NIAID will not move forward with the PAVE 100 HIV Vaccine Trial

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After soliciting and considering broad input from the scientific and HIV advocacy communities, the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), has determined that it will not conduct the HIV vaccine study known as PAVE 100.

However, NIAID believes the vaccine developed by its Vaccine Research Center (VRC) is scientifically intriguing and sufficiently different from previously tested HIV vaccines to consider testing it in a smaller, more focused clinical study. Therefore, NIAID will entertain a proposal for an alternative study with one specific goal: to determine if the vaccine regimen significantly lowers viral load—the amount of HIV in the blood of vaccinated individuals who may later become infected with HIV.

The original PAVE 100 study, as presented to NIAID's AIDS Research Advisory Committee in January 2007, proposed to test the VRC's HIV vaccine regimen in a trial initially designed to enroll 8,500 volunteers in the United States, South America, the Caribbean and Eastern and Southern Africa. The study was to begin U.S. recruitment in October 2007 but was postponed last fall following the decision to halt immunizations in the STEP HIV vaccine study. That decision was made after it was determined that the vaccine used in the STEP trial, an investigational product developed by Merck & Co. Inc., failed to prevent HIV infection or reduce viral load.

Subsequent analyses of the STEP trial found increased numbers of HIV infections among those volunteers who received the vaccine in comparison to those who received the placebo; the Merck vaccine itself did not cause HIV infection. The highest risk of HIV infection among vaccinees compared with placebo recipients appeared to be among males who were both uncircumcised and had pre-existing neutralizing antibodies to adenovirus type 5 (Ad5), the common cold virus used in the vaccine as a carrier for the HIV genes. Vaccination resulted in no apparent increased risk in men who were circumcised and who lacked pre-existing neutralizing antibodies to Ad5. The VRC vaccine regimen that was to be tested in the PAVE 100 study has two components, one of which includes an Ad5-based carrier, which is administered to boost immune responses that are first stimulated with a DNA vaccine.

Based on the analyses of the STEP study results, PAVE 100 was redesigned and reduced somewhat in its proposed scope, although it remained a scientifically and logistically complex study. The redesigned PAVE 100 study would have involved testing the VRC vaccine in 2,400 U.S.-based, circumcised men who have sex with men and who lack preexisting neutralizing antibodies to Ad5. The redesigned study would have tested the vaccine's effect on viral load, provided additional safety information about the product, and examined in detail immune responses to the vaccine and their impact on viral load.

Based on the available scientific information, NIAID has decided that the VRC vaccine regimen did not warrant a trial of this size and scope and that PAVE 100 will not proceed. However, NIAID will entertain a smaller, more focused clinical trial designed to answer one important question: Does the product have a significant effect on HIV viral load? If such an effect is noted, then additional studies or expansion of the study to carefully examine immunological correlates could be performed. NIAID will consider such an alternative study and will announce its decision at a later time.

Source: National Institute of Allergy and Infectious Diseases