Study Suggests Genetic Tests Could Predict HIV Drug Side Effects

January 3, 2011

A new study published in the January 15 issue of *The Journal of Infectious Diseases* suggests genetic testing might help predict whether a person will have side effects from some HIV drugs. This could allow people to avoid those drugs or at least take them with greater caution.

Previous studies have found that side effects can result in switching meds or discontinuing treatment in up to 45 percent of people starting HIV therapy for the first time. Thus far, however, researchers have found only one form of a gene (an allele) conclusively responsible for side effects: The HLA-B5701 allele, which causes people to have a hypersensitivity reaction to abacavir (found in Ziagen and Epzicom).

Other alleles have been linked to changes in drug blood levels or increased side effect risks for other HIV medications, but the influence of these alleles isn't as predictable as that of the HLA-B5701 allele.

To determine whether other alleles might predict poor tolerability to drugs other than abacavir, Rubin Lubomirov, MD, PhD, from the University of Lausanne in Switzerland, and his colleagues analyzed data from 577 people enrolled in the Swiss HIV Cohort study. All of the people were starting HIV treatment for the first time.

The specific drugs they studied were abacavir, tenofovir (found in Viread, Truvada and Atripla), efavirenz (found in Sustiva and Atripla), Kaletra (which contains lopinavir and ritonavir) and Norvir (ritonavir)–boosted Reyataz (atazanavir).

Based on data linking alleles to side effects or drug level changes in previous studies, Lubomirov and his colleagues tested collected blood samples for 23 alleles in 15 genes.

The only significant genetic switch not included was the HLA-B5701 allele, because all people who took abacavir had already been tested for the allele and only those without it were allowed to take abacavir. With some drugs, the researchers looked at whether a single allele affected a drug's tolerability, and with other drugs, Lubomirov's team looked at the combined effect of several alleles.

The team did not directly assess the effect of certain alleles on specific side effects. They focused

only on whether the alleles predicted dose adjustments or treatment discontinuation (though the most common reason for switching treatment in the study was side effects).

The team found that the presence of drug-specific alleles was highly predictive of a switch from efavirenz or Reyataz, but not for the other drugs.

Lubomirov's group found that 71 percent of people with alleles in the CYP2B6 gene combined with secondary alleles to other genes had to switch off efavirenz or change the dose of the drug compared with only 28 percent of those who did not have the alleles. The risk was even higher in women.

Likewise, Lubomirov and his colleagues found that 62 percent of people with a double substitution in the UGT1A1 gene had to change or discontinue Reyataz, compared with 24 percent with a single substitution and only 15 percent with no substitutions.

"The study suggests that assessment of the genetic markers could lead to improved prescription of atazanavir and efavirenz," the authors state. They conclude that "a prospective clinical trial should ideally formalize the analysis and provide the basis for measuring the cost effectiveness of this approach."

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