Switching From Kaletra to Isentress: Benefits and Hazards

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Switching from Kaletra (lopinavir plus ritonavir) to Isentress (raltegravir) when viral load is undetectable might help reduce elevated cholesterol and triglyceride (lipid) levels, but it might also raise the risk of losing control of the virus, according to two studies published online January 13 in *The Lancet* and reported by MedPage Today.

The studies, SWITCHMRK 1 and 2, were originally presented February 2009 at the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal. A total of 702 people living with HIV who were on a stable Kaletra regimen and had less than 50 copies of HIV were randomized to either stay on Kaletra or switch to Isentress. The participants kept the rest of their regimen as is. The studies included a mix of people using Kaletra as a component of their first treatment regimen and individuals using Kaletra in a new regimen after previously experiencing treatment failure.

The studies' primary aim were to determine whether Isentress maintained undetectable virus levels and had fewer side effects, compared with continued Kaletra therapy, for 24 weeks. If Isentress were statistically equivalent to Kaletra in terms of viral suppression, it would be considered "non-inferior." The studies were originally slated to continue for 48 weeks.

In both studies, people who switched to Isentress were more likely to see virus levels creep back up, called virological failure. When the results of both studies were combined, 90.6 percent of those who stayed on Kaletra maintained an undetectable viral load, compared with just 84.4 percent of those who switched to Isentress. The difference between Kaletra and Isentress in terms of virological failure meant Isentress did not meet the goal of non-inferiority. For this reason, the trials were halted after 24 weeks.

Those on Isentress did, however, see significant reductions in harmful lipids, including cholesterol and triglycerides.

When the researchers reanalyzed the efficacy data and excluded people who had a history of previous treatment failure, people who switched to Isentress were about as likely as people who stayed on Kaletra to maintain an undetectable viral load: 89 percent for those on Isentress compared with 90 percent for those on Kaletra. In other words, most people who start HIV therapy for the first time with a regimen containing Kaletra and maintain an undetectable viral load can switch to Isentress.

In an accompanying editorial in The Lancet, J. Michael Kirby, MD, from the Medical University of South Carolina in Charleston, predicted the results “will probably generate some debate and controversy.” He added that the results are “a reminder that…even our most promising antiretroviral agents should be used in combination with two or more fully active drugs.”
