Experimental HIV vaccine regimens likely to be ineffective in preventing HIV acquisition, research finds

December 7 2023

The first PrEPVacc volunteer participant receives an injection at the launch of the launch of the PrePVacc Trial at the Masaka site of the MRC/UVRI and LSHTM Uganda Research Unit, on Tuesday 15 December 2020. Credit: PrEPVacc Investigators

The PrEPVacc HIV prevention study of experimental vaccine regimens and a new form of oral pre-exposure prophylaxis (PrEP) running in East and Southern Africa among 1,500 volunteer participants has stopped further vaccinations as there is little or no chance of the trial demonstrating vaccine efficacy in preventing HIV acquisition.

PrEPVacc's leadership decided to stop vaccinations immediately based on the recommendation of its independent data monitoring committee (IDMC), which also recommended that the oral PrEP component of the study continue to completion.

Follow-up of all participants will continue for additional safety data collection, HIV testing, and referral for ongoing care for six months after the last vaccine injection for all participants or until the end of the oral PrEP trial, whichever is longest.

PrEPVacc's trial safety group reviews the safety information of participants twice a month and has no concerns about the safety of the vaccines.

Trial leaders shared news about PrEPVacc publicly at the International Conference on AIDS and STIs in Africa (ICASA 2023) today in Zimbabwe.

PrEPVacc, led by African researchers with support from European scientists, is three trials in one. It is testing two different combinations of HIV vaccines to find out if either can prevent HIV infection in populations at risk of acquiring HIV.

Participants received injections of either one regimen combining a DNA vaccine with a protein-based vaccine (AIDSVAX), a regimen combining DNA, MVA and a protein-based vaccine (CN54gp140), or a placebo (saline). Participants received four injections in each regimen or of the

placebo.

At the same time as participants receive vaccinations, PrEPVacc is also testing a new oral PrEP drug formulation (TAF/FTC, Descovy) to see if it is as good as the drugs already approved for PrEP (TDF/FTC, Truvada), in a study population that is 87% female. Participants received study PrEP as either Descovy or Truvada up to two weeks after the third vaccine injection.

After that, the study teams either provide non-study PrEP in a clinic or refer the participants to access non-study PrEP at the local service providers. Participants received information and counseling on how best to incorporate PrEP in combination with other available prevention methods against HIV acquisition.

Enrollment of healthy adults aged 18-40 in PrEPVacc began in December 2020 and was completed on 1 March 2023 with 1,512 participants. At enrollment, participants reported behaviors that made them more vulnerable to acquiring HIV.

Despite the delays experienced due to the COVID-19 pandemic, all but 10 participants had passed the time point for the third set of vaccinations by 2 October 2023, and 1,016 had received all four vaccinations. Almost all the participants received oral PrEP, with only 6% deciding they did not want oral PrEP. Overall, most participants reported taking oral PrEP two days before or after their last condomless sex act.

PrEPVacc's study sites are Masaka, Uganda; Mbeya, Tanzania; Dar es Salaam, Tanzania; and Durban, South Africa. The Masaka and Durban sites enrolled men and women, while the Mbeya and Dar es Salaam sites enrolled only women. Across all sites, 13% of participants are men, and 87% are women.

Vaccinations were stopped immediately following the recommendation by PrEPVacc's IDMC after a scheduled interim review on 9 November of PrEPVacc data collected up to 2 October 2023.

PrEPVacc's Trial Steering Committee accepted the recommendation that vaccinations be permanently discontinued on 22 November, after which the study team began communicating the news to participants and their local communities, other stakeholders, and regulatory and ethics groups.

The stopping of further vaccinations in PrEPVacc underlines how challenging it is to develop an effective HIV vaccine. To date, only the RV144 'Thai trial' showed some efficacy in reducing HIV acquisition by 31.5% at three years.

The full results of the vaccine trial will not be known until all the study visits have been completed, which the study teams aim to do by June 2024. Full results will be analyzed and shared with participants, study teams, and the public in the second half of 2024.

PrEPVacc's Trial Director, Dr. Eugene Ruzagira, based at the MRC/UVRI & LSHTM Uganda Research Unit in Uganda, who announced the news at ICASA, said, "Vaccinations to PrEPVacc trial participants have been stopped because an analysis of the data collected so far by our Independent Data Monitoring Committee has led them to conclude that there is little or no chance of demonstrating that the vaccines we are testing are reducing the risk of acquiring HIV."

"PrEPVacc clinicians and scientists will not know the vaccine trial's full results until after June 2024, when the collection of all the trial data is complete, and they can be analyzed. A report will be available in the later months of 2024."

"The scientific hurdles are high, but I have equally high hopes that an

HIV vaccine will be developed one day. Every day, all around the world, important research like PrEPVacc is moving us forward, and participants are willing to step forward with us and make a difference in the health of their communities."

"Throughout this HIV prevention study, we have built very good relations with participants and our communities using the principles and techniques of Good Participatory Practice. As we move towards a new era of HIV prevention studies and vaccine efficacy trials, the lessons of Good Participatory Practice have never been more important to apply."

PrEPVacc's Chief Investigator, Professor Pontiano Kaleebu, based at the MRC/UVRI & LSHTM Uganda Research Unit in Uganda, said, "The development of a vaccine preventing HIV is a critical goal for Africa. It is a goal that must have even greater urgency now that no HIV vaccines are being trialed for efficacy anywhere in the world."

"We have come so far in our HIV prevention journey, but we must look to a new generation of vaccine approaches and technology to take us forward again."

"We must also look to a new generation of leaders. We set up PrEPVacc to grow our capacity in Africa to do future trials ourselves and to develop those who will lead them here in Africa."

"Our participants and collaborators should be very proud that PrEPVacc is the largest HIV vaccine efficacy trial to run in East Africa."

Professor Sheena McCormack, PrEPVacc Project Lead based at the Medical Research Council clinical trials unit at University College London, UK, said, "It is important to remember that PrEPVacc is three studies in one, and the PrEP part is continuing. Almost all participants received oral PrEP as a study drug, but far fewer continued on non-study

PrEP. We hope that we will have valuable insights from the quantitative and qualitative findings to guide the use of oral PrEP beyond the trial."

Professor Jonathan Weber of Imperial College London, UK, the sponsor of PrEPVacc, said, "The most important people to thank and to credit in PrEPVacc are our participants. Each one has made a tremendous ongoing commitment to this study. The schedule of visits is demanding, and each research clinic visit can take a long time. Our participants' willingness to continue this study with us is heroic and greatly appreciated by the research community."

"We do clinical trials because we don't know the answer to questions. It was important to find out whether the combination vaccine regimens in PrEPVacc, developed over 20 years, should be ruled out or further developed for preventing HIV. While we await the final results and analysis of individual products, I believe that our interim result puts this generation of putative HIV vaccines to bed."

"It has been a tremendous achievement by PrEPVacc's study staff to successfully conduct the trial through COVID-19. We must also acknowledge those who have designed the PrEPVacc trial. PrEPVacc's novel methodology was intended to reach a clear result with the minimum number of volunteers."

Olivia Nakanwagi, a member of the Masaka site, Uganda, Community Advisory Board, said, "Without community trust and engagement, we will not be able to advance the search for new ways of preventing HIV. PrEPVacc has tried new ways to bring the community's voice into decision-making. I'm proud to represent my community among the study leaders, scientists, and staff at my site and guide them in engaging well with that community."

"The participants in PrEPVacc have the deep gratitude of their

communities for their dedication to this study and helping to test two ways of preventing HIV at the same time."

Provided by PrEPVacc

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