Project Summary of Publication

Period covered: 01 January 2022 to 31 December 2022

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 evaluate the effect of co-infections, such as malaria and helminths, on the immune response to vaccination.

Main results achieved so far

The M36 follow-up of the study was completed on 12 April 2022. The attendance rate for the M36 visit is high at 90.5%. M48 visits started on 21 April 2022. In 2022, participants who received the placebo or an incomplete strategy were invited to receive the Ebola vaccine if they wished. Only a single vaccine strategy was used in each country. 79.5% of the participants eligible for the revaccination have been revaccinated. The manuscript of the M12 results was submitted to the New England Journal of Medicine and published online on 14 December 2022.

Follow-up visits and PBMC isolations were performed at the Landreah/Conakry site. Evaluation of the functional cellular response was performed on 31 participants at M36. Results showed that EBOV-specific CD4 and CD8 T cells were detected at M36 post-vaccination with no major differences compared to the M24 time point.

A parasitological survey was completed successfully in Mambolo district Sierra Leone, and a report on its findings submitted to the Sierra Leonean Ministry of Health and the Helen Keller Foundation. A laboratory assay was developed which measures antibodies to malaria and helminth infections. This test has now been used to measure antibodies in PREVAC-UP study participants from Sierra Leone.

EDCTP

PREVAC-UP project is funded by the European and Developing Countries Clinical Trials Partnership (EDCTP2) programme supported by the European Union. PREVAC-UP also benefits from co-funding from Inserm, the NIAID, the LSHTM and the COMAHS as well as host country support from Liberia, Sierra Leone, Guinea and Mali.

The methods for the identification of key early correlates of protection were evaluated. We performed a linear descriptive analysis and have based subsequent work on our model on the published mechanistic model for the antibodies kinetics on the data accumulated on the Ad27.Zebov/MVA Ebola vaccine (Journal of Virology, Pasin et al. 2019), further completed by new research on SARS-CoV-2 (Clairon et al. 2022 under revision). The model also includes the maintenance and reactivation of immune response after vaccination, adding immunological memory to the model (Balelli et al. 2020 Journal of Theoretical Biology).

Extensive community engagement work has been carried out to improve trial participant recruitment. Social science work has been conducted to understand acceptability, uptake and social impact of the trial. PREVAC-UP has created a new university degree in Global Health and Emerging at Gamal Abdel Nasser University of Conakry in partnership with Montpellier University and organised training for PREVAC-UP site staff. Laboratory staff have been trained on Immunology Capacity Building in the Kambia Health Research Centre Laboratory in Sierra Leone including further development of the Luminex Platform and Cell-mediated immune assays. A 4-day workshop on clinical research and a symposium on cancer research were organized at University Gamal Abdel Nasser of Conakry in September 2022.

Progress beyond the state of the art and expected potential impact

PREVAC-UP produces much needed data regarding long-term immunogenicity and safety of the three different Ebola vaccine regimens tested in PREVAC trial. The follow-up of vaccinated participants will enable long-term cellular immune responses to the vaccines to be evaluated and will contribute to determining if new vaccination campaigns are necessary to ensure the protection.

The parasitological study has had a practical impact by providing the Ministry of Health and the Helen Keller Foundation with important information on the success of their helminth mass treatment programme in Mambolo. The Luminex assay in Kambia is being used to measure antibody concentrations in the samples collected in Sierra Leone rather than outside the country. Establishment of the versatile Luminex technique in Kambia has allowed serological studies on other important infections including COVID-19 and Lassa fever.

Work on the mechanistic model is well advanced. Work on the key correlate of protection has also begun. The project generates understanding of different models of community engagement and the long-term impact of epidemics on people's lives. PREVAC-UP strengthens the clinical capacities of both individuals and institutions.

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