

Thigh Injections Might Be an Option for Cabenuva and Apretude

Some people found thigh injections less painful than butt shots, and this could potentially enable self-administration at home.

March 22, 2023 By [Liz Highleyman](#)

Injecting long-acting cabotegravir and rilpivirine in the thigh may be an option for people who are unable to receive, can't tolerate or want a break from butt injections, according to study results reported at the [30th Conference on Retroviruses and Opportunistic Infections \(CROI\)](#). This could potentially help overcome one of the barriers to wider adoption of the long-acting injectables.

Injectable cabotegravir and rilpivirine, sold together as [Cabenuva](#), is the first complete antiretroviral regimen that does not require daily pills. Injectable cabotegravir alone, sold as Apretude, was [approved last year](#) as the first long-acting pre-exposure prophylaxis (PrEP) option. Cabenuva currently involves two separate intramuscular injections in the buttocks administered by a health care provider either once monthly or every other month. Apretude is always given every other month. The shots contain a relatively large volume of liquid compared with a typical vaccine.

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 with an undetectable viral load, while the [FLAIR study](#) assessed first-line therapy after achieving initial viral suppression using oral drugs. The follow-up [ATLAS-2M study](#) showed that administering the injections every other month works as well as once-monthly dosing. [Another study presented at CROI](#) showed that the long-acting regimen also works well for people starting the injections without viral suppression, although this indication is not yet approved. In addition, two large trials, [HPTN 083](#) and [HPTN 084](#), showed that Apretude is even more effective than daily PrEP pills for HIV prevention.

Participants in these studies generally expressed a high level of satisfaction with the injections and said they preferred them over daily pills. But HIV-positive people using Cabenuva and HIV-negative people using Apretude must visit a health care provider for injections at least six times a year.

In [a study presented](#) last summer at the International AIDS Conference in Montreal, researchers from ViiV and GSK evaluated the pharmacokinetics and tolerability of injecting cabotegravir and rilpivirine into the outer side of the thigh rather than the buttocks. That study, which enrolled 15 healthy HIV-negative adults, found that people who received 600 milligrams of cabotegravir plus

900 mg rilpivirine (the standard doses when using the every-other-month schedule) had drug concentrations comparable to those of buttocks shots. Injection site reactions, such as pain, swelling, induration (hardness) and redness, were common; these were usually mild or moderate and lasted about a week.

With evidence that thigh injections are feasible for healthy volunteers, Franco Felizarta, MD, a private practice physician in Sacramento, and colleagues went on to evaluate the pharmacokinetics, safety, tolerability and efficacy of thigh injections of cabotegravir and rilpivirine for people living with HIV.

This analysis included 118 participants in the ATLAS-2M trial who had received buttocks injections for at least three years. A majority (62%) were men, more than 80% were white and the median age was 48 years. They switched to thigh injections for four months on the same schedule they were initially randomized to: 400 mg cabotegravir plus 600 mg rilpivirine once monthly (54 people) or 600 mg cabotegravir plus 900 mg rilpivirine every other month (64 people). Most received cabotegravir shots in the left thigh and rilpivirine in the right thigh. After four months, they went back to butt injections.

All study participants maintained an undetectable viral load. The lowest levels of cabotegravir and rilpivirine in the blood between doses remained well above the active levels for both the once-monthly and every-other-month regimens. In the every-other-month group, maximum drug concentrations and the area under the curve (a measure of total drug exposure) were statistically higher with thigh injections, but there were no significant differences in the once-monthly group. Overall, differences in drug concentrations between thigh and butt injections “were not considered clinically relevant,” according to the researchers.

Again, injection site reactions were common, occurring after about 40% of the monthly injections and about 60% of the larger-volume every-other-month shots. Pain was most frequently reported, and one person stopped thigh injections for this reason. More than 90% of the reactions were described as mild or moderate, but 4% to 7% were more severe. The median duration was about three days.

Overall, nearly one third of participants said they preferred thigh injections, about 60% preferred buttocks injections and about 10% had no preference. Interestingly, the most common reason for preferring either thigh or butt shots was less pain during or after the injection, highlighting the importance of individual choice. Another reason for preferring thigh injections was convenience or easy access. Conversely, some people preferred butt shots because the thigh shots led to more muscle pain or stiffness when walking or doing other physical activity.

Thigh injections could be a better option, for example, for transgender women who have gluteal implants. Other people may have different contraindications or may simply want a periodic break from butt shots.

These results, the researchers concluded, support rotational or short-term thigh administration of

injectable cabotegravir and rilpivirine for people with an established buttocks regimen. They added that further studies will be done to assess the potential for earlier or ongoing thigh injections.

This and [another study presented at the Montreal conference](#), which evaluated a high-concentration formulation of cabotegravir that reduces the volume of injections, suggest that long-acting therapy could potentially be self-administered. To date, uptake of Cabenuva for HIV treatment and Apretude for PrEP have been limited. Enabling people to administer the shots themselves at home instead of visiting a clinic every six months could make these options more attractive.

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