Simplified HIV Treatment Linked to Greater Inflammation

Two-drug antiretroviral regimens suppress viral load, but three-drug combos may offer additional benefits.

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Antiretroviral regimens containing two medications suppress HIV as well as standard three-drug combinations, but they may not be enough to prevent all the detrimental consequences of chronic HIV, a new study suggests.

Research presented at the International AIDS Conference, being held virtually this week, showed that people who switched from three to two drugs maintained viral suppression and were no more likely to experience serious non-AIDS health events or to die, but they did have higher levels of biomarkers linked to increased inflammation.

As they face a lifetime of treatment, many people living with HIV and their clinicians are interested in simpler regimens that could lower the likelihood of side effects and ease long-term adherence.

One such approach is antiretroviral regimens that contain two rather than the standard three drugs. Studies have shown that two-drug combos that include a potent integrase inhibitor or a boosted protease inhibitor can maintain viral suppression in people who switch from three-drug regimens, and some can be used as initial treatment. Two dual combos—Dovato (dolutegravir/lamivudine) and Juluca (dolutegravir/rilpivirine)—are available as single-tablet regimens. However, simplifying further to a single drug (known as monotherapy) is less effective.

Sergio Serrano-Villar, MD, PhD, of University Hospital Ramón y Cajal in Madrid, and colleagues evaluated the long-term consequences of switching from triple to dual regimens or protease inhibitor monotherapy. They looked at outcomes including virological treatment failure, clinical events and systemic inflammation.

Chronic HIV can lead to persistent inflammation even among people on effective treatment, and this has been linked to serious non-AIDS health problems including heart disease, non-AIDS-related cancers and severe kidney and liver disease.

This analysis included more than 8,400 people in the Spanish AIDS Research Network cohort who started antiretroviral treatment with a three-drug regimen between 2004 and 2018. More than

80% were men, the median age was 37, 12% were over 50 and about 12% had been diagnosed with AIDS.

Eligible participants who achieved viral suppression during the first 48 weeks on treatment either stayed on a three-drug regimen (7,665 people), switched to a two-drug regimen (424 people) or switched to monotherapy (327 people).

The two-drug regimens used were dolutegravir plus lamivudine, dolutegravir plus rilpivirine or a boosted protease inhibitor plus lamivudine. The single drug regimens consisted of a boosted protease inhibitor such as darunavir (Prezista or Prezcobix) or lopinavir/ritonavir (Kaletra).

The risk of virological failure (at least two viral load measurements above 50) did not differ significantly among the three groups during the first two years following treatment simplification. After two years, those on a two-drug regimen fared about equally well, but those who switched to monotherapy had a three-fold higher risk of treatment failure.

Because this cohort had an average age under 40 and started treatment in the era of effective therapy, the total number of serious non-AIDS events (cardiovascular disease or severe kidney or liver disease) and non-AIDS-related deaths was small, Serrano-Villar noted. In fact, there were only a few deaths from any cause in the two-drug and monotherapy groups.

After six months, people who switched to a two-drug regimen or monotherapy had a higher risk of serious non-AIDS events or non-AIDS death, but these differences did not reach the threshold for statistical significance, meaning they could have been due to chance. The risk of death from any cause likewise did not differ significantly among the three groups.

The study also looked at levels of the inflammation biomarkers interleukin 6 (IL-6) and C-reactive protein (CRP); D-dimer, a byproduct associated with blood clotting; and intestinal fatty-acid binding protein (IFABP), a protein released when the lining of the gut is damaged. HIV damages the gut lining starting at the earliest stages of infection.

The researchers analyzed blood samples from 180 participants with at least three available samples, of whom 90 were on three-drug regimens, 60 were on two-drug therapy and 30 were on monotherapy.

Compared with those who stayed on triple therapy, people who switched to two-drug regimens had significantly increased levels of IL-6, CRP and D-dimer starting around three years after achieving viral suppression. The effect did not appear to differ between those taking dolutegravir or protease inhibitors. Those who switched to monotherapy also showed more evidence of inflammation.

In this large cohort of people with viral suppression, single-drug HIV treatment was associated with a greater risk of virological failure, with no significant differences between those taking two or three medications, the researchers concluded. However, staying on three-drug treatment “was associated with a more favorable long-term anti-inflammatory profile” than switching to two drugs

or monotherapy.

“The potential clinical implications of these findings on the development of non-AIDS events deserve further investigation,” they recommended.

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