After 2 Years, Drug Regimen Works Well Among Treatment-Experienced

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A drug regimen containing Isentress (raltegravir), Intelence (etravirine) and Norvir (ritonavir)–boosted Prezista (darunavir) continues to work well in a French clinical trial involving heavily treatment-experienced people living with HIV. About 88 percent of those using this potent regimen active against drug-resistant virus have undetectable viral loads after nearly two years of treatment, reported researchers on Wednesday, March 2, at the 18th Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

Isentress, Intelence and Prezista are three of the newest antiretrovirals (ARVs), initially approved specifically for treatment-experienced people living with HIV. Because these compounds—an integrase inhibitor, a non-nucleoside reverse transcriptase inhibitor (NNRTI) and a protease inhibitor (PI), respectively—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.

Only recently have researchers begun to understand exactly how much these drugs—especially when used in combination with each other—have to offer patients with a great deal of previous treatment experience under their belts.

Results thus far have been encouraging. Forty-eight 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 patients 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 96-week follow-up data from TRIO were reported in Boston by Catherine Fagard, MD.

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 patients 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 254. Patients had been on ARV treatment for an average of 13 years.

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 patients 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, 88 percent of the 100 patients who continued in the study had viral loads below 50 copies per milliliter (ml) at the 96-week time point. Though 19 patients 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 180 cells after 96 weeks.

The regimens containing Isentress, Intelence and Norvir-boosted Prezista were generally well tolerated, according the 24- and 48-week data reported previously. Serious adverse effects were reported in 15 patients, but only four of these were believed to be related to the treatment regimen. One patient with a rash and fever discontinued treatment.

Significant increases in creatinine levels—a sign of muscle damage—were noted in 11 patients, and in four patients, sharp increases in the liver enzyme GGT were reported. However, none of these individuals has discontinued treatment.
As for lipid levels, Fagard reported that triglyceride and cholesterol levels remained unchanged over the entire study period.
The Isentress, Intelence and Norvir-boosted Prezista combination, Fagard's group concluded, "is highly efficacious and safe over at least two years of continuous treatment. Virologic failure was rare and occurred at low level viremia. Only one patient stopped a study drug [Isentress, due to severe skin rash], and this was during the first 48 weeks of the study. Clinical events were mild in general, and no serious adverse event reported during the extended follow-up was related to study drugs. This new potent antiretroviral combination [should] become a standard of care in treatment-experienced patients."
