HIV Vaccines

An Introductory Factsheet

January 2023

This factsheet provides basic information on preventive HIV vaccines. For more basic fact sheets in this series on emerging HIV prevention strategies visit [www.avac.org/intro.](www.avac.org/intro)

What is an HIV vaccine?

Researchers are working to come up with two kinds of vaccines against HIV. One kind, a **preventive vaccine**, would reduce HIV risk in people who are HIV negative. It would teach their immune systems to recognize the virus right away (for example, during sex), and block it from causing an infection. No preventive HIV vaccine exists yet.

A therapeutic HIV vaccine is also being pursued. People living with HIV would take a therapeutic vaccine to strengthen their immune systems for better control the virus. This kind of vaccine could, in theory, help people control the virus without anti-retroviral drugs (ART), or be used as a supplement to ART regimens. Research on therapeutic vaccines may also inform research on how to cure HIV. No therapeutic HIV vaccine has been proven to work yet.

This fact sheet is about research to find **preventive vaccines** for use by HIV-negative people.

Resources and links

AVAC (www.avac.org/vaccines)

Global HIV Vaccine Enterprise (www.iasociety.org/Global-HIV-Vaccine-Enterprise)

HIV Vaccine Trials Network (www.hvtn.org)

International AIDS Vaccine Initiative (www.iavi.org)

US MHRP (www.hivresearch.org)

NIH-NIAID (www.niaid.nih.gov)

What is happening in HIV vaccine research now?

As of January 2023, one HIV vaccine efficacy trial is underway, known as PrEPVacc. Three additional efficacy trials—Uhambo/HVTN 702 and Imbokodo/HVTN 705 and Mosiaco/HVTN 706—have ended since early 2020, after findings showed the vaccine candidates they were testing did not significantly reduce the risk of HIV infection. But analysis in these trials will help inform future research.

The PrEPVacc trial is simultaneously testing experimental HIV vaccines and oral PrEP against a placebo. Participants are randomized to receive one of two experimental vaccines, which have both been tested before but did not advance to late-stage trials on their own. PrEPVacc is testing if they work better in combination. Participants are also randomized to receive one of two types of daily oral PrEP: F/TDF (Truvada) or F/TAF (Descovy). Participants receive the daily oral PrEP over weeks 0–26; test vaccine injections are received over weeks 0–48. This Phase IIb trial is enrolling 1,668 participants from Mozambique, South Africa, Tanzania, and Uganda, and results are expected in 2023. Learn more at: *www.prepvacc.org/*.

Mosaico, also known as HVTN 706/HPX3002, was a Phase III trial that was stopped in January of 2023 after a routine review of the data found the regimen to be safe but not efficacious— the regimen did not significantly reduce the risk of HIV acquisition. Mosaico enrolled 3,800 men and trans people who have sex with cis-gender men or trans individuals. Trial sites were in Argentina, Brazil, Italy, Mexico, Peru, Poland, Spain and the United States. Mosaico tested an Adenovirus 26-based vaccine candidate designed to protect against multiple subtypes of HIV—referred to as a mosaic vaccine. Learn more at: *www.mosaicostudy.com*.

The Imbokodo trial, also known as HVTN 705/HPX2008, is a companion study to Mosaico, but it stopped at the end of its first phase, in August 2021. The vaccine candidate, an Adenovirus 26-based mosaic vaccine, was found to be safe, but did not significantly reduce risk of HIV infection. While both the Mosaico and Imbokodo studies used mosaic vaccines, the regimens used different ingredients in the follow-up boost. Imbokodo enrolled 2,637 women from

Malawi, Mozambique, South Africa, Zambia and Zimbabwe. Imbokodo's participants will be linked to existing treatment or prevention programs. Learn more at: *https://imbokodo.org.za/*.

The Uhambo trial, also known as HVTN 702, enrolled 5,407 South African men and women and was testing a vaccine candidate designed for clade C, the most common type of HIV in Southern Africa (see below for details). Unfortunately, results showed this vaccine did not reduce risk of HIV infection and the trial was stopped in February 2020. Learn more at: *http://uhambo.org.za/*.

For a view of ongoing vaccine trials, visit the HIV vaccine Track the Research page on *avac.org*.

What are the discoveries in HIV vaccine research so far?

In 2009, a trial in Thailand called RV144 showed that people who got the test vaccine were 31 percent less likely to get HIV during the trial than those who got the placebo. Since that trial, researchers reviewed the data and identified immune responses that might have led to protection. They also identified changes to the regimen to potentially improve efficacy and adapt it for use in other parts of the world. Those changes were reflected in the regimen tested in the Uhambo trial (HVTN 702) described above, which included some refined components of the RV144 vaccine strategy.

On February 3, 2020, the Uhambo Trial (HVTN 702) trial stopped vaccinations early because data showed the vaccine did not prevent HIV acquisition. The vaccine was safe but not effective. Participants were monitored through a follow-up period, and researchers hope to further analyze data from participants who remained uninfected versus those who were not protected by the vaccine to better understand why the vaccine did not show efficacy overall. Further research will be needed to understand how genetics of the virus or human genetics or differences in the vaccine regimen contributed to the different outcomes in this trial and the study in Thailand.

On August 31, 2021, Johnson & Johnson and partners announced that the vaccine regimen in the Imbokodo trial (HVTN 705) was safe but did not provide sufficient protection against HIV for the women enrolled in the study. An analysis of the data found an efficacy estimate of 25.2 percent, but with a wide confidence interval that crossed zero, which means the finding was not statistically significant and that the vaccine may not offer any protection. Researchers expect to learn critical information from the trial data to inform future research.

On January 18th, 2023 Johnson and Johnson and partners announced that the vaccine regimen in the Mosaico trial (HVTN 706) was safe but was not effective in preventing HIV infection compared to placebo among study participants. Furter analysis of the data will contribute to a field wide considerations for next generation strategies to develop an effective HIV vaccine.

How is antibody research helping us advance HIV vaccine research?

Antibodies play a big part in fighting off disease. The body naturally produces antibodies, as a part of the immune system. Vaccines are designed to induce a range of antibodies that fight off pathogens. Broadly neutralizing antibodies (bNAbs) are of particular interest in HIV prevention. They are Y-shaped proteins made by B cells, which are part of the immune system. They attach to a specific target on HIV's surface and stop the virus from infecting healthy cells. "Broadly neutralizing" refers to the ability of an antibody to recognize and neutralize many of the types of a virus circulating around the world.

It often takes a long time after HIV infection, even years, for a person's body to produce bNAbs, and many people never produce them. HIV also continues to mutate and change. Scientists sometimes say that, "Today's antibodies can neutralize yesterday's virus." Scientists hope to develop a vaccine that will induce bNAbs in people who are HIV-negative, protecting them from the risk of HIV.

BNAbs have been studied for "antibody-mediated prevention" using a method called "passive immunization". Traditional immunization involves a vaccine that teaches your body to make its own antibodies to fight infection. With passive immunization, bNAbs are brought into the body through an infusion, or "drip". Once received, these

bNAbs might be able to fight off HIV for a period of time. Two large clinical trials tested this idea in the Americas, Europe, and several countries in Africa. Called the Antibody Mediated Prevention (AMP) Study, these companion trials—HVTN 704/HPTN 085 and HVTN 703/HPTN 081-tested the safety and efficacy of using an antibody known as VRC01 for HIV prevention. In February 2021, the National Institute of Allergy and Infectious Diseases (NIAID) announced that VRC01 did not significantly reduce the overall risk of HIV infection. However, VRC01 did safely and effectively reduce the risk of acquiring HIV from strains of the virus that were "highly sensitive" to VRC01. The trials suggest that a single bNAb, such as VRC01, cannot offer sufficient protection against a broad range of HIV types, and a combination of bNAbs might be needed. Plans to test bNAb combinations, delivered through an injection, are advancing.

A growing number of antibodies are going through animal testing and smaller, early-phase clinical trials. For an ongoing list of bNAbs as they are discovered, visit *www.bnaber.org*.

About AVAC | AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic.