Treatment Is Affected by the T-Cell Coreceptor HIV Uses

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The coreceptor used by HIV to infect CD4 cells (referred to as its tropism) affects how well standard HIV treatment works, according to a study published in the July 1 issue of *The Journal of Infectious Diseases*. This is the first study to suggest that viral tropism affects the response to treatments other than the drug Selzentry (maraviroc).

Toward the end of the last decade, scientists at the National Institutes of Health (NIH) made one of the most important discoveries regarding HIV: that the virus uses receptors other than CD4 to enter and infect T-cells. These coreceptors function somewhat like doorknobs, and HIV must first bind and attach to CD4, and then to one of two other coreceptors, either CCR5 or CXCR4, to enter cells.

After detecting these coreceptors, researchers made several other key discoveries. First, they found that people whose virus prefers to use CXCR4 tended to have lower CD4 counts and faster HIV disease progression than people whose virus prefers CCR5. Second, they found that those born without the ability to make the CCR5 coreceptor were highly resistant to HIV infection. This led to the development and approval of a drug to block CCR5, that drug being Selzentry. For Selzentry to work, however, a person must only carry CCR5-tropic virus and not CXCR4-tropic or mixed-tropic virus.

What hasn't been studied until now, however, is whether a person's viral tropism would have an effect on antiretroviral (ARV) treatment responses to drugs other than Selzentry. To explore this, Eduardo Seclén, MD, and his colleagues from the Hospital Carlos III in Madrid, examined blood samples from HIV-positive people enrolled in the ARTEN study, which compared a regimen containing Viramune (nevirapine) to a regimen containing Norvir (ritonavir)–boosted Reyataz (atazanavir).

The participants in both groups were similar in most respects, and overall the study found that the two different regimens had similar efficacy. Seclén's group, however, was interested not in how those treatments compared with one another, but in how a person's HIV tropism would affect his or her response to starting either treatment.

Of the 482 participants in the study who were treated for at least 48 weeks, 14 percent had CXCR4-tropic virus at the start of the study. The rest had CCR5-tropic virus. Also, 22 percent had a

strain of HIV (called a clade) other than clade B, the most common strain in Western Europe and the United States.

Seclén and his colleagues found that a person's tropism significantly affected the response to treatment. Overall, while 92 percent of those with CCR5-tropic virus had an undetectable viral load after 48 weeks of treatment, this was true in only 77 percent of those with CXCR4-tropic virus. When multiple factors were considered, a person's tropism remained significant until the 24-week point. In people with clade B virus, however, tropism was significant at both 24 and 48 weeks. Contrary to other studies, those with CXCR4-tropic virus had similar increases in CD4 counts as those with CCR5-tropic virus.

"In antiretroviral-naïve patients beginning antiretroviral therapy, baseline…tropism seems to be an independent predictor of virologic response," conclude the authors, adding that "this observation may have important clinical implications for the monitoring of antiretroviral therapy and interpretation of comparative trials."
