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Starting antiretroviral therapy earlier yields better clinical outcomes

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A clinical trial has demonstrated that HIV-infected adults in a resource-limited setting are more likely to survive if they start antiretroviral therapy (ART) before their immune systems are severely compromised.

On May 28, 2009, an independent data and safety monitoring board (DSMB) met to conduct a planned interim review of an ongoing clinical study known as CIPRA HT 001, which is being conducted in Haiti. The DSMB found overwhelming evidence that starting ART at CD4+ T cell counts—a measure of immune health—between 200 and 350 cells per cubic millimeter (mm3) improves survival compared with deferring treatment until CD4+ T cells drop below 200 cells/mm3. In light of these results, the DSMB recommended that the trial sponsor—the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health—end the trial immediately, before its scheduled conclusion. NIAID agreed with the DSMB recommendation, and all study participants who have fewer than 350 CD4+ T cells/mm3 will be offered ART.

The study investigators say this new finding has the potential to change the standard of care for HIV infection in dozens of countries around the world where ART is initiated only when CD4+ T cell counts drop below 200 cells/mm3. Like the results of several recent epidemiologic studies in developed countries that examined the optimal time to begin ART, the new finding underscores the importance of identifying people who are HIV-infected earlier in the course of their infection and starting ART earlier.

"The public health community now has evidence from a randomized, controlled clinical trial—the gold standard—that starting ART at CD4+ T cell counts between 200 and 350 cells/mm3 in resource-limited settings yields better health outcomes than deferring treatment until CD4+ T cell counts drop below 200 cells/mm3," says NIAID Director Anthony S. Fauci, M.D.

"The number of people who meet the medical criteria for receiving ART likely will grow as treatment guidelines are revised as a consequence of this finding, challenging the global community to supply antiretroviral drugs to all who need them," adds Carl Dieffenbach, Ph.D., director of the NIAID Division of AIDS. "Today, only 30 percent of HIV-infected individuals in low- and middle-income countries who need ART are receiving it."

The clinical trial CIPRA HT 001 began in 2005. It is funded by NIAID through the Comprehensive International Program of Research on AIDS (CIPRA) and is being carried out by the Haitian Group for the Study of Kaposi's Sarcoma and Immune Deficiency Disorders (GHESKIO) Centers in Port-au-Prince, Haiti. The principal investigator is Jean William Pape, M.D., the director of the GHESKIO Centers and a professor of medicine at Weill Medical College of Cornell University.

The trial enrolled 816 HIV-infected adults ages 18 and older with early HIV disease and CD4+ T cell counts between 200 and 350 cells/mm3. Half of the participants were assigned at random to begin ART within two weeks of enrollment, and the other half were assigned to defer treatment until their CD4+ T cell counts dropped below 200 cells/mm3 or they were diagnosed with AIDS. This deferred treatment is in keeping with the standard of care in Haiti and the current guidelines of the World Health Organization (WHO). The first-line treatment regimen consisted of the anti-HIV drugs zidovudine, lamivudine and efavirenz.

At the time of the DSMB interim review, six participants in the early treatment group had died, while 23 participants in the standard-of-care group had died—nearly four times as many. The DSMB also found that, among participants who began the study without tuberculosis (TB) infection, 18 people in the early treatment had developed TB, while 36 people—twice as many—in the standard-of-care group had developed TB. These results were statistically significant.

In light of these results, the DSMB recommended that NIAID end the trial immediately and that the study team offer ART to all participants in the standard-of-care group who have fewer than 350 CD4+ T cells/mm3. The DSMB also recommended that the study team continue to follow all participants for another year and make every effort to ensure that participants receiving ART continue their therapy. NIAID concurred with these recommendations.

The study investigators are notifying all participants and have notified institutional review boards and national ethics committees involved with CIPRA HT 001 as well as the Haitian Ministry of Health about the findings of the DSMB. Investigators also have shared the information with WHO, the U.S. President's Emergency Plan for AIDS Relief, and the Global Fund to Fight AIDS, Tuberculosis and Malaria.

Source: NIH/National Institute of Allergy and Infectious Diseases (news : web)