Switching to Dolutegravir and Lamivudine Works for People With Drug-Resistant HIV

People who switched to the two-drug regimen maintained viral suppression even if they had common resistance mutations.

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Switching from another antiretroviral regimen to a dual combination of dolutegravir and lamivudine is a feasible option even for people who have HIV with M184V/I drug-resistance mutations and experienced prior virological failure, according to study results presented at the International AIDS Conference (#AIDS2024) in July.

Dolutegravir (sold alone as Tivicay) is a potent integrase inhibitor with a high barrier to resistance, and lamivudine (3TC or Epivir) is an inexpensive nucleoside reverse transcriptase inhibitor (NRTI). The two drugs make up ViiV Healthcare's Dovato combination pill. M184V/I is the most common substitution associated with lamivudine resistance. Some studies have found that HIV with these mutations have reduced fitness or lower replication capacity. Among people with prolonged viral suppression, M184V/I may disappear from the viral reservoir.

Dolutegravir/lamivudine (DTG/3TC) is approved for people starting treatment for the first time and as a switch option for people with an undetectable viral load, no history of treatment failure and no known mutations associated with resistance to either drug. This means a majority of highly treatment-experienced people do not qualify for a switch to DTG/3TC.

Gary Blick, MD, of Health Care Advocates International, and colleagues conducted the SOLAR-3D trial to evaluate whether DTG/3TC is a feasible switch option for people with viral suppression on another regimen who have a history of prior virological failure, defined as never achieving a viral load below 50 copies or confirmed viral rebound above 200 copies while on treatment.

This prospective open-label trial enrolled 100 adults in Connecticut who were currently on a stable two-, three- or four-drug regimen with viral suppression (below 50 copies) for at least six months. Most (85%) were men, and the median age was 58 years. There were no exclusions based on prior integrase inhibitor use, CD4 count or NRTI resistance mutations, including M184V/I and K65R.

The participants had been on HIV treatment for a median of 22 years and had used at least two

(median seven) prior antiretroviral regimens. Half had ever tested positive for M184V/I mutations, and 37% currently had these mutations according to a sensitive genotypic resistance test. Current K65R mutations were rare. People with the mutations were, on average, older than those without and had been living with HIV longer (28.4 versus 15.5 years), had a lower nadir (lowest-ever) CD4 count, had been on treatment longer (24.6 versus 15.2 years), had tried more regimens and had more instances of prior treatment failure (nine versus four). They were taking a variety of regimens when they switched, about three quarters of which include lamivudine or the related drug emtricitabine (FTC).

At last year's 12th International AIDS Society Conference on HIV Science, Blick reported that a history of virological failure and resistance does not affect response to DTG/3TC. None of the participants with a history of M184V/I mutations who switched to the two-drug regimen experienced confirmed virological failure, defined as a viral load above 50 followed by a measurement above 200, at two years.

This year, Blick presented updated findings showing that study participants maintained viral suppression at three years, with no cases of confirmed virological failure among those with M184V/I resistance mutations. Looking at those who stayed on treatment, efficacy was similar for people with and without a history of M184V/I mutations (94.9% versus 92.3%). The likelihood of viral blips was also similar. Two people with a history of mutations had a viral load above 50 but experienced viral resuppression without changing their regimen. Three people without the mutations had a viral load above 50, one of whom had confirmed virological failure due to poor adherence. No cases of new treatment-emergent resistance were observed.

"SOLAR-3D is the largest prospective comparative trial with the longest follow-up to date to demonstrate that neither prior/current M184V/I nor multiple prior virological failures impact the efficacy and durability of switching virologically suppressed [people living with HIV] to DTG/3TC through 144-weeks," the researchers concluded.

Blick noted that switching to DTG/3TC could be cost-saving and could have a safety advantage over regimens containing tenofovir disoproxil fumarate (which can cause kidney and bone problems), suggesting that this approach should be explored in economically developing countries.

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