Vir Launches Trial of a New Type of HIV Vaccine

The vaccine, dubbed VIR-1388, is designed to stimulate the production of T cells to fight HIV.

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Vir Biotechnology announced this week that the first participant in a Phase I trial has received an experimental preventive vaccine known as VIR-1388 that is designed to help the immune system produce T cells that recognize HIV.

So far, traditional HIV vaccines that stimulate the production of antibodies have failed in large trials. A more sophisticated approach known as germline targeting, which aims to spur the development of specialized B cells that can produce broadly neutralizing antibodies (bnAbs), is still in early stages. Vir is taking a different approach based on T-cell immunity.

Vaccine Research to Date

HIV vaccine research has led to a string of disappointments over the past four decades. Only one large study—the RV144 trial in Thailand—has shown any effectiveness for preventing HIV. That trial tested a vaccine dubbed ALVAC-HIV, which used a canarypox virus vector to deliver genetic instructions for HIV proteins plus another vaccine that contained engineered HIV gp120 envelope proteins. In 2009, researchers reported that this prime-boost regimen reduced new infections by 31%.

Following up on those findings, the Uhambo trial tested ALVAC-HIV plus gp120 proteins from the HIV subtype most common in southern Africa. But this regimen did not prevent HIV acquisition, and the study was discontinued ahead of schedule in 2020.

That left two large Phase III vaccine trials underway, Imbokodo and Mosaico. In both studies, participants received a vaccine dubbed Ad26.Mos4.HIV that uses an adenovirus vector to deliver a "mosaic" of antigens from multiple HIV strains plus an additional vaccine containing gp140 envelope proteins. Earlier studies showed that the regimen induced potent antibody and T-cell responses and protected monkeys exposed to an HIV-related virus. However, it did not generate bnAbs that target a hidden portion of HIV that does not change much as the virus evolves.

In August 2021, Imbokodo was stopped early after the vaccine regimen failed to protect young

women in Africa. Likewise, Mosaico was discontinued this past January because it did not reduce the risk of HIV acquisition among gay and bisexual men and transgender women in North and South America and Europe.

An ongoing African-led trial called PrEPVacc is testing two vaccine regimens based on the one that showed some efficacy in RV144 along with oral pre-exposure prophylaxis (PrEP). The trial, which includes 1,513 men and women at risk for HIV in South Africa, Tanzania and Uganda, enrolled its final participants in March. PrEPVacc appears to be "the last roll of the dice" for traditional HIV vaccines, study coordinator Jonathan Weber, of Imperial College London, told CNN. Results are expected in late 2024, but interpretation could be challenging because PrEP alone is so effective for preventing HIV.

Many experts think a successful prevention vaccine will need to trigger production of bnAbs that can recognize multiple strains of HIV. The germline targeting approach uses a series of vaccines in a stepwise manner to encourage the development of specialized B cells and train them to produce bnAbs.

Last December, researchers reported that all but one of the 36 participants in the Phase I IAVI G001 trial who received a vaccine containing a so-called immunogen consisting of 60 engineered copies of gp120 developed specialized precursor B cells. After a booster, these cells produced antibodies with greater affinity for the HIV proteins. In June, the team reported that the vaccine regimen also stimulated a vigorous CD4 helper T-cell response.

The researchers are now employing Moderna's messenger RNA (mRNA) technology to speed up the development of successive versions of the vaccine. Two trials, IAVI G002 and IAVI G003, are testing a candidate dubbed mRNA-1644 that uses mRNA to deliver the immunogens. Moderna is also testing a vaccine called mRNA-1574 that delivers stabilized trimer configurations of HIV envelope proteins.

VIR-1388

Vir is taking a different tack, focusing on T cells that recognize HIV proteins, rather than antibodies, in an effort to prevent the virus from establishing chronic infection. VIR-1388 uses a weakened cytomegalovirus (CMV) vector to deliver HIV antigens. An initial T-cell vaccine dubbed VIR-1111 did not elicit the desired responses, but it provided clues to inform the development of VIR-1388.

The new Phase I trial (HVTN 142), sponsored by the Bill & Melinda Gates Foundation and the National Institute of Allergy and Infectious Diseases and conducted by the HIV Vaccine Trials Network, is enrolling people at low risk for HIV in the United States and South Africa who already have asymptomatic CMV infection. The 95 participants will be randomly assigned to receive one of three doses of VIR-1388 or placebo injections. Initial results are expected in the second half of 2024.

"HIV continues to be a major global public health challenge with no approved vaccines despite

decades of research efforts," Carey Hwang, MD, PhD, Vir's senior vice president for clinical research, said in a company press release. "We are hopeful that our unique approach will help close the longstanding public health gap in HIV prevention."

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