Cabenuva Every Other Month Maintains Viral Suppression for Two Years

Injectable cabotegravir and rilpivirine are approved for people with viral suppression who want monthly injections instead of daily pills.

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ViiV Healthcare recently requested Food and Drug Administration (FDA) approval of Cabenuva administered every other month. This regimen maintains viral suppression for two years, according to follow-up study results presented this week at the Conference on Retroviruses and Opportunistic Infections (CROI).

Cabenuva consists of an extended-release formulation of the integrase inhibitor cabotegravir plus an injectable version of Janssen's non-nucleoside reverse transcriptase inhibitor rilpivirine. It is the first complete injectable HIV treatment regimen that does not require daily pills.

Cabenuva is indicated as maintenance therapy for adults who have achieved viral suppression (a viral load less than 50) on daily oral treatment and have no history of treatment failure and no known or suspected resistance to either cabotegravir or rilpivirine.

The FDA initially approved Cabenuva only as a once-monthly regimen, while the European Medicines Agency approved both once-monthly and every-other-month administration.

The Phase III ATLAS study, which included more than 600 participants who started with an undetectable viral load on a standard daily oral regimen, showed that 93% of people randomly assigned to switch to once-monthly Cabenuva maintained viral suppression at 48 weeks, as did 96% of those who stayed on their daily regimen.

Findings from a follow-up study, ATLAS-2M (NCT03299049), showed that once-monthly and every-other-month dosing of the injectable regimen were equally effective, with 94% in both groups maintaining viral suppression.

At CROI, Hans Jaeger, MD, of MVZ Karlsplatz HIV Research and Clinical Care Center in Munich, presented longer-term results from ATLAS-2M, extending follow-up to 96 weeks.

This analysis included 654 participants with an undetectable load who switched from a daily oral regimen and 391 people who rolled over from the monthly Cabenuva arm of the original ATLAS

trial. About 70% were men, and the median age was 42 years. Three quarters were white, and 18% were Black. The median CD4 count exceeded 600.

The participants were evenly randomized to receive injections of either 400 milligrams of cabotegravir and 600 mg of rilpivirine every four weeks or 600 mg of cabotegravir and 900 mg of rilpivirine every eight weeks after a two-week oral lead-in period using cabotegravir and rilpivirine pills (Vocabria and Edurant, respectively). Cabenuva involves two separate injections in the buttocks administered by a health care provider.

At 96 weeks, 90% of people in the once-monthly Cabenuva group and 91% in the every-other-month group maintained viral suppression; 1% and 2%, respectively, had a viral load of 50 or higher (data were missing for the rest).

Just 1% of study participants— two in the once-monthly group and nine in the every-other month group—experienced confirmed virological failure, defined as two consecutive viral load measurements above 200; only one person in the latter group met the criteria during the second year of follow-up. Most of them were found to have viral mutations associated with resistance to rilpivirine and integrase inhibitors. However, all but one regained viral suppression when they switched to another regimen, and all had virus that remained susceptible to dolutegravir, another integrase inhibitor.

But two other analyses presented at CROI suggest that sticking to the dosing schedule is especially important for those on the every-other-month regimen. Researchers from GlaxoSmithKline, ViiV and Janssen reported that delaying cabotegravir or rilpivirine injections by up to a week should have minimal impact, but longer delays could be a problem. Adherence to the dosing schedule is “strongly recommended,” they concluded. People who expect to miss an injection visit can use Vocabria and Edurant pills as a “bridging” strategy.

Cabenuva was safe and generally well tolerated. About 12% in both groups experienced severe side effects. Adverse events leading to study discontinuation were uncommon (3% in the every-other-month group and 4% in the once-monthly group). The most common side effect was pain at the injection site, mostly reported as mild and lasting a median of three days.

Previous analyses from ATLAS and another trial of people new to treatment (FLAIR) found that most study participants preferred monthly injections over daily pills. Reasons included greater convenience and not having to think about HIV every day. The drawback is needing to see a provider more often than most people do for viral load monitoring while on stable oral therapy.

“The ATLAS-2M 96-week data reinforces the therapeutic potential of this long-acting regimen for the treatment of HIV,” Jaeger said in a ViiV press release. “It provides an option that could change the treatment experience for some people living with HIV by removing the need for daily pills for the treatment of HIV. Taking a pill every day can come as an unwelcome daily reminder of their HIV status, or it may add to their fears that their HIV status might be disclosed by someone seeing their HIV medication. This regimen can enable people living with HIV to reduce the days they receive treatment from 365 to 12 or six per year, representing a paradigm shift in their experience

of HIV treatment.”

Injectable cabotegravir alone is also being studied for pre-exposure prophylaxis (PrEP). Cabotegravir injections given every other month were found to be more effective for HIV prevention than daily oral Truvada (tenofovir disoproxil fumarate/emtricitabine) both for cisgender men and trans women who have sex with men in the HPTN 083 study and for cisgender women in the HPTN 084 study.

Click here to read the CROI abstract.
Click here for more news about Cabenuva.
