

Bictegravir/Lenacapavir Combo Pill Could Replace Complex HIV Treatment

The two-drug single-tablet regimen could enable people to switch from antiretroviral regimens containing multiple pills.

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A once-daily combination pill containing bictegravir and lenacapavir could offer a simpler alternative for people with HIV who are taking complex antiretroviral regimens, according to study results presented at the [Conference on Retroviruses and Opportunistic Infections \(CROI 2026\)](#) this week in Denver. Gilead Sciences plans to submit data from the ARTISTRY-1 and ARTISTRY-2 trials to the Food and Drug Administration for approval.

Gilead is testing a new single-tablet regimen consisting of 75 milligrams of bictegravir and 50 mg lenacapavir (BIC/LEN). Bictegravir is an oral integrase inhibitor best known as a component of the widely used Biktarvy combination pill (bictegravir/tenofovir alafenamide/emtricitabine). Lenacapavir is the first HIV capsid inhibitor. A twice-yearly injectable formulation is currently approved [as a component of combination therapy for multidrug-resistant HIV](#) (brand name Sunlenca) and [for pre-exposure prophylaxis](#) (brand name Yeztugo). It is also available as a pill used as an initial loading dose before starting injections.

While most people living with HIV can take a single daily combination pill or injections every other month, some individuals who have used multiple antiretrovirals and developed drug resistance need more complex regimens. Others are unable to tolerate the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) in existing single-tablet regimens or must manage potential drug interactions with medications they take for other conditions.

“In many cases, these individuals are our elders, diagnosed early in the pandemic,” said presenter Chloe Orkin, MD, of Queen Mary University of London. “They may experience a high pill burden and challenges with adherence and may be at risk for drug interactions due to the boosted protease inhibitors they’re taking. So this is a clear unmet need, and a novel drug such as BIC/LEN could optimize treatment for individuals with viral suppression who are on these complex regimens.”

ARTISTRY-1

Orkin presented findings from the open-label ARTISTRY-1 trial ([NCT05502341](#)), which evaluated bictegravir plus lenacapavir as a switch option for people taking complex regimens. The Phase II portion of the study tested bictegravir and lenacapavir as separate pills, while the Phase III portion used the new single-tablet regimen.

At the 2024 International AIDS Conference, [researchers reported](#) results from the Phase II portion, showing that about 90% of people assigned to bictegravir plus one of two doses of lenacapavir had a viral load below 50 at 48 weeks, as did everyone who stayed on their existing regimen; these results held at 96 weeks.

Late last year, Gilead announced [top-line results](#) from the Phase III portion, showing that the BIC/LEN combination pill worked as well as continuing on complex regimens. Orkin presented the details at CROI, and they were also published in [The Lancet](#).

The Phase III portion enrolled 557 adults in 15 countries who were on stable complex multi-tablet regimens that included two or more pills per day, required more than once-daily dosing or contained a boosted protease inhibitor, an NNRTI plus two other drug classes or injected HIV medications besides Cabenuva (cabotegravir and rilpivirine). They had an undetectable viral load at baseline. They were randomly assigned in a two-to-one ratio to switch to BIC/LEN or stay on their existing regimen.

This study population was older than that of most HIV trials; the median age was 60 years, and three quarters were older than 55. About one in five were women. Most (69%) were white, 17% were Black, 5% were Asian and 22% were Latino. Comorbidities were common, including elevated blood lipids (68%), high blood pressure (50%), high blood sugar or diabetes (24%) and chronic kidney disease (14%). More than half had two or more comorbidities, and 61% were taking at least two medications besides antiretrovirals. The current median CD4 T-cell count exceeded 600, but two thirds had a history of AIDS.

At study entry, the participants had been on antiretroviral therapy for a median of 28 years. Three quarters were taking boosted protease inhibitors, and a majority used both a protease inhibitor and an integrase inhibitor. Most were taking two (41%) or three (26%) pills per day, but 22% were taking five or more; 39% took their pills twice daily. The most common reason for using a complex regimen was drug resistance (81%), followed by intolerance (23%) or contraindications (6%) to single-tablet regimens. Many had a history of resistance to NRTIs (67%), NNRTIs (55%) or protease inhibitors (41%), but integrase inhibitor resistance was uncommon (5%).

BIC/LEN was shown to be noninferior to staying on a complex regimen, Orkin reported. At 48 weeks, 96% of those on the single-tablet regimen had an undetectable viral load, compared with 94% of those who stayed on their existing regimen. Three people in the BIC/LEN group (0.8%) and two in the complex regimen group (1.1%) had a viral load above 50. No treatment-emergent resistance to the study drugs was observed. CD4 counts remained stable in both groups.

BIC/LEN was generally safe and well tolerated. While overall adverse event rates were similar in

both groups, people assigned to BIC/LEN were more likely to experience drug-related events (14% versus 2%)—not surprising, as side effects typically occur when people start new medications. Two people taking BIC/LEN had severe drug-related adverse events, and one had a serious side effect (diabetes). People taking BIC/LEN saw decreases in cholesterol and triglycerides—largely attributable to stopping a protease inhibitor—while those on complex regimens had a small increase. Orkin said that a detailed analysis of cardiometabolic outcomes, including weight changes, is underway.

Six people on BIC/LEN and one person on a complex regimen discontinued treatment due to adverse events, including one who showed evidence of hepatitis B reactivation. This is a potential risk when people stop taking drugs, such as tenofovir, that are active against both HIV and hepatitis B virus. This underscores the importance of hepatitis B vaccination for those who are not already immune.

Looking at patient-reported outcomes, people in both groups had similar satisfaction scores, but those who switched from a complex regimen to BIC/LEN reported increased satisfaction with their treatment.

“These data suggest that the BIC/LEN single-tablet regimen is an important option enabling treatment to be tailored for people with virological suppression on a complex regimen,” the researchers concluded.

“Finding new effective and convenient dosing with single-tablet regimens is key to optimizing treatment, ensuring that more people can benefit from recent advances in medical research like bictegravir and lenacapavir,” said in a [Gilead news release](#).

ARTISTRY-2

Researchers also presented results from the ARTISTRY-2 trial ([NCT06333808](#)) in a poster at the conference. This study evaluated the BIC/LEN single-tablet regimen as a switch option for people currently taking Biktarvy.

In this trial, 574 people with viral suppression on Biktarvy were randomly assigned in a two-to-one ratio to either switch to BIC/LEN or stay on their current treatment. Unlike the open-label ARTISTRY-1 study, this trial was double-blind, meaning neither the participants nor the investigators knew who was assigned to which group.

This study population was younger; the median age of 49 years, and about a third were age 55 or older. Again, nearly 20% were women, but participants were more racially diverse (54% white, 27% Black, 13% Asian and 27% Latino). The participants were generally healthier, but comorbidities were still common.

Here, too, the new single-tablet regimen was shown to be noninferior. At 48 weeks, 94% of people assigned to BIC/LEN had an undetectable viral load, as did 91% of those who stayed on Biktarvy. Five people in the BIC/LEN group (1.3%) and two in the Biktarvy group (1.0%) had a viral load

above 50. One person in the former group, who had previously used integrase inhibitors, had an integrase resistance mutation. Again, CD4 counts stayed about the same in both groups.

Both regimens were safe and generally well tolerated. The likelihood of drug-related adverse events was similar in the BIC/LEN and Biktarvy groups (10% and 12%, respectively). Only one person in the BIC/LEN group had a severe side effect (rhabdomyolysis, or muscle damage). Six people in the BIC/LEN group and three in the Biktarvy group stopped treatment due to adverse events. Weight and body mass index (BMI) remained stable in both groups.

“The findings from ARTISTRY-2 support the potential of the BIC/LEN regimen to expand the range of single-tablet antiretroviral treatments available to people living with HIV,” lead investigator Eric Meissner, MD, PhD, of the Medical University of South Carolina, said in the news release. “With efficacy shown to be comparable to a guideline-recommended therapy, we look forward to the prospect of having another meaningful treatment option for adults with HIV who are virologically suppressed.”

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