Another HIV Treatment Option—But With Less Weight Gain

South African study finds doravirine works as well as dolutegravir to suppress HIV viral load, enabling choice for those living with HIV.

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If you're a black, 34-year-old South African woman living with HIV, antiretroviral (ARV) treatment options have likely been limited to tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and the "gold standard" dolutegravir (DTG).

Now, another once-a-day, three-drug regimen has been found to be as effective as DTG in suppressing HIV viral load.

Not only is the once-daily regimen of TDF, 3TC and doravirine non-inferior to DTG, it is associated with significantly less weight gain and has a better lipid profile than the combination favored and recommended as first-line in many countries, and increasingly in low- and middle-income countries. [Editor's note: This three-drug combination is sold as a single-tablet regimen branded as Delstrigo in the United States, but generic versions are generally used in lower-income countries.]

These were the endpoint findings of the South African Opti-DOR study presented at the 2026 International AIDS Conference July 31 and published in the Journal of the American Medical Association (JAMA).

Dr. Joana Woods, senior research clinician at Ezintsha at the University of the Witwatersrand (Wits), and lead author, says, "The findings are important because although second-generation ARVs such as dolutegravir and bictegravir are highly effective HIV medicines, they have been consistently associated with substantial weight gain and new onset obesity, particularly among women and black populations and especially when combined with TAF [tenofovir alafenamide]. This has raised concern about long-term cardiometabolic risk, including diabetes and cardiovascular disease."

Why weight gain matters

Research consistently confirms that if you gain excess weight, it puts you at risk of diabetes, hypertension, cardiovascular disease, and other non-communicable diseases (NCDs).

In primary healthcare, prevention is better than having to deal with long term consequences. This is why in a country like South Africa with widespread HIV and NCDs, managing weight gain in people living with HIV is critical to their health.

“So if you can start an ARV that’s not going to cause as much weight gain, or not cause weight gain at all, or have an alternative, that would be first prize. And that’s the premise of this study,” says Woods.

About the Opti-DOR Study

The Africa Health Research Institute (AHRI) ran the rural arm of the Opti-DOR study at the AHRI-Somkhele site in rural northern KwaZulu-Natal province.

“By including participants from both rural KwaZulu-Natal and urban Gauteng, we can be confident that these findings are relevant to people living with HIV in different communities across South Africa,” says Professor Limakatso Lebina, principal investigator at the rural AHRI-Somkhele study and Director of Science at AHRI.

The AHRI site enrolled 178 participants between December 2023 and March 2025, with the Johannesburg site enrolling the rest, for a total of 600.

Participants were randomised in a 1:1 ratio to receive either oral daily doravirine/TDF/3TC (DOR/TDF/3TC) or dolutegravir/TAF/emtricitabine (DTGTAF/FTC).

Weight gain differed significantly between the two study groups. Median weight gain at week 48 was 3.0 kg [6.6 lb] with DOR/TDF/3TC compared with 5.0 kg [11.0 lb] with DTG/TAF/FTC. Increases in total body fat percentage were also significantly lower with DOR/TDF/3TC at 1.5%, versus 2.2%.

“These results add some clarity to a challenge that has frustrated both doctors and patients for years: how to treat HIV effectively without causing significant weight gain,” says Lebina. “For many patients, especially black women who are disproportionately affected by treatment-associated weight gain, this could be a game changer. It offers an important new treatment option that supports long-term health while maintaining excellent HIV control.”

Noninferior yet drug resistance risk

Woods emphasises that the efficacy of doravirine is dependent on patients’ absolute adherence to taking it. If doravirine is taken properly, HIV viral load will be suppressed. However, failure to adhere can cause drug resistance.

“Doravirine is noninferior to dolutegravir in the sense that if you take the drug properly, you will suppress it [HIV viral load]. If you don’t take it properly, you will likely become resistant. That unfortunately is one of the downsides of using doravirine.”

In the Opti-DOR clinical trial, seven patients developed resistance to the drug. These participants

were then switched over to dolutegravir and successfully suppressed [HIV] again.

Woods emphasises that doravirine is unlikely to be a replacement for DTG: “It is not a replacement. It has to be targeted to patients who are at risk of gaining more weight—and complications thereof.”

Despite drug resistance, the data prove that doravirine is not inferior to dolutegravir and that it causes less weight gain.

Research into action

Doravarine is already an available and registered drug.

The researchers have alerted the South African National Department of Health and the South African Health Products Regulatory Authority.

“Imagine you’re a diabetic and you only have access to one drug? It’s the same thing with HIV. Yes, the drug they have at the moment is really top of the tops, but it doesn’t suit everybody. You have to have options. Until we can cure HIV, you’ve got to make it as easy as possible for people to take their treatment. That’s what it comes down to.”

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