RELEASE IN PART B6

From: Mills, Cheryl D <MillsCD@state.gov>
Sent: Thursday, May 12, 2011 4:02 PM
To: H
Subject: Fw: New HIV Prevention news breaking today
Attachments: NIH HPTN 052 Final.docx; NIH HPTN 052 Final.docx

---

From: Von Zinkernagel, Deborah J
Sent: Thursday, May 12, 2011 11:40 AM
To: Mills, Cheryl D
Cc: Quam, Lois E; Hyde, Dana; Goosby, Eric; 'lorriemchugh[redacted] <lorriemchugh[redacted] B6
Subject: New HIV Prevention news breaking today

Good morning,

I am sending this on behalf of Eric, who is heavily engaged with the Global Fund today. We wanted to give you a heads up on new data that NIH will be releasing today, which shows a strong HIV prevention benefit resulting from antiretroviral treatment.

The study, HPTN 052, is a rigorous randomized control trial of 1763 HIV discordant couples (97% heterosexual). In half of the couples, the HIV+ partner was started on ARVs with a CD4 count between 350 – 550, the ' early treatment group' ; the remaining couples had a delayed start of ARVs (HIV+ partner CD4 $\leq$ 250 cells, or symptomatic).

In the early treatment group, there was only 1 new HIV infection among 882 couples. There were 27 new infections among HIV negative partners in the delayed treatment group. The Data Safety Monitoring Board has stopped the study early and discontinued the delayed treatment arm, given the significance of these results.

This study will have significant implications for HIV prevention where the epidemic is driven by heterosexual transmission. Five PEPFAR countries were involved as trial sites (Botswana, South Africa, Malawi, Kenya, Zimbabwe). We will follow up with an information memo to you and a briefing for Lois and Dana.

Thanks,

Deborah
Ext 32802

SBU
This email is UNCLASSIFIED.

Contact: Kathy Stover
stoverk@niaid.nih.gov
301-402-1663
NIH/National Institute of Allergy and Infectious Diseases

Treating HIV-infected people with antiretrovirals significantly reduces transmission to partners

Findings result from NIH-funded international study

Men and women infected with HIV reduced the risk of transmitting the virus to their sexual partners by taking oral antiretroviral medicines when their immune systems were relatively healthy, according to findings from a large-scale clinical study sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

The clinical trial, known as HPTN 052, was slated to end in 2015 but the findings are being released early as the result of a scheduled interim review of the study data by an independent data and safety monitoring board (DSMB). The DSMB concluded that it was clear that use of antiretrovirals by HIV-infected individuals with relatively healthier immune systems substantially reduced transmission to their partners. The results are the first from a major randomized clinical trial to indicate that treating an HIV-infected individual can reduce the risk of sexual transmission of HIV to an uninfected partner.

"Previous data about the potential value of antiretrovirals in making HIV-infected individuals less infectious to their sexual partners came largely from observational and epidemiological studies," said NIAID Director Anthony S. Fauci, M.D. "This new finding convincingly demonstrates that treating the infected individual—and doing so sooner rather than later—can have a major impact on reducing HIV transmission."

Led by study chair Myron Cohen, M.D., director of the Institute for Global Health and Infectious Diseases at the University of North Carolina at Chapel Hill, HPTN 052 began in April 2005 and enrolled 1,763 couples, all at least 18 years of age. The vast majority of the couples (97 percent) were heterosexual, which precludes any definitive conclusions about effectiveness in men who have sex with men. The study was conducted at 13 sites in Botswana, Brazil, India, Kenya, Malawi, South Africa, Thailand, the United States and Zimbabwe. The U.S. site collected only limited data because of difficulties enrolling participants into the study. However, data from one serodiscordant couple at the site was included in the DSMB's analysis. At the time of enrollment, the HIV-infected partners (890 men, 873 women) had CD4+ T-cell levels—a key measure of immune system health—between 350 and 550 cells per cubic millimeter (mm^3) within 60 days of entering the study. The HIV-uninfected partners had tested negative for the virus within 14 days of entering the study.

The investigators randomly assigned the couples to either one of two study groups. In the first group, the HIV-infected partner immediately began taking a combination of three antiretroviral drugs. In the second group (the deferred group), the HIV-infected partners began antiretroviral therapy when their CD4 counts fell below 250 cells/mm^3 or an AIDS-related event, such as Pneumocystis pneumonia, occurred. Throughout the study, both groups received HIV-related care that included counseling on safe sex practices, free condoms, treatment for sexually transmitted infections, regular HIV testing, and frequent evaluation and treatment for any complications related to HIV infection. Each group received the same amount of care and counseling.

In its review, the DSMB found a total of 39 cases of HIV infection among the previously uninfected partners. Of those, 28 were linked through genetic analysis to the HIV-infected partner as the source of infection. Seven infections were not linked to the HIV-infected partner, and four infections are still undergoing analysis. Of the 28 linked infections, 27 infections occurred among the 877 couples in which the HIV-infected partner did not begin antiretroviral therapy immediately. Only one case of HIV infection occurred among those couples where the HIV-infected partner began immediate antiretroviral therapy. This finding was statistically significant and means that earlier initiation of

antiretrovirals led to a 96 percent reduction in HIV transmission to the HIV-uninfected partner. The infections were confirmed by genetic analysis of viruses from both partners.

Additionally, 17 cases of extrapulmonary tuberculosis occurred in the HIV-infected partners in the deferred treatment arm compared with three cases in the immediate treatment arm, a statistically significant difference. There were also 23 deaths during the study. Ten occurred in the immediate treatment group and 13 in the deferred treatment group, a difference that did not reach statistical significance.

The study was designed to evaluate whether antiretroviral use by the HIV-infected individual reduced HIV transmission to the uninfected partner and potentially benefited the HIV-infected individual as well. Additionally, the study was designed to evaluate the optimal time for a person infected with HIV to initiate antiretrovirals in order to reduce HIV-related sickness and death. Based on their analysis, the DSMB recommended that the deferred study arm be discontinued and that the study participants be informed of the trial's outcome.

"We want to thank the study participants for making such an important contribution in the fight against HIV/AIDS. We think that these results will be important to help improve both HIV treatment and prevention," said Dr. Cohen.

Study participants are being informed of the results. Individuals who became HIV-infected during the course of the study were referred to local services for appropriate medical care and treatment. HIV-infected participants in the deferred treatment group will be offered antiretroviral therapy. The study investigators will continue following the study participants for at least one year.

The study was conducted by the HIV Prevention Trials Network, which is largely funded by NIAID with additional funding from the National Institute on Drug Abuse and the National Institute of Mental Health, both part of the NIH. Additional support was provided by the NIAID-funded AIDS Clinical Trials Group. The antiretroviral drugs used in the study were made available by Abbott Laboratories, Boehringer Ingelheim Pharmaceuticals, Inc., Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline/Viiv Healthcare and Merck & Co., Inc.

The 11 HIV drugs that were used in various combinations included the following:

atazanavir (300 mg once daily)
didanosine (400 mg once daily)
efavirenz (600 mg once daily)
emtricitabine/tenofovir disoproxil fumarate (200 mg emtricitabine/300 mg tenofovir disoproxil fumarate once daily)
lamivudine (300 mg once daily)
lopinavir/ritonavir 800/200 mg once daily (QD) or lopinavir/ritonavir 400/100 mg twice daily (BID)
nevirapine (200 mg taken once daily for 14 days followed by 200 mg taken twice daily)
ritonavir (100 mg once daily, used only to boost atazanavir)
stavudine (weight-dependent dosage)
tenofovir disoproxil fumarate (300 mg once daily)
zidovudine/lamivudine (150 mg lamivudine/300 mg zidovudine taken orally twice daily)

In an ongoing international clinical study called Strategic Timing of Antiretroviral Therapy (http://www.niaid.nih.gov/news/newsreleases/2011/Pages/START.aspx), NIAID is examining the optimal time for asymptomatic HIV-infected individuals to begin antiretrovirals.

###

For additional information about the HPTN 052 study, see the Questions and Answers (http://www.niaid.nih.gov/news/QA/Pages/HPTN052qa.aspx) . Visit the NIAID HIV/AIDS Web portal

(http://www.niaid.nih.gov/topics/hivaids/Pages/Default.aspx) for more information about NIAID's HIV/AIDS research.

NIAID conducts and supports research—at NIH, throughout the United States, and worldwide—to study the causes of infectious and immune-mediated diseases, and to develop better means of preventing, diagnosing and treating these illnesses. News releases, fact sheets and other NIAID-related materials are available on the NIAID website at www.niaid.nih.gov.

About the National Institutes of Health (NIH): NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.