Project Summary of Publication

Period covered: 1 January 2019 – 31 December 2019

Context and Overall objectives

Human-to-human transmission of Ebola virus in West Africa was interrupted in 2016 but the risk of reemergence of the disease is real. Thus, efforts to develop a safe and effective vaccine against Ebola virus disease with a durable prophylactic effect in communities must continue. 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 either the Ad26.ZEBOV (rHAd26) vaccine with a MVA-BN-Filo (MVA) boost, 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 of follow up. 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 mobilisation efforts previously generated through PREVAC to provide a trans-national platform for social and health science research and training. Finally, this project will expand and sustain capacity building and training of scientists in the four participant African countries.

To reach its objectives, PREVAC-UP consortium has assembled a network of leading scientists and clinicians from seven countries distributed in Europe (France and UK), Africa (Guinea, Sierra Leone, Mali and Liberia) and USA with expertise in clinical trials and Ebola research.

Main results achieved so far

2019 marks the transition between PREVAC and PREVAC-UP. Regarding the clinical trial, the activities focused on the preparation of the long-term follow-up with the update of the ethical and regulatory documents, Standard Operating Procedures, monitoring plan, statistical analysis plan and timelines, and community engagement strategies.

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.

In order to evaluate the impact of malaria and other parasitic infections on the persistence of the antibody response to two EBOLA vaccines, a parasitological survey is being conducted in the Mambolo district, Sierra Leone where these vaccine trials were conducted. Preliminary findings suggest that the prevalence of helminth infections in Mabolo district is low, probably the consequence of successful mass drug administration programmes conducted in this community during the past few years.

Extensive community engagement work has been carried out alongside the trial in each site. This has been used to improve trial participant recruitment, lost to follow-up, retention, as well as to understand acceptability, uptake and social impact of the trial. Long term in situ ethnography and interviews with trial participants and community members has begun alongside the trial to understand participant experiences of the vaccine trials and vaccine deployment including the long-term impact of the Ebola epidemic.

As for capacity building, a new university degree in Global Health and Emerging was created at Gamal Abdel Nasser University of Conakry, short-term courses and international exchange in Epidemiology with the Bordeaux School of Public Health were launched, and several training courses were offered on the site of the clinicals trial.

Progress beyond the state of the art and expected potential impact

In addition of the devastating effects on the population, Ebola outbreaks have a pronounced socioeconomic impact in affected countries. Thus it is of utmost importance to produce scientific evidence supporting health authorities in the definition of the safest and most efficient approach to better protect populations at risk of Ebola. Despite numerous clinical trials involving Ebola vaccines implemented worldwide, durability of the immune response following vaccination with rVSV or with Ad26.ZEBOV/MVA vaccines still remains unknown. PREVAC-UP comes to bring 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 persistance on the antibody response.

The transnational platform for social science research will generate understanding of 1) Different models of community engagement at each trial site; 2) participant experiences of vaccine development and the clinical trials; and 3) the longer term impact of epidemics on people's lives, and their experiences of epidemic responses as well as their understandings and experiences of health care. In terms of impact, this research is contributing to our understanding of how trial strategies can be adapted to ensure community acceptance and is expected to contribute to learning and scientific knowledge about community acceptance of and attitudes towards medical research that will be of crucial importance for future outbreaks and medical interventions.

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