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; 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 Colleen F Kelley at HIVR4P 2024 (Twice-Yearly Lenacapavir for HIV Prevention in Cisgender Gay, Bisexual, and Other Men, Transgender Women, Transgender Men, and Gender-Nonbinary People Who Have Sex With Partners Assigned Male at Birth: Interim Analysis Results From the PURPOSE 2 Study). 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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Background

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

Standard-of-care 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 non-White and gender-diverse people who may be more likely to be affected by HIV.

Lenacapavir is an investigational medication for HIV prevention that is given as an injection every 6 months.

In the PURPOSE 2 study, researchers looked at cisgender gay, bisexual, and other men; transgender; and gender nonbinary individuals who have sex with partners assigned male at birth, who received lenacapavir over 12 months, 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) is unethical. 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 to which group participants were assigned. **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

HIV positive: HIV test and recency test results from the beginning of the study were used to calculate the background HIV rate. These people were immediately referred to receive HIV care.

What was measured?

Researchers measured the **incidence of HIV in each medication 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 also looked at **whether the drugs were safe**.

PURPOSE 2 enrolled a diverse population of people of different races, ethnicities, and genders, across a broad age range, including adolescents

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What were the results?

Lenacapavir reduced the risk of acquiring HIV by 96% when compared with the background HIV rate

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

Background HIV rate in 4634 people

2.37 cases

per 100 person-years

Lenacapavir was also **89%** more effective than **F/TDF** at preventing people from acquiring HIV

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.

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 15,239 lenacapavir or placebo injections administered during the study, only 29 people discontinued due to injection-site reactions.

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

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

Conclusions

- Only two people receiving lenacapavir acquired HIV; it reduced the risk of acquiring HIV by 96% and was better than F/TDF
- 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 prevents HIV, and is a safe and well-tolerated choice to potentially improve PrEP use among cisgender gay men, transgender, and gender-diverse people that will hopefully reduce HIV in populations who have not benefitted from PrEP previously

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 Oct. 4, 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 Oct. 4, 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.

References: Kelley C, et al. Oral presented at: HIVR4P; Oct. 6-10, 2024; Lima, Peru

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