Two-Drug HIV Regimens Struggle to Match Triple Therapy for Long-Term Survivors

Many participants on two-drug regimens had more treatment under their belt and more chronic conditions.

June 2, 2021 By Heather Boerner

According to an analysis published in PLoS One, two-drug antiretroviral (ARV) regimens couldn't stand up to three-drug regimens in heavily pretreated long-term survivors with multiple chronic conditions.

Numerous studies have found that two-drug regimens, such as Juluca (dolutegravir/rilpivirine) and Dovato (dolutegravir/lamivudine), are noninferior to, or work at least as well as, standard three-drug regimens. But that was in clinical trials that often included the people most likely to be successful on two drugs: those for whom antiretroviral drugs or classes never stopped working, those with no previous resistance to any of the major drug classes and those with durably undetectable viral loads. That was the case in the major studies of Juluca and Dovato.

So Ramón Teira, of Hospital de Sierrallana in Spain, and colleagues decided to see how people with multiple chronic conditions and with all viral load levels did on two-drug regimens in the real world.

The researchers looked at a cohort of people living with HIV who received care at 23 sites around Spain, pulling data on 7,481 people who started or switched to a two-drug or three-drug regimen between January 2012 and June 2017. The three-drug regimens contained an integrase inhibitor plus two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), either tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) and emtricitabine or abacavir/lamivudine—for example, Stribild, Genvoya or Triumeq. The two-drug regimens contained dolutegravir or a boosted protease inhibitor plus one other drug—for example, Dovato, Juluca, boosted Prezista (darunavir) or Kaletra (lopinavir/ritonavir) plus lamivudine, Prezista or Kaletra plus Isentress (raltegravir), or Prezista plus Tivicay (dolutegravir).

Participants on triple therapy had a median age of 47 years, and three out of four of them were men; there was no mention of transgender participation. The cohort was a third gay or bisexual men (35%), a third people who inject drugs (34%) and nearly a third heterosexuals (29%). One

quarter had previously been diagnosed with AIDS, and participants had been living with HIV for a median of 12 years. Those taking a two-drug regimen were significantly older (a median of 50 years old), had been living with HIV for 15 years and were more likely to be women.

Notably, people on two-drug regimens were more likely to have had a diagnosis of AIDS (32% versus 25%), were more likely to use illicit drugs (40% versus 33%) and more likely to be living with hepatitis C (47% versus 39%). What's more, those switching to two-drug regimens had more previous ARV regimens under their belts (seven versus four) and had experienced twice as many virologic treatment failures (two versus one).

At the end of the analysis period, only 20% of all participants were put on a two-drug regimen. But those people were more likely to have had to switch away from their two-drug combos than their peers on triple regimens (31% versus 24%). What's more, they were twice as likely to switch because their two-drug regimen was unable to control their virus (14% in the two-drug arm versus 7% in the three-drug arm). The flip side was that four and a half times as many people switched from a triple combo to another three-drug regimen to avoid long-term toxicities compared with people taking a two-drug regimen (4.5% versus 1.0%). People on a three-drug regimen also stayed on the triple therapy longer.

Even after adjusting the odds of virologic failure for the differences between the groups, people taking a two-drug combo were still 29% more likely to discontinue their regimen for any reason. When the researchers narrowed it down to switches due to lack of effectiveness, people on a two-drug regimen were twice as likely to switch.

However, when participants started with an undetectable viral load and switched to a dolutegravir-containing combo, they were more likely to stay on their new regimen: 80% of those on a dolutegravir-based triple combo and 72% of those on a dolutegravir-based two-drug combo were still on their regimen at the end of the analysis period.

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