Intermittent Antiretroviral Therapy Can Work as Well as Daily Treatment

Taking medications three to five days a week could stretch limited drug supplies due to global funding cuts, but this approach is not appropriate for everyone.

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Switching to intermittent antiretroviral treatment—such as taking weekends off—can work as well as daily medication for people with well-controlled HIV, according to a study presented at the International AIDS Society Conference on HIV Science (IAS 2025) in Rwanda. This strategy could help stretch limited drug supplies, but another trial showed that it's a risky approach for adolescents.

"For countries with urgent drug shortages, extending antiretroviral therapy supplies could have clinical benefits for people with HIV and population benefits of minimizing HIV transmission," said presenter Cassandra Fairhead, MD, of the Royal Free Hospital in London.

U.S. funding cuts were an unavoidable focus of the conference. After the Trump administration slashed funding for USAID, which oversees PEPFAR (the U.S. President's Emergency Plan for AIDS Relief), health officials and providers in low- and middle-income countries reported that their ability to provide continued HIV care and services has been sharply curtailed. A UNAIDS survey in May found that 46% of countries affected by the funding cuts reported supply chain disruptions, and 14% had less than a six-month stock of at least one antiretroviral drug.

Intermittent HIV treatment could potentially help limited drug supplies go further. Several studies have assessed less frequent dosing of antiretrovirals approved for daily use, often in an effort to give people brief breaks from treatment. While longer treatment interruptions can lead to viral rebound, drug resistance, disease progression and HIV transmission, some antiretrovirals remain at adequate levels for a few days.

Fairhead and colleagues performed a systematic review and meta-analysis of studies comparing the efficacy of intermittent and daily antiretroviral therapy. Using PubMed, MEDLINE and ClinicalTrials.gov, they identified eight randomized controlled trials comparing intermittent three-drug regimens versus daily treatment. They also did a rapid scoping review of observational studies of intermittent therapy without a control group.

Altogether, the randomized trials included 1,346 people on daily treatment with viral suppression

for at least three months at baseline who had a high CD4 count and, in most studies, no known drug resistance; people who were pregnant or had hepatitis B were generally excluded. Four trials were conducted in Europe, one each in the United States, Taiwan and Uganda, and the largest (BREATHER) in 11 countries.

Four of the randomized trials assessed five-days-on/two-days-off treatment, one used four-days-on/three-days-off dosing, two used three-days-on/four-days-off and one looked at administration on alternating days. Five trials evaluated regimens containing non-nucleoside reverse transcriptase inhibitors (NNRTIs), two assessed the integrase inhibitor-based single-tablet regimen Biktarvy (bictegravir/tenofovir alafenamide/emtricitabine) and one evaluated various triple regimens.

Overall, there was no difference in efficacy between intermittent and daily treatment, with 3.1% and 3.3% of participants, respectively, experiencing viral rebound at 48 weeks. Across the studies, the proportion of people with a viral load above 50 was comparable in the intermittent and continuous therapy groups. Viral levels were typically low, and participants regained suppression after adherence counseling or returning to daily dosing. Results were similar when using more sensitive viral load tests measuring down to 2 copies. In the six observational studies of intermittent treatment, 4.4% of participants had a detectable viral load.

The likelihood of emergent drug resistance was also comparable in the intermittent and daily treatment groups (1.9% versus 2.1%), as were biomarkers of inflammation in the studies where these were measured. Adherence was mostly high and similar with intermittent and daily schedules, but participants reported higher satisfaction with less frequent dosing.

While this analysis showed that intermittent treatment is an effective approach for people with prior viral suppression, good adherence, no pre-existing drug resistance, “in settings with less frequent viral load monitoring or resistance testing, switching after treatment failure may be less rapid, potentially compromising outcomes,” the researchers cautioned. “Studies of intermittent antiretroviral therapy closer to these real-word scenarios are urgently warranted.”

Adding to the caution, another study presented at the conference, BREATHER Plus, found that intermittent treatment did not work so well for adolescents who received infrequent viral load monitoring.

Adeodata Kekitiinwa, MD, director of the Baylor College of Medicine Children’s Foundation-Uganda, and colleagues, enrolled 470 adolescents ages 12 to 19 years (median 16.5) in Kenya, South Africa, Uganda and Zimbabwe, most of whom had acquired HIV via vertical transmission. At baseline, they were on daily treatment using tenofovir disoproxil fumarate/lamivudine/dolutegravir (known as TLD) with viral suppression and no history of treatment failure. They were randomized to stay on the daily regimen or switch to a short-cycle five-days-on/two-days-off schedule. They received viral load tests every six to 12 months.

At 96 weeks, adolescents assigned to intermittent dosing were twice as likely as those on daily treatment to have a detectable viral load (10% versus 5%, respectively), showing that the

intermittent schedule was “not non-inferior” to and, in fact, “significantly worse” than continuous therapy.

Drug resistance was uncommon, and participants regained viral suppression after resuming daily therapy, Kekitiinwa reported. In a subgroup of participants who used pill bottles will electronic caps to monitor adherence, those on both intermittent and continuous treatment took 92% of their pills.

“Short-cycle therapy cannot be recommended as a strategy in adolescents on TLD with standard-of-care six-to-12 monthly viral loads in Africa,” the researchers concluded.

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