HIV mRNA Vaccine Trial Is Now Underway

The experimental vaccine regimen aims to train B cells to produce broadly neutralizing antibodies against HIV.

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The first doses of an experimental HIV vaccine regimen using the same messenger RNA (mRNA) technology as highly effective COVID-19 vaccines have been administered to clinical trial participants, according to an announcement from Moderna and the International AIDS Vaccine Initiative (IAVI).

The Phase I study (IAVI G002; ClinicalTrials.gov NCT05001373) is testing whether sequential administration of a series of primer and booster shots can trigger the development and maturation of specialized B cells that can produce broadly neutralizing antibodies (bnAbs) that target multiple strains of HIV.

#Breaking: IAVI and @moderna_tx are partnering to advance promising #HIV vaccine candidates ???? delivered through messenger RNA (mRNA) technology.

Learn more about this exciting new trial:

https://t.co/MDMES8vY5V

— IAVI (@IAVI) January 27, 2022

The vaccine candidates, dubbed mRNA-1644 (eOD-GT8 60mer mRNA) and mRNA-1644v2-Core (Core-g28v2 60mer mRNA), were developed by researchers at Scripps Research in collaboration with IAVI and Moderna. The study is underway at George Washington University School of

Medicine and Health Sciences in Washington, DC. Other collaborators include the University of Texas Health Science Center in San Antonio, the Fred Hutchinson Cancer Research Center in Seattle, Emory University in Atlanta, the Karolinska Institute in Stockholm, the Bill & Melinda Gates Foundation and the National Institute of Allergy and Infectious Diseases.

“We are tremendously excited to be advancing this new direction in HIV vaccine design with Moderna’s mRNA platform,” said IAVI president and CEO Mark Feinberg, MD, PhD. “The search for an HIV vaccine has been long and challenging, and having new tools in terms of immunogens and platforms could be the key to making rapid progress toward an urgently needed, effective HIV vaccine.”

A New Approach

Researchers have spent more than three decades and billions of dollars studying vaccines to prevent HIV, with little success. The virus mutates rapidly, and there are many different strains around the world, making it difficult to develop broadly effective vaccines. But experts hope the mRNA technology used in the Moderna and Pfizer-BioNTech COVID-19 vaccines can help turn things around for HIV.

The mRNA vaccine technology uses lipid nanoparticles, or fat bubbles, to deliver bits of genetic material that encode instructions for making proteins. The mRNA COVID-19 vaccines, for example, deliver blueprints for making the SARS-CoV-2 spike protein, which the virus uses to enter cells. When the vaccine is injected into a muscle, cells produce the protein, triggering an immune response.

To date, only one HIV vaccine regimen—a canarypox vector primer followed by a gp120 envelope protein booster—has demonstrated partial protection in a human study, but it was not effective in the larger Uhambo trial. Two ongoing trials, Mosaico and Imbokodo, are testing an approach that uses an adenovirus primer (similar to the one used in the Johnson & Johnson COVID-19 vaccine) followed by a booster that contains a mosaic of proteins from multiple HIV strains.

The IAVI G002 trial takes a different approach, known as germline targeting, which aims to train immature B cells in a stepwise fashion to generate broadly neutralizing antibodies against HIV. People with HIV do produce antibodies against the virus, but they usually target parts that are highly variable, so they don’t recognize new viral mutations. However, a small proportion of individuals naturally produce bnAbs that target hidden, conserved parts of the virus.

In an early study (IAVI G001), eOD-GT8 60mer, a so-called immunogen consisting of engineered HIV envelope proteins, triggered production of specialized B cells—the first step in the pathway for generating bnAbs. Almost all vaccine recipients produced the desired immune cells. Using mRNA technology to rapidly generate and deliver successive versions of the immunogen is expected to speed up the process. So far, the mRNA approach was shown to prevent or delay infection in monkeys exposed to an HIV-like virus.

IAVI G002 will enroll 56 healthy HIV-negative adult volunteers at low risk for acquiring the virus. Most participants (48) will receive one or two doses of mRNA-1644; 32 of them will also receive an mRNA-1644v2-Core booster. The rest will receive the booster immunogen alone.

While the new approach appears promising so far, the research is only in its early stages. If the current study pans out, it will still take years before the vaccine regimen can be evaluated in large clinical trials and deployed worldwide.

Click here to see the study description and eligibility criteria.
Click here for more news about HIV vaccines.
Click here for a POZ feature on HIV vaccine development.
