



Human Clinical Trial of DNA-MVA HIV Vaccine Candidate Begins

Phase I study of PENNVAX™-G / MVA-CMDR will assess safety and immune responses in HIV-uninfected volunteers at five sites on three continents

September 28, 2010 - A Phase I study, called RV262, recently began to evaluate a combination DNA prime/MVA vector boost vaccine regimen that was developed to protect against diverse subtypes of HIV-1 prevalent in North America, Europe, Africa and South America.

The National Institute of Allergy and Infectious Diseases (NIAID), part of the U.S. National Institutes of Health (NIH), is sponsoring the study, which will enroll 92 total participants and is designed to assess safety and immune responses. The study is being conducted by the U.S. Military HIV Research Program (MHRP) through its clinical research network in the U.S., East Africa and Thailand.

This clinical trial was designed to test a unique prime-boost preventive HIV vaccination strategy aimed at global coverage. The prime is a plasmid DNA vaccine, PENNVAX™-G, and the boost is a virus vector vaccine, Modified Vaccinia Ankara-Chiang Mai Double Recombinant (MVA-CMDR). Together, the vaccines are designed to deliver a diverse mixture of antigens for HIV-1 subtypes A, B, C, D and E.

Taken separately, DNA based and MVA based strategies have been shown to be safe and immunogenic in pre-clinical and clinical trials. Researchers hope they can enhance immune responses by using this prime-boost strategy. Another distinguishing feature of this study is the use of different HIV antigens during the priming (A,B,C,D) and boosting (A/E), which is being studied as a means to increase the breadth of the immune response.

"We hypothesize that this vaccine regimen, which has subtype-mismatched inserts, will facilitate the emergence of subdominant epitopes and increase the overall breadth of the immune response," noted Dr. Mary Marovich, Chief of the Department of Vaccine Research and Development at MHRP and the Protocol Chair for the study.

The DNA vaccine was designed in Prof. David B. Weiner's laboratory at the University of Pennsylvania and licensed by Inovio Pharmaceuticals for further clinical product development. The boost vaccine component, based on Modified Vaccinia Ankara (MVA), is a modified version of the smallpox vaccine that has been used safely and effectively to eradicate that disease worldwide. Researchers at MHRP and NIAID developed the MVA vaccine.

Historically, DNA vaccine potency has been constrained by the inability to deliver enough DNA into cells, which express the antigens coded by the DNA. To address this, researchers will also test two intramuscular delivery methods for the DNA prime (PENNVAX™-G) to compare their effects on immune response. The two devices that will be tested in this study are the Biojector® 2000 and the CELLECTRA® EP (electroporation) device.

The Biojector is a needle-free injection system that has FDA clearance for delivering vaccines and other injected medications. The CELLECTRA EP system is an intramuscular electroporation device currently being evaluated in clinical trials as an alternative vaccine delivery system to increase immune responses above those elicited by standard needle and syringe injections. Electroporation involves the application of controlled, millisecond electrical pulses to cells to enhance their uptake of the vaccine.

"We are very excited about the launch of this important clinical trial exploring the role of newer HIV vaccine approaches building on the success of the RV144 Thai prime boost trial," said COL Nelson Michael, Director of MHRP and the Division of Retrovirology at the Walter Reed Army Institute of Research (WRAIR). "The role of electroporation as a method of delivery of the priming DNA vaccine will be an especially critical factor to assess in this initial phase I safety and immunogenicity trial."

Once the vaccine combination has been assessed as safe and acceptable in 12 HIV-uninfected participants in the U.S., the study will begin at four MHRP sites: Kericho, Kenya; Kampala, Uganda; Mbeya, Tanzania; and Bangkok, Thailand. Twenty healthy, HIV-uninfected participants will be enrolled at each of these sites for a total of 80 international participants.

This clinical trial is a collaboration that includes Bioject Medical Technologies Inc., Inovio Pharmaceuticals, Inc., Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., NIAID and the U.S. Army/MHRP.

About MHRP

The U.S. Military HIV Research Program (MHRP)—centered at Walter Reed Army Institute of Research (WRAIR) and part of the US Medical Research and Materiel Command—conducts research to develop an effective HIV vaccine and integrates prevention, treatment, diagnosis and monitoring as part of an international effort to protect troops and reduce the risk of HIV infection worldwide. MHRP has developed five state-of-the-art international research sites in the U.S., Africa and Asia. The program collaborates on HIV prevention care and treatment services, funded by the President's Emergency Plan for AIDS Relief (PEPFAR), with African militaries and in the communities where it conducts research.

In 2009, MHRP announced results of an Army-sponsored clinical trial in Thailand that demonstrated for the first time a modest ability to protect against HIV infection, reducing the number of infections by 31.2 percent. MHRP researchers are now working with scientists around the world, with the support of NIAID, to dissect the trial results to inform basic research and design future clinical trials to translate this scientific milestone into a deployable vaccine. For more information, visit www.hivresearch.org.