Weekly Oral HIV Treatment Continues to Look Promising

A once-weekly combination of lenacapavir and islatravir pills maintained viral suppression for 48 weeks.

October 23, 2024 By Liz Highleyman

A weekly oral regimen of Gilead Sciences' HIV capsid inhibitor lenacapavir and Merck's experimental antiretroviral islatravir kept the virus suppressed as well as daily pills for a year, according to study results presented at IDWeek 2024 in Los Angeles.

[Update: Study findings were also presented at the Glasgow HIV Drug Therapy meeting in November.]

The latest data show that more than 94% of people who switched to weekly lenacapavir and islatravir pills maintained an undetectable viral load, similar to the viral suppression rate of those who stayed on the daily regimen. If data continue to look promising, this could become the longest-acting regimen that doesn't involve injections.

Once-daily antiretroviral regimens are highly effective, but some people have trouble taking pills every day. And while long-acting injectable regimens like Cabenuva (cabotegravir and rilpivirine) are the answer for some people, others find it inconvenient to schedule injection appointments—or they simply don't like shots.

"Daily single-tablet regimens have helped to transform HIV care but can be challenging for some people to maintain," Elizabeth Rhee, vice president of global clinical development for Merck Research Laboratories, said in a news release. "Novel HIV treatment options that allow for less frequent oral dosing have the potential to help support adherence and address stigma faced by some individuals taking daily oral therapy."

Amy Colson, MD, MPH, research director at the Community Resource Initiative in Boston, presented the latest findings from a Phase II trial (NCT05052996) evaluating once-weekly oral lenacapavir plus islatravir as a switch option for people currently on daily Biktarvy (bictegravir/tenofovir alafenamide/emtricitabine) with an undetectable viral load.

Lenacapavir works differently than other antiretrovirals, so it remains active against HIV that has developed extensive resistance. A twice-yearly injectable version, sold as Sunlenca, was approved

in 2022 for heavily treatment-experienced people with multidrug-resistant HIV. What's more, lenacapavir injections every six months were recently shown to be highly effective as pre-exposure prophylaxis (PrEP) both for cisgender women and for gay and bisexual men and gender-diverse people. Gilead also makes a lenacapavir pill that is used as an initial treatment loading dose and may be used for temporary "bridging" if an injection must be missed.

Islatravir (also known as EFdA or MK-8591) is a first-in-class nucleoside reverse transcriptase translocation inhibitor. In prior studies, a daily regimen of islatravir plus doravirine (Pifeltro) demonstrated good activity in previously untreated people and maintained viral suppression in those who switched from another regimen. But the drug's long half-life in the body makes it a candidate for longer-acting treatment and prevention.

The development of islatravir hit a snag when studies found that HIV-positive participants in treatment trials experienced a decline in CD4 T-cell counts and HIV-negative volunteers in prevention studies saw a drop in total lymphocyte counts, prompting the Food and Drug Administration (FDA) to place a clinical hold on the drug in late 2021. Merck scientists conducted an extensive analysis, determining that the doses used in these trials were too high. The FDA subsequently lifted the hold, and studies of islatravir with doravirine and islatravir with lenacapavir resumed using a lower dose; however, its development for PrEP was halted.

The Phase II trial of lenacapavir and islatravir enrolled 104 adults with viral suppression (less than 50 copies) on daily Biktarvy, no history of virological failure, a CD4 count of at least 350 and a total lymphocyte count of at least 900. The median age was 40, about 80% were men and the diverse study population was 50% white, 36% Black, 29% Latino and 7% Asian, Native American or Pacific Islander. The participants were randomly assigned to either stay on Biktarvy once daily or switch to lenacapavir (300 mg) and islatravir (2 mg) pills once weekly.

Colson presented 24-week results at this year's Conference on Retroviruses and Opportunistic Infections, showing that the rate of viral suppression was the same in both groups (94.2%) after accounting for people with missing data. Only one person in the lenacapavir plus islatravir group had a viral load above 50 at 24 weeks, and he went on to achieve viral suppression by 30 weeks.

At IDWeek, Colson presented follow-up data showing that the weekly combination remains effective at 48 weeks. The viral suppression rate was still 94.2%, and no one who switched to lenacapavir and islatravir had a viral load of 50 or higher at this time point. The viral suppression rate in the Biktarvy group was 92.3%.

Both treatment regimens were safe and generally well tolerated. As of 48 weeks, 19.2% of participants in the lenacapavir plus islatravir group and 5.8% in the Biktarvy group experienced treatment-related adverse events, all mild to moderate. The most common adverse events in the lenacapavir plus islatravir group were dry mouth and nausea (both 3.8%). Two participants discontinued the weekly regimen due to adverse events unrelated to the drugs. Careful monitoring of CD4 and total lymphocyte counts revealed no clinically significant decreases and no differences between the two treatment groups.

These new study results support the continued development of lenacapavir and islatravir as a once-weekly oral treatment regimen for people with viral suppression. A fixed-dose combination pill containing the two drugs is now being tested in the Phase III ISLEND-1 (NCT06630286) and ISLEND-2 (NCT06630299) trials.

“The future of HIV treatment is person-centered, with long-acting options tailored to help meet the needs and preferences of people affected by HIV,” said Gilead senior vice president Jared Baeten, MD, PhD. “There is no ‘one size fits all’ approach. The complexities of HIV care require putting people first in the development of biomedical innovations as we keep striving to offer options for all those living with HIV.”

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