Kaletra-to-Isentress Switch Helps Lipids, but With Viral Rebound Risk

February 9, 2009 By Tim Horn

Patients with undetectable viral loads—but struggling with elevated lipids—while on a Kaletra (lopinavir and ritonavir)-based regimen are likely to see marked improvements in their cholesterol and triglyceride levels upon swapping Kaletra for Isentress (raltegravir), but they may be less likely to keep their viral loads below 50 copies. This was the joint finding of the halted SWITCHMRK 1 and 2 studies, reported by Joe Eron, MD, of the University of North Carolina in Chapel Hill and his colleagues on Monday, February 9, at the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal.

Another study reported on Monday by a team of French researchers indicates that treatment-experienced patients switching from Fuzeon (enfuvirtide) to Isentress were no more likely to see rebounds in their viral loads, compared with those remaining on Fuzeon.

The SWITCHMRK clinical trials, also known as Merck-sponsored studies 032 and 033, were designed to evaluate the safety and effectiveness of switching to integrase inhibitor Isentress in patients with well-controlled HIV—defined as a viral load below 50 copies—while on a Kaletra-based regimen. In these trials, 348 patients in study 032 and 354 patients in study 033 were randomized to either remain on their Kaletra-based regimen or switch to Isentress (400 mg twice daily) in combination with their other antiretrovirals.

The major objectives, or endpoints, of the studies included changes in fasting lipids—including total cholesterol, triglycerides and “bad” non-HDL and LDL levels—at week 12, as well as the proportion of patients with viral loads below 50 copies at week 24. If the percentage of patients with viral loads below 50 copies was similar in both groups, Isentress would be considered “non-inferior” to, or statistically no worse than, Kaletra, according to the particular study designs chosen for SWITCHMRK 1 and 2.

Not surprisingly, patients who switched to Isentress experienced significant decreases in cholesterol, triglycerides and non-HDL levels in both studies. In SWITCHMRK 1, for example, non-HDL levels—total cholesterol minus any good HDL cholesterol in a blood sample—at study entry were 158 milligrams per deciliter (mg/dL) in the Kaletra group and 166 mg/dL in the Isentress group. After 12 weeks, non-HDL cholesterol increased by 2 percent in the Kaletra group but decreased by 15 percent in the Isentress group.

Switching to Isentress also had a profound effect on triglyceride levels. In SWITCHMRK 2, triglycerides averaged 219 mg/dL in the Kaletra group and 210 mg/dL in the Isentress group at study entry. After 12 weeks, levels increased by 8 percent in the Kaletra group, but fell by about 42 percent in the Isentress group.

Isentress did not, however, demonstrate non-inferiority with respect to maintaining viral load suppression. In the SWITCHMRK 1 study, 87.4 percent of patients who continued on Kaletra maintained viral loads below 50 copies for 24 weeks, compared with 80.8 percent of patients in the Isentress group. In the SWITCHMRK 2 study, 93.8 percent of patients who continued on Kaletra maintained viral loads below 50, compared with 88 percent in the Isentress group.

An analysis combining data from both studies found that 94 percent of patients in the Kaletra groups, compared with 88 percent of patients in the Isentress groups, had viral loads below 50 copies at week 24.

Merck has halted SWITCHMRK 1 and 2 based on these results and is currently conducting a thorough analysis of both studies to better understand the results.

A possible reason for the somewhat poorer viral load control in the Isentress group, Eron explained, may be due to the fact that many patients in the studies who had viral load rebounds were treatment experienced. Twenty-seven of the 32 patients (84 percent) who saw their viral loads rebound after switching to Isentress in SWITCHMRK 1 and 2 had been on other regimens before initiating Kaletra. In fact, 18 (66 percent) of these patients reported a history of virologic failure—possibly due to the emergence of drug-resistant virus—on earlier regimens.

A similarly designed study involving highly treatment-experienced patients, presented at CROI by Nathalie de Castro, MD, of the St.-Louis Hospital in Paris and her French colleagues, explored the safety and effectiveness of switching off Fuzeon—an injectable fusion inhibitor—to the easier-to-take Isentress. In this clinical trial, dubbed INSERT SC10, switching to Isentress was associated with non-inferior antiviral activity—only one patient in each group experienced virologic failure during the 24-week study.

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