Isentress, Intelence, Prezista Regimen Goes the Distance for HIV Treatment Veterans

February 2, 2012

A drug regimen containing Isentress (raltegravir), Intelence (etravirine) and Norvir (ritonavir)–boosted Prezista (darunavir) has been shown to be "highly potent and durable in terms of efficacy and safety" in a French clinical trial involving heavily treatment-experienced people living with HIV. According to the research paper published ahead of print by the Journal of Acquired Immune Deficiency Syndromes (JAIDS), 88 percent of those using this regimen had undetectable viral loads after nearly two years of treatment.

The arrivals of Isentress, Intelence and Prezista—approved by the U.S. Food and Drug Administration in 2007, 2008 and 2006, respectively—were considerable milestones in our ability to treat people living with HIV resistant to many of the longstanding antiretroviral (ARV) options. Isentress was the first of the new class of integrase inhibitors, whereas Intelence, a non-nucleoside reverse transcriptase inhibitor (NNRTI) and Prezista, a protease inhibitor (PI), showed early promise against HIV with mutations conferring resistance to other members of their respective drug classes.

Because these compounds were being evaluated in clinical trials around the same time, studies evaluating the use of all three agents together were not possible. However, because these drugs each demonstrated effectiveness against HIV resistant to older ARVs, they were expected to perform well when used together.

Early results from a French study were highly encouraging. Preliminary 48-week data from the Agence Nationale de Recherches sur le Sida et les Hépatites Virales (ANRS) 139 TRIO study, testing all three drugs in combination with other ARVs as needed, found that 86 percent of heavily treatment-experienced people using the regimen had undetectable viral loads—a degree of success similar to that expected in first-time treatment takers receiving standard ARV drug combinations.

The final 96-week follow-up data from TRIO have now been published by Catherine Fagard, MD, and her colleagues by JAIDS. The results are similar to those reported in 2011 at the 18th Conference on Retroviruses and Opportunistic Infections in Boston.

The study enrolled 103 HIV-positive patients to take Isentress, Intelence and Norvir-boosted Prezista with an optional background regimen of nucleoside reverse transcriptase inhibitors

(NRTIs) with or without Fuzeon (enfuvirtide). Researchers continued to follow 100 study volunteers for 96 weeks.

Eighty-eight percent of the participants were male, and the average age was 45. The average viral load upon entering the study was 16,000 copies, and the average CD4 cell count was 258. Volunteers had been on ARV treatment for an average of 13 years, and about 40 percent had a CD4 count below 200 upon entering the trial.

As for pre-treatment resistance profiles, patients in TRIO had an average of four major PI mutations, five major NRTI mutations and one major NNRTI mutation in their HIV, which was evidence of significant drug resistance. In addition, 96 percent and 65 percent of participants had between one and three HIV mutations conferring at least partial resistance to Prezista and Intelence, respectively. The authors also reported that 59 percent of the patients were using a background regimen that didn't contain any ARVs that were fully active against their HIV.

Yet the results after nearly two years are remarkable. According to Fagard and her colleagues, 88 percent of the 100 patients enrolled in the study had viral loads below 50 copies per milliliter (ml) at the 96-week time point.

Though 19 people in the study had two repeated episodes of detectable viral load—changes to the background drugs used with the TRIO regimen were made in five cases—14 of these patients had undetectable viral loads at 96 weeks.

Fagard and her colleagues also observed an average CD4 count increase of 110 cells after 96 weeks. What's more, the proportion of patients with CD4 counts below 200 decreased from 40 percent at study entry to 16 percent at the 96-week mark.

The regimens containing Isentress, Intelence and Norvir-boosted Prezista were generally well tolerated. Moderate-to-severe abnormalities in lab results were reported in 25 people, usually during the first 48 weeks of treatment, none of which required discontinuing treatment.

Fagard's group reported that lipid levels, notably triglyceride and cholesterol levels, remained largely unchanged over the entire study period.

Clinical side effects were reported in 93 percent of the study participants, mostly during the first year of the study. Twenty-six patients experienced moderate-to-severe side effects, but only four of these were believed to be related to the treatment regimen. One patient with a rash and fever discontinued treatment.

"This study confirms that in treatment-experienced patients, an antiretroviral regimen containing raltegravir, etravirine and darunavir/ritonavir showed high efficacy, with a good safety profile," Fagard's team concludes. "Long-term efficacy in this population appeared to be as high as that reported for treatment-naive patients receiving either PI-containing regimens associated with NRTIs or combinations containing new antiretroviral drugs, such as raltegravir."

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