Merck’s Experimental HIV Drug Islatravir Proves Effective and Well Tolerated

This finding did not vary based on the dose of the nucleoside reverse transcriptase translocation inhibitor, formerly called MK-8591.

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Merck’s investigational antiretroviral (ARV) islatravir (formerly MK-8591) was safe and kept HIV fully suppressed regardless of the dose when paired with Pifeltro (doravirine) in a recent mid-stage trial. The two-drug regimen was also comparable in efficacy to Delstrigo (doravirine/ tenofovir disoproxil fumarate/lamivudine).

Islatravir is the first in a new class of ARVs, a nucleoside reverse transcriptase translocation inhibitor (NRTTI), to reach clinical trials. Merck is investigating it both as a treatment for HIV and for prevention of the virus. Pifeltro is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that was recently approved. Lamivudine belongs to the nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) class of ARVs.

Previous research has indicated that islatravir has at least a 10-fold greater potency over approved ARVs, meaning that a much lower dose can be used.

Jean-Michel Molina, MD, PhD, of the Hôpital Saint-Louis in Paris,presented findings from a randomized, double-blind, active comparator-controlled, dose-ranging Phase IIb trial of these three ARVs at the 10th International AIDS Society Conference on HIV Science in Mexico City (IAS 2019). The study evaluated the safety, tolerability and efficacy of islatravir in combination with Pifeltro therapy to which individuals with an undetectable viral load switch, known as maintenance therapy.

A separate small human trial presented at the conference suggested that an islatravir-infused implant likely has the potential to work as pre-exposure prophylaxis (PrEP) for an entire year before it needs replacing.

Molina’s study enrolled people with HIV who had not previously received ARVs and who had a viral load of at least 1,000 and a CD4 count of at least 200 upon enrolling in the study. Potential participants were excluded if they had hepatitis B or C viruses and if their HIV was drug resistant.

A total of 121 participants were randomized into four groups. They received either 0.25 milligrams (29 people), 0.75 mg (30 people) or 2.25 mg (31 people) of islatravir plus, for at least the first 24 weeks of the study, both Pifeltro and lamivudine. A fourth group (31 people) received Delstrigo along with a placebo tablet so that they were taking the same number of tablets that the other three groups took.

At the 24-week mark, those taking islatravir, Pifeltra and lamivudine who had a viral load below 50 were permitted to drop the lamivudine and thus switch to a two-drug regimen of islatravir plus Pifeltro.

The group that transitioned to the second 24 weeks of the study included 29 (100%) of the 0.25 mg group, 30 (100%) of the 0.75 mg group, 27 (87.1%) of the 2.25 mg group and 28 (90.3%) of the Delstrigo group. There were 48-week data about a respective 27 (93.1%), 29 (96.7%), 24 (77.4%) and 28 (83.9%) of each study group.

The participants had an average age of 28 years old. A total of 92.6% of them were male, 76.0% were white and 22.3% started the study with a viral load above 100,000.

At week 48, a respective 89.7% (26 of 29), 90.0% (27 of 30) and 77.4% (24 of 31) of those in the 0.25 mg, 0.75 mg and 2.25 mg of islatravir groups and 83.9% (26 of 31) of those in the Delstrigo group had a viral load below 50.A respective 6.9% (2 of 29), 6.7% (2 of 30), 12.9% (4 of 27) and 6.5 % (2 of 31) of the members of each group had a viral load of 50 or greater at this point.

None of the participants died. In the 0.25 mg, 0.75 mg and 2.25 mg of islatravir and Delstrigo groups, the respective proportions of participants experiencing drug-related nonserious adverse health events were zero percent (0 of 29), 10.0% (3 of 30), 12.9% (4 of 31) and 19.4% (6 of 31).

Two participants in the 2.25 mg group stopped treatment because of an adverse health event, one who had diarrhea, nausea and vomiting starting at day 200 of treatment and lasting for about two weeks and the other whose hep B reactivated starting at day 201 of treatment.

The researchers concluded that islatravir plus Pifeltro has the potential to be a potent two-ARV regimen and that a Phase III study is warranted.

To read the study abstract, click here.

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