Can People Without Viral Suppression Benefit From Cabenuva?

Most people in a pilot program at a safety-net HIV clinic achieved viral suppression on the long-acting injectable regimen.

August 19, 2022 By Liz Highleyman

Long-acting Cabenuva (cabotegravir and rilpivirine) injections may be an option for people with HIV who are unable to achieve viral suppression due to challenges with treatment adherence, according to a small pilot study presented at the 24th International AIDS Conference in Montreal and published in Clinical Infectious Diseases.

Researchers at San Francisco's Ward 86 HIV clinic found that 80% of people who started Cabenuva with a detectable viral load achieved and maintained viral suppression, some of them for the first time.

Injectable cabotegravir, a new integrase inhibitor from ViiV Healthcare, plus Janssen's non-nucleoside reverse transcriptase inhibitor rilpivirine (NNRTI) is the first complete antiretroviral regimen that doesn't require daily pills. The treatment involves two intramuscular injections in the buttocks administered by a healthcare provider once monthly or every other month.

Two Phase III clinical trials showed that Cabenuva leads to 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.

The Food and Drug Administration (FDA) approved Cabenuva only for people whose HIV is currently under control on a stable oral regimen, have no prior history of treatment failure and have no evidence of resistance to the two drugs.

Katerina Christopoulos, MD, MPH, Monica Gandhi, MD, MPH, and colleagues at Zuckerberg San Francisco General Hospital (SFGH) wanted to know whether Cabenuva could be a feasible option for people who are unable to achieve or maintain viral suppression due to challenges adhering to oral treatment.

The researchers evaluated a demonstration project that included 51 people who started the long-

acting regimen at SFGH's Ward 86 HIV clinic between June 2021 and April 2022. Of these, 39 had at least two follow-up injection visits. A majority (24 people) had viral suppression and a high CD4 count (median 706 cells) when they started the injections, but 15 had a detectable viral load and substantial immune suppression (median 99 CD4 cells).

> Totally agree @paulsaxMD; this is why we have started very hard to reach adherence-challenged patients on IM cabotegravir/rilpivirine as "Hail Mary"s when need be:https://t.co/rVWmJAC2Z9 https://t.co/93wZtMjb6l
> — Monica Gandhi MD, MPH (@MonicaGandhi9) August 8, 2022

Ward 86 is a safety-net clinic for low-income people living with HIV who are uninsured or rely on Medicaid or Medicare. Overall, the clinic serves more than 2,400 clients. About 10% have chronic unsuppressed HIV, a group with high rates of substance use, mental illness and homelessness. In 2019, Ward 86 started the POP-UP program to provide care for unstably housed people who struggle to engage with traditional HIV care.

Most participants in this analysis were men, except for one transgender and two cisgender women. The median age was 46 years; none were under 30. About 60% were Black or Latino, and three were monolingual Spanish speakers. Just over 40% were homeless or unstably housed, and half reported current stimulant drug use. People with rilpivirine resistance were excluded, but one person had an integrase inhibitor resistance mutation.

Participants in the pilot project typically start Cabenuva injections without an oral lead-in period using cabotegravir and rilpivirine pills, which has been shown to be safe and effective. Viral load testing is conducted monthly, with resistance testing done at the second injection visit if it remains detectable. Participants who maintain viral suppression after half a year of monthly injections may switch to the every-other-month schedule, which was found to be equally effective in the ATLAS-2M trial. People who expect to miss an injection visit by more than seven days are advised to take their previous oral regimen until injections resume.

The program offers a wide range of support. Participants can drop into the Ward 86 clinic for their injections any time on the designated day. A bilingual pharmacy technician calls or sends text messages to remind people of upcoming visits or to follow up if they miss an appointment. If a person can't be contacted, staff attempt to reach them in person. Clinic staff develop

individualized plans for people without viral suppression, which may include community-based support, case managers, home care, street-based nursing services and financial incentives for visits and blood draws. Two homeless people in this analysis received Cabenuva injections and viral load monitoring at a community clinic or from a mobile harm reduction van.

Of the 24 people who started Cabenuva with an undetectable viral load, 100% maintained viral suppression after a median of six injections, consistent with outcomes in the ATLAS and FLAIR trials.

But the most exciting finding was that 12 of the 15 people (80%) who started with a detectable viral load achieved and maintained viral suppression after a median of six injections, and the other three had at least a 2-log decline in viral load. Two of these individuals had been living with HIV for over 10 years and had never previously achieved viral suppression, the researchers noted. One of them—the person with the baseline resistance mutation—has now had an undetectable viral load for more than eight months.

Overall adherence was good. Most participants (87%) attended all injection appointments on time. One person was late for one injection, and two were late for two shots. One man traveled to his home country and took oral antiretrovirals while he was away. All of them still had viral suppression after the delayed visits. One other person was seven days late for an appointment at the data cut-off for this analysis.

Cabenuva was safe and generally well tolerated. Injection site reactions were mostly mild to moderate, but one person developed cellulitis at the injection site. No one decided to stop the injectable regimen due to side effects.

“This small demonstration project of [long-acting injectable treatment] in a diverse group of patients with high levels of substance use and marginal housing demonstrated promising early treatment outcomes, including in those with detectable viremia due to adherence challenges,” the study authors concluded.

They noted that five participants were receiving other long-acting injections (psychiatric medications or naltrexone to manage alcohol or opioid use disorders), highlighting the promise of leveraging attendance at other injection visits to deliver long-acting HIV treatment.

The researchers acknowledged that Cabenuva might not be an option for people who do not have access to such intensive support. San Francisco offers excellent HIV care, and the city provides extensive services for people experiencing homelessness. Unlike many other states, California covers Cabenuva through Medicaid and its AIDS Drug Assistance Program (ADAP). Most people on Medicare had their co-pays covered by ADAP. But getting prior authorization for private insurance coverage could be a challenge, since the FDA indication for Cabenuva does not include people without viral suppression.

While these results are promising, the approach warrants caution because inconsistent use of Cabenuva could lead to dual NNRTI and integrase inhibitor resistance that limits other treatment

options.

“Ward 86 is a special place, hardly representative of most HIV, ID [infectious disease] or primary care clinics,” Paul Sax, MD, of Brigham and Women’s Hospital in Boston wrote in a blog post about the study. “They have tons of dedicated on-site resources to enhance the care of their difficult-to-reach patient population. This includes doctors, nurses, pharmacists, social workers—a veritable army of people available to support and chase down people who might go astray while on HIV therapy….How many of us HIV providers have access to this kind of wraparound care? In other words, if you’re in a standard ID or HIV clinical practice, don’t try this at home quite yet.”

“Up to this point, our options for people who won’t take oral ART [antiretroviral therapy] have been highly limited,” he continued. “The alternative to trying this might be an HIV-related death. And no one in 2022 should die of AIDS without our doing everything we possibly can to get them on antiretroviral therapy. Even if that includes an unapproved use of cabotegravir and rilpivirine.”

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