New vaccine effective in preventing TB in African patients with HIV infection

January 29 2010

Investigators from Dartmouth Medical School (DMS) have reported results of a clinical trial showing that a new vaccine against tuberculosis, Mycobacterium vaccae (MV), is effective in preventing tuberculosis in people with HIV infection. The DarDar Health Study, named for Dartmouth and Dar es Salaam, Tanzania, found that MV immunization reduced the rate of definite tuberculosis by 39 percent among 2,000 HIV-infected patients in Tanzania.

The study appears in the January 29, 2010 online issue of the journal AIDS, and it will be published in the March print issue of AIDS.

"Since development of a new vaccine against tuberculosis is a major international health priority, especially for patients with HIV infection, we and our Tanzanian collaborators are very encouraged by the results of the DarDar Study," said Principal Investigator Ford von Reyn, M.D., director of the DarDar International Programs for the Section on Infectious Disease and International Health at DMS.

The 7-year, randomized, placebo-controlled trial was conducted in Tanzania with collaborators at the Muhimbili University of Health and Allied Sciences (MUHAS) in Dar es Salaam, and was supported by a grant from the National Institutes of Health (NIH) in the United States. According to Kisali Pallangyo, M.D., the senior collaborator at MUHAS, "The study confirms that University institutions from the northern and southern hemispheres can establish partnerships to perform quality clinical research work with global importance. The results of the study

are not only good news for people living in regions with high infection rates of HIV and tuberculosis but has also contributed to capacity building in performing TB vaccine trials among HIV infected persons in Tanzania."

TB is the most common cause of death from HIV in developing countries. Since newly-infected HIV patients risk contracting TB almost immediately, Dartmouth investigators are targeting a strategy for immunization with MV before patients need to start taking antiretroviral drugs.

The Dartmouth group began Phase-I human studies with MV in the United States in 1994, in collaboration with Robert Arbeit, M.D., now affiliated with Tufts University School of Medicine, and demonstrated that a multiple-dose series of MV was safe in both healthy subjects and patients with HIV infection.

The group then conducted Phase-II studies in larger groups of adults in Zambia and in Finland. In the Zambian trial, Richard Waddell, D.Sc., a research assistant professor at DMS, found that MV boosted immune responses against tuberculosis that had first been primed in childhood with the current TB vaccine, BCG.

Subsequently the DarDar group received NIH funding to conduct the large Phase-III efficacy trial among HIV-infected patients with prior BCG immunization in Tanzania, under the direction of Lillian Mtei, M.D., in Dar es Salaam, with von Reyn and collaborators Drs. Muhammed Bakari and Mecky Matee at MUHAS with Waddell, Arbeit and C. Robert Horsburgh M.D, Chairman of Epidemiology at Boston University School of Public Health.

Von Reyn, a Professor in the Department of Medicine at DMS, described the DarDar trial as "a significant milestone" - the first to

demonstrate that any type of vaccine can prevent an infectious complication of HIV in adults. He added that the next steps are to improve the manufacturing methods to support the production of the larger quantities of the TB vaccine needed for further studies and subsequent clinical use. Development work on manufacturing will be conducted by the Aeras Global TB Vaccine Foundation in Rockville, Maryland, in conjunction with the London-based manufacturer, Immodulon Therapeutics.

"Aeras' goal is to speed the development and distribution of new TB vaccines for those who need them most," said Jerald C. Sadoff, MD President and Chief Executive Officer of Aeras Global TB Vaccine Foundation. "We are pleased that our internal manufacturing capacity can assist in the further development of this TB vaccine."

The vaccine is a type known as an inactivated, whole-cell mycobacterial vaccine and is expected to be economical to produce and distribute, von Reyn said.

Provided by Dartmouth College