Selzentry Dosing May Be Inadequate for HIV-Positive Blacks

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HIV-positive African Americans may not be able to maintain effective drug levels of Selzentry (maraviroc) at the antiretroviral's standard dose, thanks to a protein that is more common in blacks than among whites. Publishing their findings in Drug Metabolism and Disposition, researchers conducted a dosing study in 24 HIV-negative people who had either zero, one or two functioning copies of the CYP3A5 gene, which yields a protein of the same name that is key to removing Selzentry from the body.

Eighty percent to 90 percent of European Americans lack the CYP3A5 protein entirely because they have two dysfunctional copies of the gene, while 45 percent of African Americans have two functional copies of the gene. Unfortunately, the 2007 dosing studies of Selzentry were conducted with mostly white participants, leading to a dearth of understanding about the pharmacokinetics of the drug among blacks.

"Because African Americans are disproportionately affected by HIV infection, it is doubly important that we get the dosing right," Namandje Bumpus, PhD, an assistant professor of pharmacology and molecular sciences at the Johns Hopkins University School of Medicine, said in a release.

All participants in this study were given a single dose of Selzentry at the recommended level of 300 milligrams. Blood samples were then taken at 10 points over the subsequent 32 hours.

The Selzentry concentration was comparable among those with either zero or one functional copy of CYP3A5 at almost all the blood draws. Meanwhile, those with two functional copies of CYP3A5 had a 41 percent lower overall concentration of Selzentry when compared with those with two poorly functioning copies of the gene. The average drug concentration among those participants with two functioning copies of the gene was just above the floor that is necessary for Selzentry to fight HIV effectively. The individual average drug concentrations were below that floor among four out of the eight participants with two functioning copies of the gene.

"The trend we saw was that the more functional CYP3A5 a person had, the faster maraviroc was processed and left the body, so the lower its concentration in the bloodstream," Bumpus said. "What's nice is that, if a larger study confirms that we are underdosing this group, a simple genetic test prior to dosing decisions could rectify the situation."

The findings underscore the need for clinical trials to have study populations that reflect the diversity of those who will need the drug once it is approved.

To read the press release, click here.

To read the study abstract, click here.

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http://beta.docker.poz.com/article/Selzentry-drug-levels-26098-6600