HIV VACCINE
TRIALS NETWORK

Frequently asked questions

HVTN 307 vaccine study

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1. What is a vaccine study?

A vaccine teaches the body how to prevent a particular infection or fight a disease. In order to develop a vaccine, researchers need to test it in people. A vaccine study tests whether the vaccine is safe (does not cause health problems) and whether people's immune systems respond to the study vaccines. The immune system protects people from disease. A vaccine must cause people to have immune responses in order to prevent a disease. Sometimes a vaccine is given with an adjuvant. An adjuvant is a substance added to a vaccine to help the immune system respond better. Researchers only need to test a vaccine in a small number of people to learn if the immune system responds to it. If a study vaccine produces the desired immune responses, this helps researchers decide whether to do more studies of the vaccine. A vaccine study can also be used to find out if a vaccine might help prevent or fight an infection or disease. It takes many vaccine studies to produce a safe, effective vaccine.

Currently, there is no licensed vaccine against HIV or AIDS.

2. What is the HVTN 307 study?

HVTN 307 tests 2 experimental vaccines against HIV. The study vaccines are called:

- V3G CH848 Pr-NP1 (the Protein study vaccine)
- V3G CH848 mRNA-Tr2 (the messenger ribonucleic acid [mRNA] study vaccine)

The Protein study vaccine and the mRNA study vaccine will be given by injection into the upper arm muscle. The products used in this study are not made from live HIV, killed HIV, or HIV-infected human cells. These study vaccines cannot cause HIV infection or AIDS.

The Protein study vaccine was designed to look like a piece of protein on HIV. Proteins are natural substances. They help build and maintain the body, and do the same for viruses, such as HIV. The body's immune system may respond to these proteins; this is called an immune response. An immune response prepares the body to recognize the same proteins in HIV and fight the virus if a person is exposed to HIV in the future.

The Protein study vaccine was developed by the Duke Human Vaccine Institute (DHVI) and is being provided by Duke University in Durham, North Carolina, USA.

In this study, the Protein study vaccine will be given with 1 of 2 different experimental adjuvants. Adjuvants are products that help alert the immune system to make a stronger response. The adjuvants used with the Protein study vaccine are called:

- 3M-052-AF + Alum
- ACU-026-001-1

3M-052 was originally developed by the 3M Corporation to treat skin conditions and tumors, and to make vaccines more effective. It is designed to stimulate parts of the immune system that recognize invaders like viruses. This study will use the improved version called 3M-052-AF that is dissolved in water. This mixture is being supplied by Access to Advanced Health Institute (AAHI) in Seattle, Washington. 3M-052-AF will be combined with Alum, which is made from aluminum hydroxide. Alum is an adjuvant with a long-standing safety record that has been used in approved vaccines for more than 90 years. It is being supplied by the Division of AIDS (DAIDS) at the National Institute of Allergy and Infectious Diseases (NIAID), in Bethesda, Maryland.

The ACU-026-001-1 study adjuvant is an experimental lipid nanoparticle (LNP) adjuvant that contains 4 different lipid (fat) molecules. A nanoparticle (NP) is a tiny piece of matter. The adjuvant was developed by Acuitas Therapeutics and is being provided by Duke University. It is designed to stimulate parts of the immune system that recognize invaders like viruses and is similar to the adjuvant used in the Pfizer/BioNTech COVID-19 vaccines.

The mRNA study vaccine is made using messenger ribonucleic acid (mRNA) technology. mRNA is a piece of genetic code carried into the body by the vaccine as a message with instructions in the same way that the mRNA vaccines against COVID instruct the body's cells to make the SARS-CoV-2 spike protein. Instead of showing the immune system actual pieces of HIV, the vaccine carries instructions that show human muscle cells how to make small pieces that look like parts of HIV.

When the vaccine gets injected in the muscle of the arm, the cells in that muscle will get the instructions and start to make the different types of HIV-like pieces and display these pieces on the muscle cell's surface. The immune system will be able to see these HIV-like pieces and learn how to recognize them. Researchers hope that the immune system will respond by making antibodies and T cells that could fight HIV if a person is ever exposed to the real virus in the future.

The mRNA instructions do their work in the part of the muscle cell called the cytoplasm. The mRNA does not get into the nucleus of the cells, which is where human DNA is located. The mRNA cannot interact with the DNA. The mRNA instructions only remain in the body for a couple of days before they break down naturally.

The mRNA study vaccine was developed by the Duke Human Vaccine Institute (DHVI) and is being provided by Duke University in Durham, North Carolina, USA.

3. What organizations are involved in this study?

The National Institute of Allergy and Infectious Diseases (NIAID) and the HIV Vaccine Trials Network (HVTN) developed this study, along with the groups that are supplying study vaccines and adjuvants mentioned above. NIAID is part of the National Institutes of Health (NIH), which is part of the United States government.

The HVTN is an international collaboration of scientists, educators, and community members searching for an effective and safe HIV vaccine. The HVTN is funded by NIAID.

In Nashville, the study is taking place at the Vanderbilt HIV Vaccine Trials Unit, which is part of the Fred Hutchinson Cancer Research Center and the University of Washington."

4. When and where will this study be done?

Vanderbilt University Medical Center

The study is expected to begin enrolling participants around June 2023. It will be done in these locations in the US:

- Atlanta-Ponce
- Birmingham
- Boston-BIDMC
- Boston-Brigham
- Nashville
- Seattle

5. Why is this study being done?

All of the HVTN's studies work toward the mission of finding a safe and effective HIV vaccine. The main purpose of this study is to see if the study vaccines are safe to give to people, and whether people are able to take the study vaccines without becoming too uncomfortable. Another important goal of the study is to test if people's immune systems respond to the study vaccines.

6. How many people will be in this study, and who can join?

The study will involve about 36 participants who will receive study vaccines.

To join this study, a person must not be living with HIV, must be in overall good health, and be between 18 and 55 years of age. They cannot be pregnant or breastfeeding. There are also other criteria that must be met. People will be asked about their medical history, will be given a physical exam, and will have their blood and urine samples taken for testing. People will also be asked about their sexual activity and drug use.

7. Are the study vaccines safe?

The study vaccines have not been given to people before, so we do not know all of the risks of these study vaccines. Based on the results from studies of the vaccines in animals, researchers believe that these study vaccines appear to be safe to give to people. However, results in animals do not always predict the results in people.

That is why the main purpose of this study is to test whether the study vaccines are safe to give to people. Each participant's health will be watched closely throughout the study.

Those receiving the mRNA study vaccine and the ACU-026-001-1 study adjuvant might have side effects like those seen with mRNA COVID-19 vaccines. Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining around the heart) have occurred very rarely in some people who got mRNA vaccines against COVID-19. It is not known whether the risk of myocarditis or pericarditis is increased following mRNA vaccines for other diseases.

Participants should seek medical attention right away and inform the study staff if they have any of the following symptoms after getting the mRNA study vaccine:

- Chest pain
- Shortness of breath
- Fainting
- A fast-beating, fluttering, or pounding heart.

There have been reports that some people have experienced hives (urticaria) in the days to weeks after receiving mRNA vaccines.

The 3M-052-AF + Alum adjuvant combination has been tested before in 2 other studies with a different protein vaccine in about 50 people. This study is the first time the Protein study vaccine will be given to people in combination with the 3M-052-AF + Alum adjuvant. Although no one in these earlier studies had any serious health problems related to the 3M-052-AF + Alum adjuvant, there is always a possibility that there could be unexpected problems.

8. Can these study vaccines protect participants from acquiring HIV?

Participants should not expect to be protected from HIV by these study vaccines.

This study is not designed to find out if the study vaccines work to prevent or fight HIV. More studies will need to be done to learn if they do.

Because it is not expected that the study vaccines will prevent HIV/AIDS, participants in this study will be counseled on how to avoid behaviors that will put them at risk of HIV infection.

9. How long will it take to find out if the study vaccines work?

The results of HVTN 307 will help researchers to know if they should do more studies on the vaccines. These additional studies would give the study vaccines to more people to see if they are safe. These studies would also give researchers a better understanding of how the immune system responds and whether the vaccines can prevent HIV acquisition. If more studies are done, it could take several years to find out if the study vaccines work. This study is expected to take about 2 years to answer the research questions about safety and immune responses.

10. How will the health and rights of participants be protected?

Protecting the health and respecting the rights of participants are top priorities for everyone in the HVTN. Without volunteers, we would never be able to find a safe and effective HIV vaccine.

A first step in protecting the rights of study participants is to give them information about the study before they join. Clinic staff will give volunteers information about the study products and procedures, the possible risks and benefits to participants, and the rights that participants have. These rights include the right to receive any new information about the study that could affect whether a participant wants to remain in the study, and the right to leave the study at any time.

During the study, the clinic staff will monitor participants to make sure the study vaccines are not causing any health problems. The clinic staff will also ask participants about any social problems they may experience from being in the study. If a participant has a health or social problem related to being in the study, clinic staff will help them.

There are also several groups involved in protecting participants' rights and well-beings:

- A study safety review team and an independent safety monitoring board regularly look at the health information from the study to decide whether it appears safe to continue giving study injections.

- An Institutional Review Board (IRB) or Ethics Committee (EC) reviews and monitors the study plan for each clinic doing the study, including the information that is given to people about the study, study progress, and health problems in participants. The IRB/EC also looks at whether participant rights are being respected.

- The US Food and Drug Administration (FDA) also reviews the study. The FDA enforces US laws about research in humans and the use of study vaccines in research.

- Each study clinic has a Community Advisory Board (CAB). Each CAB's members are local people who bring the concerns and interests of the community and study participants to the researchers. CAB members are part of the team that develops each study. They also help develop or review the information that is given to participants.

11. Could the study vaccines cause a positive result on an HIV test?

Yes, the study vaccines are likely to cause people to test positive on some types of HIV tests. If a participant gets an HIV study vaccine, their body may make antibodies to HIV. Antibodies help people fight infection. Standard HIV tests search for HIV antibodies as a sign of infection. Because of this, a person could have a positive HIV test result even if they do not have HIV. This is called a vaccine-induced seropositivity (VISP) test result. This may also be referred to as "vaccine-induced seroreactivity" or VISP/R. It is not known who will have VISP test results or how long these test results may last.

People with VISP test results need specific HIV tests to determine if a positive test result is due to VISP or having HIV. Clinics participating in this study have access to these specific tests that look for the virus itself instead of looking for antibodies.

No health problems are associated with a VISP test result, but VISP test results may cause problems in several areas of life, such as medical or dental care, employment, insurance, visas for traveling, or entry into the military. People with VISP might not be allowed to donate blood or other organs. If they are planning to apply for insurance, employment, or the military, they are asked to inform their study site right away. The insurance company, employer, or military agency may not accept HIV test results from the HVTN. However, the HVTN can work with them to ensure the right test is done that will show their true HIV status.

12. Where can I find more information?

About HIV vaccine clinical studies: **www.clinicaltrials.gov**

About the HVTN: **www.hvtn.org**

About VISP: **https://www.hvtn.org/participate/visp-and-hiv-testing.html**

If you have additional questions that were not answered by this document, please ask us.

You can contact: *Shonda Sumner, Clinic Coordinator at* ***shonda.sumner@vumc.org*** *or 615-343-6906*