

## Study summary

### Evaluation of a heterologous, two-dose preventive Ebola vaccine for effectiveness and safety in the Democratic Republic of the Congo

Ebola virus disease (EVD) is a highly fatal acute systemic febrile syndrome caused by six known viruses of the Filoviridae family under the genus Ebolavirus. Case fatality rates tend to average around 50%, though Zaire ebolavirus has been recorded as reaching a case fatality rate of 90%. There is currently no licensed vaccine or treatment for EVD.

The current outbreak of Ebola was declared in the Democratic Republic of Congo on 1 August, 2018. As of 8 October, 2019, there have been over 3000 confirmed cases and 2000 deaths confirmed to be the result of EVD, with a case fatality rate of approximately 67%. While it does not reflect the steep epidemic curves seen in many large Ebola outbreaks, this epidemic became the second largest Ebola outbreak in history by November 2018. On 17 July, 2019, the World Health Organization declared the outbreak a Public Health Emergency of International Concern. One of the many challenges of the outbreak is not only the community engagement and trust, but additionally the current security situation in North Kivu. Front line workers have found it increasingly difficult to reach the necessary communities to implement prevention and treatment strategies.

One of these strategies includes ring vaccination out to the third level of contacts with the rVSV-ZEBOV-GP (rVSV) vaccine, which has a published efficacy of 100% using ring vaccination. In addition, rVSV is being offered to healthcare personnel and front line workers in areas of active transmission. After a year of outbreak, new cases continue to appear, including those outside of the purview of the ring vaccination strategy. Therefore, the Strategic Advisory Group of Experts (SAGE) on Immunization recommended not only to continue ring vaccination with rVSV but to explore alternative products for protection of the population.

The Janssen Ebola vaccine is a two dose vaccine regimen, the first dose being a primer vaccine of Zaire ebolavirus known as Ad26.ZEBOV and the second, a booster with other Ebolavirus types, trademarked as MVN-BN-Filo. The two doses are given 56 days apart (-14 days; +28 days). The Janssen Ebola vaccine was chosen over other candidates by a series of comparisons, including a WHO in depth comparison of the current safety and immunogenicity data against another vaccine developed by CanSino Beijing. Clinical studies found no safety signals, with a profile of mild to moderate AEs that did not last for an extended time nor led to sequelae. SAEs were reported at the same level in both the active and control groups. Immunogenicity trials found that over 98% of participants had at minimum a 2.5 fold increase in antibody concentration beyond baseline. There were also several promising results on long-term follow up studies indicating good persistence of antibody response.

The primary object of this study is to estimate vaccine effectiveness of the Janssen Ebola vaccine for EVD prevention. Our primary endpoint is a lab-confirmed case of EVD. Secondary objectives include safety assessment, coverage estimation, and exploring knowledge and perceptions of the vaccine. Rigorous follow up is planned for a safety cohort as well as all pregnant participants, who are considered eligible for the vaccine.