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Cabenuva Works Well Regardless of Body Weight

The long-acting injectable regimen suppressed HIV in more than 90% of study participants, including those with obesity.

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Long-acting Cabenuva works well in people with obesity, according to research presented last week at the European AIDS Conference—the first HIV conference to resume in person since the start of the COVID-19 pandemic. But researchers also found that longer needles yielded higher drug levels in people with a high body mass index (BMI).

Cabenuva consists of an extended-release formulation of ViiV Healthcare's integrase inhibitor cabotegravir plus an injectable version of Janssen's non-nucleoside reverse transcriptase inhibitor rilpivirine (sold in pill form as Edurant). It is the first complete injectable HIV treatment regimen that does not require daily pills.

The Food and Drug Administration (FDA) approved once-monthly Cabenuva in January 2021 as maintenance therapy for adults who have achieved an undetectable viral load on daily oral medications. The treatment involves two separate monthly shots in the buttocks administered by a health care provider.

The approval was supported by the Phase III ATLAS trial, which showed that 93% of people randomly assigned to switch to Cabenuva maintained viral suppression at 48 weeks, as did 96% of those who stayed on their daily oral regimen. The follow-up ATLAS-2M study showed that every-other-month dosing works as well as once-monthly administration. (ViiV has requested FDA approval of the less frequent schedule.) The FLAIR trial, which enrolled participants new to HIV treatment, found that 94% maintained viral suppression at 48 weeks.

Some drugs can be metabolized and distributed differently in the body in people with obesity. To see whether this occurs with Cabenuva, ViiV scientist Emilie Elliott, MD, PhD, and colleagues conducted a pooled subanalysis of the three trials, stratifying participants by baseline body weight.

In the combined study population, 154 people who received Cabenuva once monthly and 59 of those treated every other month had a BMI of 30.0 or greater (classified as obesity), while 764 and 268, respectively, had a BMI below 30.0 (18.5 to 24.9 is considered normal weight, 25.0 to 29.9 is

considered overweight). In the latter group, about 15% had a BMI over 40.0. The median age (approximately 40 years) was similar across groups, but people with obesity were more likely to be women (42% versus about 20% in the normal/overweight group) and Black (about 33% versus about 13%, respectively).

At week 48, viral suppression rates were high and similar across groups. Among participants with obesity, 92.2% of those who received Cabenuva every month and 91.5% of those who did so every other month had a viral load below 50, compared with 92.7% and 94.0%, respectively, in the normal/overweight group.

However, people with obesity were more likely to have a viral load above 50 (4.5% on monthly and 6.8% on every-other-month Cabenuva), compared with the normal/overweight group (1.2% and 0.4%, respectively). More people with obesity stopped treatment due to lack of efficacy, while more normal/overweight participants did so due to adverse events or for other reasons. Eight people with obesity and five in the normal/overweight group met the criteria for confirmed virological failure. But no one in the former group had high BMI as their only risk factor; all also had either rilpivirine resistance mutations or an HIV subtype associated with treatment failure.

Cabenuva was safe and generally well tolerated, with comparable rates of adverse events across groups. No participants with obesity experienced severe drug-related adverse events, and only one stopped treatment because of an adverse event.

The most common side effect was injection site reactions, including pain, redness or swelling. People with obesity were somewhat less likely to report such reactions. The reactions were usually mild or moderate, transient (lasting a median of three days) and diminished over time.

Looking at drug levels, cabotegravir and rilpivirine trough concentrations (the lowest level between doses) remained above the target level known to suppress HIV, regardless of BMI. Median cabotegravir trough levels tended to be lower initially in people with obesity, but this trend disappeared by week 48, Elliott reported. Rilpivirine concentrations were unaffected by BMI.

But the researchers found that using a longer two-inch needle for injection led to higher cabotegravir trough concentrations for participants with obesity. They recommended that longer needles be used for people with a BMI over 30.0 to ensure appropriate administration into the gluteal muscle.

“These data support the use of [Cabenuva] dosed monthly or every two months as a complete regimen for the maintenance of HIV-1 virological suppression in adults regardless of BMI category,” the researchers concluded.

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. Cabotegravir PrEP could be approved early next year.

Click here for more news about Cabenuva.
