NIH launches large clinical trials of antibody-based HIV prevention

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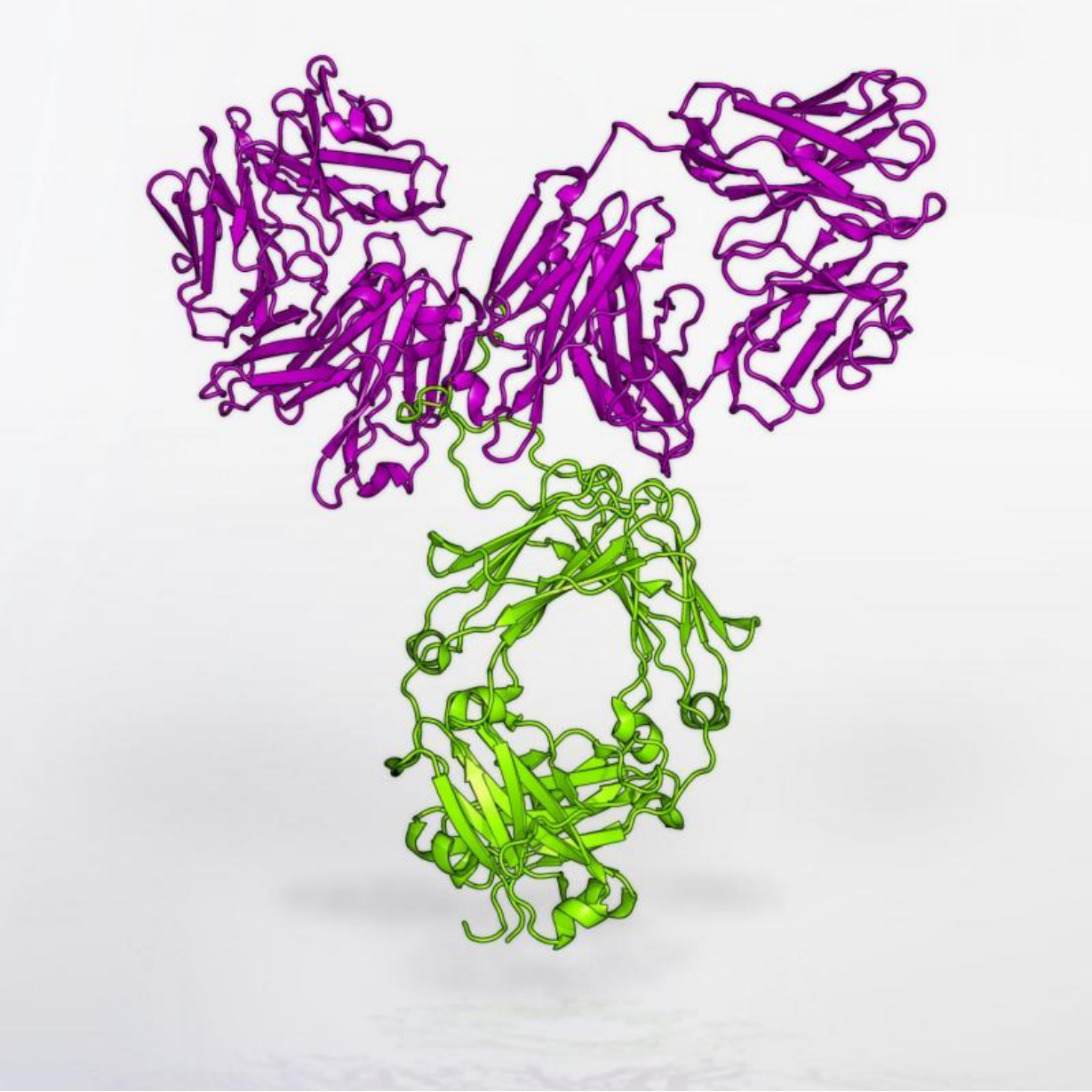

Model of the VRC01 antibody. Credit: NIAID

Enrollment has begun in the first of two multinational clinical trials of an intravenously delivered investigational antibody for preventing HIV infection. Known as the AMP Studies, for antibody-mediated prevention, the trials will test whether giving people an investigational anti-HIV antibody called VRC01 as an intravenous infusion every 8 weeks is safe, tolerable and effective at preventing HIV infection. With a projected enrollment of 4,200 adults, the trials also are designed to answer fundamental scientific questions for the fields of HIV prevention and vaccine research.

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), is sponsoring and funding the AMP Studies.

The NIAID Vaccine Research Center (VRC) discovered the VRC01 antibody in the blood of an HIV-infected person in 2010 and subsequently manufactured the antibody for these trials. Laboratory studies have shown that VRC01 stops up to 90 percent of HIV strains worldwide from infecting human cells, and thus it is considered to be a broadly neutralizing antibody.

"The AMP Studies could have a major impact on the future of HIV prevention and may be especially informative to HIV vaccine research," said NIAID Director Anthony S. Fauci, M.D. "Many scientists believe that if a vaccine were developed that elicited broadly neutralizing antibodies in healthy people, it would protect them from HIV infection. The AMP Studies will test this hypothesis by directly giving people the VRC01 antibody."

In addition, the studies could clarify what level of broadly neutralizing antibodies a vaccine or other long-acting HIV prevention method needs to achieve and maintain to provide sustained protection from the virus.

The AMP Studies are being conducted jointly by the NIAID-funded HIV Vaccine Trials Network (HVTN) and HIV Prevention Trials Network (HPTN). The National Institute for Drug Abuse and the National Institute of Mental Health, both part of NIH, also fund HPTN. The studies individually are known as HVTN 703/HPTN 081 and HVTN 704/HPTN 085.

"The immediate goal of antibody-mediated prevention of HIV is for each VRC01 infusion to have a protective effect that lasts for many weeks," said Protocol Chair Myron Cohen, M.D. "Such a long-acting HIV prevention regimen might be easier for some people to follow than a daily regimen of oral medication, as currently required to prevent HIV infection." Dr. Cohen is a principal investigator of the HPTN, associate vice chancellor for global health at the University of North Carolina at Chapel Hill and director of the university's Institute for Global Health and Infectious Diseases.

The AMP Study that just launched , HVTN 704/HPTN 085, will take place at 24 sites in Brazil, Peru and the United States, and will enroll 2,700 men and transgender people who have sex with men.

The second of the two AMP Studies, HVTN 703/HPTN 081, is planned to launch later this spring, enrolling 1,500 sexually active women at 15 sites in Botswana, Kenya, Malawi, Mozambique, South Africa, Tanzania and Zimbabwe.

The volunteers in both studies will be adults at high risk for HIV infection, but HIV-negative when they enter the study.

In each trial, volunteers will be assigned at random to receive an intravenous infusion of either VRC01 at a dose of 30 milligrams per kilogram (mg/kg), VRC01 at a dose of 10 mg/kg, or a saline solution (a placebo). Neither the volunteers nor the study investigators will know who receives which type of infusion until the end of the study. Volunteers will receive a total of 10 infusions, once every 8 weeks, and then will be followed for 20 more weeks. The results of the trials are expected in 2022.

"Injections or infusions of antibodies to prevent acquisition of an infectious disease have been utilized in medicine for decades," said Protocol Chair Larry Corey, M.D. "The remarkable advance in technologies to isolate and manufacture human monoclonal antibodies in concentrations high enough to potentially prevent HIV is a major development that makes these exciting trials possible." Dr. Corey is principal investigator of the HVTN, past president and director of the Fred Hutchinson Cancer Research Center in Seattle, and a professor of medicine and laboratory medicine at the University of Washington.

Volunteers will be tested for HIV infection once every 4 weeks and at any time after reporting possible exposure to the virus. Those who test positive for HIV will stop receiving infusions but will remain in the study for follow-up and will be referred to professionals in their communities for appropriate medical care.

All volunteers will receive the standard care for preventing HIV infection, including condoms and lubricant, counseling on how to reduce behaviors that increase risk for infection, and counseling and referral for antiretrovirals to take immediately following suspected exposure to HIV (post-exposure prophylaxis). In addition, volunteers in the AMP Studies will be referred to available local programs where they may obtain the oral medication Truvada to take daily for HIV prevention, a highly effective practice called pre-exposure prophylaxis (PrEP). Volunteers'

access to PrEP will expand as more host countries approve Truvada for PrEP and develop the infrastructure to support its use. The AMP Studies have been designed so investigators will be able to discern a preventive effect from VRC01 even if some participants are taking PrEP.

"I am gratified that seven southern African nations are taking part in a clinical trial that could have far-reaching implications for the future of HIV prevention," said Protocol Co-Chair Nyaradzo Mgodi, MBChB, MMed. "With 5 to 25 percent of adults in the participating African countries infected with HIV, more and stronger HIV prevention options—especially a vaccine—would make a huge difference here." Dr. Mgodi is a principal investigator at the University of Zimbabwe-University of California San Francisco Collaborative Research Program in Zimbabwe.

Provided by NIH/National Institute of Allergy and Infectious Diseases