HUTCH NEWS

HVTN moves forward with Africa's first major HIV-vaccine trial

Three thousand South Africans may enroll in continent's first large-scale HIV-vaccine study

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The HIV Vaccine Trials Network's Dr. James Kublin is one of the lead investigators in South Africa's Phambili HIV-vaccine trial. Kublin, also a physician in the Clinical Research Division, said that high levels of HIV infection, good clinical infrastructure, community involvement and education make South Africa an excellent location for the trial

Photo by Stephanie Cartier

The first large-scale HIV-vaccine trial on the African continent is now under way in South Africa, a country where 5.5 million people live with the deadly virus. Led by scientists from the Hutchinson Center and South Africa, the trial is called Phambili or "moving forward" in the Xhosa language. It is expected to run four years and enroll up to 3,000 participants at five sites thorough the country.

The sites are part of the HIV Vaccine Trials Network (HVTN), which is based at the Center and supported through a cooperative agreement with the National Institute of Allergy and Infectious Diseases of the National Institutes of Health. The trial sites also receive funding from the South African AIDS Vaccine Initiative. The Center's Statistical Center for HIV/AIDS Research and Prevention is the statistical data-management center for the study.

"This trial will answer several major scientific issues that face all of us in the field of HIV-vaccine development," said Dr. Lawrence Corey, principal investigator of the HVTN. "It will determine the usefulness of vaccines that induce high immune response to the parts of the virus that are similar between different strains of HIV-1."

A 'test of concept' trial

The study is known as a phase IIb or "test of concept" efficacy trial because it enables researchers to determine whether the test vaccine prevents HIV infection, results in lower HIV levels in those who become infected after vaccination, or both. In addition, trial investigators will determine if the vaccine has the potential to protect against the subtype of the virus that is prevalent in South Africa.

Phase IIb trials cannot be used to support licensure of a vaccine. However, the data from this study will guide whether this type of vaccine approach offers the promise of interrupting the spread of the virus, which currently leaves every 15-year old South African boy and girl with an 85 percent chance of losing his or her life to AIDS.

The South African study is likely to provide important new data on how the test vaccine might work in a predominantly heterosexual HIV epidemic, how well the vaccine works in women, and whether the vaccine works in populations with pre-existing immunity to the viral vector used in the vaccine, said Corey, also an investigator in the Center's Clinical Research Division and head of the Infectious Diseases Program and Virology Division at the University of Washington School of Medicine.

"South Africa is an excellent location for this trial due to the high levels of infection coupled with the good clinical infrastructure, including internationally recognized immunology laboratories, a well-established national vaccine initiative and experience in running clinical trials," said Dr. James Kublin, one of the study's lead investigators from the HVTN, working in collaboration with Dr. Glenda Gray, of the Perinatal HIV Research Unit, University of the Witwatersrand, based at the Chris Hani Baragwanath Hospital in Soweto.

"Community involvement and education initiatives in South Africa are robust and mature, and they are essential for running trials involving thousands of volunteers," said Kublin, a physician in the Clinical Research Division and a clinical associate professor of health services at the University of Washington School of Public Health and Community Medicine. Volunteers for the trial will be healthy HIV negative males and females, aged 18 to 35 years, who are sexually active and not pregnant.

The test vaccine, known as the MRKAd5 HIV-1 trivalent vaccine, is manufactured by Merck & Co., Inc. and already has been studied for several years in phase I and phase II trials involving thousands of volunteers in the Americas, Africa and Australia. In those previous trials, the vaccine was found to be safe and to stimulate cellular immune responses against HIV in more than half of volunteers.

Developed by Merck Research Laboratories, the test vaccine is based on an adenovirus — a common cold virus that has been modified so that it cannot cause a cold in humans or be passed from person to person. The adenovirus is the carrier or vector, which transports copies of three HIV genes called gag, pol and nef. The vaccine is made in the laboratory. It does not contain live HIV; therefore, it cannot cause infection.

The hope is that these HIV genes will produce a cellular immune response to HIV and cause the body to make killer cells that are programmed to recognize and destroy cells that are infected with HIV. The previous studies with this vaccine suggest that it is generally well tolerated and that the response of the immune system or immunogenicity is high.

Long-term commitment

The trial design will compare the test vaccine to a placebo (a harmless substance). To eliminate bias, neither volunteers nor researchers will know who receives the vaccine and who receives the placebo. The trial will last about four years. The South African Medicines Control Council and the South African Department of Agriculture have approved the trial, which has also been reviewed by the U.S. Food and Drug Administration. A group of independent experts, not affiliated with Merck and Co. Inc, the HVTN, or the clinical-trial investigators, will carefully monitor the safety of the trial participants.

A cornerstone of this vaccine trial is a commitment to the highest level of preventive care for all participants. To meet this commitment, all participants will receive extensive, state-of-the-art risk-reduction counseling on a regular basis throughout the study, and high-quality male and female condoms will be provided to participants.

Participants also will be provided access to treatment for any sexually transmitted infection acquired during the study. Recent research has shown that men who are circumcised are less likely to become HIV infected when they have sexual relations with women. As a result, medical circumcision also will be provided to male participants who choose to undergo the procedure.

What is the HVTN?

The HIV Vaccine Trials Network is an international collaboration of scientists and institutions whose goal is to accelerate the search for an HIV vaccine by sharing trial results and facilitating parallel, concurrent testing.

The HVTN is a unique hybrid that combines the depth and diversity of the academic community and the flexibility of a commercial drug company. Working with industry and government, the HVTN seeks to expedite and coordinate the trial process — advancing vaccine candidates and building a body of knowledge around HIV-vaccine trials.

Volunteer for vaccine studies

The HIV Vaccine Trials Unit seeks healthy men and women ages 18-50 of all sexual orientations who are HIV negative and have no major medical problems to participate in studies to test potential vaccine candidates.

Learn more about how you can make a difference in the fight against HIV/AIDS. Contact the Seattle HIV Vacciine Trials Unit at (206) 667-2300 or visiting **www.seattlevaccines.org**.

TAGS: Clinical Research, HIV AIDS, Jim Kublin, Lawrence Corey, Vaccine and Infectious Disease

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