Similar Efficacy, Better Triglycerides with Invirase vs. Kaletra

October 26, 2007 By Tim Horn

Final 48-week results from a clinical trial comparing Norvir (ritonavir)-boosted Invirase (saquinavir) to Kaletra (lopinavir/ritonavir) conclude that, among HIV-positive patients starting treatment for the first time, both protease inhibitors are comparable. Additional data from the GEMINI study, reported this week at the 11th European AIDS Conference (EACS) in Madrid, suggest that Norvir/Invirase may be less likely to increase triglycerides than Kaletra.

The GEMINI study was a Phase III clinical trial designed to compare twice-daily doses of Kaletra and Norvir-boosted Invirase, both combined with Truvada (tenofovir plus emtricitabine) in 337 HIV-positive people starting HIV treatment for the first time. The primary goal of the trial is to assess the number of patients with viral loads below 50 after 48 weeks of treatment.

The final results were reported in Madrid by Sharon Walmsley, MD, associate professor of medicine at the University of Toronto and her colleagues. The final data follow on the heels of 24-week data reported at the fourth IAS Conference on HIV Pathogenesis, Treatment and Prevention this past summer in Sydney.

After 48 weeks of treatment, 63.5 percent of patients in the Kaletra group had viral loads below 50, compared with 64.7 percent of patients taking Norvir-boosted Invirase. The difference between the two groups was not statistically significant, meaning it could have been due to chance.

CD4 count increases were also similar between the two groups, with gains of 178 cells seen in the Norvir/Invirase group and 204 cells in the Kaletra group—again, indicating no statistically significant difference.

Dr. Walmsley reported that there were eleven virologic failures—defined as incomplete viral suppression—in the Norvir/Invirase group and five virologic failures in the Kaletra group. However, this difference was not statistically significant.

Five of the Norvir/Invirase-treated patients started therapy with a at least one HIV mutation conferring resistance to protease inhibitors, compared to no PI mutations in the Kaletra group. The most common mutation to arise during therapy with either Norvir/Invirase or Kaletra was M184V in HIV's reverse transcriptase enzyme, which causes high-level resistance to the emtricitabine in Truvada (and lamivudine in Epivir, Combivir, and Trizivir). Only one new mutation in the protease enzyme was documented in the study, occurring in a patient receiving Norvir/Invirase.

Dr. Walmsley indicated that poor adherence was likely to blame for several of the Norvir/Invirase failures.

Dr. Walmsley also noted that 48 weeks of Norvir-boosted Invirase therapy was associated with better triglyceride results. Approximately 1.9 percent of patients in the Norvir/Invirase group had triglyceride levels two times the upper limit of normal upon entering the study. After 48 weeks, the rate dropped to 1.4 percent. Among those in the Kaletra group, 2.4 percent had elevated triglyceride levels at the start of the study and 9 percent had elevated levels after 48 weeks.

As for cholesterol, the proportion of patients with elevated total cholesterol levels after 48 weeks was 31 percent in the Norvir/Invirase group and 39 percent in the Kaletra group. Rates of elevated "bad" LDL cholesterol, however, were higher in the Norvir/Invirase group compared to those in the Kaletra group after 48 weeks (34 vs. 24 percent).

The researchers also said there were fewer cases of diarrhea among those treated with Norvir-boosted Invirase (17 percent) compared with those taking Kaletra (27 percent). It is worth noting, however, that most patients in the Kaletra group began therapy using the older gel-cap formulation of the drug, which is known to have a more pronounced effect on the gastrointestinal tract than the current tablet version of the medication.

Dr. Walmsley noted, "These data are of considerable importance because they confirm that Invirase offers treatment-naïve patients an effective treatment to control the virus with significantly smaller increases in triglyceride levels than lopinavir, the most commonly prescribed PI."
