# Doravirine/Islatravir Combo Pill Works Well for First-Line HIV Treatment

The once-daily dual oral regimen is well tolerated and suppresses viral load as well as Biktarvy.

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An experimental single-tablet regimen containing doravirine and islatravir worked as well as a widely used combination pill for people starting HIV treatment for the first time, according to an announcement from Merck.

Top-line results from an ongoing Phase III clinical trial (MK-8591A-053; NCT05705349) showed that rates of viral suppression—defined as HIV RNA viral load below 50—were similar at 48 weeks in people randomly assigned to receive doravirine/islatravir or Gilead Sciences' Biktarvy (bictegravir/tenofovir alafenamide/emtricitabine). Safety profiles were also comparable.

"These data support the potential for this regimen to be a meaningful treatment option for virally suppressed people living with HIV who are looking to switch to a new regimen or people who have not previously been on antiretroviral therapy to start treatment," Merck senior vice president and chief medical officer Eliav Barr, MD, said in the news release.

Doravirine (sold alone as Pifeltro and part of the Delstrigo coformulation) is a next-generation non-nucleoside reverse transcriptase inhibitor (NNRTI) with a high barrier to resistance. Islatravir is Merck's first-in-class nucleoside reverse transcriptase translocation inhibitor. Development of islatravir hit a snag in 2021 when some participants in earlier trials experienced a decrease in their CD4 T-cell or total lymphocyte counts. But scientists determined that the doses used in these studies were too high, and this side effect has not been seen using the lower 0.25 milligram dose in the new combination pill.

Merck's recent announcement did not include details about the treatment-naive study population demographics, virological outcomes or tolerability, but noted that these findings will be presented at a future scientific meeting (possibly the Conference on Retroviruses and Opportunistic Infections in February 2026).

Merck plans to submit the new data for consideration by the Food and Drug Administration (FDA). The FDA has already accepted a New Drug Application for the doravirine/islatravir coformulation as a switch option for people with viral suppression on a stable antiretroviral regimen, with a target action date of April 28, 2026.

A pair of Phase III trials (MK-8591A-051; NCT05631093 and MK-8591A-052 (NCT05630755) showed that people who were randomized to switch from standard oral regimens to the doravirine/islatravir combination pill were as likely to maintain an undetectable viral load as those who stayed on their existing regimen. As reported at this year's Conference on Retroviruses and Opportunistic Infections, viral suppression rates exceeded 90% in all treatment arms at 48 weeks.

Further data from these trials, presented at this year's European AIDS Conference (EACS 2025), showed that doravirine/islatravir was associated with minimal changes in weight or body composition and had no clinically meaningful effect on lipid or blood sugar levels or insulin resistance.

In these studies, doravirine/islatravir was safe and generally well tolerated, and participants did not experience the kind of white blood cell declines that doomed higher doses of islatravir. Doravirine and islatravir are not active against hepatitis B virus (HBV), unlike tenofovir, emtricitabine or lamivudine in many other widely used antiretroviral regimens, so it may not be an appropriate option for people with HIV/HBV coinfection, and those who are HBV negative should be vaccinated.

Islatravir has a long half-life in the body, making it a potential candidate for longer-acting treatment. It has also shown good results as part of a once-weekly oral regimen in combination with Gilead's capsid inhibitor lenacapavir (Sunlenca); two-year Phase II data were presented at EACS 2025. An islatravir/lenacapavir fixed-dose combination pill is being tested as a switch option in the Phase III ISLEND-1 (NCT06630286) and ISLEND-2 (NCT06630299) trials, with initial results expected next Spring. Merck is also testing a once-weekly regimen of islatravir and its investigational NNRTI ulonivirine in a Phase II trial (MK-8591B-060; NCT06891066).

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