Genes, Not Race, Should Guide Antiretroviral Treatment

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A person's genetic sequence, and not his or her race, should guide scientists and health care providers in the design of clinical trials and treatment decisions with antiretroviral (ARV) drugs such as efavirenz (found in Sustiva and Atripla), according to a review article published in the September 1 issue of *AIDS*.

Data analysis from several studies have suggested that there may be racial differences in response to some ARV drugs, most notably efavirenz. Two early studies suggested that black patients might experience greater central nervous system (CNS) side effects from efavirenz. More recently, study ACTG5095 reported that black patients taking an efavirenz-containing regimen had a shorter time to virologic failure—the virus became detectable after being undetectable for several weeks or months—than white patients. Though the black patients as a whole reported more challenges with adherence than white patients, the study's authors found that adherence alone could not explain the differences in virologic failure. In a comparison of black and white patients with equal levels of self-reported adherence challenges, black patients still had virologic failure sooner than white patients.

In an attempt to offer guidance to scientists and health care providers, Jennifer King, PharmD, from the University of Alabama in Birmingham, and Judith Aberg, MD, from the New York University School of Medicine in New York City, conducted a thorough analysis of published studies that compared the effects of race and genetic makeup on efavirenz blood concentration levels, side effects and efficacy.

King and Dr. Aberg found that the data were quite inconsistent. In fact, in a majority of studies, there were no significant differences in efficacy or side effects between blacks, whites and Hispanics. A few studies, however, did find differences in efavirenz blood levels, and the possibility of greater CNS side effects in the first week or two of treatment, in people who carried a version of a gene responsible for making one of the liver enzymes that metabolizes efavirenz, called CYP2B6*6. People with this gene mutation had much slower metabolism, and therefore higher blood concentrations, of efavirenz than people without the mutation. Notably, people of African descent were about four times as likely as people of European descent to carry this mutation. In the few small studies that examined this genetic mutation's impact on the incidence of CNS side effects; however, the results were not consistent. Some showed that people with higher blood levels of efavirenz had a greater incidence of CNS side effects in the first several days after

starting treatment, while others showed no difference at all.

The authors suggest that further studies be conducted to compare efavirenz levels in spinal fluid in people with and without specific genetic mutations to help narrow down the possibility of gene-based differences in treatment response. Until those studies are conducted, however, King and Aberg conclude that the data do not support making treatment decisions based solely on race.
