PURPOSE

A summary of PURPOSE 1, a study looking at how well lenacapavir and F/TAF work for HIV prevention in cisgender women

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This is a summary of a scientific presentation that was originally presented by Dr Linda-Gail Bekker at AIDS 2024 (Twice-Yearly Lenacapavir or Daily Oral Emtricitabine/Tenofovir Alafenamide for HIV Prevention in Cisgender Women: Interim Analysis Results from the PURPOSE 1 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.
*For a list of co-authors, please see the original presentation

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

Background

"PrEP" (pre-exposure prophylaxis) medications can be taken to reduce the chances of a person getting HIV.

Even though the standard-of-care once-daily emtricitabine and tenofovir disoproxil fumarate (F/TDF) tablet used for HIV prevention works very well, some people are unable to take it as prescribed. A newer, once-daily HIV-prevention tablet called emtricitabine and tenofovir alafenamide (F/TAF) is available, but it is not yet approved for people at risk of HIV from receptive vaginal sex. There is an urgent need for more PrEP options, especially for women.

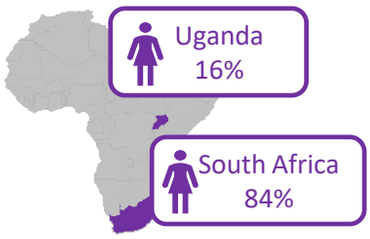
Lenacapavir is a new, investigational medication for HIV prevention that works by targeting the capsid protein, which is needed for the HIV virus to replicate. Lenacapavir is given as an injection every 6 months.

In the PURPOSE 1 study, researchers looked at cisgender women who received lenacapavir or F/TAF for HIV prevention over 12 months, to see how well these medicines worked at preventing HIV.

Why did researchers do this analysis?

Researchers wanted to know how well lenacapavir and F/TAF work to prevent HIV in cisgender women.

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



8094 women were tested for HIV at the start of the study. The results of this testing were used to calculate **the background HIV rate.**

Because effective PrEP options exist, a true placebo group (with no active drug) is unethical. So, researchers used the "background HIV rate" to compare medications against. The background HIV rate was calculated by testing women for HIV at a screening visit. Researchers took positive samples and tested them with a special recency test, which determined if people had acquired HIV recently, then used that information to calculate the expected rate of new HIV infections in women not on PrEP

5338 women tested negative for HIV and received one of the study drugs (lenacapavir, F/TAF, or F/TDF). Women were randomly assigned to each group, and neither the doctors nor the study participants knew which group participants were assigned to.

Women in the study

16-25† years of age

> 99% Black

> 80% had prior HIV testing

†One participant was 25 years of age when they entered the study but turned 26 years of age by the time they were assigned to a treatment group.

Study design

8094 women tested for HIV

HIV negative

Group 1 (2134 women) — **Lenacapavir injections every 6 months** (and F/TAF or F/TDF placebo‡ tablet daily)

Group 2 (2136 women) — **F/TAF tablet once daily** (and lenacapavir placebo‡ injection every 6 months)

Group 3 (1068 women) — **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**

HIV positive: HIV test and recency test results from the beginning of the study were used to calculate the background HIV rate. These women 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.**

The study design using the estimation of background HIV incidence for understanding efficacy of lenacapavir and F/TAF was innovative. Other groundbreaking features included showing that the first twice-yearly product studied for PrEP worked, and it included pregnant and lactating women and adolescents (16 and 17 years of age) for the first time in an adult pivotal PrEP trial

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What were the results?

Lenacapavir was 100% effective, with zero cases of HIV

0 out of 2134 women taking lenacapavir got HIV

0 cases

per 100 person-years

39 out of 2136 women taking F/TAF got HIV

2.02 cases

per 100 person-years

16 out of 1068 women taking F/TDF got HIV

1.69 cases

per 100 person-years

Background HIV rate in 8094 women

2.41 cases

per 100 person-years

Lenacapavir prevented 100% of women from acquiring HIV (**zero cases**), when compared with the background HIV rate. Most people were able to take lenacapavir as prescribed.

> 90% of lenacapavir and placebo injections were given on time

Taking **F/TAF** did not reduce the incidence of HIV in the overall F/TAF group compared with the background rate. However, this was because most people did not take F/TAF as prescribed. **F/TAF** was protective against HIV in women who took it as prescribed.

Adherence to F/TAF was low and decreased over time

Almost all women who acquired HIV in the group taking F/TAF were taking their tablets less than twice a week (instead of every day, as prescribed)

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

Lenacapavir and F/TAF were safe and well tolerated

Lenacapavir and F/TAF were well tolerated by the women in the study, and few people stopped receiving the medications because of side effects.

There were 510 confirmed pregnancies during the study. Pregnancy outcomes were as expected for this population.

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

Conclusions

- Zero women receiving lenacapavir acquired HIV; it was 100% efficacious, and better than F/TDF
- The rate of HIV infections was not reduced by F/TAF; however, women who took the F/TAF tablets as prescribed had a lower chance of HIV infection than those who did not
- Lenacapavir, F/TAF, and F/TDF were safe and well tolerated
- Twice-yearly lenacapavir works well, is safe, and is a discreet choice to potentially help more cisgender women use and stay on PrEP and hopefully reduce HIV in cisgender women worldwide

ACCESS: Please see the full access statement here.
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: Bekker L-G, et al. Oral SS0407 presented at: AIDS; July 22-26, 2024; Munich, Germany; Bekker L-G, et al. N Engl J Med. July 2024. doi:10.1056/NEJMoa2407001. [https://www.nejm.org/doi/full/10.1056/NEJMoa2407001]

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