Islatravir Plus Pifeltro Shows Promise as 2-Drug HIV Regimen

A mid-stage trial showed the combo suppressed HIV, was well tolerated and resulted in a low rate of virologic failure.

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The experimental antiretroviral (ARV) islatravir plus Pifeltro (doravirine) suppressed HIV well, led to a low rate of virologic failure and was well tolerated in a recent mid-stage clinical trial, aidsmap reports.

If approved following late-stage trials now in the works, islatravir (formerly known as MK-8591 or EFdA) would be the first nucleoside reverse transcriptase translocation inhibitor to hit the market. Pifeltro is a non-nucleoside reverse transcriptase inhibitor.

Two researchers presented findings from the Phase IIb study comparing the two-drug regimen of islatravir plus Pifeltro to the three-drug regimen Delstrigo (doravirine/tenofovir disoproxil fumarate/lamivudine) at the International AIDS Conference (AIDS 2020), which is being held virtually this week.

Chloe Orkin, MBBCH, MSc, of Queen Mary University of London presented findings about the treatment's efficacy and rate of virologic failure, while Edwin DeJesus, MD, of the Orlando Immunology Center in Florida presented safety findings.

The randomized, double-blind trial enrolled 121 people with HIV who had not previously taken treatment for the virus and had no known resistance to ARVs.

More than 9 out of 10 of the participants were men, and three out of four were white. The median age was 28. About one in four had a viral load higher than 100,000 when they entered the study.

The study had two parts. In part one, the participants were randomized to receive islatravir at either 0.25 milligrams, 0.75 mg or 2.25 mg plus 100 mg of Pifeltro and 300 mg of lamivudine or to receive Delstrigo. Twenty-four weeks later, in part two, those who received islatravir and who had an undetectable viral load (below 50) stopped taking lamivudine and kept taking the remaining two-drug regimen of islatravir plus Pifeltro for another 24 weeks.

Findings presented at the 2019 International AIDS Society Conference on HIV Science in Mexico

City indicated that 90% of those who took 0.75 mg of islatravir—the dose that will continue on to Phase III trials—had a fully suppressed viral load at the trial's 48-week mark, compared with 84% of those on the three-drug regimen. These rates were considered comparable.

Orkin's presentation at AIDS 2020 focused on cases of virologic failure, which the study defined as either having a nonresponse to treatment or a viral rebound. A nonresponse was defined as having a viral load of 200 or higher at any time during part two of the study or a viral load of 50 or higher at week 48 confirmed by a second test taken within two weeks. Viral rebound was defined in one of two ways: having a viral load of 50 or higher after having achieved an undetectable viral load, or experiencing a greater than tenfold increase in viral load after experiencing at least a tenfold decrease from the viral load seen at the start of the study.

People with virologic failure had to stop the study and return to a standard ARV regimen.

Six people experienced virologic failure. Viral rebound occurred in two people (7%) in the 0.25 mg islatravir group, two people (7%) in the 0.75 mg group and one person (3%) in the Delstrigo group. One person (3%) in the 2.25 mg group experienced nonresponse to treatment.

The viral load in all these people, once suppressed by treatment, remained under 100, which is below the threshold of 200 that would make such a viral load "clinically significant" according to the study's authors.

After those who experienced virologic failure switched to another regimen, three continued to have a low-level detectable viral load during the 42 weeks they were followed.

A separate recent study published in Clinical Infectious Diseases found that maintaining a low-level detectable viral load—between 50 and 999—was associated with worse health outcomes as well as a higher risk of death.

At AIDS 2020, DeJesus presented the safety findings about the islatravir plus Pifeltro versus Delstrigo regimens.

Both regimens proved safe and well tolerated. Side effect rates were similar between the two main study groups.

During the first 24 weeks of the study, five people (6%) in the islatravir groups and six people (19%) in the Delstrigo group reported any drug-related adverse health events. During the second period, a respective three people (4%) and one person (4%) reported such health events. Two people (2%) in the islatravir group and one person (4%) in the Delstrigo group stopped treatment due to adverse health events.

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