Double-blind study shows HIV vaccine not effective in viral suppression

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Credit: National Cancer Institute

(Medical Xpress)—A large team of researchers from the U.S. and Canada has conducted a randomized double-blind study of the effectiveness of an HIV vaccine and has found it to be ineffective in suppressing the virus. In their paper published in *Science Translational Medicine*, the group describes the study, what they found and why they believe their work has provided the medical research community a

valuable lesson on the importance of placebo-controlled studies. Michael Nelson with Walter Reed Army Institute of Research offers a FOCUS piece on the work done by the team in the same journal issue.

A lot of research has gone into curing people infected with HIV, but that goal has still not been achieved. In the meantime, antiretroviral therapy (ART) drugs allow people infected with the virus to live an almost normal existence. But the goal of developing a vaccine remains. One approach has been to provide a two-stage attack, injecting patients first with a HIV multi-antigen and a DNA plasmid encoding human interleukin proteins and then following up with a booster containing a viral vector. The idea behind this approach is to nudge the immune system into learning how to combat the virus so that ART drugs are no longer needed. But, the approach has not been proven. In this new effort, the research team conducted a study designed to test the effectiveness of the vaccine.

The study consisted of enlisting the assistance of 30 early-stage patients (one dropped out) with HIV infections who were already being treated with ARTs and assigning them to one of two groups—14 patients got the vaccine while 15 got a placebo. Injections took place at 0, 4, 12, 24, 36 and 48 weeks. ART drug administration was halted for all of the volunteers starting at week 56 and lasting until week 72. All of the volunteers were tested regularly throughout the study for viral loads, a measure of how well the body, along with ARTs and/or the vaccine, was working to suppress the virus.

The researchers report that they found no measurable increase in effectiveness in any of the volunteers who were given the vaccine. They also report that they were surprised to see that four of the volunteers who had received the placebo had lower than normal viral loads for a short time. This finding was particularly important, the researchers note, because it showed that if the study not been conducted with placebos, the

results would have showed that the vaccine had worked to a limited extent. And that, Nelson notes, is the real lesson learned from this study.

More information: Michael C. Sneller et al. A randomized controlled safety/efficacy trial of therapeutic vaccination in HIV-infected individuals who initiated antiretroviral therapy early in infection, *Science Translational Medicine* (2017). DOI: 10.1126/scitranslmed.aan8848

Abstract

Despite substantial clinical benefits, complete eradication of HIV has not been possible using antiretroviral therapy (ART) alone. Strategies that can either eliminate persistent viral reservoirs or boost host immunity to prevent rebound of virus from these reservoirs after discontinuation of ART are needed; one possibility is therapeutic vaccination. We report the results of a randomized, placebo-controlled trial of a therapeutic vaccine regimen in patients in whom ART was initiated during the early stage of HIV infection and whose immune system was anticipated to be relatively intact. The objectives of our study were to determine whether the vaccine was safe and could induce an immune response that would maintain suppression of plasma viremia after discontinuation of ART. Vaccinations were well tolerated with no serious adverse events but produced only modest augmentation of existing HIV-specific CD4+ T cell responses, with little augmentation of CD8+ T cell responses. Compared with placebo, the vaccination regimen had no significant effect on the kinetics or magnitude of viral rebound after interruption of ART and no impact on the size of the HIV reservoir in the CD4+ T cell compartment. Notably, 26% of subjects in the placebo arm exhibited sustained suppression of viremia (