Reactions to HIV drug have autoimmune cause, reports AIDS journal

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Potentially severe hypersensitivity reactions to the anti-HIV drug abacavir occur through an autoimmune mechanism, resulting from the creation of drug-induced immunogens that are attacked by the body's immune system, according to a study published online by the journal AIDS, official journal of the International AIDS Society.

The study is the first to explain how hypersensitivity reactions to abacavir develop in genetically predisposed patients—and suggests that similar autoimmune mechanisms might account for other types of drug reactions related to variants in the human leukocyte antigen (HLA) system. The lead author is Dr Michael A. Norcross of the U.S. Food and Drug Administration's Center for Drug Evaluation and Research. The publish-ahead-of-print article is currently available on the *AIDS* journal homepage and will be available in the July 17, 2012 print edition.

Abacavir Hypersensitivity Results from 'Drug-Induced Autoimmunity'

Dr Norcross and colleagues performed a series of laboratory experiments to examine why some patients develop hypersensitivity reactions to the antiretroviral drug abacavir (Ziagen—also included in combination products such as Epzicom and Trizivir). Developing a few weeks after the start of treatment, the reactions cause a wide range of symptoms including fever, rash, nausea, muscle soreness, and shortness of breath.

The reactions have been linked to a gene variant called HLA-B*57:01, found in up to eight percent of people of European descent (lower in other racial/ethnic groups). However, the molecular basis by which people with the HLA-B*57:01 gene develop hypersensitivity reactions to abacavir has been unclear.

In model cells expressing the HLA-B*57:01 gene product, the researchers found that abacavir induced a set of unique changes. Abacavir exposure led to the formation of new peptide molecules that bound to specific HLA-B*57:01 binding sites. The result was the creation of new drug-induced immunogens, which triggered attacks by immune cells.

These findings suggest that abacavir hypersensitivity reactions occur through an autoimmune mechanism—the immune system attacks cells it doesn't recognize as "self." This is the same basic mechanism that causes autoimmune diseases such as lupus, inflammatory bowel disease, and type 1 diabetes.

This autoimmune mechanism helps to explain why abacavir hypersensitivity reactions can affect such a wide range of different organs and tissues. It also helps in understanding why the reactions clear up promptly when abacavir is stopped, and why more severe reactions can rapidly develop if treatment is restarted.

"Our data support a model of drug-induced autoimmunity as a consequence of abacavir exposure," Dr Norcross and colleagues write. They believe that a similar molecular mechanism could potentially explain other types of drug reactions involving HLA gene variants. It's also important to identify other factors influencing the development of hypersensitivity, since not all patients with the HLA-B*57:01 gene react to abacavir.

"This study provides important insight into why only certain people show this severe hypersensitivity to this valuable anti-HIV drug," comments Dr J.A. Levy, Editor-in-Chief of AIDS. "The finding represents an example of how approaches to personalized medicine can identify patients who would be sensitive to this side effect of abacavir."

Provided by Wolters Kluwer Health