Therapeutic Vaccines May Help Control HIV Off Treatment

HTI vaccines could become the backbone of a combination approach for achieving a functional cure.

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A set of therapeutic vaccines that help the immune system control HIV may contribute to prolonged viral suppression after interrupting antiretroviral treatment, researchers reported at the recent Conference on Retroviruses and Opportunistic Infections (CROI). Although this work is still in its early stages, HTI vaccines might one day become part of a combination strategy for achieving a functional cure.

HTI vaccines contain HIV peptides commonly recognized by people who control HIV naturally. (HTI stands for "HIVACAT T-cell immunogen," named after the Spanish research program that's developing it.) Some study participants who started with an undetectable viral load and interrupted treatment after receiving a series of vaccines using different technologies were able to maintain a low viral load for six months, reported Beatriz Mothe, MD, PhD, of IrsiCaixa Institute for AIDS Research in Spain.

"[T]he beneficial effect of immunization on controlling viral load was clear and represents the first proof of concept in people living with HIV that stimulation of HIV-specific T cells can contribute to cure strategies," International AIDS Society president Adeeba Kamarulzaman, MBBS, said in a statement.

While most familiar vaccines are designed to prevent infection in the first place, therapeutic vaccines are used to treat people who have already acquired a pathogen. In effect, therapeutic vaccines aim to make the immune system of a typical person with HIV work more like that of an elite controller.

Mothe presented findings from AELIX-002, the first human study of HTI vaccines, which are designed to help T cells recognize parts of HIV that are known to trigger an immune response in people who naturally control the virus. One reason HIV is so hard to prevent and cure is that it mutates rapidly, creating a wide variety of viral variants. The novel HTI immunogen was designed based on an analysis of immune responses in nearly 1,000 people with HIV on three continents.

The researchers created a set of HTI vaccines using different technologies, including one that

delivers HIV DNA directly, one that uses a modified vaccinia Ankara (MVA) viral vector and one that uses a chimpanzee adenovirus vector (ChAdOx1)—similar to the one used in the AstraZeneca COVID-19 vaccine.

This Phase I/IIa trial enrolled participants who started antiretroviral therapy less than six months after initial HIV acquisition, had an undetectable viral load for at least a year and had a CD4 T-cell count above 400 for at least six months. All but one of the 45 participants were men, and most were in their mid-30s.

First, 30 participants were randomly assigned to receive the vaccine regimen while 15 received matching placebo injections. The vaccine group received three doses of the HTI immunogen delivered via DNA (at baseline and weeks 4 and 8) followed by two doses of the MVA vector vaccine (at weeks 12 and 20). Most participants later received the chimpanzee adenovirus vector vaccine (two doses 12 weeks apart) and a final booster of the MVA vaccine.

After vaccination, the participants could decide whether to undergo a closely monitored treatment interruption lasting up to 24 weeks. Their viral load was measured weekly, and antiretrovirals were resumed immediately if their HIV RNA level rose above a prespecified threshold (above 100,000 at any point or above 10,000 for more than eight weeks) or their CD4 count dropped below 350.

Almost everyone in the vaccine group showed strong and broad T-cell responses to the HIV peptides delivered by the HTI vaccines—and the strength of these responses predicted how long they could stay off treatment. All participants in both groups showed a decline in HIV DNA, the form of HIV genetic material in the long-lived viral reservoir that makes HIV so difficult to eradicate.

Among the 41 people who opted for treatment interruption, HIV viral load rebounded in all cases—typically within the expected two to three weeks. But the new viral setpoint, or stable level, was lower in the vaccine group.

Among the 32 participants who lacked a favorable genetic profile (HLA class I allelles) associated with spontaneous HIV control, eight vaccine recipients (40%) and one placebo recipient (8%) were able to remain off antiretrovirals for 22 weeks. Due to the COVID-19 pandemic, two people decided to restart treatment even though they still had a low viral load.

Five vaccine recipients and one placebo recipient have maintained a viral load below 2,000 despite treatment interruption. But even a low viral load like this could lead to adverse health consequences, perhaps due to chronic immune activation and inflammmation. What’s more, people with a detectable viral load are at risk of transmitting HIV via sex; one study participant chose to resume treatment for this reason.

The vaccine regimen was well tolerated, with mostly mild to moderate side effects. Muscle pain was more common in the vaccine group than in the placebo group.

HTI vaccines could be a good backbone of a combination strategy to achieve a functional cure of HIV, Mothe suggested. She added that it's probably critical to start antiretroviral therapy early, while the viral reservoir is still low, or the vaccines may need to be combined with agents that lower the reservoir. The AELIX-003 trial (NCT04364035), now underway in Spain, is evaluating HTI vaccines in combination with Gilead Sciences' reservoir-reducing TLR7 agonist vesatolimod (GS-9620).

While stressting that the results are still early, other experts concurred that the findings are promising.

"I think the study has convincingly shown that the HTI vaccines can generate immune control; it is clear that they should be considered as a backbone for future HIV cure eradication trials," HIV cure researcher Sharon Lewin, MD, of the Peter Doherty Institute for Infection and Immunity in Melbourne commented in an AELIX Therapeutics press release.

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