'Elite neutralizing' antibody demonstrates long-term viral suppression in persons living with HIV in phase 1 trial

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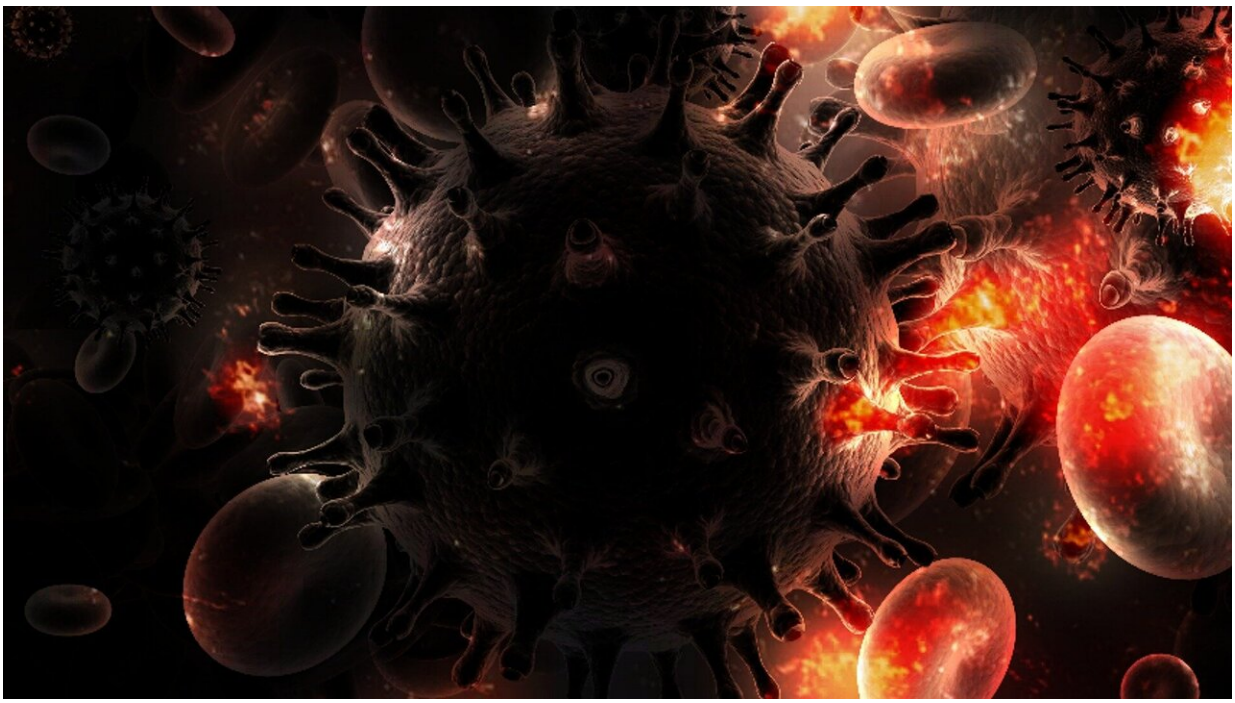

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In the 40 years since the first published reports of the syndrome known as AIDS, more than 32 million people have died from the virus that causes it, the human immunodeficiency virus (HIV). With more than 35 million people worldwide living with HIV today and nearly two million

new cases each year, HIV remains a major global epidemic.

Broadly neutralizing monoclonal antibodies (bNAB) target specific proteins on the outside of the virus. In a phase 1 clinical trial, researchers led by physicians-scientists at Beth Israel Deaconess Medical Center (BIDMC) evaluated an antibody known as PGT121 for its ability to treat and prevent HIV-1 infection. The scientists found that the antibody was safe and well-tolerated by trial participants and also demonstrated antiviral activity in adults living with HIV. The team's results appear in *Nature Medicine*.

After establishing the antibody's safety and tolerability in a placebo-controlled trial including adults living with and without HIV and adults living with HIV taking anti-retroviral therapy (ART) to suppress their viral infection, the scientists next evaluated the antibody in adults living with HIV who were not taking ART who therefore had detectible viral loads. Among the 13 participants enrolled in this part of the trial, nine participants were found to have high viral loads at baseline (more than 2,000 viral copies per milliliter of blood) and four were found to have low baseline viral loads (fewer than 2,000 copies).

Following a single dose of the antibody, viral load declined among those with high baseline viral counts and continued to decrease for seven to 10 days before rebounding to baseline by day 28. In the low viral load group, all four participants saw a decrease in viral load, with two participants' numbers rebounding to baseline by day 28. However, two participants exhibited much longer viral suppression.

"Notably, two individuals with a low viral load at baseline demonstrated drug-free viral suppression for more than 168 days—nearly six months—following a single infusion of the antibody," said corresponding author Dan H. Barouch, MD, Ph.D., director of the Center for Virology and Vaccine Research at BIDMC. "Viral rebound

was not detected in one participant until the individual was brought back for a long-term extension of the study at day 252. To our knowledge, this is the longest observed ART-free viral load suppression reported in the literature following one dose of any single or combined broadly neutralizing antibody treatment for HIV."

Consistent with previous studies of antibody treatments for HIV, the scientists also observed the emergence of at least partial resistance to the antibody in 12 of the 13 participants—HIV's ability to rapidly evolve resistance to drug therapies and vaccine strategies is one reason the virus has been so difficult to eradicate. However, the current study's findings suggest the investigative antibody may have greater potency than other single broadly neutralizing antibodies tested thus far, the researchers noted.

"In summary, the antibody treatment was safe, well-tolerated and had a brisk antiviral affect in participants living with HIV-1 who had a detectable viral load," said co-first author Kathryn E. Stephenson, MD, MPH, an investigator in the Center for Virology and Vaccine Research at BIDMC and protocol co-chair with Boris Julg, MD, Ph.D. of the "T001" Clinical Trial. "These data suggest that this antibody should be tested further for its ability to maintain viral suppression or to block HIV infection, particularly in combination with other broadly neutralizing antibodies."

More information: Kathryn E. Stephenson et al, Safety, pharmacokinetics and antiviral activity of PGT121, a broadly neutralizing monoclonal antibody against HIV-1: a randomized, placebo-controlled, phase 1 clinical trial, *Nature Medicine* (2021). DOI: 10.1038/s41591-021-01509-0

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