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Re-evaluating optimal vaccine schedules against Ebola in Senegal

Submission date
05/06/2018

Recruitment status
No longer recruiting

Registration date
12/07/2018

Overall study status
Completed

Last Edited
22/08/2022

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Ebola outbreaks have been occurring in Africa for the past 40 years with several hundreds of people being infected and a high number of them dying quickly. The major outbreak in West Africa was the largest in history and recorded more than 11, 000 deaths. One case was reported in Senegal that was imported from Conakry. This means that the outbreak can quickly spread in many other countries. Participants involved in the study EBL06 received 2 vaccines. The first was ChAd3-EBO Z and 7 days later the second vaccine was MVA-EBO Z. The results from this study show that both the vaccines were safe and well tolerated, and induced a strong immune response. In this study the participants are invited back to receive another vaccine and have some further blood tests to find out how long the immune response has lasted, and if the vaccine is potentially capable of providing protection against the Ebola virus infection. The study will also look at whether giving another vaccine will increase the duration of this response. An Ebola vaccine called Ad26-ZEBOV is being tested as a booster to see if it will be an effective vaccination strategy against Ebola.

Who can participate?
Senegalese adult men and women who took part in the EBL 06 study

What does the study involve?
Participants come for five study visits over a period of one year. At the screening visit they are asked to provide information about their medical history. The study doctor also performs a medical examination and laboratory tests including urinary and blood tests to ensure that they are eligible for this study. A maximum of 8 ml of blood is collected for this (about half a tablespoon). All female volunteers must be willing to practice effective contraception from the time of consent until 3 months after they have had the vaccine. Pregnancy tests are conducted on the day of vaccination. Female volunteers must also not be breastfeeding or planning to until 3 months after they have had the vaccine. An HIV test is carried out on the blood collected. Before the test, a trained counsellor explains the HIV test to the participant. They are told the result and given advice about the meaning of it. Only the investigators and authorised personnel have access to the results of the blood tests. If participants are found to be HIV infected, they are referred to an approved HIV clinic for further care. If they do not want to have an HIV test they do not have to but they cannot participate in this study. If the results of the tests indicate

that they can participate in the study and they still want to participate, participants attend an appointment at IRESSEF for the enrolment visit. If the results of the tests indicate that they have conditions that do not allow them to take part in the study, they are referred for medical care and do not participate in the study. If for any number of reasons the vaccine study needs to be stopped, participants are informed and have normal medical care. The vaccines are given into the muscle of the non-dominant upper arm (deltoid). Participants are requested to wait at the IRESSEF clinic for one hour after the vaccination to check if they are well before going home. If they experience an immediate adverse reaction after the vaccination, they are requested to stay at the clinic until the emergency physician decides to send them home. After they have gone home, if they have difficulty in using the diary card with a thermometer and a ruler, staff visit them at home every day to assess if they have any side effects of the vaccine, until six days after vaccination. Literate participants complete the diary card at home for 6 days after the vaccination. Participants are asked to attend the clinic at the trial site on Days 7, 28, and 365 after vaccination. Over one year five blood samples are collected with 8-36 ml (about one to two tablespoons) taken at each visit; the total amount of blood taken is about 9 tablespoons (134 ml). The blood samples are needed to see whether the body is building a response to the vaccines, indicating that the vaccines are working.

What are the possible benefits and risks of participating?
If participants are sick at any time during the study, they receive free treatment. Participants do not get paid for participation in the study, but the costs for the transport will be reimbursed. The vaccine may not provide protection against Ebola so participants should follow all known preventive measures against Ebola. The vaccine may cause some changes in colour of the skin at the injection site, which should go away in a few days. Also, there could be pain, swelling or itching at the injection site. Participants may experience a mild fever lasting for two or three days after vaccination. Other common side effects that may occur include headache, muscle pain, tiredness, loss of appetite, nausea and rarely, fast breathing, convulsion and unknown reactions may occur. A few people reported ‘tingling’ in their hands and feet, and muscle weakness, but it is not known if they received AD26.ZEBOV or a placebo. These symptoms usually got better after 24-48 hours, but sometimes lasted for a few weeks before going away on their own. In one more serious case the tingling, numbness and loss of pain sensation has been ongoing for several months, which may be due to nerve damage. With any vaccine, there is a small risk of more serious reactions such as a bad allergic reaction (anaphylaxis), including a rash, hives, or difficulty breathing. Some allergic reactions can be life-threatening, therefore trained personnel with resuscitation equipment will be immediately available to treat any such reactions. Changes in blood tests have been seen in some people after the vaccine. These include anaemia (low levels of red blood cells) and low levels of potassium, but the people with these changes did not have any symptoms. The effect of the study vaccine(s) on sperm, egg, conception, pregnancy, an unborn child or a breastfed infant has not been studied. There is currently no information on possible effects of the study vaccine(s) in these cases. Insurance cover and treatment is provided for any injury caused by procedures related to this study.

Where is the study run from?
Institut de Recherche en Santé, de Surveillance Epidemiologique et de Formation (IRESSEF) (Senegal)

When is the study starting and how long is it expected to run for?
March 2018 to December 2020

Who is funding the study?
Innovate UK

Who is the main contact?
1. Dr Mehreen Datoo, mehreen.datoo@ndm.ox.ac.uk
2. Mrs Sarah Kelly, sarah.kelly@paediatrics.ox.ac.uk

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

Protocol serial number
OVG 2018/03

Study information

Scientific Title
Evaluating the long-term immunogenicity of Ad / MVA Ebola Virus Vaccines following late boosting with AD26-ZEBOV vaccine administered after heterologous prime/boost schedules of adenoviral and MVA vectored Ebola vaccines in healthy Senegalese adult volunteers aged 18-50 years: an open-label clinical trial

Acronym
RESOLVE

Study objectives
To assess humoral and cellular immunity against Ebola virus glycoprotein at 1 year following a late booster dose of Ad26-ZEBOV administered 3 to 4 years after receiving heterologous prime /boost of ChAd3- EBO Z /MVA –EBO Z administered at a 7-day interval.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 01/08/2018, Oxford Tropical Research Ethics Committee (OxTREC)
2. Approved 07/01/2019, Comité National d'Ethique pour la Recherche en Santé (CNERS) de Senegal

Study design
Open-label single-centre phase II clinical trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Ebola virus disease

Interventions
The Senegalese study team will approach approximately 40 participants from a previous Ebola Vaccine study (EBL06). It is anticipated that approximately 50% of participants will be subsequently recruited into this study. These volunteers will have previously received ChAd3-EBO Z (2.5-3.7 x 1010 vp) with a boost of MVA-EBO Z (1.0 x 108 pfu) in 2015. Those who are interested in taking part will be invited to the research centre for further discussion. The study will be explained in more detail to eligible participants on an individual basis and informed consent will be taken if they wish to proceed. Screening and enrolment will then follow with all participants receiving one booster dose of AD26-ZEBOV (5 x 1010 vp) injected intramuscularly into the deltoid region of the non-dominant arm. Overall the trial will involve 5 study visits with a total duration of 1 year.

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
AD26-ZEBOV

Primary outcome(s)

Measured at 1 year following late booster dose of Ad26-ZEBOV:
1. Ebola GP specific IgG measured by ELISA
2. Ebola GP specific T cell cytokine response measured using ex vivo interferon-γ enzyme-linked immunosorbent spot (ELISPOT)

Key secondary outcome(s))
Safety and reactogenicity of late booster dose of Ad26-ZEBO
The specific endpoints for safety and reactogenicity will be actively and passively collected data on adverse events. The following parameters will be assessed for both groups:
1. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following the vaccination
2. Occurrence of unsolicited adverse events for 28 days following the vaccination
3. Change from baseline for safety laboratory measures at 7 days following immunisation
4. Occurrence of serious adverse events for 1 year following immunisation

Immunogenicity
1. Humoral - Ebola GP specific IgG measured by ELISA
2. Cellular - Ebola GP specific T cell cytokine response measured using ex vivo interferon-γ enzyme-linked immunosorbent spot (ELISPOT)
These secondary immunological endpoints will be determined at baseline, and at 7 and 28 days following immunisation.

Completion date
21/10/2020

Eligibility

Key inclusion criteria
Current inclusion criteria as of 23/07/2019:
1. Participants must have completed one of the Ebola vaccine immunisation schedules as part of the EBL06 study
2. Able and willing (in the Investigator's opinion) to comply with all study requirements
3. For females only, willingness to use an effective form of contraception from the time of consent until 3 months after they have had the vaccine and a negative pregnancy test on the day (s) of screening and vaccination
4. Agreement to refrain from blood donation during the course of the study
5. Provide written informed consent

Previous inclusion criteria:
1. Participants must have completed one of the Ebola vaccine immunisation schedules as part of the EBL06 study
2. Able and willing (in the Investigator's opinion) to comply with all study requirements
3. For females only, willingness to practice continuous effective contraception during the study and a negative pregnancy test on the day(s) of screening and vaccination
4. Agreement to refrain from blood donation during the course of the study
5. Provide written informed consent

Participant type(s)
Healthy volunteer

Healthy volunteers allowed

No

Age group
Adult

Sex
All

Total final enrolment
28

Key exclusion criteria
1. Participation in another research study involving receipt of an investigational product in the 30 days preceding enrolment, or planned participation during the study period
2. Receipt of any live, attenuated vaccine within 28 days prior to enrolment
3. Receipt of any subunit or killed vaccine within 14 days prior to enrolment
4. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate
5. Any confirmed or suspected immunosuppressive or immunodeficient state, including HIV infection; asplenia; recurrent, severe infections and chronic (more than 14 days) immunosuppressant medication within the past 6 months (inhaled and topical steroids are allowed)
6. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine, (e.g. egg products) including urticaria, respiratory difficulty or abdominal pain
7. Any history of hereditary angioedema, acquired angioedema, or idiopathic angioedema.
8. Any history of anaphylaxis in reaction to vaccination
9. Pregnancy, lactation or willingness/intention to become pregnant during the study
10. History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ)
11. History of current or previous psychiatric illness.
12. Poorly controlled asthma or thyroid disease
13. Seizure in the past 3 years or treatment for seizure disorder in the past 3 years
14. Bleeding disorder (eg. Factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture
15. Any other serious chronic illness
16. Current anti-tuberculosis prophylaxis or therapy
17. Suspected or known current alcohol abuse as defined by an alcohol intake of greater than 42 units every week
18. Suspected or known injecting drug abuse in the 5 years preceding enrolment
19. Seropositive for hepatitis B surface antigen (HBsAg)
20. History of contact with suspected, probable or confirmed cases of Ebola in the previous 21 days
21. Any clinically significant abnormal finding on screening biochemistry or haematology blood tests or urinalysis
22. Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study or impair interpretation of the study data

Date of first enrolment
01/10/2019

Date of final enrolment

30/10/2019

Locations

Countries of recruitment
Senegal

Study participating centre
Institut de Recherche en Santé, de Surveillance Epidemiologique et de Formation (IRESSEF)
Dakar
Senegal
7325

Sponsor information

Organisation
Oxford Tropical Research Ethics Committee (OxTREC), University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Innovate UK (Grant Reference Number 971553)

Alternative Name(s)
UK Research and Innovation Innovate UK, innovateuk

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Matthew Snape (matthew.snape@paediatrics.ox.ac.uk).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet version 4.0	11/11/2025	11/11/2025	No	Yes
Protocol file		20/02/2019	22/08/2022	No	No