Treating HIV-infected infants early helps them live longer

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Hundreds of thousands of babies around the world are born each year with HIV--more than half a million in 2006 alone. Caring for these children is complicated by the fact that their immune systems are not fully developed in the first year of life, which makes them especially susceptible to rapid HIV disease progression and death. The current standard of HIV care in many parts of the world is to treat infants with antiretroviral therapy--but only after they show signs of illness or a weakened immune system.

Now the initial results of an ongoing clinical trial sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), suggests that more HIV-infected infants survive if they are given therapy early on, regardless of their apparent state of health.

This trial, called the “Children with HIV Early Antiretroviral Therapy” (CHER) study, is a phase III, randomized clinical trial led by Avy Violari, M.D., FCPaed (SA), of the University of the Witwatersrand in Johannesburg, South Africa, and Mark Cotton, MBChB, MMed, of the University of Stellenbosch in Cape Town, South Africa. Dr. Violari will present these findings on Wednesday, July 25 at the 2007 International AIDS Society Conference in Sydney, Australia.

“Children with HIV infection frequently show rapid disease progression within the first year of life due to their developing immune systems and susceptibility to other serious infections,” says NIH Director Elias A.

Zerhouni, M.D. “This is the first randomized clinical trial that shows that infants treated before three months of age will do better than infants who have their treatment delayed.”

“The results of this trial could have significant public health implications worldwide,” says NIAID Director Anthony S. Fauci, M.D. “Because these findings will cause experts to consider changes in standards of care in many parts of the world, NIAID has released details of the interim results to the World Health Organization, local ethics committees, regulatory authorities and other key stakeholders for their consideration and evaluation for possible implementation.”

"These initial results also highlight the importance of diagnosing HIV infections early--within the first six to twelve weeks of life,” says Edward Handelsman, M.D., chief of the Pediatric Medicine Branch in NIAID’s Division of AIDS, which is overseeing the CHER study. Dr. Handelsman stresses, however, that the study results cannot necessarily be generalized to asymptomatic adults or older children because young infants are very different in immune function, time since HIV infection and susceptibility to other serious illnesses.

The evidence came to light last month after a routine review by the trial’s data and safety monitoring board (DSMB), an independent committee composed of clinical research experts, statisticians, ethicists and community representatives from Africa, Europe and the United States that regularly reviews interim data from the CHER study to ensure the safety of study participants.

CHER had begun two years earlier to evaluate whether early antiretroviral therapy given over a limited period of time would delay disease progression. The idea was that this approach might allow the immune system to develop and possibly allow the child to stop treatment for a period of time and therefore avoid continuous therapy from an

early age.

Starting in July 2005, HIV-infected infants between 6 and 12 weeks old without immune suppression or severe symptoms of clinical disease were enrolled at the Perinatal HIV Research Unit in Soweto and Tygerberg Children's Hospital in Cape Town. By early 2007, 377 babies were enrolled in one of three groups--those receiving immediate antiretroviral therapy for 40 weeks, those receiving immediate antiretroviral therapy for 96 weeks, and a control group whose treatment was initiated after doctors observed signs of clinical or immunological progression toward the development of AIDS (the current standard of HIV care in many parts of the world).

The trial is designed to continue through 2011, but after reviewing early trial data on June 20, 2007, the DSMB found a significant increase in survival among infants who received immediate antiretroviral therapy. At the time of the DSMB review, 96 percent of these children were alive, compared to only 84 percent of the children in the control group. Based on this finding, the DSMB concluded that providing early antiretroviral therapy to infants is more effective in preventing early death than delaying treatment until clinical or immunological disease triggers are observed.

The DSMB recommended that no additional infants be placed in the deferred-treatment arm of the study and infants previously enrolled in this arm be evaluated for potential initiation of antiretroviral therapy. NIAID accepted these recommendations and informed the study investigators at each site. The doctors at those sites have been contacting the parents and legal guardians of the infants involved in the study to inform them of the interim findings and call them in for evaluation. The DSMB also recommended that all infants enrolled in the study be followed for the planned duration of approximately 3.5 years and those in the 40- and 96-week treatment groups continue with the study.

Source: NIH/National Institute of Allergy and Infectious Diseases