Five-Year Follow-Up: Isentress Comparable to Sustiva

July 21, 2011 By Tim Horn

Merck's integrase inhibitor Isentress (raltegravir) works just as well as mainstay therapy efavirenz (found in Sustiva and Atripla) in HIV-positive individuals starting treatment for the first time, according to final five-year follow-up results from a Phase II clinical trial. These encouraging results were reported Wednesday, July 20, by Eduardo Gotuzzo, MD, of the Hospital Nacional Cayetano Heredia in Lima, Peru, and his colleagues at the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention in Rome.

Isentress was originally approved for treatment-experienced people living with HIV. In July 2009, however, the U.S. Food and Drug Administration allowed its use in patients beginning HIV treatment for the first time.

Isentress and efavirenz—particularly when efavirenz is taken as Atripla, which also contains tenofovir and emtricitabine—are both "preferred" antiretrovirals (ARVs) for people living with HIV starting therapy for the first time, according to guidelines maintained by the U.S. Department of Health and Human Services.

Gotuzzo's group enrolled 198 HIV-positive people starting treatment for the first time to receive either Isentress at one of the six doses—explored in the first 48 weeks of the study, with all participants in the Isentress group then switching to 400 milligrams (mg) twice daily—or 600 mg Sustiva once daily. All patients in the study also received Viread (tenofovir) and Epivir (lamivudine).

Upon entering the study, the average viral load was 55,000 copies in the Isentress group and 67,000 in the Sustiva group.

After 240 weeks of therapy—about five years—nearly 69 percent of people in the Isentress group maintained viral loads below 50 copies/mL. In the Sustiva group, about 63 percent of patients maintained viral loads below 50 copies/mL. This difference was not statistically significant, meaning that the variation could have been due to chance.

CD4 counts, averaging 305 cells in the Isentress group and 280 cells in the Sustiva group at the start of the study, increased in all participants after 240 weeks of treatment. Among those in the Isentress group, CD4 counts increased by 301 cells. In the Sustiva group, CD4 counts increased by 275 cells. As with the viral load results, this minute difference was not statistically significant.

Ten patients (6 percent) in the Isentress groups and five patients (13 percent) in the Sustiva group experienced virologic failure while in the study, defined as either a viral load that failed to go undetectable by week 24 or a viral load rebound after an initial undetectable result. Only three of the virologic failures noted in the Isentress group occurred in the two final years of the study.

Gotuzzo reported that side effects were lower among those receiving Isentress compared with Sustiva. Overall, 55 percent of those in the Isentress group experienced a drug-related adverse event, compared with 76 percent of those in the Sustiva group.

Diarrhea, nausea, dizziness and headache were documented in both groups of participants, with headaches being more common among those receiving Sustiva (24 percent versus 9 percent). Neuropsychiatric adverse events—such as abnormal dreams, depression and suicidal thoughts—were, not surprisingly, less common among those in the Isentress group compared with those in the Sustiva group.

As for lipid levels, total cholesterol increased by 11.7 milligrams per deciliter (mg/dL) in the Isentress group, compared with a 26.4 mg/dL increase in the Sustiva group. This difference was statistically significant, meaning that it was too great to have occurred by chance.

“Good” HDL cholesterol was higher among those receiving Sustiva compared with those in the Isentress group (14.2 versus 7.4 mg/dL), also a statistically significant difference.

Moderate increases in “bad” LDL cholesterol and triglycerides were reported in both groups, with no statistically significant differences between the groups.

In the final five-year analysis of first-time treatment takers, Gotuzzo reiterated in his concluding remarks, Isentress with Truvada had durable efficacy with few late virologic failures. The regimen was generally well-tolerated during long-term therapy, with fewer drug-related side effects than efavirenz, and minimal effects on lipid levels.
