

Are Long-Acting Injectables Feasible for People Without Viral Suppression?

People at a safety-net HIV clinic who struggle with adherence had viral suppression rates comparable to those seen in clinical trials.

February 23, 2023 By [Liz Highleyman](#)

Long-acting [Cabenuva \(cabotegravir and rilpivirine\)](#) injections may be an option for people who struggle to stay engaged with traditional HIV care and who have been unable to maintain an undetectable viral load on oral antiretroviral treatment, researchers reported this week at the [30th Conference on Retroviruses and Opportunistic Infections \(CROI\)](#) in Seattle.

“For those of us treating HIV on a daily basis, we know that some patients have challenges taking pills, including substance use, housing and food insecurity and stigma,” Monica Gandhi, MD, MPH, medical director of the [Ward 86 HIV clinic](#) at Zuckerberg San Francisco General Hospital, told POZ. “We tried the long-acting regimen in adherence-challenged patients—even those with viremia—and saw high success rates that were equivalent to those in clinical trials.”

Some experts caution, however, that this approach might not be feasible for people who don’t have the same level of support offered by Gandhi’s clinic.

Cabenuva consists of two separate injections of cabotegravir, a new integrase inhibitor from ViiV Healthcare, and Janssen’s non-nucleoside reverse transcriptase inhibitor rilpivirine. It is the first complete antiretroviral regimen that doesn’t require daily pills. The treatment involves two intramuscular injections administered by a health care provider once monthly or every other month.

Two Phase III clinical trials showed that Cabenuva produces sustained viral suppression. The [ATLAS study](#) evaluated the regimen as maintenance therapy for treatment-experienced people who already had a stable undetectable viral load on a standard oral regimen. The [FLAIR study](#) enrolled previously untreated people, but they achieved viral suppression on a temporary oral regimen before switching to the injections.

In January 2021, the Food and Drug Administration (FDA) [approved Cabenuva](#) only for people whose HIV is currently suppressed on a stable oral regimen. But the new study suggests that the long-acting injectables may also work well for those without viral suppression.

Gandhi's team first conducted a pilot study to assess whether Cabenuva, if provided along with extensive support, could be an option for people who have been unable to achieve or maintain viral suppression due to adherence challenges. That study included about 50 people who received care at Ward 86, a safety-net HIV clinic that serves mostly low-income people covered by Medicaid or Medicare, many of whom are dealing with substance use, mental health problems and unstable housing.

At the International AIDS Conference last July, [the team reported initial results](#) for 51 patients, showing that everyone who switched to the injections with an undetectable viral load maintained viral suppression, while 80% of those with detectable HIV at baseline achieved viral suppression, some for the first time.

This set the stage for SPLASH, the Special Program on Long-Acting Antiretrovirals to Stop HIV. The program offers extensive support, including case management, phone or text reminders of upcoming injection visits, follow-up for those who miss appointments and street-based nursing services. Gandhi noted that if a person misses an injection, clinic staff will call them and even go look for them in the community.

At CROI, Gandhi reported results from a larger group of 133 people who started Cabenuva between June 2021 and November 2022. Unlike the clinical trials of the regimen, participants did not need to have viral suppression at baseline, and they were not required to start with an oral lead-in before the injections. They started with monthly injections, but those who maintained viral suppression for six months could switch to every other month. Initially, people with minor integrase inhibitor or rilpivirine resistance mutations could join, but the criteria were later tightened.

Most participants (88%) were men, 8% were cisgender women and 4% were transgender women. The median age was 45 years. Most were Latino (38%) or white (32%), and 16% were Black. Only one third had stable housing; the rest were either unstably housed (58%) or homeless (8%). A majority reported active substance use—including a third who reported current stimulant use—and 38% had a major mental illness.

When they entered the program, 76 people already had an undetectable viral load on their existing oral regimen. A majority of the 57 people who had detectable HIV had never achieved viral suppression using oral therapy. Not surprisingly, those who did not have viral suppression had a lower median CD4 T-cell count than those who did (about 200 versus about 600), and some people with uncontrolled HIV had advanced immune suppression.

Overall, 74% of participants received their injections on time. Once again, all 76 people with undetectable HIV maintained viral suppression after switching to Cabenuva. The more exciting finding is that 55 of the 57 people with a detectable viral load were able to achieve viral suppression, comparable to response rates seen in the major clinical trials.

The two people who did not achieve viral suppression had minor drug-resistance mutations, which is what led the team to tighten the entry criteria. However, neither one of them was able to take

oral antiretrovirals, so trying the injectables was deemed worthwhile.

But Is It Feasible?

New approaches for making antiretroviral treatment more accessible are sorely needed. Only two thirds of people diagnosed with HIV in the United States have achieved viral suppression, [according to the Centers for Disease Control and Prevention](#), and rates are even lower in some other countries.

“Making progress against the HIV pandemic necessitates that societies prioritize reaching those who have historically been left behind yet stand to benefit the most from making newer, easier formulations of antiretroviral treatment available,” [said Carl Dieffenbach, PhD](#), director of the National Institute of Allergy and Infectious Diseases Division of AIDS within the National Institutes of Health, which supported the study.

But during the discussion after the presentation, several audience members pointed out that this approach might not work for people without viral suppression who do not have intensive support like that provided at Ward 86.

San Francisco offers excellent HIV care, and the city provides extensive services for people experiencing homelessness. Unlike some other states, California covers Cabenuva through its Medicaid program and AIDS Drug Assistance Program. Ward 86 is able to leverage funding from the Ryan White HIV/AIDS Program to pay for case managers and social workers.

Joseph Eron, MD, of the University of North Carolina at Chapel Hill, wondered what sort of evidence would be required to convince regulators and guidelines committees that the approach is feasible, given that randomized controlled trials might not be possible for a population that can’t take oral therapy. And what would persuade health insurers to cover the treatment outside its approved indication?

Session moderator Babafemi Taiwo, MD, of Northwestern University in Chicago, asked audience members whether they had ever prescribed Cabenuva for people without viral suppression, and about two dozen raised their hands. He said he thinks we do not yet have enough evidence, but this approach is “a new paradigm that’s worth exploring.”

One commenter recalled that during the early years of the AIDS epidemic, clinicians “did a lot of things without a lot of data and saved a lot of lives.”

“If used creatively and used boldly, long-acting antiretroviral treatment could really make a dent in the epidemic,” Gandhi said. “We hope that innovative approaches to treating marginalized patients will help us achieve the [Ending the HIV Epidemic](#) goals.”

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