



The HVTN 505 Study

ITS ROLE IN HELPING FIGHT AIDS

The world needs an HIV vaccine. We can't educate or treat ourselves out of the epidemic—we have to prevent it, and vaccines have historically been the best tool in our arsenal for preventing disease. But HIV has proven itself to be a challenging virus to vaccinate against during the more than two decades of HIV vaccine research efforts.

Because of the complex scientific hurdles involved with developing an HIV vaccine, products tested to date haven't worked. One approach, called T-cell-based vaccines, was recently examined in efficacy trials called Step and Phambili. These studies asked if a particular vaccine would prevent HIV infection or delay progression of disease. The Step Study demonstrated that the vaccine did not prevent infection, nor did it lower the viral load in those who became infected. Additionally, the results showed that some groups of men who received the vaccine (those who had antibodies to a common cold virus and were uncircumcised) may have been more likely to become infected when exposed to the virus than those who received the placebo. Those study results made the entire HIV vaccine research field evaluate the situation carefully.

WHY THIS STUDY?

As HIV vaccine research efforts continue, we're learning a lot about what kinds of studies will help move us closer to success while ensuring participant safety. Each new study is a part of a larger mosaic of research efforts, designed to give us a clearer picture of the pathway to a successful vaccine, particularly in light of the fact that for HIV, no animal model can clearly predict the results found in humans. This particular study—called HVTN 505—will use a DNA prime/rAd5 boost vaccine regimen developed by the Vaccine Research Center at the National Institutes of Health (NIH). Parts of this vaccine regimen are similar to the vaccine used in Step and Phambili. While this vaccine is not on the path to licensure and is not expected to prevent HIV infection, the results of HVTN 505 will help us to better understand and develop T-cell-based vaccines.

SAFETY FIRST

Safety is always our top priority, and the design of HVTN 505 reflects this. Key safety considerations built into this study include:

- The vaccine used in this study *cannot* cause HIV infection.
- For HVTN 505, we are limiting the study population to U.S. men who have sex with men (MSM) who are circumcised and do not have antibodies to Adenovirus type 5. In the Step Study, men who fit these criteria and received the vaccine had the same rates of HIV infection as the men who received the placebo. This study will not enroll the populations where there was a trend toward higher rates of HIV infection among people who received the vaccine in the Step Study.
- We are proposing real-time monitoring of safety by an independent Data and Safety Monitoring Board (DSMB). In addition to interim analyses of the data, the DSMB will review new infections as they are diagnosed to keep the closest possible watch on the study participants and their safety.
- All participants will receive the best available prevention services, including risk reduction assessment and counseling, condoms, and access to local prevention services.
- The protocol team for this study includes HVTN study investigators and study site staff, among them clinic coordinators, community educators and community advisory board members, as well as staff from the Division of AIDS, part of the National Institute of Allergy and Infectious Diseases.

HVTN 505's RESEARCH OBJECTIVE

HVTN 505 is an exploratory study designed to answer one specific question: **will the VRC's DNA/rAd5 vaccine regimen significantly reduce viral load in individuals who become infected with HIV?** This is important because viral load is a marker of potential vaccine effect on disease progression, and therefore a signal of potential vaccine efficacy. Typically, the lower the viral load, the longer it may take before the person develops symptoms of AIDS. So, an HIV vaccine that lowers viral load may delay the onset of illness, even if it doesn't prevent HIV infection. The lower viral load may also reduce transmission of the virus to others. Once we have the results of this study, we may have a better understanding of how to focus future efforts to design and test vaccine candidates. For example, if this regimen is shown to lower HIV viral load, it will be an indication of promise for the development of T-cell-based vaccines and may also provide information on what specific T-cell responses are most beneficial.

HVTN 505 moves us past the Step Study in several ways. It uses a different vaccine regimen that combines 10 different genes. Looking across non-human primate studies, the VRC regimen produces a different immune response that may be stronger than the Step Study vaccine.

As mentioned above, for safety reasons, HVTN 505 is being tested only in people who don't have antibodies to Adenovirus type 5, a small subset of the population. But as an approach, once we know if this regimen works, we can modify the adenovirus strain to be safely used in larger populations.

THE LARGER RESEARCH AGENDA

Hundreds of scientists around the world are working on finding a vaccine that will be safe and prevent HIV/AIDS, but finding a vaccine is a long-term process that involves many studies, each designed to learn specific information. For example, one study (such as HVTN 505) might evaluate effects on viral load, one might evaluate immune responses, one might evaluate prevention of infection in individuals and one might evaluate prevention of infection among partners. Ultimately, as this larger effort generates and refines new vaccine candidates, they will need to be tested on large numbers of study volunteers, in every population and across the globe.

AT HVTN, OUR CURRENT RESEARCH GOALS INCLUDE:

- Using the research results from Step and Phambili to develop conceptual improvements to T-cell-based vaccines,
- Conducting trials that define how to improve T-cell responses in the body after vaccination,
- Carrying out studies with women to learn more about the patterns of the epidemic in their demographic, and
- Evaluating conceptual improvements in both human and non-human primate studies.

HOW YOU CAN HELP

The fight against AIDS is far from over. Millions of people become newly infected each year. A comprehensive program to fight AIDS must include prevention, treatment and research. HIV research explores a variety of approaches to prevention, including behavioral intervention, vaccines and microbicides. But as history has shown us, a vaccine is our best hope for fighting this epidemic. For the AIDS research community the challenge is clear: find an AIDS vaccine that is safe, and that works.

There are many ways you can help in the effort to find an AIDS vaccine.

Stay informed.

Sign up for an e-Newsletter about HIV vaccine research at <http://www.bethegeneration.org>.

Stay connected.

Join the AIDS Vaccine Advocacy Coalition Advocates Network at <http://www.avac.org>.

Stay involved.

Join an HVTN Community Advisory Board. Find the site nearest you at <http://www.hvtn.org/about/sites.html>.



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