Africa's first large-scale HIV vaccine study launches

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The launch of the first large-scale study to evaluate a candidate HIV vaccine on the African continent was announced today by study collaborators in the United States and South Africa. The trial will involve up to 3,000 participants at five sites throughout South Africa and is expected to continue for four years.

The sites are part of the HIV Vaccine Trials Network (HVTN), which is headquartered at Fred Hutchinson Cancer Research Center in Seattle 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.

"This trial will answer several major scientific issues that face all of us in the field of HIV-vaccine development," said Lawrence Corey, M.D., principal investigator of the HVTN and a member of the Hutchinson Center's Clinical Research Division. "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."

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, investigators for the South Africa vaccine trial will determine if this vaccine, which is based on clade B HIV, has the potential to protect against the clade C virus, the

subtype 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 promise to interrupt the continued spread of HIV.

Additionally, 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, according to Corey, who is also 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 James Kublin, M.D., M.P.H., one of study's lead investigators, along with Glenda Gray, MBBCH, FCPaeds (SA), 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, who is a staff physician in the Hutchinson Center's Clinical Research Division and a clinical associate professor of health services at the University of Washington School of Public Health and Community Medicine.

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 II trials involving thousands of volunteers in the Americas, Africa and Australia to evaluate safety and immune responses. In those previous trials this vaccine was found to be safe and

to stimulate cellular immune responses against HIV in more than half of volunteers.

Merck Research Laboratories developed the test vaccine that 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 and does not contain live HIV. The test vaccine therefore 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 studies already completed with this vaccine suggest that it is generally well tolerated and that the response of the immune system or immunogenicity is high.

In South Africa, the vaccine trial is called "Phambili," which means "moving forward" in the Xhosa language. Volunteers will be healthy HIV negative males and females, aged 18 to 35 years, who are sexually active and not pregnant.

The trial design will compare the test vaccine to a placebo (a harmless substance) and, 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 trial has been approved by the South African Medicines Control Council and the South African Department of Agriculture, and has been reviewed by the US Food and Drug Administration. Approval has also been given or is pending by institutional ethics and bio-safety committees at all the trial sites. In addition, there will be an independent Data and Safety Monitoring Board, a group of independent experts, not affiliated with Merck and

Co. Inc, the HVTN, or the clinical trial investigators, who 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, access to medical circumcision also will be provided to male participants who choose to undergo the procedure.

Source: Fred Hutchinson Cancer Research Center