Drug Resistance Shouldn't Preclude Using NRTIs in an HIV Salvage Regimen

February 1, 2011

People with heavily drug-resistant HIV benefit from adding two nucleoside reverse transcriptase inhibitors (NRTIs) to a regimen that contains Isentress (raltegravir), even if their virus is partially or fully resistant to the NRTIs. These data were published online January 28 in the *Journal of Acquired Immune Deficiency Syndromes*.

Constructing effective new antiretroviral (ARV) regimens for people with significant HIV drug resistance often involves at least some guess work, and this is particularly true when deciding whether to add NRTIs when drug-resistance testing suggests they may not work. There have been hints that using the drugs despite the resistance does add some additional HIV-fighting power to the regimen, in part due to the fact that the drug-resistance mutations they're associated with may retard HIV's ability to reproduce. This theory, however, has not been well studied. This means that providers and their patients must make a difficult choice with limited information: Do they add two additional drugs—both of which are expensive and might cause additional side effects—without knowing for sure whether the meds will add any benefit?

To shed more light on the subject, Alexandra Scherrer, MSc, from the University of Zurich in Switzerland, and her colleagues analyzed data collected as part of the Swiss HIV Cohort. They found 118 people who had started a new regimen containing Isentress and who added either zero, one or two NRTIs to that regimen. Scherrer's team only included individuals who had full genotypic resistance results from before starting the new regimen and who had viral load results 24 weeks after beginning treatment.

Scherrer and her colleagues compared the individuals who added only zero or one NRTI—combined because the two groups were similar in characteristics and treatment outcomes—with people who added two NRTIs. Both groups were further broken down by whether their genotypic resistance results indicated that they had no resistance, partial resistance or full resistance to any NRTIs included in the regimen.

Given the limitations of the study design—people were not randomly assigned to the various groups, and the groups differed in some key respects—Scherrer's team used a variety of statistical methods to strengthen their analysis.

Overall, the team found that the NRTIs did contribute to the likelihood that people would have

undetectable viral loads 24 weeks after starting therapy, even when they had partial or full resistance to the NRTIs in the regimen. In fact, based on two types of analysis, those who added two NRTIs actually did somewhat better than those who used one or zero NRTIs, and the results held up even if a person's HIV was partially or fully resistant to the NRTIs. What's more, people who added two NRTIs to their regimen got their virus under control faster than those who added fewer NRTIs.

"Our study supports the strategy to administer two NRTIs in salvage therapy with [Isentress] even if inactive or only partially active according to [genotypic testing]," state the authors. "The negative impact on viral fitness by maintaining drug resistance mutations and the residual activity of NRTIs must not be underestimated."

The authors further state, however, that the risk of additional side effects must still be considered, as should the cost of the additional drugs when used in resource poor settings. "Further studies and collaborations are needed to support our findings and to analyze the long-term benefit of partially active or inactive NRTIs," they conclude.
