TuSalud

Twice-Yearly Lenacapavir PrEP Is 100% Effective for Women

Advocates stress that the highly effective prevention tool must be available at an affordable cost to the people most affected by HIV worldwide.

July 24, 2024 By Liz Highleyman

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Lenacapavir, Gilead Sciences twice-yearly capsid inhibitor, demonstrated 100% efficacy for preventing HIV acquisition in a large study of young women in Africa, according to long-awaited results from the PURPOSE 1 trial. As previously reported, top-line findings were announced in June, and full details were presented today at the International AIDS Conference (#AIDS2024) in Munich. The study results were also published in The New England Journal of Medicine.

The Phase III trial showed that lenacapavir pre-exposure prophylaxis (PrEP), administered by subcutaneous injection once every six months, significantly reduced HIV incidence compared with the background rate and was superior to daily oral Truvada (tenofovir disoproxil fumarate/emtricitabine). There were no new infections among women randomly assigned to receive lenacapavir.

“These stellar results show that twice-yearly lenacapavir for PrEP, if approved, could offer a highly effective, tolerable and discreet choice that could potentially improve PrEP uptake and persistence, helping us to reduce HIV in cisgender women globally,” said presenter Linda-Gail Bekker, MBChB, PhD, of the Desmond Tutu HIV Centre at the University of Cape Town in South Africa.

@DTHF_SA’s @LindaGailBekker receives a standing ovation after presenting full results from the PURPOSE 1 study. The results confirm #lenacapavir demonstrated

100% efficacy for #HIV prevention in cisgender women.

pic.twitter.com/dr2Q94XH9N

— IAC - the International AIDS Conference (@AIDS_conference) July 24, 2024

Like other antiretrovirals, lenacapavir stops HIV replication. It is not a vaccine that trains the immune system to fight the virus. After four decades of effort, there are still no effective HIV vaccines, but twice-yearly PrEP could be the next best thing. Currently, the longest-acting PrEP method is ViiV Healthcare's Apretude (long-acting cabotegravir), which is administered once every other month.

Lenacapavir, sold as Sunlenca, is now approved only as part of an HIV treatment regimen for people with multidrug-resistant virus. Before it can receive Food and Drug Administration (FDA) approval for PrEP, it must demonstrate effectiveness in other populations. Results from the PURPOSE 2 study of gay and bisexual men, transgender women and men and nonbinary individuals are expected in late 2024 or early 2025. Trials for cisgender women in the United States (PURPOSE 3), people who inject drugs (PURPOSE 4) and people at high risk for HIV in Europe (PURPOSE 5) are also underway.

Although lenacapavir for PrEP is not yet approved in any country, activists are already demanding that the drug be made available at an affordable cost to people who need it most worldwide.

[Update: On September 12, Gilead announced that twice-yearly lenacapavir PrEP was also highly effective for gay and bisexual men and gender-diverse people in PURPOSE 2.]

[Update: On December 19, 2024, Gilead announced that it has completed New Drug Application submissions to the Food and Drug Administration seeking approval of twice-yearly lenacapavir PrEP based on the results of PURPOSE 1 and PURPOSE 2.]

[Update: On June 18, 2025, twice-yearly lenacapavir, brand name Yeztugo, was approved by the Food and Drug Administration for prevention of sexually acquired HIV.]

PURPOSE 1 Findings

Oral PrEP is highly effective when used consistently, but additional options are still needed. Prior studies have shown that women tend to have more difficulty achieving good adherence to daily PrEP. Some people have trouble remembering to take a pill every day, and others are hesitant to have pill bottles that could be lost or stolen or reveal that they are at risk for HIV. Having multiple prevention options ensures that everyone can find a method that works for them.

PURPOSE 1 (NCT04994509) is essentially two studies in one, evaluating both lenacapavir and daily oral Descovy (tenofovir alafenamide/emtricitabine). It therefore helps fill the data gap that has held up approval of Descovy PrEP for cisgender women and others exposed to HIV via vaginal sex.

The study enrolled more than 5,300 cisgender adolescent girls and young women ages 16 to 25 in South Africa and Uganda. Almost all were Black, most were single and the median age was 21 years. More than a third tested positive for sexually transmitted infections at study entry, indicating that the population was at high risk for HIV.

Three groups were randomly assigned to receive lenacapavir injections every six months, daily Descovy pills or daily Truvada pills in a 2:2:1 ratio. Now that oral and injectable PrEP are proven effective, it would be unethical to compare experimental prevention methods to a placebo. Lenacapavir and Descovy were separately compared against the background HIV incidence rate.

Adherence to lenacapavir was high, with more than 90% of participants receiving their injections on time, Bekker reported. But adherence to both daily pills was poor and declined over the course of the study.

Slide comparing efficacy of lenacapavir, Descovy (F/TAF) and Truvada (F/TDF)vada (Bekker et al, AIDS 2024.

After a year on their assigned PrEP regimen, there were zero new infections among the 2,134 women who received lenacapavir, 39 among the 2,136 women who received Descovy and 16 among the 1,068 participants assigned to Truvada. The corresponding HIV incidence rates were 0.00, 2.02 and 1.69 per 100 person-years, respectively. Meanwhile, the background HIV incidence rate was 2.41 per 100 person-years.

The study therefore met its primary efficacy endpoint of showing that lenacapavir significantly

reduced the risk of HIV acquisition compared with the background incidence rate, as well as the secondary endpoint of showing that lenacapavir is more effective than Truvada.

In contrast, the findings were not good news for Descovy, which did not provide statistically superior protection relative to the background incidence. However, women who achieved medium or high adherence to the daily pill did have a lower risk of infection than those who did not take it as directed, according to Bekker. The trial was not designed to directly compare Descovy versus Truvada, but infection rates for the two pills were numerically similar. This leaves open the question of whether Descovy will win FDA approval as PrEP for women.

All three PrEP methods were generally well tolerated, and no new safety concerns were identified. Less than 5% of participants in each group experienced severe (Grade 3) adverse events. Across all groups, the most common adverse events—not necessarily attributable to the drugs—were headache, urinary tract infections, chlamydia and upper respiratory tract infections. Women assigned to Truvada or Descovy were more likely to experience nausea and vomiting than those who received lenacapavir.

Long-acting lenacapavir injections form a depot in the subcutaneous fat layer of the abdomen that slowly releases the drug, Bekker explained. This can sometimes be felt as a nodule that shrinks over time. In addition to nodules, some women experienced injection site reactions such as pain or swelling. Four women discontinued lenacapavir due to injection site reactions.

Women in the trial were not required to use contraception and were not removed from the study if they became pregnant or were breastfeeding. About 500 women got pregnant during follow-up. Pregnancy rates were similar across the three PrEP groups, and there were no notable differences in pregnancy outcomes between the groups or compared with the background rate.

“These data confirm that twice-yearly lenacapavir for HIV prevention is a breakthrough advance with huge public health potential. If approved and delivered—rapidly, affordably and equitably—to those who need or want it, this long-acting tool could help accelerate global progress in HIV prevention,” International AIDS Society president and conference cochair Sharon Lewin, MD, said in a statement. “[A]ll stakeholders must work together to accelerate equitable delivery of existing HIV prevention options and do more to prepare for future options, such as lenacapavir for PrEP.”

Access Is Key

Bekker’s presentation received a standing ovation, and researchers, policymakers and advocates lauded the findings. Speaking at a media briefing, incoming International AIDS Society president Beatriz Grinsztejn, MD, PhD, called twice-yearly lenacapavir PrEP a “game-changer.”

But many expressed concern that lenacapavir will not be available at an affordable price to the populations with the greatest need for new prevention methods, repeating inequities in the rollout of antiretroviral therapy and existing PrEP methods. Even before the interim PURPOSE 1 results were announced, the People’s Medical Alliance, made up of people living with HIV, medical providers and allies, urged Gilead to ensure access to lenacapavir in low- and middle-income

countries. In particular, Bekker suggested, people in countries where trials are conducted should be first in line for access.

Lenacapavir for HIV treatment now costs about $40,000 per year, but the price could be brought down to around $40 with voluntary licensing and competition between generic suppliers, according to a study by Andrew Hill, MD, of Liverpool University, and colleagues. Gilead stressed that prior to approval, it has not yet set a price for lenacapavir PrEP.

Happening now at #AIDS2024!

We're asking @GileadSciences to immediately license groundbreaking #HIV prevention drug, #lenacapavir, to make it affordable for all! #PeopleOverProfits

pic.twitter.com/p2g53mXnlH

— MSF Access Campaign (@MSF_access) July 23, 2024

As activists at the conference called on Gilead to promptly license generic versions of lenacapavir, the company is building an access strategy that prioritizes speedy regulatory approval and, if approved, broad access in countries that account for most of the global HIV burden, Jared Baeten, MD, PhD, Gilead's vice president of HIV clinical development, said at the briefing.

"In advance of today's milestone and in view of the company's ongoing commitment to communities affected by HIV, we have been developing a strategy to enable broad, sustainable access globally," Gilead said in a statement. "A key component of this strategy is to deliver lenacapavir swiftly, sustainably and in sufficient volumes, if approved, to high-incidence, resource-limited countries, which are primarily low- and lower-middle-income countries."

As the world awaits findings from PURPOSE 2, which will be submitted along with the PURPOSE 1 results for FDA consideration, advocates vow to keep up the pressure.

"We are only six years away from 2030, and we still have 1.3 million new HIV infections per year. We want this miracle prevention to reach all those who need it now, not in six years' time," said UNAIDS executive director Winnie Byanyima. "This is not a Gucci handbag for rich people," she added. "This is a feminist product. It is a product for Africa."

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