WHO Vaccine Prioritization Working Group

Summary of the evaluations and recommendations on the three *Sudan ebolavirus* vaccines that are candidates for inclusion in the planned ring vaccination trial in Uganda ("Tokomeza Ebola)

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Background

With the rapidly evolving outbreak of Ebola in Uganda with the Sudan ebolavirus strain, WHO and the MoH Uganda are co-sponsoring a randomised ring vaccination trial with one or more candidate vaccines. The design of the trial is similar to that successfully conducted during the outbreak in Guinea and Sierra Leone involving the Zaire ebolavirus strain.[1-5]

Due to the urgency of the situation in Uganda, WHO asked the existing COVID-19 Vaccine Prioritisation Working Group (WG) to extend its COVID-19 remit to rapidly evaluate the suitability of candidate Ebola vaccines for inclusion in the planned trial in Uganda using similar considerations on safety, likely efficacy and logistic issues relating to availability and implementation.

Working Group (WG) membership and meeting attendees

Three candidate vaccines were evaluated at meetings that took place between 13th October and 8th November 2022.

The meetings were chaired by Prof Myron M Levine. The following voting WG members took part in the evaluations: Dr Rebecca E. Chandler, Prof Dani Cohen, Dr Subhash Kapre, Dr Sergio Nishioka, Dr Sue-Nie Park, Dr. Sudhanshu Vrati, Dr Junzhi Wang. Together these WG members have expertise in the areas of vaccine safety, clinical immunology, vaccine trials, virology, regulatory science, vaccine manufacturing and pre-clinical evaluation of vaccines. Prof Elizabeth Miller acted as rapporteur and Prof César Muñoz-Fontela and Dr Simon Funnell provided specialist expert advice to the WG.

Process

Manufacturers of each of the three candidate vaccines provided written material for the WG to review prior to the meeting. This comprised as appropriate Investigator's Brochures and pre-clinical or clinical study reports. Each manufacturer made a live presentation to the WG and responded to questions either in the meeting or through written responses. The WG members were asked to make a recommendation after each meeting as to whether the candidate vaccine was suitable for inclusion in the trial. After the individual evaluations were completed the WG members were asked to rank the three vaccine candidates, should a prioritisation be needed on which vaccine(s) to include.

Summary reports of each meeting, the questions raised by the WG, the manufacturers' responses and the recommendations made by the WG on each candidate were produced and, after approval by the Chairman, were submitted to the WHO Secretariat as the formal record of the meeting and the WG's recommendations.

Candidate vaccines

The following candidate vaccines were evaluated:

1. A bivalent adenovirus vectored vaccine (biEBOV) which consists of the replication-deficient simian adenovirus vector ChAdOx1 encoding two antigens: EBOV glycoprotein (Zaire) and SUDV glycoprotein (Sudan) developed by the University of Oxford and the Jenner Institute UK

2. A monovalent adenovirus vectored vaccines consisting of the simian adenovirus vector ChAd3 encoding the Sudan (SUDV) glycoprotein (ChAd3-SUDV) and produced by the Sabin Vaccine Institute USA

3. A monovalent vaccine which consists of the vesicular stomatitis virus (VSV) as the backbone with the VSV-G gene replaced with the Ebola-GP gene from the Sudan strain (VSV-SUDV) from the International Aids Vaccine Initiative (IAVI).

Evaluation criteria

The WG assessed safety and potential for efficacy based on the following criteria in descending order of importance under each of the two headings:

Safety: experience with the vaccine platform with a different ebolavirus strain or when used with a different antigen; safety data from clinical trials with the candidate vaccine, toxicity studies in animals.

Potential for efficacy: proven efficacy with the vaccine platform with a different ebolavirus strain; immunogenicity in clinical trials including rapidity of response and potential for interference with naturally-acquired or vaccine-induced antibodies to the vaccine backbone, challenge data in non-human primates (the preferred animal model for predicting efficacy of Ebola vaccines in humans), challenge data in a rodent model.

Availability and implementation: took account of the delivery timeline for product to be ready for use in Uganda having successfully completed all release tests, stability data and storage temperature, method of administration, and injected volume, need for dilution of product at study site, potential for scale-up, and commitment by the manufacturer to take the product to licensure.

Conclusions and recommendations of the WG

The WG commended all three manufacturers on the excellence of their presentations and of the clarity of the material provided for review.

There was a consensus among voting WG members, the Chairman, and the non-voting meeting attendees that all three candidate vaccines should be recommended for inclusion in the planned ring vaccination trial in Uganda on the grounds of safety, potential for efficacy, timely availability of vaccine at the study sites and commitment to take the vaccine to licensure.

Should it not be possible to include all three vaccines, then the consensus of the WG, the Chairman and the non-voting meeting attendees on the order of priority for inclusion was as follows:

1. **VSV-SUDV from IAVI**. This was ranked highest on the basis of the proven safety and efficacy of the rVSV ZEBOV GP (ERVEBO™) vaccine with the Zaire strain developed by Merck and for which IAVI now held the licensure rights for the technology. ERVEBO is licensed in the USA, UK, EU, Switzerland, and 10 African countries. ERVEBO's efficacy was shown in a pivotal ring vaccination trial using a single intramuscular dose.[1] There is extensive experience with use of rVSV ZEBOV GP in the field with approaching 400,000 doses given as part of outbreak control measures and experience with compassionate use in over one thousand pregnant women. The SAGE recommendation on this vaccine now includes pregnant women. In addition to adults, tens of thousands of children have been vaccinated with ERVEBO, most of whom are under 10 years of age. No safety signals have emerged to date for the VSV platform. It was deemed valid to extrapolate the efficacy and safety experience with ERVEBO to VSV-SUDV, as the only difference was the glycoprotein insert. The NHP data for VSV-SUDV was supportive of protection, including when NHPs were vaccinated shortly after challenge. There was confidence that the yields and ease of growth of the vaccine would make this an affordable product.

2. **ChAd3-SUDV from the Sabin Institute**. This was ranked second as there was considerable clinical trial experience with the company's ChAd3 vaccine with the Zaire strain involving over 5000 recipients including 600 children plus over 50 recipients of the ChAd3-SUDV strain vaccine. Immunogenicity and challenge studies involving 123 NHPs had been conducted at two independent laboratories. Protection was rapid and durable over 12 months

3. **biEBOV from Oxford University/Jenner Institute**. This was ranked third. There is extensive experience with use of ChAdOx1 platform in the field with over two billion doses given as part of the COVID-19 pandemic outbreak control measures. There is limited clinical trial experience with the ChAdOx1 platform encoding an ebolavirus insert (74 recipients). Also, this vaccine had not yet been tested in an NHP challenge model, nor in Syrian hamsters, only mice and guinea pigs.

References

1. Ebola ça Suffit Ring Vaccination Trial Consortium. The ring vaccination trial: a novel cluster randomised controlled trial design to evaluate vaccine efficacy and effectiveness during outbreaks, with special reference to Ebola. BMJ. 2015 Jul 27;351:h3740. doi: 10.1136/bmj.h3740.
2. Henao-Restrepo AM, Longini IM, Egger M, et al. Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial. Lancet. 2015 Aug 29;386(9996):857-66. doi: 10.1016/S0140-6736(15)61117-5.
3. Henao-Restrepo A-M, Camacho A, Longini IM, et al.: Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!). The Lancet 389, 505-18 (2017)
4. Foege WH, Millar JD, Henderson DA. Smallpox eradication in West and Central Africa. Bull World Health Organ. 1975;52(2):209-22. PMID: 1083309; PMCID: PMC2366358.
5. Henderson DA. Principles and lessons from the smallpox eradication programme. Bull World Health Organ. 1987;65(4):535-46. PMID: 3319270; PMCID: PMC2491023