

Fast-tracking the development and prospective roll-out of vaccines, therapies and diagnostics in response to Ebola virus disease

Special Session of the Executive Board on the Ebola Emergency

1. Prior to the 2014 outbreak, Ebola virus disease (EVD) had not been considered a public health challenge of great magnitude. Scientific research on the virus had been limited to experimental studies and early stage development work on vaccines within public entities interested in lines of defence against potential biological warfare.
2. After the current outbreak was declared a public health emergency, WHO quickly convened a series of expert committees to gauge the viability of existing and experimental medical products that could be tested for safety and efficacy against Ebola. Subsequent to committee findings and discussions, WHO actively engaged with partners, industry and regulatory authorities to expedite clinical trials and regulatory approval pathways for the potential deployment of proven medical products in the affected countries.
3. Two seminal meetings took place on 11 August and 4–5 September. During the first meeting, ethicists and scientific experts concluded that it would be acceptable to offer to EVD patients as potential treatments unregistered interventions that have shown promising results in the laboratory and in animal models, but have not yet been evaluated for safety and efficacy in humans. The second meeting convened experts, country representatives and industry, to review potential Ebola therapies and vaccines. The consultation concluded that whole blood therapies and convalescent blood serums should be considered as a matter of priority. Both innovative, Ebola-specific medicines and existing antivirals for other diseases were considered and prioritized for additional study and evaluation. In addition, two candidate vaccines – the cAd3-ZEBOV vaccine, developed by GlaxoSmithKline in collaboration with the United States National Institutes for Health, and the rVSV-ZEBOV vaccine, developed by NewLink Genetics (and later licenced to Merck Vaccines USA), in collaboration with Health Canada – were identified for further clinical studies.
4. The following sections provide an outline of progress since September 2014, as well as a Status of product development and clinical trials.

Blood Therapies

5. WHO issued a guidance document on the “Use of convalescent whole blood or plasma collected from patients recovered from Ebola virus disease: Empirical treatment during outbreaks” to guide countries on the safe collection and use of blood. Recognizing that supportive care is critical to the survival of Ebola patients, WHO also developed an interim list of essential medicines necessary to treat Ebola patients, based on existing guidelines, a list of essential medical devices, and guidelines for medical donations.

6. Convalescent whole blood donated by EVD recovered patients is currently being administered in Sierra Leone. Convalescent plasma entered trial phase in Guinea and Liberia in December.

Drug therapies

7. On 11 November, the Organization convened a meeting of the newly created Scientific and Technical Advisory Group on Ebola Experimental Interventions (STAC-EE). The STAC-EE reviewed clinical trial protocols and data for blood products and medicines. A number of pre-existing medicines were considered for re-purposing to treat Ebola because they have demonstrated efficacy against the virus in test tubes (in vitro). Only two of these – favipiravir and brincidofovir – demonstrated sufficient activity in non-human primates infected with EV to warrant further investigation. Favipiravir entered clinical trials in early December in Guinea. Clinical evaluation of brincidofovir is planned to start in early 2015 in Liberia.

Vaccines

8. Phase I clinical trials of the two lead vaccine candidates started in September and are ongoing in Canada, Germany, Gabon, Kenya, Mali, Switzerland, United Kingdom of Great Britain and Northern Ireland and the United States, with early results released in December 2014 and more becoming available in January 2015. Initial findings are that both vaccines are safe and induce promising immune responses in human volunteers.

9. In late September, at a WHO consultation on Ebola vaccines, participants agreed to a clinical regulatory pathway for the rapid evaluation of vaccines for safety, immunogenicity, and efficacy. The road map was further developed at an early November meeting of the African Vaccine Regulators Forum (AVAREF), where regulators and ethicists agreed to conduct joint ethical and regulatory reviews to expedite approval of later phase vaccine clinical trials in African countries. On December 15–16, National ethics and regulatory authorities from Cameroon, Ghana, Mali, Nigeria and Senegal met at WHO to expedite approval through a joint review of GSK’s phase 2 clinical trial application for the cAd3-ZEBOV vaccine. Experts from the countries requested some minor modifications to the study protocol and agreed to give a final answer by early January 2015. Accordingly, Phase 2 clinical trials of the ChAd3-ZEBOV vaccine are expected to begin in the five countries in late January 2015.

10. On October 23rd, WHO hosted a high-level meeting on Ebola vaccines access and financing. The purpose of the meeting was to address prioritization, ascertain how much vaccine is needed where and when, discuss clinical studies, and determine the source of financing for vaccines and vaccination programmes. Another topic discussed was how to mitigate the risks and liabilities associated with a possible accelerated distribution of millions of doses of new vaccines. WHO, partners and industry agreed on a road map for larger-scale Phase 3 efficacy trials, covering the first half of 2015, with

possible deployment in the third quarter of that year. Plans for Phase 3 trials are well advanced to start in January or February in Liberia, Sierra Leone and Guinea, using the following clinical trial designs: randomized-controlled, stepped-wedge and ring vaccination, respectively. It was agreed that initially the quantities of vaccines might be constrained, depending on which vaccine candidate would prove to be efficacious in Phase 3, and that this might result in an associated need for prioritization regarding which populations should be vaccinated first. Moreover, organizing vaccination campaigns in the particular situation of the three EDV-affected countries was recognized as a significant challenge, especially on logistical grounds and due to the imperative need to mobilize the communities.

11. The WHO Strategic Advisory Group on Immunization (SAGE) on 24 October established a working group to provide expert advice on immunization against EVD on an emergency basis, as needed, in response to requests from the Secretariat.

12. On December 11, the Gavi Alliance's Board committed up to US\$ 300 million to procure Ebola vaccines and to immunize at risk populations in affected countries. Up to an additional US\$ 90 million could be used to support countries to introduce the vaccines, to rebuild devastated health systems and to restore immunization services in Ebola-affected countries. The Alliance is ready to begin procurement as soon as WHO recommends a vaccine for use.

13. Two other vaccine candidates – one being developed by Johnson & Johnson and the other by Novavax – are due to enter clinical trials in January 2015, and more vaccine candidates are advancing towards clinical evaluation later in the year.

Diagnostics

14. In October, manufacturers of Ebola virus in vitro diagnostics were invited to submit their products for emergency assessment for procurement by UN agencies. A first test was found acceptable by WHO in mid-November.

15. At a meeting held on 12 December by WHO, accelerated pathways were identified for the development and roll-out of rapid and safe diagnostics and laboratory systems for improving diagnosis and treatment of EVD patients. Two types of rapid diagnostics are expected to be ready for clinical trials in the first quarter of 2015. The most promising type is a rapid, integrated nucleic acid PCR test, which is believed to be more effective in case tracing. The other is an antigen test that is easier to use but may be less reliable.

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