Skip the Switch? HIV Integrase Inhibitors Have a High Barrier to Resistance

People whose viral load rebounds on Tivicay may not need to switch medications.

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Two thirds of people who had a detectable viral load after missing doses of Tivicay (dolutegravir) returned to undetectable status within nine months without changing medications, researchers reported recently in Clinical Infectious Diseases.

This led investigators with the ADVANCE trial to suggest that the term "virologic failure"—that is, the failure of antiretroviral treatment to keep viral load at an undetectable level—may not apply to regimens containing integrase inhibitors like dolutegravir. (Dolutegravir is sold alone as Tivicay and is part of the Triumeq, Juluca and Dovato combination pills.)

"The findings support the argument for a shift away from the term 'virologic failure' for [integrase inhibitor]-containing regimens," wrote Toby Pepperell, BSc, of Imperial College London, and colleagues. "This may be inappropriate in an era where viral suppression can be achieved routinely with enhanced adherence counseling."

These updated data add to what's already been published in The New England Journal of Medicine and The Lancet HIV. For background, in 2019, the ADVANCE trial showed that Tivicay plus Truvada (tenofovir disoproxil fumarate/emtricitabine) or Tivicay plus Descovy (tenofovir alafenamide/emtricitabine) were as effective at getting people to an undetectable viral load as Atripla (efavirenz/emtricitabine/tenofovir disoproxil fumarate). The study also showed that weight gain was a problem, especially for women using Tivicay plus Descovy.

The original trial, conducted in South Africa, randomized 1,053 people into three groups of 351 participants; each group received one of the three regimens. After the first year of the trial, 85% of people on Tivicay plus Truvada, 84% of people on Tivicay plus Descovy and 79% of people on Atripla had a viral load of 50 or less—the study's definition of undetectable. Statistically, this meant that the Tivicay-based regimens were noninferior to Atripla.

This updated post hoc analysis asked whether dolutegravir-containing regimens could also enable people to return to an undetectable viral load after HIV rebounds substantially, reaching 1,000 or

more. The analysis followed the participants, who received viral load tests every 12 weeks, until the 96-week cutoff.

Of the original 1,053 participants, 196 experienced a viral load rebound to 1,000 or more after having an undetectable viral load at least once during the 96-week study: 70 (20%) in the Tivicay plus Truvada arm, 74 (21%) in the Tivicay plus Descovy arm and 52 (15%) in the Atripla arm. These numbers update an October 2020 report on the overall 96 weeks of ADVANCE results in The Lancet HIV.

Each person who saw their viral load rebound during treatment received additional adherence counseling. Adherence was assessed by self-report, so it's impossible to know just how regularly participants with a viral load of 1,000 or more took their medications, the researchers noted. The participants then came back for three more visits, each 12 weeks apart, for viral load testing. The participants switched to a different regimen only if after the third visit, their viral load was still above 1,000 or they developed drug resistance.

There wasn't much difference in the proportion of participants with viral load rebound, with roughly 4% in each arm reaching 1,000 or more. But after three consecutive visits and adherence counseling, people taking the Tivicay-based regimens were about twice as likely to have an undetectable viral load than those using Atripla (64% and 67%, respectively, for Tivicay plus Descovy and Tivicay plus Truvada, versus 32% for Atripla).

At 96 weeks, 22% of people on Tivicay plus Descovy, 12% of those on Tivicay plus Truvada and 46% on Atripla had a detectable viral load. In the end, one person using a Tivicay plus Truvada combination switched regimens, compared with eight on Atripla.

Click here to read the study abstract.

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