Project Summary of Publication

Period covered: 01January 2021 to 31 December 2021

Context and Overall objectives

PREVAC-UP is built around the PREVAC trial, a phase IIB, randomised, placebo controlled, multicentre trial evaluating the safety and immunogenicity over 12 months of three vaccine strategies in children and adults.

Participants received a two-dose heterologous vaccine regimen consisting of Ad26.ZEBOV (rHAd26) as dose 1 and MVA-BN-Filo (MVA) as dose 2, or the rVSVΔG-ZEBOV-GP (rVSV) vaccine with or without boosting, or placebo.

PREVAC-UP aims to extend the follow-up of 2,802 participants included under PREVAC in Guinea, Liberia, Sierra Leone and Mali, for four additional years. PREVAC-UP will also evaluate the effect of co-infections, such as malaria and helminths, on the immune response to vaccination. An integrative statistical analysis of the immune response will be used to explore the mechanism of action of the vaccines and to identify early correlates of durable antibody induction. PREVAC-UP will build on the extensive community mobilization efforts previously generated through PREVAC to provide a trans-national platform for social and health science research and training. PREVAC-UP will expand and sustain capacity building and training of scientists in the four participant African countries.

Main results achieved so far

For the second successive year, PREVAC-UP activities in 2021 were influenced by the COVID-19 pandemic, which led to situations of suspension/resuming of activities. The year 2021 was also marked by the Marburg epidemic and Ebola epidemic in Guinea, which accelerated the discussion on the participant unblinding and the vaccination of those who received the placebo or an incomplete vaccination. The revaccination process started in December 2021 in Liberia. The primary paper for the M12 data for PREVAC is in progress.

In order to evaluate the impact of malaria and other parasitic infections on the persistence of the antibody response to two Ebola vaccines, a survey was completed successfully in Mambolo district Sierra Leone. Results of the survey, which have been presented in a manuscript accepted for publication, were used to inform selection of antigens for the Luminex helminth/malaria antibody assay, in the Kambia laboratory. Staff from Sierra Leone

EDCTP

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have received training on operation of the Luminex machine and on performing multiplex bead assays.

Regarding the data processing of the immunological study in Guinea, samples were shipped to Inserm-VRI in January and December 2021. All the consumables needed for the experiment on the field were shipped to Conakry.

As for capacity building, which aims at strengthening and maintaining capacity in clinical research for site staff during the trial, some academic achievements were carried out, with notably the creation of a new university degree in Global Health and Emerging at Gamal Abdel Nasser University of Conakry in partnership with Montpellier University, and applications by Bordeaux School of Public Health (ISPED)/University of Bordeaux for an international exchange program at Bordeaux School of Public Health (ISPED). Furthermore, three scholarships for a distance-learning short course in epidemiology organized by Bordeaux School of Public Health (ISPED) graduated in 2020.

Progress beyond the state of the art and expected potential impact

Besides of the devastating effects on the population, Ebola outbreaks have a pronounced socio-economic impact in affected countries. To date, two vaccines have obtained authorization from international drugs, agencies to be used to control Ebola virus disease and they have been used during epidemics. Yet, data on the durability of the immune response following vaccination with rVSV or with Ad26.ZEBOV/MVA vaccines remain limited. Outbreaks sporadically occur in different countries on the African continent and authorities need to provide the safest and most efficient approach to better protect populations and control the spread of the virus. PREVAC-UP brings much needed data regarding long-term immunogenicity and safety of the three different Ebola vaccine regimens tested in PREVAC, as well as the impact of co-infections on the persistence on the antibody response. In terms of impact the Ministry of Health and the Helen Keller Foundation have been given important information on the success of their helminth mass treatment programme in areas such as Mambolo. Once the Luminex assay has been established and validated in Kambia district, this will be used to measure antibody concentrations in the samples collected each year in Sierra Leone rather than requiring the samples to be sent outside the country.

The follow-up of vaccinated participants during these 5 years will enable long-term cellular immune responses to the vaccines to be evaluated and to describe the durability of the immune response. The societal impact is strong as it will help to determine if new vaccination campaigns are necessary to ensure the protection of the population in the event of a new epidemic.

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