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Re-evaluating Optimal Vaccine Schedules Against Ebola (REVOLVE)

Submission date
13/08/2018

Recruitment status
No longer recruiting

Registration date
17/08/2018

Overall study status
Completed

Last Edited
09/09/2020

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
This study will evaluate the duration of the immune response of a late booster dose of a vaccine against Ebola Virus Disease (EVD), AD26.ZEBOV, in healthy adults previously immunised with investigational Ebola vaccine schedules. This will generate data crucial to the understanding of persistence of immunity after initial immunisation, and whether a late booster dose confers additional benefit in the long-term persistence of immunity. These data are critical for showing whether the investigational vaccines schedules provide sustained immunity to those at ongoing risk of EVD (e.g. health care workers), and whether this can be significantly altered by the additional dose of AD26.ZEBOV.

Who can participate?
Participants who completed previous Phase 1 and 2 Ebola vaccine studies in the UK, including EBL01, EBL04 and EBL05

What does the study involve?
Blood tests are taken at 2 to 5 years after initial immunisation. Participants who are willing to take part in the follow-on study are invited to receive a booster dose of AD26.ZEBOV, but this is not a requirement of participation. Blood tests are taken 7 days and 1 month after Ad26.ZEBOV in those receiving the booster dose with this vaccine. All participants have a further blood test one year later to evaluate the persistence of vaccine-induced immunity with and without a late booster dose of Ad26.ZEBOV.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Oxford Vaccine Group and Imperial College (UK)

When is the study starting and how long is it expected to run for?
October 2017 to December 2020

Who is funding the study?
Innovate UK

Who is the main contact?
Dr Katja Pfafferott
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2017-004610-26

Protocol serial number
39260

Study information

Scientific Title
Evaluating the Long Term Immunogenicity of adenoviral and MVA vectored Ebola vaccine schedules and response to late boosting with AD26.ZEBOV vaccine: an open-label clinical trial

Acronym
REVOLVE

Study objectives
This study will evaluate the duration of the immune response of a late booster dose of a vaccine against Ebola Virus Disease (EVD), AD26.ZEBOV, in healthy adults previously immunised with investigational Ebola vaccine schedules. This will generate data crucial to the understanding of persistence of immunity after initial immunisation, and whether a late booster dose confers additional benefit in long term persistence of immunity. These data are critical in informing the

potential for the investigational vaccines schedules to provide sustained immunity to those at ongoing risk of EVD (e.g. health care workers) and whether this can be significantly altered by the additional dose of AD26.ZEBOV.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/09/2018, South Central – Berkshire B Research Ethics Committee (Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT; Tel: +44 (0)207 104 8059; Email: NRESCommittee.southcentral-berkshireB@nhs.net), ref: 18/SC/0399

Primary study design
Interventional

Study design
Non-randomised; Interventional; Design type: Prevention, Vaccine

Study type(s)
Prevention

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

Interventions
This is a Phase 2, multi-centre, open-label, follow-on study of clinical trials of investigational vaccines against Ebola.

The participants for this study will be volunteers from previous Ebola vaccine studies led by the Oxford Vaccine Centre, who were vaccinated approximately 2-5 years previously with investigational Ebola vaccines (ChAd3-EBO Z, MVA–BN-FILO, MVA-EBO-Z and Ad26.ZEBOV) given as a prime (first) dose followed after a variable time interval by a booster (second) dose of a different vaccine.

156 participants took part in the previous Ebola vaccine studies. All of those who have consented to be contacted again will be invited to take part in this follow-on study. The trialists anticipate approximately 50% recruitment which equates to 80 participants. Participants will be contacted and invited to take part in the study and to receive booster doses of Ad26.ZEBOV. However, if they do not wish to receive a booster, they may opt to remain in the study and become part of the "control" (unboosted) cohort. These participants will have their immune response to the initial Ebola vaccines followed up with blood tests but will receive no vaccines.

Those who express an interest in the study will be provided with an information booklet. If participants are willing to proceed after having read this information they will be invited for their first visit.

There will be a total of four visits for those participants who receive a booster dose and two visits for those who do not. All clinical visits will take place either at the Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), Churchill Hospital or at the NIHR/Wellcome Trust Imperial Clinical Research Facility, Hammersmith Hospital depending on where the participants attended their visits during the parent studies.

At Visit 1 (V1) the contents of the information booklet will be discussed with a doctor or nurse, including:
• the exact nature of and the rationale for performing the study
• implications and constraints of the protocol
• the risks and benefits involved in taking part

The participant will have ample time to consider whether they wish to take part in the study and to ask questions.

If the participant wishes to take part in the study they will be asked to provide written informed consent by personally signing and dating the latest approved version of an informed consent form. This form will also be signed by the study staff member who took part in the informed consent discussion. A copy of the signed informed consent form will be given to the participant and the original will be retained at the study site.

Once informed written consent has been obtained, baseline assessments and information collection are carried out by an appropriately trained member of the study team (usually a nurse or doctor) as part of the assessment of inclusion/exclusion criteria.

To summarise, the following will occur at V1 (Day 1: all participants):
• The nature of the study will be discussed in detail, including the option of receiving no booster vaccine. Obtain informed consent.
• Assess eligibility (inclusion/exclusion criteria: section 7.2), including re-assessment of criteria submitted on pre-screening questionnaire.
• Perform blood draw: 50 ml of blood will be collected at each visit from each participant. The date of sample collection will be recorded in the CRF and the laboratory requisition form.
• If the participant has opted to receive the booster vaccine:
o Carry out physical examination and record oral temperature, pulse and blood pressure
o Perform urine pregnancy test for females
o Administer vaccine by IM injection
o Observe for immediate adverse events for 30 minutes
o Provide participant with a Medic Alert Contact Card with 24 hour telephone number to reach a study doctor
o Remind participants to contact the study team if they have any concerns regarding their wellbeing, symptoms and/or admission to hospital.
o Distribute eDiary log in details will be distributed to participants receiving a boost vaccine, along with training on how to complete. Additional paper backup copies of the eDiary will also be provided.
• Schedule next visit

Participants will be asked if they would consent for their samples to be stored following the end of the study in the Oxford Vaccine Centre BioBank (‘Oxford Vaccine Centre Biobank’ Southampton & South West Hampshire LREC (B) 10/H0504/25). Biobank is a separate study and optional to all participants of studies conducted by OVC. Separate consent is sought for this. Study participants who consent for the Biobank, will have their samples stored according to local SOPs for future research.

Added 04/06/2019: Visit 2 (V2) (Day 7: only those who have received booster vaccine)
The following will occur at Visit 2:
• Review electronic diary entries, any relevant adverse events and use of any concomitant medication since the last visit

• Check for serious adverse events
• Record oral temperature, pulse and blood pressure
• Perform blood draw: 50 ml of blood will be collected. The date of sample collection will be recorded in the CRF and the laboratory requisition form.
• Schedule next visit
• Remind participants to contact the study team if they have any concerns regarding their wellbeing, symptoms and/or admission to hospital

Visit 3 (V3) (Day 28: only those who have received booster vaccine)
The following will occur at Visit 3:
• Review electronic diary entries, any relevant adverse events and use of any concomitant medication since the last visit
• Check for serious adverse events
• Record oral temperature, pulse and blood pressure
• Perform blood draw: 50 ml of blood will be collected. The date of sample collection will be recorded in the CRF and the laboratory requisition form.
• Schedule next visit
• Remind participants to contact the study team if they have any concerns regarding their wellbeing, symptoms and/or admission to hospital

Visit 4 (V4) (Day 365: all participants)
The following will occur at Visit 4:
• Check for serious adverse events
• Perform blood draw: 50 ml of blood will be collected at each visit from each participant. The date of sample collection will be recorded in the CRF and the laboratory requisition form.

In the event of an unexpected or serious adverse event, a participant may need to have unscheduled clinic visit at any point during the study. Safety bloods might be sent at these visits, at the discretion of the investigator.

When all participants have completed their fourth visit, data cleaning and analysis will commence. When this is complete a publication will be prepared and submitted for publication. Participants will be informed when publication is to take place.

Intervention Type
Biological/Vaccine

Phase
Phase II

Primary outcome(s)
Humoral and cellular immunity against Ebola virus glycoprotein at baseline and at 1 year following a late booster dose of Ad26-ZEBOV administered 2 to 5 years after receiving heterologous prime/boost of ChAd3- EBO Z /MVA –EBO Z and at the same time points (baseline and 1 year post-baseline) in participants who opt not to receive a booster dose of Ad26-ZEBOV.

Key secondary outcome(s)
Safety and reactogenicity of late booster dose of Ad26-ZEBO:
1. Occurrence of solicited systemic reactogenicity signs and symptoms for 3 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 3 days following immunisation
4. Occurrence of serious adverse events for 1 year following immunisation

Immunogenicity:
1. Humoral - Ebola GP specific IgG as 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, 7 days (added 04/06/2019), 28 days and 1 year following immunisation (baseline and 1 year for those opting not to receive a booster in this study)

Completion date
31/12/2020

Eligibility

Key inclusion criteria
1. Participants must have completed one of the following Ebola vaccine immunisation schedules; ChAd3-EBO-Z + Ad26.ZEBOV (or vice-versa), ChAd3-EBO-Z +/- MVA–BN-FILO or ChAd3-EBO-Z + MVA-EBO-Z
2. Willing and able to give written informed consent for participation in the study
3. In good health as determined by medical history, physical examination and clinical judgement of the investigators
4. Females of childbearing potential: willing to use effective contraception (the oral contraceptive pill, contraceptive implant, contraceptive injection, intrauterine device, intrauterine hormone-releasing systems (IUS) barrier methods, vasectomized partner or abstinence) from one month prior to three months after the vaccine. Vaccination will be delayed in female participants who have not used effective contraception for one month prior to Visit 1*
5. Able to attend the scheduled visits and to comply with all study procedures, including internet access for the recording of diary cards*
6. Willing to allow his or her General Practitioner to be notified of participation in the study
7. Agree to be registered on the Trial Over-Volunteering Prevention Service (TOPS) and agree to provide their National Insurance number or passport number (if not a British citizen) for the purposes of registration*
8. Agree to provide National Insurance number and Bank details for reimbursement purposes
* Participants intending to receive booster dose only

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
48

Key exclusion criteria
1. History of malignancy
2. Pregnancy or breastfeeding
3. New significant medical or surgical history since completion of the previous study (based on participant recall)
4. Receipt or planned receipt of adenovirus based vaccine since the parent Ebola vaccine studies
5. Chronic or recurrent use of medication which modify host immune response
6. Any contraindication to venepuncture, as determined by clinical judgement
7. History of allergy or anaphylaxis to a vaccine or any component within the vaccines used in this study (booster group only)
8. Have any known or suspected impairment or alteration of immune function, resulting from, for example:
8.1. Congenital or acquired immunodeficiency
8.2. Human Immunodeficiency Virus infection or symptoms/signs suggestive of an HIV-associated condition
8.3. Autoimmune disease
8.4. Receipt of immunosuppressive therapy such as anti-cancer chemotherapy or radiation therapy within the preceding 12 months or long-term systemic corticosteroid therapy (10mg daily or higher) or any systemic corticosteroid (or equivalent) treatment within 14 days prior to vaccination, or for more than 7 days consecutively within the previous 3 months

Date of first enrolment
05/09/2019

Date of final enrolment
03/12/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford Vaccine Centre (lead site)
University of Oxford
Centre for Clinical Vaccinology and Tropical Medicine
Churchill Hospital
Old Road
Oxford
United Kingdom
OX3 7LJ

Study participating centre

NIHR/Wellcome Trust Imperial Research Facility
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 OHS

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Innovate UK; Grant Codes: 971553

Alternative Name(s)
Technology Strategy Board

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 not expected to be made available due to limits set by the terms of vaccine supply from the vaccine manufacturer.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No