Researchers Launch Trial of mRNA Vaccines for HIV

The experimental vaccines use the same technology as the highly effective Moderna COVID-19 shot.

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The International AIDS Vaccine Initiative and Moderna have launched a Phase I study of a pair of HIV vaccines that use the same messenger RNA (mRNA) technology as the highly effective Moderna and Pfizer-BioNTech COVID-19 vaccines.

This open-label study (ClinicalTrials.gov NCT05001373) will evaluate two vaccine candidates dubbed mRNA-1644 (eOD-GT8 60mer mRNA) and mRNA-1644v2-Core (Core-g28v2 60mer mRNA).

The trial aims to enroll 56 healthy HIV-negative adults at low risk for acquiring the virus. They will be randomly assigned to receive one of the two vaccines or both in combination. In addition to safety, the study will evaluate whether the vaccines induce production of broadly neutralizing antibodies (nbAbs) that target various strains of HIV. The trial is expected to begin enrolling participants in September and to conclude in the spring of 2023.

The University of Texas at San Antonio; George Washington University in Washington, DC; the Fred Hutchinson Cancer Research Center in Seattle; and Emory University in Atlanta are also collaborating on the research.

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 strains around the world, making it difficult to develop broadly effective vaccines.

To date, only one vaccine regimen—a canarypox vector primer followed by a gp120 booster used in the RV144 trial in Thailand—has demonstrated partial protection in a human study, but it was not effective in the larger Uhambo trial. Two other large trials, Mosaico and Imbokodo, are currently testing an approach that uses an adenovirus primer (similar to the one used for the Johnson & Johnson COVID-19 vaccine) followed by a booster that contains a mosaic of proteins from multiple HIV strains.

The newly launched trial will take a different approach. 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. In addition to HIV, Moderna is working on mRNA vaccines for influenza, Epstein-Barr virus, multiple sclerosis, cancer and other disease. So far, the mRNA approach was shown to prevent or delay infection in monkeys exposed to an HIV-like virus.

The new study will evaluate an approach known as germline targeting 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. A small proportion of individuals naturally produce bnAbs that target hidden, conserved parts of the virus that do not change very much. While most people possess specialized B cells capable of producing bnAbs, they are few in number.

In an early study, eOD-GT8 60mer, a so-called immunogen consisting of engineered HIV envelope proteins, triggered production of these rare immune cells—the first step in the pathway for generating bnAbs. Almost all vaccine recipients (97%) produced the desired B cells, offering proof of concept that the approach could work. That study, however, did not use mRNA technology, which is expected to speed up production of successive versions of the vaccine.

While the new vaccine approach appears to hold promise, experts caution that HIV is much more difficult to prevent than SARS-CoV-2, in part because the immune system usually does not naturally fight HIV and confer lasting protection, as it does for the coronavirus.

Click here to see the study description and eligibility criteria.
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