NRTI Resistance May Blunt PI-to-Isentress Switch Effectiveness

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HIV-positive individuals with a history of nucleoside reverse transcriptase inhibitor (NRTI) resistance may be more likely to experience viral load rebounds upon switching to Isentress (raltegravir) from a protease inhibitor (PI), according to new data reported at the International HIV and Hepatitis Drug Resistance Workshop earlier this month in Dubrovnik, Croatia.

The study results, summarized by the National AIDS Treatment Advocacy Project (NATAP), may clarify data from the SWITCHMRK trials, in which people replacing Kaletra (lopinavir/ritonavir) with Isentress had a higher 24-week failure rate than people who continued Kaletra.

Archived NRTI mutations, NATAP explains, would put Merck's integrase inhibitor Isentress at a disadvantage in the study because it has a lower barrier to resistance than Kaletra and because everyone who entered the trials had controlled HIV with PIs plus NRTIs.

In the study reported in Dubrovnik, Vincent Soriano, MD, and his colleagues at Madrid's Carlos III Hospital randomized more than 200 patients, all of whom had an undetectable viral load for at least 24 weeks, to receive either once- or twice-daily Isentress.

According to NATAP's report, 13 people (6 percent) experienced virologic failure within 24 weeks of switching from the PI to Isentress, including 12 in the once-daily Isentress group and one in the twice-daily group (this difference, however, was not statistically significant).

Twelve of 13 people with virologic failure had prior NRTI resistance—and only one person with virologic failure had no record of NRTI resistance—a difference that was statistically significant, meaning too great to have occurred by chance.

In an analysis conducted by the researcher, prior NRTI resistance raised the risk of Isentress failure more than 28 times.

The new study is not definitive, NATAP warns, because there was no control group in the study involving patients who continued their PI, similar to the SWITCHMRK design.

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