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NIH and partners launch HIV vaccine efficacy study

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The National Institutes of Health and partners have launched a large clinical trial to assess whether an experimental HIV vaccine regimen is safe and able to prevent HIV infection. The new Phase 2b proof-of-concept study, called Imbokodo, aims to enroll 2,600 HIV-negative women in sub-Saharan Africa. Of 1.8 million new HIV infections worldwide in 2016, 43 percent occurred in eastern and southern Africa, with women and girls disproportionately affected.

"Imbokodo," the Zulu word for rock, is part of a well-known proverb in South Africa that refers to the strength of women and their importance in the community. The study is sponsored by Janssen Vaccines & Prevention, B.V., part of the Janssen Pharmaceutical Companies of Johnson & Johnson, with co-funding from two primary partners, the Bill & Melinda Gates Foundation (BMGF) and NIH's National Institute of Allergy and Infectious Diseases (NIAID).

The vaccine regimen being tested in Imbokodo is based on "mosaic" immunogens—vaccine components designed to induce immune responses against a wide variety of global HIV strains. This regimen differs from the one being tested in the Phase 2b/3 HVTN 702 study, an ongoing HIV vaccine efficacy trial sponsored by NIAID that launched late last year in South Africa with major co-funding from NIAID and BMGF. HVTN 702 is evaluating a newer version of the vaccine regimen tested in the RV144 Thai trial—the only candidate HIV vaccine regimen ever shown to provide some protection against the virus.

"Together with the implementation of existing HIV prevention and treatment strategies, the development and delivery of a preventive HIV vaccine that is safe and at least moderately effective would help bring about a durable end to the HIV/AIDS pandemic," said NIAID Director Anthony S. Fauci, M.D. "We are committed to pursuing multiple vaccine development strategies to achieve this goal."

The first Imbokodo participants have received vaccinations at clinical research sites in South Africa. Regulatory approvals are being sought to conduct the study at additional sites in Malawi, Mozambique, Zambia and Zimbabwe. With the start of Imbokodo, two HIV vaccine efficacy trials now are taking place in sub-Saharan Africa. Results from HVTN 702, which is enrolling HIV-negative men and women in South Africa, are expected in late 2020. Results from Imbokodo are expected in 2021.

"Both Imbokodo and HVTN 702 have resulted from years of scientific testing and clinical development, and they represent science's current best efforts to develop a vaccine to prevent HIV infection," said Kathy Mngadi, M.B.Ch.B., M.Phil., senior scientist at the Centre for the AIDS Programme of Research in South Africa (CAPRISA) and Imbokodo co-chair. "We are grateful to the people of southern Africa who volunteer for these trials, and the communities in which the trials are conducted to help develop what could be a true game-changer for the HIV/AIDS pandemic."

The NIAID-funded HIV Vaccine Trials Network (HVTN), headquartered at Fred Hutchinson Cancer Research Center in Seattle, is implementing Imbokodo. The South African Medical Research Council (SAMRC) is helping implement the study in South Africa. Additional partners providing support include the U.S. Military HIV Research Program at the Walter Reed Army Institute of Research, the U.S. Army Medical Materiel Development Activity, and the Ragon Institute of MGH, MIT and Harvard.

NIAID provided funding for preclinical and early phase clinical development of the mosaic-based vaccine, which was initially developed by the laboratory of Dan H. Barouch, M.D., Ph.D., at Beth Israel Deaconess Medical Center, together with Janssen and other partners. The mosaic immunogens incorporated in the vaccine were designed by the Los Alamos National Laboratory.

In preclinical studies, regimens with mosaic-based vaccines protected monkeys against infection with an HIV-like virus. Findings from two early-stage human clinical trials suggest that these vaccines are well-tolerated and can generate anti-HIV immune responses in healthy adult volunteers. Based on results from an early-stage clinical trial called APPROACH, reported in July 2017, as well as findings from a second early-stage trial called TRAVERSE, researchers selected a lead candidate regimen for further evaluation.

Data from TRAVERSE confirmed the decision to move forward with the larger trial to evaluate whether the experimental regimen can prevent HIV infection. The ongoing TRAVERSE study is comparing two regimens containing vaccines that use a strain of common-cold virus engineered so that it does not cause illness (adenovirus serotype 26, or Ad26) to deliver either three (trivalent) or four (quadrivalent) mosaic antigens among 198 healthy, HIV-negative adult volunteers in the United States and Rwanda. Interim data indicate that both are well-tolerated and can elicit anti-HIV immune responses. Imbokodo is evaluating the quadrivalent vaccine.

All Imbokodo participants will receive vaccinations at four timepoints over one year. They will be randomly assigned to receive either the experimental vaccine regimen or placebo. The experimental regimen includes four doses of the quadrivalent mosaic vaccine. The final two doses will be given together with doses of an HIV protein, clade C gp140, and an aluminum phosphate adjuvant to boost immune responses.

Participants will be followed for at least two years.

Provided by NIH/National Institute of Allergy and Infectious Diseases