Cabenuva Can Be an Option for People Without Viral Suppression

Most people who started the long-acting injectables with a detectable viral load were able to bring their HIV under control.

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Long-acting HIV treatment with injectable cabotegravir and rilpivirine (Cabenuva) may be a good choice for people who have been unable to maintain viral suppression on daily oral therapy, according to a pair of studies presented at the International AIDS Society Conference on HIV Science (IAS 2025) in Rwanda.

The IMPALA trial in Africa found that Cabenuva matched the effectiveness of daily pills for people who first reached an undetectable viral load on an oral regimen. A second study in the United States found that the long-acting injectables also work well for those who start without viral suppression.

Modern antiretroviral therapy is highly effective and generally well tolerated, so treatment success often comes down to consistent use. Some people have difficulty maintaining good adherence, for example, because they have trouble remembering to take a pill every day or are concerned about having pill bottles that could reveal their HIV status. For these individuals, long-acting treatment may be a better option.

Cabenuva, the first complete HIV regimen that doesn't require daily pills, is administered by injection once monthly or every other month. The Food and Drug Administration approved Cabenuva in 2021 for people with viral suppression on a stable antiretroviral regimen, no history of treatment failure and no resistance to cabotegravir or rilpivirine. The World Health Organization also recommends Cabenuva as a switch option for people whose HIV is already under control.

While people without viral suppression were not included in the pivotal trials that led to Cabenuva's approval, growing real-world evidence shows that the long-acting injectables can be a feasible option for this population as well.

IMPALA trial

Fiona Cresswell, MBCHB, PhD, of the London School of Hygiene and Tropical Medicine, presented findings from the Phase IIIb IMPALA trial (NCT05546242), which enrolled adults with HIV in Kenya,

South Africa and Uganda who had viral load above 1,000 copies or poor engagement in care, defined as not being linked to care three months or more after their diagnosis or loss to follow-up lasting four weeks or more. According to UNAIDS, around a million people in eastern and southern Africa do not have viral suppression despite oral antiretroviral treatment.

The study participants were first put on a daily oral regimen of dolutegravir plus two nucleoside/nucleotide reverse transcriptase inhibitors, such as the widely used "TLD" single-tablet regimen (tenofovir disoproxil fumarate/lamivudine/dolutegravir). Only those who maintained a viral load below 200 for at least three months were randomized to Cabenuva or continued oral therapy. This is the same approach used in the LATITUTDE trial, in which participants in the United States were given intensive support to achieve viral suppression on a daily oral regimen before switching to Cabenuva.

Among participants who achieved viral suppression on oral treatment, 271 were randomly assigned to switch to Cabenuva administered every two months, while 269 remained on a dolutegravir-based daily oral regimen. About 60% were women, almost all were Black and the median age was 40 years. They had been on HIV treatment for a median of 7.5 years, and the median current CD4 cell count was high (629), though a quarter had a history of AIDS-defining illnesses.

Almost all participants stayed on their assigned treatment, and 98% of Cabenuva injections were given on time. At 48 weeks, 91% of people who switched to Cabenuva and 89% who stayed on an oral regimen had a viral load below 50, showing that the long-acting injectables were non-inferior. Results were similar regardless of body mass index. Five Cabenuva recipients (1.9%) had confirmed virological failure, defined as two consecutive viral loads above 200, compared with zero people on oral therapy. The four people with successful virus sequencing showed high-level resistance to cabotegravir, and three were also resistant to rilpivirine. All five regained viral suppression when switched back to an oral regimen.

Safety and tolerability of the two regimens were comparable, with less than 1% in both groups discontinuing due to drug-related adverse events. Although 37% participants on Cabenuva experienced mild to moderate injection-site reactions, no one stopped for this reason. Most of those on Cabenuva (94%) said they preferred it over daily pills, with many citing increased privacy and reduced stigma.

"Long-acting treatment has an important role as a management option in people who struggle with daily pill-taking in Africa," the researchers concluded. Cresswell noted that these favorable outcomes were achieved without baseline drug resistance testing, which is often not available in lower-income countries.

OPERA Cohort

Ricky Hsu, MD, of the AIDS Healthcare Foundation, presented new results from the OPERA Cohort, confirming other real-world findings showing that Cabenuva works well for people who start the

injectables without viral suppression.

This longitudinal cohort includes more than 150,000 people with HIV seen at clinics throughout the United States. Within the cohort, 3,304 treatment-experienced adults switched to Cabenuva between January 2021 and December 2023. Of these, 368 people (11%) started Cabenuva off-label without viral suppression, with viral loads ranging from 61 to 2,535 copies; 40% had a viral load above 200. More than two thirds were men, the median age was 41 and they had been diagnosed with HIV for a median of nine years. A majority (57%) were Black, 18% were Latino and 63% received care in the South.

Most completed Cabenuva initiation, defined as receiving at least two injections no more than 67 days apart. Nearly 60% received all their shots on time, but a third had delayed injections, and 13% missed injections. Among those who completed initiation, 78% were still on Cabenuva after a median 12 months of follow-up.

Among participants who completed initiation, 85% reached an undetectable viral load (below 50 copies) within six months, but 36 people (12%) never achieved viral suppression. Just three complete initiators (about 1%) had confirmed virological failure, two of them despite good adherence. Both of those with available virus sequencing results showed evidence of major drug resistance.

“Given the high effectiveness observed in a real-world setting in the U.S., [long-acting cabotegravir plus rilpivirine] may have a role for individuals with viral load ≥50 copies/ml who may be struggling with adherence or tolerability to oral therapy,” the researchers concluded.

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