Large-scale HIV vaccine trial to launch in South Africa

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An early-stage HIV vaccine clinical trial in South Africa has determined that an investigational vaccine regimen is safe and generates comparable immune responses to those reported in a landmark 2009 study showing that a vaccine can protect people from HIV infection. Consequently, the National Institute of Allergy and Infectious Diseases (NIAID) and its partners have decided to advance the experimental HIV vaccine regimen into a large clinical trial. This new study, called HVTN 702, is designed to determine whether the regimen is safe, tolerable and effective at preventing HIV infection among South African adults. The trial is slated to begin in November 2016, pending regulatory approval.

"For the first time in seven years, the scientific community is embarking on a large-scale clinical trial of an HIV vaccine, the product of years of study and experimentation," said Anthony S. Fauci, M.D., director of NIAID, part of the National Institutes of Health and a co-funder of the trial. "A safe and effective HIV vaccine could help bring about a durable end to the HIV/AIDS pandemic and is particularly needed in southern Africa, where HIV is more pervasive than anywhere else in the world."

The experimental vaccine regimen that will be studied in HVTN 702 is now being tested in the smaller initial trial, named HVTN 100, and is based on the regimen investigated in the U.S. Military HIV Research Program-led RV144 clinical trial in Thailand that delivered landmark results in 2009. The current regimen is designed to provide greater protection than the RV144 regimen and has been adapted to the HIV subtype that predominates in southern Africa.

The experimental vaccine regimen tested in the RV144 trial was found to be 31.2 percent effective at preventing HIV infection during the 3.5 years after vaccination, although the regimen appears to have been 60 percent effective one year after vaccination. In the HVTN 702 study, the design and schedule of the RV144 vaccine regimen have been adjusted to try to increase the magnitude and duration of vaccine-elicited immune responses.

NIAID is responsible for all operational aspects of the pivotal Phase 2b/3 trial, which will enroll 5,400 HIV-uninfected men and women ages 18 to 35 years who are at risk for HIV infection. The NIAID-funded HIV Vaccine Trials Network (HVTN) will conduct the study. Results are expected in late 2020.

The HVTN 702 study will be led by Protocol Chair Glenda Gray, MBBCH, FCPaed (SA). Dr. Gray is president and chief executive officer of the South African Medical Research Council, research professor of pediatrics at the University of the Witwatersrand, Johannesburg, and a director of the Perinatal HIV Research Unit at Chris Hani Baragwanath Hospital in Soweto, South Africa.

"HVTN 702 will tell us whether the initial success observed in HVTN 100 will bear fruit in the form of a safe and effective HIV vaccine designed for the people of southern Africa," said Dr. Gray.

HVTN 100 and HVTN 702 are part of a larger HIV vaccine research endeavor led by a group called the Pox-Protein Public-Private Partnership, or P5—a diverse set of public and private organizations committed to building on the success of the RV144 trial. The P5 aims to produce an HIV vaccine that could have a significant public health benefit in southern Africa and to deepen scientists' understanding of the immune responses associated with preventing HIV infection. P5 members are NIAID, the Bill & Melinda Gates Foundation, the South African Medical Research Council, HVTN, Sanofi Pasteur, GSK and the U.S. Military HIV Research Program.

The HVTN 702 vaccine regimen consists of two experimental vaccines: a canarypox-based vaccine

called ALVAC-HIV and a bivalent gp120 protein subunit vaccine with an adjuvant that enhances the body's immune response to the vaccine. Both ALVAC-HIV (supplied by Sanofi Pasteur) and the protein vaccine (supplied by GSK) have been modified from RV144 to be specific to HIV subtype C, the predominant HIV subtype in southern Africa. In addition, the protein subunit vaccine in HVTN 702 is combined with MF59 (also supplied by GSK), a different adjuvant than the one used in RV144, in the hope of generating a more robust immune response. Finally, the HVTN 702 vaccine regimen will include booster shots at the one-year mark in an effort to prolong the early protective effect observed in RV144.

All study participants will receive a total of five injections over one year. The volunteers will be randomly assigned to receive either the investigational vaccine regimen or a placebo.

The safety of HVTN 702 study participants will be closely monitored throughout the trial, and participants will receive the standard of care for preventing HIV infection. Study participants who become infected with HIV during the trial will be referred to local medical providers for care and treatment and will be counseled on how to reduce their risk of transmitting the virus.

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