Request for Research Proposals: Imbokodo HIV Vaccine Efficacy Trial (HVTN 705/VAC89220HPX2008)

February 7th, 2023

The HIV Vaccine Trials Network (HVTN), the NIH/NIAID Division of AIDS (DAIDS), and Janssen Vaccines and Prevention are pleased to welcome scientific study proposals involving specimens and/or study data from the Imbokodo (HVTN 705/VAC89220HPX2008) HIV vaccine clinical trial.

Background

The Imbokodo study tested an investigational HIV vaccine regimen of Ad26.Mos4.HIV (adenoviral vectors encoding four mosaic immunogens) administered at four vaccination visits over one year. The Imbokodo regimen also included a soluble protein component (subtype C gp140) adjuvanted with aluminum phosphate, which was administered at vaccination visits three and four. The primary analysis was conducted 24 months after participants received their first vaccinations. The study's primary endpoint was based on the difference in cumulative incidence of HIV acquisition between the placebo and vaccine recipient groups, from month seven (one month after the third vaccination) through month 24.

Sampling during the study:

The sampling design of the Imbokodo efficacy study was unique in its extensive and longitudinal sampling for serum, PBMC, and mucosal specimens. An overview of sample types available, sampling schedule and volumes, and details on number of acquisitions and statistical analysis populations is available at hvtn.org/imbokodo-rfp.

Summary of findings:

The investigational HIV vaccine evaluated in Imbokodo was found to have a favorable safety profile with no serious adverse events related to vaccine administration. However, this vaccine regimen did not provide sufficient protection against HIV acquisition in a sub-Saharan African population of young cisgender women (18–35 years old) who had a high likelihood of acquiring HIV. After two years of follow-up, 65 of 1,108 participants who received placebo compared to 54 of 1,080 participants who received active vaccine acquired HIV. This analysis demonstrated a vaccine efficacy point estimate of 14% (95% confidence interval of -22% to 40%). Based on the efficacy results, the study did not proceed to a second stage with a longer follow-up period, and study participants were informed about the trial results and whether they received the vaccine or the placebo.

Ongoing research:

Immunological correlates research is ongoing in the Imbokodo study to investigate associations between HIV-1 infection risk, vaccine efficacy and both humoral and cellular immunity:

- Serum antibody binding to vaccine-matched antigens as well as to diverse panels of subtype C and cross-subtype HIV-1 antigens are being assessed through ELISA and a binding antibody multiplex assay (BAMA).
- Antibody functionality is being evaluated through antibody-dependent cellular cytotoxicity (ADCC) and phagocytosis (ADCP), and systems serology analyses are being done that cover a diverse array of antibody binding and functional responses.
- Functional T-cell responses are being investigated through IFN-ɣ ELISpot and intracellular cytokine staining (ICS) responses to vaccine-matched and potential T-cell Epitope (PTE) peptide pools, as well as T-cell breadth mapping via IFN-ɣ ELISpot.
- Viral sequencing of *gag*, *pol* and *env* genes is ongoing from all participants who acquired HIV-1 between months 7 and 24, to enable sieve analysis.
- Mucosal antibody responses will be assayed by multiplex binding assays.
- The impact of vaginal microbial composition on vaccine efficacy and the likelihood of acquiring HIV is being explored.
- Host genetic factors (including Fc receptor, IGHG variation and HLA genotype) are being assessed to investigate if these impact the vaccine efficacy.

Call for Proposals

We welcome proposals for research projects that will potentially extend, complement, or advance key hypotheses from the areas detailed above, or investigate other novel research questions beyond those listed to further the understanding of the outcomes in this clinical trial.

Proposal Submission and Review Process

To submit a proposal, complete the Imbokodo Study Proposal Template available at hvtn.org/imbokodo-rfp and submit to Imbokodo@hvtn.org.

The submission period opens on February 7, 2023 and closes on April 4, 2023. Late proposals will be considered in the order of their submission, after those submitted in the initial proposal period are reviewed.

Proposals will undergo an initial feasibility assessment, which includes administrative and regulatory review and subject matter expert review (where applicable). This process will be

managed by the Imbokodo Study Management Group (SMG), which includes representatives from the HVTN Leadership and Operations Center (LOC), Laboratory Center (LC), and Statistical and Data Management Center (SDMC), and representatives from Janssen's Clinical Immunology and Biomarkers groups. Together, the SMG and investigators will refine proposals prior to submission to the Review Committee, which is comprised of the Imbokodo Protocol Team and the Imbokodo Oversight Group.

Available Resources

Explicit funds for these studies are not available through the HVTN or Janssen. However, we are committed to assisting investigators who are submitting proposals by providing administrative and regulatory review, subject matter expert consultation, and access to HIV vaccine research expertise at the network's LOC, LC, and SDMC

Find additional information about Imbokodo, the sampling schema, and the process for proposal development and review on the HVTN website hvtn.org/imbokodo-rfp.

Contact Imbokodo@hvtn.org with any questions about this call for proposals or for support with proposal completion and submission.

Imbokodo was supported by a public-private partnership led by Janssen Vaccines & Prevention B.V., part of the Janssen Pharmaceutical Companies of Johnson & Johnson; the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health; the Bill & Melinda Gates Foundation; and the HIV Vaccine Trials Network (HVTN). Additional partners providing support included the U.S. Army Medical Research and Development Command (USAMRDC) and the Ragon Institute of MGH, MIT and Harvard. The study was conducted at clinical sites coordinated by HVTN, and the South African Medical Research Council (SAMRC) helped to implement Imbokodo in South Africa.

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