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STATEMENT

NIH Discontinues Immunizations in HIV Vaccine Study

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, will stop administering injections in its HVTN 505 clinical trial of an investigational HIV vaccine regimen because an independent data and safety monitoring board (DSMB) found during a scheduled interim review that the vaccine regimen did not prevent HIV infection nor reduce viral load (the amount of HIV in the blood) among vaccine recipients who became infected with HIV.

The HVTN 505 study began in 2009 and was testing an investigational prime-boost vaccine regimen developed by NIAID's Vaccine Research Center. The Phase IIb study, conducted by the NIAID-funded HIV Vaccine Trials Network (HVTN), was designed to determine whether the vaccine regimen could prevent HIV infection and/or reduce the amount of virus in the blood of vaccine recipients who became infected with HIV.

The investigational HIV vaccine regimen involved a series of three immunizations over the course of eight weeks, beginning with a DNA-based vaccine designed to prime the immune system. The DNA priming vaccine contained genetic material expressing antigens representing proteins from both the surface and internal structures of HIV. Immunizations with the priming vaccine were followed by a single injection at week 24 with a recombinant vaccine (the booster vaccine) based on a weakened adenovirus type 5 (Ad 5). The adenovirus was used as a vector, or carrier, of genetic material expressing a matching set of HIV antigens. Structures from all three major HIV clades, or subtypes, were included. Adenoviruses are a common cold virus, but the Ad5 virus used in the study's vaccine regimen was disabled so that it could not cause a cold or other respiratory illness. The two investigational vaccines tested in HVTN 505 cannot cause HIV infection because neither contains live or weakened versions of HIV.

The HVTN 505 study enrolled 2,504 volunteers at 21 sites in 19 U.S. cities. The study population consisted of men who have sex with men and transgender people who have sex with men. In its April 22 interim review, the DSMB examined the information gathered from 1,250 volunteers who received the investigational vaccine regimen and 1,244 volunteers who received the placebo vaccine. The primary analysis looked at volunteers who were diagnosed with HIV infection after having been in the study a minimum of 28 weeks. This was done to enable enough time for the vaccine regimen to be given and stimulate an immune response. In this analysis, 27 HIV infections occurred among the vaccine recipients, and 21 HIV infections occurred among the placebo vaccine recipients. Among volunteers who became HIV-infected during the first 28 weeks of the study, 14 cases of HIV infection occurred among those who received the

investigational vaccine regimen, and 9 HIV infections occurred among the placebo vaccine recipients. Overall in the study from the day of enrollment through the month 24 study visit, a total of 41 cases of HIV infection occurred in the volunteers who received the investigational vaccine regimen and 30 cases of HIV infection occurred among the placebo vaccine recipients.

Additionally, the DSMB found that the vaccine failed to reduce viral load among volunteers who acquired HIV infection at least 28 weeks after entering the study and who had been followed for at least 20 weeks after diagnosis. There were 30 participants with measurable viral load (15 vaccine recipients; 15 placebo recipients).

Based on these findings, the DSMB recommended that no further vaccinations with the investigational vaccine regimen be administered. As the trial's sponsor, NIAID concurred with the DSMB's recommendation and has instructed all HVTN 505 study sites to immediately cease administering injections but continue follow-up with study participants to further evaluate the trial data.

It should be noted that there was a non-statistically significant increase in HIV acquisition among volunteers in the investigational vaccine group compared to those in the placebo group. It is not clear why this occurred and further analysis is needed to draw any firm conclusions. Based on the finding, the DSMB recommended closer follow-up of participants beyond their month 24 study visit. NIAID concurred, and will, in concert with the study investigators, be amending the study protocol to allow for closer, extended follow up of the vaccine recipients.

As with all NIAID-sponsored HIV prevention trials, the HVTN 505 participants were offered extensive counseling on how to reduce their risk of becoming HIV-infected and provided free condoms. As an added precaution, study participants were required at time of enrollment to be circumcised and free of antibodies to Ad5. These precautions were taken in light of an HIV vaccine clinical trial, known as the Step Study, which found in 2007 an increased number of HIV infections among vaccine recipients, particularly those who were not circumcised and/or had Ad5 antibodies.

NIAID and the HVTN 505 study team are working to thoroughly analyze the study data to better understand why the vaccine did not work and to guide future vaccine development efforts. Detailed scientific findings will be made publicly available as soon as possible.

Study investigators at each of the 21 clinical trial sites have been informed of the decision to stop immunizations in the HVTN 505 study and are contacting study volunteers to inform them of the developments. Study volunteers are being asked to report to their specific clinic sites over the next few weeks to find out whether they received the investigational vaccines or placebo. Individuals who became HIV-infected during the trial were referred to local services for appropriate medical care and treatment. The study investigators will continue following all study participants for five years from the time of enrollment.

NIAID remains committed to the pursuit of a highly effective, preventive HIV vaccine as part of a multifaceted HIV prevention research program. For more information about the HVTN 505

study, please see the updated Questions and Answers. To learn about NIAID's HIV vaccine research, please see the HIV vaccine section of the NIAID website.

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 Web site at http://www.niaid.nih.gov.

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