New NNRTI RDEA806 Shows Promise in Seven-Day Study

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An experimental non-nucleoside reverse transcriptase inhibitor (NNRTI), currently dubbed RDEA806 by its developer Ardea Biosciences in San Diego, appeared to have robust antiviral activity and a favorable safety profile in a Phase II study reported at the XVII International AIDS Conference (IAC) in Mexico City. Results from the trial, involving HIV-positive patients starting treatment for the first time who took the NNRTI without other antiretrovirals (ARVs), were reported August 7 by Graeme Moyle, MD, of Chelsea and Westminster Hospital in London.

According to Dr. Moyle, test tube studies show that RDEA806 is a potent NNRTI that has very little impact on the enzyme system responsible for metabolizing many ARVs, thus greatly reducing the risk of negative interactions with many medications.

RDEA806 also appears to have a high barrier to resistance. In test tube studies, it took about 400 days for HIV—both drug-sensitive "wild-type" virus and HIV with the K103N mutation in its reverse transcriptase gene that confers resistance to Sustiva—to develop high-level resistance to the drug when tested without other ARVs. Moyle demonstrated that this is twice as long as it takes wild-type virus to develop resistance to Sustiva in test tube studies.

In studies involving HIV-negative subjects, RDEA806 was well tolerated at single doses up to 800 mg, as well as multiple doses up to 1000 mg/day for two weeks. No evidence of central nervous system side effects or rash were seen in these studies. There was also evidence that cholesterol and triglyceride levels decreased in these HIV-negative volunteers.

The study reported at IAC by Moyle randomized 48 patients to seven days of treatment with either RDEA806 or placebo. Nine patients took a capsule version of the drug at a dose of 400 mg twice daily, without food. Nine also took a capsule version, but at a 600 mg once-daily dose without food. A third group of nine patients took an enteric-coated (EC) tablet version of the drug—designed to release the drug slowly—at a dose of 800 mg once daily, with food. A fourth group of nine patients took EC tablets, using a 1,000 mg dose, once daily without food. There was also a placebo group consisting of 12 patients.

All patients enrolled were male, either starting treatment for the first time or off treatment for at least 14 days.

On day eight of the study, viral loads dropped, on average, by 1.3 log in the 600 mg capsule group to 1.8 log in the 400 mg capsule and two EC tablet groups. There was a 0.2 log drop in the placebo group.

While no statistical comparisons were made, the most pronounced viral load reduction appeared to be in the 800 mg EC tablet group—100 percent of the patients saw their viral loads drop by at least 1 log, and 67 percent had viral loads below 400 copies on day eight.

No serious side effects were documented, Moyle reported. Side effects were generally mild, including one report of back pain, one report of diarrhea, two reports of headache, one report of difficulty sleeping and one report of itchy skin (pruritis).

There were no reports of central nervous system problems or rash. Nor were there any apparent effects of lipid levels.

Moyle concluded by saying that RDEA806 was “well tolerated with robust antiviral effect across all doses.” He added that a second Phase II study is planned to compare multiple once-daily doses in additional groups of HIV-positive patients starting therapy for the first time.
