



Injectable Cabotegravir PrEP Bests Daily Truvada for Gay Men and Trans Women

Twice monthly injections for HIV prevention could be approved early next year.

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Long-acting injections given once every two months could soon offer a new option for HIV pre-exposure prophylaxis (PrEP), according to studies showing that the shots work even better than highly effective daily pills.

The Phase IIb HPTN 083 trial ([NCT02720094](#)) enrolled 4,566 cisgender men and transgender women who have sex with men in the United States (37%), Latin America (43%), Asia (17%) and Africa (3%); 13% identified as trans women. The median age was 26 years. About a third of the U.S. participants were Black—the group at highest risk for HIV.

The participants were randomly assigned to receive injections of long-acting cabotegravir—ViiV Healthcare’s new HIV integrase inhibitor—every two months or once-daily oral tenofovir disoproxil fumarate/emtricitabine (Truvada or generic equivalents). People assigned to the cabotegravir group also received placebo pills, while those in the Truvada group got placebo injections. Those taking cabotegravir started with a four-week oral lead-in period using cabotegravir pills before the first injection to ensure they could tolerate the drug.

The blinded portion of the trial was [halted ahead of schedule](#) in May 2020 after an interim analysis showed that cabotegravir injections worked as well as daily pills. Further analysis found that the injections were actually superior to daily Truvada. The study results were [first presented](#) at last year’s International AIDS Conference and have now been [published in The New England Journal of Medicine](#).

Over a year and a half of follow-up, 52 people acquired HIV: 13 in the cabotegravir group (0.41 per 100 person-years) and 39 in the Truvada group (1.22 per 100 person-years), showing that the injections were 66% more effective at preventing HIV acquisition. This is a remarkable finding given that daily Truvada itself reduces the risk of HIV by about 99% for gay and bisexual men who

use it consistently.

“Oral PrEP options are extremely effective for prevention of HIV acquisition, but we have learned that for many reasons, the daily or planned use of oral PrEP that is currently available simply is not practical or desirable for some people who are most at risk for HIV,” lead study author Raphael Landovitz, MD, of the David Geffen School of Medicine at UCLA, said in a [university press release](#). “As we learned with birth control, we need more options for HIV prevention in hopes of finding one option that will fit with someone’s lifestyle. We also have to figure out how to make PrEP options and their surrounding services available to all, regardless of ability to pay or insurance status, and without stigma and other barriers.”

A majority of people who acquired HIV in the cabotegravir group and almost all who did so in the Truvada group were not using their assigned method consistently. An [in-depth analysis](#) revealed that four cabotegravir recipients already had HIV at study entry. Four other cabotegravir recipients acquired HIV despite receiving the injections consistently and having apparently adequate drug levels. Four people with newly acquired HIV developed integrase inhibitor resistance mutations. However, resistance did not occur during the so-called “long tail” when cabotegravir levels decline slowly after the last dose, a potential concern identified in earlier studies. But a new concern arose, as cabotegravir use appeared to [delay HIV diagnosis](#).

Cabotegravir injections were safe and well tolerated, and serious adverse events were uncommon in both groups (5%). The most frequently reported side effect was injection site reactions, including pain, redness or swelling. Just over 80% of people in the cabotegravir group reported such reactions, compared with 31% in the placebo injection group, but few stopped treatment for this reason.

“[Long-acting cabotegravir] was superior to daily oral Truvada in preventing HIV infection among men who have sex with men and transgender women,” the researchers concluded. “Strategies are needed to prevent [integrase inhibitor] resistance in cases of [long-acting cabotegravir] PrEP failure.”

A parallel study, HPTN 084 ([NCT03164564](#)), which compared the safety and effectiveness of long-acting cabotegravir versus daily Truvada for more than 3,000 mostly young cisgender women in sub-Saharan Africa, also found that [the injections worked better than daily pills](#) for HIV prevention. And in that study, the difference was even greater, as women appear more likely than men to have difficulty taking daily PrEP pills consistently.

Click here to read the [study abstract](#).

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