

A Phase I Clinical Trial to Evaluate the Safety, Tolerability and Immunogenicity of a High Dose Live Recombinant Canarypox ALVAC-HIV Vaccine (vCP1452) in Healthy HIV-1 Uninfected Adult Participants (HVTN 039)

WHY IS THE TRIAL BEING DONE?

The main purpose of this study is to see if an experimental vaccine is safe and to study how the human immune system responds to the vaccine. One of the immune responses that may be important in preventing disease from HIV is the immune response that kills HIV-infected cells. Unfortunately not all of the individuals vaccinated with the current HIV vaccines trigger these immune responses. This trial is designed to determine whether a higher vaccine dose (six times the usual dose) will elicit a higher immune response. The dose in this trial is a higher dose than the ones used in previous trials. It is important to study the immune responses and safety in more people before using these vaccines in large studies.

WHO IS SPONSORING THE STUDY?

This trial is sponsored by the Division of AIDS (DAIDS) and The National Institute of Allergy and Infectious Diseases (NIAID). The product was created by Aventis Pasteur of Lyon, France, and will be tested through the HIV Vaccine Trials Network.

WHEN AND WHERE IS THE STUDY BEING CONDUCTED?

This trial began in December of 2001 with a study duration of 18 months and is taking place in ten US cities:

- New York, NY -- Columbia University and the New York Blood Center
- Seattle, WA -- Fred Hutchinson Cancer Research Center/Univ. of Wash.
- Baltimore, MD -- Johns Hopkins University and the University of Maryland
- Nashville, TN -- Vanderbilt University
- Birmingham, AL -- University of Alabama at Birmingham
- Saint Louis, MO -- Saint Louis University
- Rochester, NY -- University of Rochester
- Boston, MA -- Harvard University
- Providence, RI -- Brown University
- San Francisco, CA -- The San Francisco Department of Public Health

WHO IS ELIGIBLE TO PARTICIPATE IN THE STUDY?

Healthy, low-risk, HIV uninfected adult participants of either gender between the ages of 18 and 60 with no more than 10% over 50 years old.

WHAT DOES THE HVTN 039 VACCINE CONTAIN?

ALVAC-HIV vCP1452 is made from a vaccine used to protect canaries against the canarypox virus. In making the vaccine, the canarypox virus is attenuated, or weakened. ALVAC-HIV vCP1452 uses the weakened canarypox virus to carry copies of HIV genes coding for the HIV envelope, core and a regulatory protein. ALVAC-HIV vCP1452 contains additional genes that may help stimulate the immune response to the vaccine.

When injected into the body, the canarypox virus can enter some human cells, but does NOT multiply in them. However, it directs the cell to make the HIV proteins encoded in the genes that are inside the canarypox virus. These proteins trick the immune system into thinking that the host is infected with HIV. The immune system of the host may then make specialized immune cells called cytotoxic T lymphocytes (CTLs) that can kill HIV-infected cells - just as if it were fighting an actual HIV infection.

Scientists chose canarypox to make ALVAC-HIV vaccines such as vCP1452 because: (1) research has shown that the virus appears to be safe to use in humans, (2) canarypox does not multiply in human cells, and (3) it carries the vaccine genes into the body's cells.

CAN THESE VACCINES CAUSE HIV INFECTION?

No. It is important for you to know that you cannot get infected from this vaccine. This vaccine is produced with only a piece of virus protein. Furthermore, this vaccine is not produced from live virus, so there is NO possibility that they can contain live or killed HIV virus. The canarypox virus itself cannot grow in human cells.

HOW DO SCIENTISTS THINK THESE VACCINES COULD HELP PREVENT HIV/AIDS?

The immune system fights viral infections with two major weapons: neutralizing antibodies and cytotoxic T lymphocytes (CTLs). This particular product focuses on the CTL response. CTLs, also known as "killer T cells", are white blood cells that can potentially kill cells infected with HIV. The results of this study are expected to determine if HIV-1 specific T cell responses will increase when vaccinating with a higher dose of ALVAC-HIV (vCP1452).

ARE THESE VACCINES SAFE?

The vaccine, at a lower dose, is already being tested in several studies in at least 300 people and so far it seems to be safe. A similar vaccine, ALVAC-HIV (vCP205) has been tested in several studies in about 500 humans, and so far it seems to be safe. High doses of a similar vaccine have been given to a few people without serious side effects.

WHAT IS THE DESIGN OF THIS STUDY?

Entering the Study. To see if one qualifies to take part in this study, they will be asked about their medical history and have a physical examination. They will also have about 4 tablespoons (60 ml) of blood drawn for routine tests and check for HIV infection. A urine specimen will also be collected for routine urinalysis. Pregnancy tests will also be administered to woman able to become pregnant. Women who are pregnant will not be allowed to enter the study. There will also be a series of questions asked about one's sexual activity and drug use.

During the study. This is a randomized, placebo-controlled, double-blinded trial. "Randomized" means that participant will be put into one of the three groups randomly, much like tossing a coin. "Placebo-controlled" means that there will be a placebo used that will not contain the investigational vaccine. "Double-blinded" means that no one directly involved in the trial will know which group participants are in until the study is completed, neither the participant, the study investigators nor the nurses.

There will be a total of 110 volunteers with 60 receiving a high dose of the vaccine, 40 receiving the normal dose of the vaccine and 10 receiving placebo. There will be 2 injections administered intramuscularly into each anterior thigh at separate visits. The reason for this particular injection site is because the volume of fluid is better tolerated in the thigh than in the deltoid muscles of the arm. In total there will be 11 visits to the vaccine trial site. Other visits involve one or a combination of the following: physical exam, pregnancy test (women), urine dipstick, blood draw, HIV testing, and behavioral questionnaires.

HAVE THESE VACCINES BEEN STUDIED BEFORE?

As of May 2001, over 200 people received the vaccine used in this study at the lower dose. The higher dose of the vaccine to be used in this study has not been given to humans previously.

WHAT IS KNOWN SO FAR ABOUT HOW PEOPLE IN CLINICAL TRIALS RESPOND TO THE VACCINES?

Nothing, this is the first time this vaccine will be tested in humans at this high of a dose. However, we do know that similar kinds of vaccines have been given to several hundred healthy people in the past without serious side effects. High doses of a similar vaccine have been given to a few people without serious side effects.

WHO REVIEWED AND APPROVED THE STUDY?

The vaccines in this study are considered investigational. This means that the U.S. Food and Drug Administration (FDA) allows the use of these products only in research with a small number of subjects. The vaccines are made according to guidelines reviewed by the U.S. Food and Drug Administration (FDA).

WHAT SAFEGUARDS AND ETHICAL PROCEDURES ARE IN PLACE FOR PROTECTING THE VOLUNTEERS?

Before deciding to enter the study, potential volunteers are provided with information about HIV and AIDS, the intent of the study, possible risks and benefits of participation, and study procedures. In addition to the unknown risks associated with any new, experimental vaccine, potential risks include side effects due to injection into a muscle and social harm issues associated with taking part in HIV studies. Volunteers will be reminded consistently that being part of this study does not mean that they are less likely to become infected with HIV.

Volunteers who are eligible and willing to participate after the study has been fully explained to them will be asked to sign an informed consent to enroll in the study. Volunteers will be given plenty of time to consider whether they want to participate. Volunteers are free to refuse to join the study or to leave the study at any time without losing the benefits of their standard medical care.

ARE THERE NON-MEDICAL RISKS?

Yes. Others may treat you unfairly if the test vaccine causes you to “appear” to be HIV positive. You will not be able to donate blood and you may also have difficulties with: getting insurance, hospitalization, traveling to other countries, employment, military/peace corps service, relationships with friends and family.

To help avoid these problems, the participant will be encouraged to talk to the study staff before getting HIV testing done outside the study. The participant will also be offered an identification card that shows that they joined this study. A toll free number will be listed on the card and may be called for help or information

WHAT WILL HAPPEN TO VOLUNTEERS IF THEY BECOME HIV-INFECTED FROM RISKY BEHAVIOR DURING THE COURSE OF THE STUDY?

Throughout the study, volunteers will receive counseling on HIV prevention. Volunteers will be instructed about the symptoms of early HIV infection and to come to the clinic if such symptoms develop. Clinical and laboratory evaluations will be done periodically throughout the study to determine HIV status. If found to be HIV-infected, a volunteer will be notified in person, as soon as possible, and counseled about what the test results mean and how to avoid passing the virus to others. The volunteer will be referred for medical care, treatment and additional counseling according to standard practices at each site. Testing and counseling will be provided to the volunteer’s partner(s), if desired. HIV-infected volunteers will continue to be followed in the study although they will no longer receive vaccinations.

HOW CAN I OBTAIN MORE INFORMATION ABOUT THE STUDY?

More information about AIDS vaccine clinical trials can be obtained by calling the AIDS Clinical Trials Information Service (1-800-TRIALS-A) or by visiting their website at www.actis.org. More information about the HIV Vaccine Trials Network (HVTN) can be found on their website at www.hvtn.org.