a study looking at how well lenacapavir works for HIV prevention in cisgender gay, bisexual, and other men, transgender people, and gender-nonbinary people who have sex with partners assigned male at birth

What were the results?

Over 99.9% of participants who took lenacapavir did not acquire HIV

Lenacapavir reduced the risk of acquiring HIV by:

96% vs the background HIV rate

89% vs F/TDF

2 out of 2179 people taking lenacapavir got HIV
➔ **0.10 cases per 100 person-years**

9 out of 1086 people taking F/TDF got HIV
➔ **0.93 cases per 100 person-years**

The background HIV rate in 4634 people was
➔ **2.37 cases per 100 person-years**

- Both people taking lenacapavir who got HIV had an N74D capsid resistance mutation.
- There was no evidence that lenacapavir delayed HIV diagnosis by standard HIV serologic testing in these two people.

Did people adhere to lenacapavir and F/TDF at 12 months?

of people received on-time lenacapavir injection (< 28 weeks from last injection)

of people in the F/TDF group were taking four or more tablets per week (**high adherence**)

The nine people in the F/TDF group who got HIV had either stopped taking F/TDF or were taking fewer than two tablets per week (**low adherence**)

How safe was 12 months of lenacapavir or F/TDF medication?

Lenacapavir and F/TDF were safe and well tolerated

- **Lenacapavir and F/TDF were well tolerated** by the people in the study, and only seven people in each group stopped receiving the medications because of side effects other than injection-site reactions.
- Aside from injection-site reactions, the most common side effects experienced by at least 10% of people during the study were rectal chlamydia infection, oropharyngeal gonococcal infection, and rectal gonococcal infection.

Lenacapavir is injected under the skin into the space between skin and muscle where it forms a collection of drug, called a drug depot. Sometimes people can feel the depot through their skin, but usually it is not visible

The most common side effects reported during the study were injection-site reactions, including **pain, redness, or a lump under the skin** at the site of the injection.

Among 10,094 lenacapavir and 5145 placebo injections administered during the study, only 26 and three people, respectively, discontinued due to injection-site reactions.

Over time, as people received more injections, they experienced fewer injection-site reactions.

Conclusions

- Lenacapavir reduced the risk of acquiring HIV by 96% vs the background HIV rate and was 89% better than F/TDF
- Most people received injections on time; F/TDF adherence was high but declined over time
- There was no delay in HIV diagnosis using standard HIV testing in people taking lenacapavir who acquired HIV
- Lenacapavir and F/TDF were safe and well tolerated
- All of the people who participated in the study are now being offered lenacapavir
- Twice-yearly lenacapavir was highly efficacious for HIV prevention among the most globally, racially, and ethnically diverse population of 17- to 74-year-old cisgender gay, bisexual, and other men; transgender women; transgender men; and gender nonbinary people

ACCESS: Please see the full access statements:
https://www.gilead.com/company/company-statements/2024/updated-statement-on-access-planning-in-high-incidence-resource-limited-countries-for-lenacapavir-for-hiv-prevention (accessed November 5, 2024).
https://www.gilead.com/news/news-details/2024/gilead-signs-royalty-free-voluntary-licensing-agreements-with-six-generic-manufacturers-to-increase-access-to-lenacapavir-for-hiv-prevention-in-high-incidence-resource-limited-countries (accessed November 5, 2024).

Gilead believes working directly with generic manufacturers (voluntary licensing) is the fastest way to create broad and sustainable access to lenacapavir for PrEP for people who need it the most.

Reference: Ogbuagu O, et al. Oral O49 presented at: HIV Glasgow; November 10-13, 2024; Glasgow, UK.

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