Experimental Antiretroviral Has Potential for Once-Weekly HIV Treatment

MK-8507, a long-acting NNRTI, will be tested in a weekly regimen with islatravir.

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An experimental non-nucleoside reverse transcriptase inhibitor (NNRTI) from Merck, dubbed MK-8507, appears to keep HIV suppressed with weekly dosing, researchers reported at the virtual Glasgow HIV Drug Therapy conference. The long-acting NNRTI has the potential to be paired with islatravir for a once-weekly oral treatment.

Wendy Ankrom, MD, of Merck, and colleagues conducted a small Phase I clinical trial to evaluate single oral doses of MK-8507, which was previously shown to have high antiviral potency, a favorable safety profile and pharmacokinetics that make it suitable for once-weekly dosing.

The study included 18 previously untreated people with high viral loads (above 10,000) and no prior resistance to NNRTIs. All were white men, and the median age was about 35.

Participants received a single dose of 40, 80 or 600 milligrams of MK-8507 followed by a standard combination antiretroviral regimen. The two higher doses reduced viral load by about 1.5 log, with about a 1.2 log reduction in the low-dose group. HIV levels continued to decline for seven days after administration. None of the 14 participants who started standard therapy at this point experienced viral rebound.

One of the four people who delayed starting standard therapy until 14 days after their MK-8507 dose did experience a rebound and was found to have an NNRTI resistance mutation (F227C). The researchers concluded that emergence of this mutation after 10 days would not be clinically relevant in the context of weekly dosing of MK-8507 as part of a combination regimen.

MK-8507 was generally safe and well tolerated at all dose levels, with no notable changes in vital signs, electrocardiograms or lab tests.

In order to be used for once-weekly treatment, MK-8507 would have to be paired with other long-acting antiretrovirals. One possible partner is Merck's islatravir (formerly known as MK-8591 or EFdA), the first nucleoside reverse transcriptase translocation inhibitor.

Another study at the conference showed that a combination of once-daily islatravir plus the NNRTI Pifeltro (doravirine) demonstrated good efficacy for 96 weeks in a Phase IIb trial that included 121 previously untreated people. The study design and 48-week results were presented last year.

The updated 96-week results, presented by Jean-Michel Molina, MD, PhD, of the University of Paris, showed that 90.0% of people treated with the selected dose of islatravir (0.75 milligrams) plus Pifeltro had an undetectable viral load.

The combined efficacy for all three tested doses of islatravir was 81.1%, indicating that the new drug is noninferior to, or works at least as well as, the three-drug Delstrigo pill (doravirine/tenofovir disoproxil fumarate/lamivudine), which had 80.6% efficacy.

Islatravir continued to be safe and well tolerated at 96 weeks. Another presentation at the conference described the uncommon cases of virologic failure in more detail, and a third study showed that people taking islatravir plus Pifeltro did not see notable changes in kidney function.

Prior research showed that islatravir has a long half-life in the body, suggesting it has the potential to be used for once-weekly HIV treatment or pre-exposure prophylaxis (PrEP). What's more, an early study found that an islatravir implant delivered protective concentrations of the drug for more than a year.

Ankrom said that Merck plans to test the combination of MK-8507 plus islatravir as a once-weekly oral HIV treatment.

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