Can HIV Treatment Be Taken Just 4 Days a Week?

Taking meds for four days followed by three days off maintained viral suppression for two years.

April 20, 2021 By Liz Highleyman

Taking antiretroviral treatment for four consecutive days each week followed by a three-day break maintains viral suppression as well as a daily regimen, according to a study presented at the recent virtual Conference on Retroviruses and Opportunistic infection (CROI).

In the era of effective antiretroviral therapy, researchers are exploring treatment approaches that do not require taking pills each day. Some studies have involved new types of treatment, like the long-acting injectable regimen Cabenuva, while others are looking at less frequent dosing of approved oral medications.

More than a decade ago, researchers reported results from the FOTO study showing that people who took antiretrovirals for five days a week followed by weekend breaks were as likely to maintain viral suppression as those who took their meds every day. Another study found that weekend treatment breaks also worked well for adolescents and young adults with HIV.

The QUATOR trial, sponsored by the French Agency for Research on AIDS and Viral Hepatitis, explored whether people with an undetectable viral load could maintain viral suppression while taking medications just four days a week.

This open-label study included more than 600 adults who had a viral load below 50 for at least a year and no evidence of drug resistance. More than 80% were men, the median age was 49 and the median CD4 count was nearly 700. They had been on treatment for a median of about seven years with viral suppression for a median of about six years.

The participants were using a variety of different antiretroviral regimens, mostly including an integrase inhibitor (48%) or a non-nucleoside reverse transcriptase inhibitor, or NNRTI (46%). About 70% were also taking tenofovir disoproxil fumarate or tenofovir alafenamide (components of the Truvada and Descovy combination pills, respectively), while the rest were taking abacavir and lamivudine (the drugs in the Epzicom combination).

For the first 48 weeks, they were randomly assigned to either stay on their existing regimen every day or take their meds Monday through Thursday followed by three days off. After that, all

participants in both groups followed the four-day schedule for another 48 weeks.

At the 2019 International AIDS Society Conference on HIV Science, Roland Landman, MD, of Hôpital Bichat in Paris, reported that 95.6% of people on the four-day schedule and 97.2% of those taking pills every day maintained an undetectable viral load at 48 weeks, showing that the intermittent regimen was non-inferior to continuous treatment. Virological failure rates were low in both groups (1.9% and 1.3%, respectively) and did not differ based on which antiretroviral drug class participants were using.

Despite these promising findings, there has been some concern about the durability of the intermittent approach, given that drug resistance can emerge over time. But follow-up findings a year later are reassuring.

At CROI, Landman presented results after participants had been followed for 96 weeks. At that point, 92.7% of the participants who had initially been randomized to the four-day schedule and 96.1% of those who switched from daily to intermittent treatment at week 48 still maintained viral suppression. Virological failure rates rose to 4.2% and 2.0%, respectively. However, in the four-day group, this differed according to the drugs used: 2.4% for those taking an integrase inhibitor versus 5.3% for those taking an NNRTI.

New drug resistance mutations were detected in three of the six people who experienced virological failure through week 48 and in four of the 13 who did so between weeks 48 and 96. All but one developed a mutation (M184) that confers resistance to lamivudine and emtricitabine. Four people developed NNRTI resistance mutations, and one developed an integrase resistance mutation.

Both treatment strategies were generally safe and well tolerated, with few differences in the frequency or type of adverse events. However, people in the four-day group saw a small but significant improvement in kidney function. (Tenofovir disoproxil fumarate can cause kidney problems, and taking it less often may be beneficial.)

What's more, Landman noted that a related analysis showed that people on the four-day schedule were no more likely to have detectable virus in their semen, which has important implications for HIV transmission. And the four-day regimen could reduce the cost of treatment by about 40%.

Landman and colleagues concluded that the intermittent treatment approach, especially using an integrase inhibitor, "represents a real, workable alternative" to taking pills every day.

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