Mosaic Vaccines: HIV Breakthrough We've Been Waiting for?

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Scientists have been trying for more than 40 years to develop an HIV vaccine. To date, only six vaccine candidates have progressed to large-scale human testing. Of these, only one—a dual vaccine approach tested in the RV144 trial in Thailand in 2009—demonstrated even partial efficacy.[1]

The challenges of developing an HIV vaccine are well known and mainly involve the virus's ability to mutate and evade the body's immune defenses. HIV's rapid mutation rate has led to a multitude of different variants that a single vaccine (or even a combination of vaccines) has yet to be able to neutralize.[2]

For this reason, the new vaccine model—known as a **mosaic-based regimen**—has reignited hopes among researchers after the much-publicized failures of the AIDSVAX trial in 2003, the STEP trial in 2007, the HVTN 505 trial in 2013, and the HVTN 702 trial in 2020.[3]

What Are Mosaic Vaccines?

Mosaic vaccines differ from previous vaccine models in that they are not constrained to only predominant variants of HIV. Instead, mosaic vaccines take pieces of different HIV strains and combine them to trigger a broader immune response.[4]

The leading mosaic vaccine, developed by Janssen Pharmaceuticals, incorporates three immune-stimulating proteins (called mosaic antigens) created from the genes of many different HIV strains. The antigens are then inserted into a disabled cold virus—known as **adenovirus serotype 26 (Ad26)**—and delivered by injection into a muscle.[5]

Positive results from the early-stage trial led to the fast-track approval of what was then only the sixth Phase 2 human efficacy trial in 35 years.[5]

The HVTN 705 trial was officially launched in 2017 to test the mosaic Ad26 vaccine on more than 2,500 non-infected women, ages 18 to 35, in South Africa, Malawi, Mozambique, Zambia, and Zimbabwe.[1]

The results of the HVTN 705 trial, released in August 2020, concluded that the mosaic Ad26 vaccine did not provide sufficient protection against HIV.[5]

Despite the setback, a new Phase 2 trial, called the HVTN 118 or ASCENT trial, was launched in 2018 in the United States and Kenya. The new study aims to see if adding a specific protein can enhance the effect of the mosaic Ad26 vaccine.[6]

Early results have shown that among the roughly 150 study participants, the revised vaccine neutralized a broader range of HIV variants.[6]

Based on the positive findings, a Phase 3 trial called MOSAICO was launched in 2019. This large-scale human trial tests the revised mosaic vaccine on 3,800 adults in eight countries across North America, South America, and Europe. Results are expected in 2024.[7]

Supporting Evidence

The optimism surrounding the Janssen vaccine was supported by research published in *The Lancet* that evaluated the effects of a mosaic vaccine candidate in humans and monkeys.[8]

Known as the APPROACH trial, the Phase 1/2 study involved 393 adults from 12 clinics in East Africa, South Africa, Thailand, and the United States. Each participant was randomly chosen to receive either one of seven variations of the mosaic vaccine or a sham drug (placebo).

At the end of the 96-week study period, the researchers reported that the mosaic vaccine was well tolerated and triggered an HIV-specific immune response irrespective of the variation used.[8]

Even more promising were the results seen in the parallel animal study. For this study, 72 rhesus monkeys were injected with the mosaic vaccine and exposed on six different occasions to SIV (the simian version of HIV). Despite the repeated exposures, 66% of vaccinated monkeys remained SIV-free.[8]

Challenges and Opportunities

According to the United Nations Programme on HIV/AIDS (UNAIDS), an estimated 1.5 million people were newly infected with HIV in 2021. Of the 38.4 million people living with HIV worldwide, 75% are on antiretroviral therapy.[9] This is short of the 90% that UNAIDS aimed for in its 90-90-90 initiative.

With monetary contributions to global HIV funds dwindling, a vaccine—even a moderately effective one—is considered by many to be the only realistic hope of ending this HIV pandemic. For this reason, the MOSAICO trial is crucial.

Even so, there are other HIV vaccine models receiving equal attention:

Antibody-Mediated Prevention (AMP)

Antibody-mediated prevention (AMP) is an approach by which scientists hope to identify and replicate a group of naturally occurring immune cells, called broadly neutralizing antibodies (bNAbs), that can kill many HIV variants.

The most advanced of these investigations involves the **VRC01 antibody,** which is known to kill over 90% of HIV variants in test tube studies. Since the isolation of the antibody in 2010, scientists have been able to manufacture a version of VRC01 in the lab. It was hoped that injecting the lab-made version into a person's body might trigger the same protective response.[10]

The first VRC01 studies were launched in 2016 with the HVTN 704 trial (involving men who have sex with men in Brazil, Peru, and the United States) and the HVTN 703 trial (involving women in sub-Saharan Africa). Collectively referred to as the AMP trial, the Phase 2 trials involved 4,623 adults who were given an intravenous (IV) infusion of VRC01 every eight weeks.[10]

Results from the AMP trials released in January 2021 reported that lab-made VRC01 was effective at neutralizing 75% of the HIV variants that "natural" VRC01 is able to kill. Even so, the vaccine was not able to stop HIV infection.[10]

Research is underway to see if scientists can broaden the immune protection offered by lab-made VRC01 as well as other bNaB candidates.

Messenger RNA (mRNA) Vaccine

The approval of the Pfizer and Moderna COVID-19 vaccines in 2021 ushered in a new era in vaccine research, creating a whole new type of vaccine that stimulates a protective immune response in an entirely different way.[11]

Rather than triggering an immune response with a dead or weakened germ as traditional vaccines do, the Pfizer and Moderna vaccines use a molecule called messenger RNA (mRNA) to "teach" cells how to produce a protein that triggers the COVID-specific immune response.[11]

Prior to the approval of the Pfizer COVID-19 vaccine in August 2021, no mRNA vaccine of any type had ever been successfully produced.[12]

Using the Pfizer and Moderna vaccines as the proof of concept, scientists at the National Institutes of Health have launched a clinical trial called the HVTN 302 to see if an mRNA vaccine can be produced for HIV.[13]

The first phase of the HVTN 302 will examine whether three different experimental mRNA vaccines are safe and can induce an HIV-specific immune response. The study will involve 108 adults from eight U.S. cities, each of whom will be given a series of vaccinations using one of the three experimental vaccines.[13]

If any or all of the vaccines are shown to be safe and able to generate an HIV-specific response, the HVTN 302 study will be expanded to investigate how effective the vaccine candidates are. The results of the Phase 1 trial are expected by late 2023.[13]

Summary

Mosaic vaccines are made by combining pieces of different HIV variants and inserting them into an inactivated cold virus. When the inactivated vaccine is injected into the body, it stimulates a broader immune response. It is hoped that a mosaic vaccine will be more effective in killing the vast multitude of HIV variants that have until now hampered the success of HIV vaccines.

Mosaic vaccines are just one of several HIV vaccine models under investigation. Others include experimental messenger RNA (mRNA) vaccines based on the same technology used to produce the Pfizer and Moderna COVID-19 vaccines.

A Word From Verywell

Until a successful HIV vaccine is produced, it is important to practice safer sex and explore the use of HIV pre-exposure prophylaxis (PrEP) if you are at high risk of exposure. PrEP involves the daily use of the drug Truvada (emtricitabine/tenofovir DF) or Descovy (emtricitabine/tenofovir AF) to reduce your risk of getting HIV by up to 99%.[14]

In 2021, the FDA approved a new form of PrEP called Apretude (cabotegravir), which can protect against HIV with only one injection every two months.[15]

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