



HIV VACCINE
TRIALS NETWORK

QUESTIONS AND ANSWERS

SAAVI 102/ HVTN 073 HIV VACCINE CLINICAL TRIAL

A phase 1 placebo-controlled clinical trial to evaluate the safety and immunogenicity of SAAVI DNA-C2 vaccine boosted by SAAVI MVA-C vaccine in HIV uninfected healthy vaccinia naïve adult participants in South Africa and the United States

1. WHAT IS THE SAAVI 102/ HVTN 073 TRIAL?

SAAVI 102/HVTN 073 is the name of a phase 1 placebo-controlled clinical trial to test the safety and immune response of two experimental (study) HIV vaccines. These vaccines do not contain any live or whole HIV cells. For more information on the vaccines, see Question 4 below.

The study vaccines cannot cause HIV infection.

Not everyone in this study will get the study vaccines. Some people will get a placebo, which is sterile salt water that does not contain the vaccine. Researchers will compare the results from people who got the placebo with results from people who got the study vaccines. Whether a trial participant receives the study vaccines or the placebo will be decided randomly. Neither the study staff nor the participants will know who gets the vaccine or placebo.

2. WHO IS CONDUCTING THIS CLINICAL TRIAL?

This trial is sponsored by the Division of AIDS (DAIDS), within the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH), an agency of the US Department of Health and Human Services (DHHS).

The HIV Vaccine Trials Network (HVTN) will run the trial. The HVTN is an academically based research organization of scientists, educators and community members committed to eliminating the spread of HIV in the world by finding a safe and effective vaccine. The Network is supported through a cooperative agreement with the National Institute of Allergy and Infectious Diseases (NIAID), part of the US National Institutes of Health (NIH). To learn more about the HVTN, please visit www.hvtn.org.

In South Africa the trial will be conducted by researchers and staff at two HVTN designated trial sites, one at the Emavundleni Centre in Crossroads, Cape Town and one at the Perinatal HIV Research Unit (PHRU), based at the Chris Hani Baragwanath Hospital, Soweto.

The South African Medical Research Council (MRC) is a statutory organisation established by an Act of Parliament in 1969. Its mission is to improve the nation's health and quality of life through promoting and conducting relevant and responsive health research. The South African AIDS Vaccine Initiative (SAAVI) was established

by the South African government and Eskom in 1999 to co-ordinate the research and development of an affordable, effective and locally relevant HIV vaccine for southern Africa. SAAVI is a lead programme of the South African MRC.

The MRC as represented by SAAVI has agreed to cooperate with the NIAID as represented by DAIDS in the conduct of the SAAVI 102/HVTN 073 clinical trial. As part of this cooperation, SAAVI will contribute towards the development of the infrastructure to conduct the clinical trial at the two designated HVTN clinical trial sites located in South Africa.

3. WHAT IS A VACCINE, AND WHAT IS A VACCINE CLINICAL TRIAL?

A vaccine is given to people to prevent infection or fight disease. Currently there is no vaccine against HIV that works. In order to find an effective HIV vaccine, researchers need to test study vaccines that seem most likely to help the body fight HIV. A vaccine clinical trial is a way to test a study vaccine to see if it is safe to give to people. It is also a way to measure the immune response caused by the study vaccine. If early trials show that the study vaccine is safe and the immune response is good, researchers may test for efficacy – whether the study vaccines work to prevent HIV infection or to slow disease progression to AIDS – in later trials.

4. WHAT KIND OF EXPERIMENTAL VACCINES, OR “STUDY VACCINES,” ARE BEING TESTED IN THE SAAVI 102/ HVTN 073 CLINICAL TRIAL?

There are two experimental vaccines that are being tested. They are called SAAVI DNA-C2 and SAAVI MVA-C. From here on, we will call them the DNA vaccine and the MVA vaccine, or the “study vaccines”. The study vaccines were developed for SAAVI by scientists at the University of Cape Town (UCT), South Africa, through joint funding from SAAVI and the NIAID. To try to get the best protection, the vaccines were designed to represent the HIV viruses circulating in South Africa, namely HIV subtype C. The DNA vaccine was constructed in South Africa using a main component (plasmid backbone) provided by the Dale and Betty Bumpers Vaccine Research Centre (VRC) of the NIAID and was manufactured in the USA. The MVA vaccine was designed by the team at UCT and constructed and manufactured in the USA.

The study vaccines will be tested in a prime-boost approach. This means that the DNA vaccine will be given to prime the immune response followed by the MVA vaccine to boost or enhance the immune response. Both study vaccines will be injected intramuscularly.

The DNA vaccine SAAVI DNA-C2 is made out of DNA. DNA is a natural substance found in all living things, including people and viruses. DNA tells cells to make proteins. In this study, the DNA vaccine will tell the body to make a small amount of some proteins that are found in HIV. The body’s immune system may recognize these proteins and prepare itself to fight HIV. This is called an immune response. The DNA vaccine is similar to natural DNA, but it was made in a laboratory. A person cannot become infected with HIV or AIDS from the DNA vaccine or from these proteins.

The MVA vaccine SAAVI MVA-C2 was made from a virus called Modified Vaccinia Ankara (MVA) virus. It is similar to the smallpox vaccine that has been used worldwide. The MVA virus in the vaccine has been changed so that it cannot grow in humans or spread to other people. Like the DNA vaccine, the MVA vaccine will tell the body to make small amounts of some proteins that are found in HIV. These proteins may cause the body to have an immune response. A person cannot become infected with HIV or AIDS from the MVA vaccine or from these proteins.

5. ARE THESE STUDY VACCINES SAFE?

Based on the data from animal studies, and the use of similar vaccines in humans, scientists believe that these study vaccines are safe for use in human trials. But there is always the possibility that there could be problems no one expected. That is why these study vaccines, like any new drugs or vaccines, need to be tested in people in a clinical setting. Each participant’s health and safety will be watched closely throughout the trial.

6. CAN THESE STUDY VACCINES CAUSE HIV INFECTION?

It is **impossible** to get HIV infection or AIDS from these study vaccines. They are not made from live HIV, killed HIV, or HIV-infected cells.

These study vaccines cannot cause HIV infection.

HIV study vaccines are designed to lower the chance of someone becoming HIV- infected if that person is exposed to HIV. We do not know if the study vaccines tested in this trial will decrease, increase, or not change a trial participant's chance of becoming infected if he or she is exposed to HIV.

There is a chance that these study vaccines could increase a trial participant's risk of becoming infected if he or she is exposed to HIV.

A previous study called the STEP Study, which was conducted in the USA, tested an HIV study vaccine that contained a weakened common cold virus called adenovirus type 5 (Ad5). In a subset of participants from this study who were previously infected with Ad5 and who were uncircumcised, there was a higher number of HIV infections in those who received the vaccine than those who received the placebo. The people who became infected with HIV in the STEP Study did not get HIV from the study vaccine. They became infected with HIV from another infected person.

There was also a South African trial of the Ad5 study vaccine called the Phambili study. It was stopped following the above results from the STEP study. The group of trial participants from Phambili who had been infected with Ad5 before entering the study and who received the study vaccine did not have more HIV infections than the group who had been infected with Ad5 before entering the study and who got the placebo. One reason could be that fewer trial participants were vaccinated in the Phambili trial compared to those who were vaccinated in the STEP Study.

Researchers are still looking at the STEP study results to try to learn more and to understand the relationship between vaccination, circumcision and prior infection to Ad5.

The study vaccines used in this trial are not like the vaccine used in the STEP study as they have a completely different design.

It is very important that participants avoid exposure to HIV during the study. The trial site staff will give trial participants comprehensive risk reduction counselling to help them learn how to reduce behaviour that puts them at risk of getting HIV.

7. HOW COULD THE STUDY VACCINES HELP PREVENT HIV AND OR AIDS?

Study vaccines are designed to mimic (look like) the structures of HIV. By doing this, the study vaccines may cause a response from a person's immune system. During this response, the immune system may learn to recognize HIV without being exposed to HIV.

If a person who received the study vaccines is later exposed to HIV, hopefully the immune system will be prepared to respond. However, it is not yet known if these study vaccines will prevent HIV infection or slow disease progression to AIDS. If the results from this phase 1 clinical trial are promising, more clinical trials need to be conducted to see if the study vaccines work.

So, it is important to remember that being given the study vaccines does not mean a trial participant is protected from HIV infection. This is explained to participants and they are counselled on how to avoid behaviour that will put them at risk of HIV infection.

8. WHY IS THIS TRIAL BEING DONE?

This is a phase 1 trial, meaning its main purpose is to test if the study vaccines are safe to give to people and how the immune system responds to the vaccines. The study vaccines have already been tested in the laboratory and in animals.

9. WHO IS ELIGIBLE TO PARTICIPATE IN SAAVI 102/HVTN 073?

Each participant must meet certain criteria to be eligible (to qualify) to participate in the trial. Participants must be healthy adults who are between 18 and 45 years old and HIV negative (free of HIV infection). Participants also must not have received the smallpox vaccine in the past. They must be at low risk of getting HIV infection.

Potential participants are asked about their medical history and are given a physical examination. They then have blood and urine samples taken for routine testing. They are also asked about their sexual activity and alcohol or drug use.

People who want to join the trial and were born female will be given a pregnancy test. Those who are pregnant or breastfeeding are not eligible to join. Anyone in the trial who was born female and who is capable of getting pregnant must agree to use effective birth control starting at least 21 days before the first injection of the clinical trial and continuing until the last clinic visit.

10. WHEN AND WHERE IS THIS TRIAL BEING CONDUCTED?

SAAVI 102/ HVTN 073 is an international trial and will be done in two countries: the US and South Africa. The trial will be conducted at two sites in South Africa, one in Cape Town and one in Soweto, and at three sites in Boston, MA, in the US. The trial began enrolling participants in the US arm in late 2008 and early 2009 and has 12 participants enrolled. South Africa will begin enrolling participants in mid 2009.

11. HOW WILL THE SAFETY AND RIGHTS OF TRIAL PARTICIPANTS BE PROTECTED?

The HVTN and SAAVI work hard to protect the safety and rights of the trial participants. Before they join the trial, volunteers will be given information about HIV vaccine trials, the reasons for the trial, possible risks and benefits, and about trial procedures. The clinic staff will allow plenty of time to talk with volunteers, answer their questions, and to give information to them in writing.

After the trial has been fully explained, volunteers are asked to sign an informed consent form. They sign this form before being screened for eligibility and before enrolling. The informed consent form helps confirm that trial participants have made an informed decision about joining the trial. Volunteers will have plenty of time to think about whether they want to join the trial. They may decide not to enrol. If they do enrol, they may still leave the trial at any time without losing the benefits of their standard medical care.

During the trial, the clinic staff will monitor trial participants to make sure the study vaccines are not causing them problems. Participants will be given any new information that could affect whether they want to stay in the study. Participants will be reminded often that being in a vaccine trial does not mean they are protected from HIV. They will be counselled at every clinic visit on ways to avoid becoming infected with HIV. (This counselling will include, for example, talking about correct condom use.) It is important for participants to understand that any new study vaccine may have both medical and nonmedical risks.

Community Advisory Boards or Groups (CAB/Gs) are also a mechanism to ensure that any human rights issues and other concerns raised by the community are addressed.

12. COULD EITHER STUDY VACCINE CAUSE A “FALSE-POSITIVE” OR “VACCINE-INDUCED POSITIVE” TEST RESULT ON AN HIV ANTIBODY TEST?

Some study vaccines may make a trial participant test positive on an HIV antibody test, even if the participant is not infected with HIV. One way study vaccines can create an immune response is by causing the body to make antibodies. Common HIV tests look for antibodies against HIV. This means that after a participant gets a study HIV vaccine, a standard HIV test may say the person has HIV, even if that isn't the case. This result is called a “false-positive” or “vaccine-induced positive” result.

Each site involved in the SAAVI 102/HVTN 073 trial will use other HIV tests that can detect whether a person is really infected with HIV. These tests can be used to determine if a positive HIV test result is a vaccine-induced positive result or due to true HIV infection.

There are no health problems associated with a false-positive HIV test result that are caused by a study HIV vaccine. However, someone who gets that type of test result may be treated unfairly by others. People with a positive HIV test result, even a vaccine-induced positive result, are not allowed to donate blood. They may also have problems getting insurance, travelling to other countries, or with their relationships with friends and family. The trial site staff can help with such problems.

13. HOW LONG WILL IT TAKE TO FIND OUT IF THIS COMBINATION OF STUDY VACCINES WORKS?

It could take several years to find out if this combination of study vaccines helps the immune system to protect against or control HIV infection. Within the next year, results from the SAAVI 102/HVTN 073 phase 1 trial will help researchers determine whether they should proceed with further clinical trials on these vaccines. The results from the phase 1 study will show whether the study vaccines are safe and immunogenic (they cause an immune response). If results from this phase are promising, phase 2 and 3 clinical trials may be conducted in bigger numbers of people. Phase 2 trials test for vaccine safety, immune response and the best way to give the study vaccine/s. Phase 3 clinical trials continue to test for safety and to see if the study vaccine/s is effective – whether it protects against HIV infection or if it slows disease progression to AIDS. Often there is a phase 2b trial – it produces further safety and efficacy data to give an idea of whether the vaccine/s is effective. The outcomes of a phase 2b study help to guide future research.

Participants who receive the study vaccines in SAAVI 102/HVTN 073 will not be eligible for any future clinical trials on these products.

14. WHO REVIEWED, APPROVED AND MONITORS THIS TRIAL?

In the US, the study vaccines are considered ‘investigational’, meaning that the US Food and Drug Administration (FDA) only allows them to be used in research. These study vaccines have been made according to FDA guidelines and the clinical trial protocol was reviewed by the FDA who allowed the protocol to move forward through the usual review process. The Protocol Team (the people who designed the trial) also carefully reviewed the information about the study vaccine before deciding to begin the trial. Similarly, the study vaccines have been approved for use in research in a phase 1 clinical trial in South Africa by the South African Medicines Control Council (MCC).

The Institutional Review Boards (IRBs) or Independent Ethics Committees (IECs) or Research Ethics Committees (RECs) at each participating research centre have also reviewed and approved the clinical trial protocol (trial plan). RECs are also involved in reviewing changes to the clinical protocol from an ethics and human rights point of view. Ethical concerns about the trial can also be directed to these bodies to be addressed. The local Institutional Biosafety Committees (IBCs) have also reviewed and approved the clinical trial protocol. Community members, for example, by way of Community Advisory Boards or Groups (CAB/Gs) are involved throughout the trial to ensure that the research is acceptable to the community. CAB/Gs are therefore one mechanism to ensure that any human rights issues and other concerns raised by the community are addressed.

15. FOR MORE INFORMATION

About the NIAID/DAIDS: www.niaid.nih.gov

About the HVTN: www.hvtn.org

About the MRC: www.mrc.ac.za

About SAAVI: www.saavi.org.za

About UCT's IIDMM: www.iidmm.uct.ac.za

About PHRU: www.hivsa.com

About DTHC: www.desmondtutuhivcentre.org.za

SAAVI Info-Line: **080 822 2463**

16. POSITIONING STATEMENTS

National Institute of Allergy and Infectious Diseases (NIAID) positioning statement

The US National Institute of Allergy and Infectious Diseases (NIAID) is part of the US National Institutes of Health (NIH), an agency of the US Department of Health and Human Services (DHHS). NIAID conducts and supports research—at NIH, throughout the United States, and worldwide—to study the causes of infectious and immune-mediated diseases, and to develop better means of preventing, diagnosing and treating these illnesses. To learn more about NIAID, please visit www.niaid.nih.gov.

Division of AIDS (DAIDS) within the NIAID positioning statement

DAIDS is a division of the US National Institute of Allergy and Infectious diseases (NIAID). It was established in 1986 to develop and implement the US national research agenda to address the HIV/AIDS epidemic. To learn more about DAIDS, please visit www.niaid.nih.gov.

HVTN positioning statement

The HIV Vaccine Trials Network (HVTN) is an academically based research organization of scientists, educators and community members committed to eliminating the spread of HIV in the world by finding a safe and effective vaccine. The Network is supported through a cooperative agreement with the National Institute of Allergy and Infectious Diseases (NIAID), part of the US National Institutes of Health (NIH). To learn more about the HVTN, please visit www.hvtn.org.

MRC positioning statement

The South African Medical Research Council (MRC) is a statutory organisation established by an Act of Parliament in 1969. Its mission is to improve the nation's health and quality of life through promoting and conducting relevant and responsive health research. To learn more about the MRC, please visit www.mrc.ac.za

SAAVI positioning statement

SAAVI was established by the South African government and Eskom in 1999 to co-ordinate the development of an affordable, effective and locally relevant HIV vaccine for southern Africa. SAAVI is a lead programme of the South African Medical Research Council (MRC). SAAVI receives direct funding from the South African government [the Departments of Health (to date) and Science & Technology (up to 2008)], ESKOM (up to end 2007) and Impala Platinum, and indirectly from international organisations including the US National Institutes of Health (NIH) and the HIV Vaccine Trials Network (HVTN). SAAVI works with local and international partners to achieve the common aim of finding a successful HIV vaccine. To learn more about SAAVI, please visit www.saavi.org.za

University of Cape Town, Institute of Infectious Disease and Molecular Medicine positioning statement

The Institute of Infectious Disease and Molecular Medicine (IIDMM) is a postgraduate research institute within the University of Cape Town's (UCT) Faculty of Health Sciences. Launched in 2005, it concentrates its efforts on infectious diseases, particularly on HIV/AIDS and tuberculosis, diseases that particularly threaten sub-Saharan Africa, as well as other prevalent non-communicable diseases.

Over the past decade, the University, and particularly the IIDMM, have transformed their research activities to meet the needs of people in Africa, ensuring that their work is translational - their discoveries and pursuits are taken from their laboratories and applied in the communities of Africa and elsewhere. To learn more about the IIDMM, please visit: www.iidmm.uct.ac.za

Desmond Tutu HIV Centre positioning statement

The Desmond Tutu HIV Foundation (DTHF) is a registered non-profit organisation focused on the pursuit of excellence in research, treatment, training and prevention of HIV and related infections in Southern Africa.

The Desmond Tutu HIV Foundation is based in Cape Town, South Africa and is run in association with the Desmond Tutu HIV Centre (DTHC) at the University of Cape Town's (UCT) Institute of Infectious Disease and Molecular Medicine. The Foundation operates community sites in greater Cape Town's Nyanga and Masiphumelele districts. To learn more about the DTHC, please visit: www.desmondtutuhivcentre.org.za

Perinatal HIV Research Unit positioning statement

The Perinatal HIV Research Unit (PHRU), established in 1996, is one of the largest AIDS research centres in Africa. The early research focus on prevention of mother-to-child-transmission has expanded and PHRU now leads studies on many different aspects of HIV prevention, treatment and care including medical and social research.

PHRU is a research unit of the University of the Witwatersrand (WITS), which is based in Soweto, South Africa, at Chris Hani Baragwanath Hospital, one of the world's biggest hospitals. To learn more about the PHRU, please visit: www.hivsa.com



HIV VACCINE INFO-LINE:

080 VACCINE
080 8222 463

www.saavi.org.za

SAAVI is an initiative of the South African government, and a lead programme of the Medical Research Council. Founded in 1999 by Eskom, the Department of Health, and the Department of Science and Technology, SAAVI seeks to co-ordinate the research, development and testing of HIV vaccines in South Africa to arrive at an effective, safe, affordable and locally relevant HIV vaccine as quickly as possible. SAAVI funds and co-ordinates activities of investigators at South African academic institutions.

An emphasis has been on creating novel biotechnology platforms to develop and test HIV vaccines, and developing the clinical and social environment conducive to running HIV vaccine trials. SAAVI works and collaborates with key national and international partners, and has both an internal research and development arm aimed at investigating and developing novel candidate vaccines, as well as extensive and widespread clinical infrastructure for testing both our own and vaccines developed internationally.

SAAVI is proudly sponsored by:

