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OXFORD VACCINE GROUP

Re-evaluating Optimal Vaccine Schedules against Ebola (REVOLVE)

Study Information Booklet

Thank you for previously taking part in a study evaluating vaccines against Ebola virus disease, conducted by the Jenner Institute, University of Oxford.

The Oxford Vaccine Group, a separate vaccine research group within the University of Oxford, would now like to invite you to take part in a study to assess the persistence of the immune responses to the Ebola virus vaccines before and after giving a booster dose of Ebola vaccine two to five years after receiving the original Ebola vaccines.

Before you decide whether to take part, it is important for you to understand what the study is about and what participation would involve. Please take time to read the information carefully, and discuss with others if you wish. If anything is unclear or you would like further information please contact the study team (details below).

Thank you for taking the time to consider taking part in this study.

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Why have I been invited to take part?

You have been approached as you received one or more investigational vaccines against Ebola virus disease in previous studies conducted by the University of Oxford and agreed to be contacted for future research.

Who is conducting this study?

This study is being conducted by the Jenner Institute and the Oxford Vaccine Group (University of Oxford) and the Imperial College Clinical Research Facility. All of these groups worked on the original Ebola Vaccine studies in 2014 to 2016, and are collaborating on this new study. Staff of the Oxford Vaccine Group will be conducting the study visits for Oxford participants, while staff of the Imperial College will perform the study visits for London participants.

Do I have to take part?

No. Taking part in this study is entirely optional. Should you volunteer and later change your mind (for whatever reason) it is your right to do so, and you would not need to provide an explanation to the study team or anyone else.

What is the purpose of this follow-on study?

Thanks to your participation in the Ebola Vaccine studies we know that administration of these vaccines as a 'prime' and 'boost' combination generates an immune response that is potentially capable of providing protection against the Ebola virus infection for 12 to 18 months after immunisation. However, we do not know the persistence of immune responses beyond this time, nor whether giving a "late" booster dose of an Ebola vaccine approximately 2-5 years after the original course of vaccines would increase the duration of the response.

Therefore, we are inviting you to participate in this study where we will take blood samples to look at your immune response against Ebola virus. We will also give you the option of receiving a late booster dose of an Ebola vaccine in development, AD26.ZEBOV. Obtaining information regarding the immune response produced by Ebola vaccines is important to help understand how these Ebola virus vaccines may be best used. We aim to recruit up to 156 participants to the study.

Which vaccines are being studied?

The studies conducted by the University of Oxford and Imperial College in 2014-2016 (EBL01, EBL04, EBL05) evaluated a range of vaccines against Ebola virus:

- AD26.ZEBOV
- MVA-EBO-Z
- MVA-BN-Filo
- ChAd3-EBO Z

In this study we would be offering a booster dose of AD26.ZEBOV.

The AD26.ZEBOV vaccine is made up of a carrier virus and a protein from the Ebola virus. As with Chad3-Ebo-Z, the carrier virus is a type of adenovirus (AD) that has been genetically modified so that it cannot replicate (multiply) in humans and expresses an Ebola protein (the Ebola glycoprotein, which is situated on the surface of the Ebola virus). The vaccine does not contain the Ebola virus and cannot cause Ebola disease.

The AD26.ZEBOV vaccine is not yet licensed but has been tested in randomised clinical studies enrolling over 4000 participants receiving either AD26.ZEBOV or placebo, of whom 3,574 have received AD26.ZEBOV itself. This includes the studies conducted in Oxford and London in 2014 – 2016.

What should I consider?

You might not be able to take part if you have any health conditions or take any medications that might suppress your immune system. You may also not be able to take part if you have received any adenovirus based vaccine since your participation in the previous studies. You cannot take part if you are pregnant or breastfeeding. If you have private medical insurance, you are advised to contact your insurance company before participating in this study.

If you opt to receive the booster vaccination and you are female of childbearing potential, we will ask you to use an effective method of contraception (this could include the oral contraceptive pill, contraceptive implant, injection, barrier methods such as condoms, or abstinence) from one month before the time of consent to participate in the study until 3 months after you have received the vaccine. This is because the effect of the study vaccine 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.

We will record any pregnancy occurring in a participant during the clinical trial and the outcome of the pregnancy will be followed up to establish whether there is any congenital abnormality. Pregnancies will be reported to the study sponsor (University of Oxford) and the AD26.ZEBOV vaccine manufacturer, Janssen Pharmaceuticals.

What will happen if I decide to take part in this study?

If you are interested in taking part, and are potentially eligible for the study, then we would contact you to organise a visit at the Oxford Vaccine Group, Centre for Clinical Vaccinology and Tropical Medicine (CCTVM) at the Churchill Hospital, where we will check your eligibility and ask you to sign a consent form.

In this study, we will take a blood sample 2-5 years following your original immunisation with the Ebola vaccines to look for the persistence of vaccine-induced immune responses (i.e. antibodies and white blood cells). We would then offer a booster dose of AD26.ZEBOV. You would then have follow-up visits 7 days, 1 month and 1 year after you had received the study vaccine.

If you do not wish to have the booster vaccine in this follow-on study, you can still take part in the study. In that case we would take a blood sample at the time of enrolment (your first visit) and one year later to assess the persistence of your immune response to your original course of Ebola vaccines.

What happens at the first study visit?

An outline of the visits for the study can be found in the Figure below. The first study visit will take 1 to 1½ hours at the Oxford Vaccine Group. A research doctor or research nurse from the study team will go through the study in detail and provide you with the opportunity to ask any questions you might have about the study and what is involved. You will be allowed as much time as you feel necessary before making any decision on whether to take part.

If you are willing to proceed, we then ask you to sign an informed consent form. Following this we will:

- Check if you meet the study inclusion/exclusion criteria
- Review any significant changes in your general health including any medication that you are taking and any vaccinations you have received since taking part in the initial Ebola studies
- Take a blood sample of approximately 50ml (5 tablespoons)
- If you opt to receive the boost vaccine, we will also:
    - Carry out a brief physical examination
    - Take your temperature, blood pressure and pulse rate
    - For female participants, carry out a urine pregnancy test
    - Administer the AD26.ZEBOV vaccine as an injection into your upper arm
    - Issue you with a 24 hour medic alert card so you can contact the study team
    - Provide you with a record of your vaccine

- Observe you for 30 minutes after immunisation
- Register you on the TOPS (The Over-volunteering Prevention System) database, which prevents participants from over-volunteering for research studies. We require your National Insurance Number or passport number (if you are not a British national) to do this. More information can be found at www.tops.org.uk.
- Ask you to complete an online diary (eDiary) to record your temperature and any reactions daily for 3 days after immunisation, and to record any medical visit or medications you are taking in the month after immunisation.
- Discuss the storage of your samples and ask for your consent to store them in a collection of samples called a Biobank

All participants will be asked to tell the study team if you have any significant medical problems for the duration of the study.

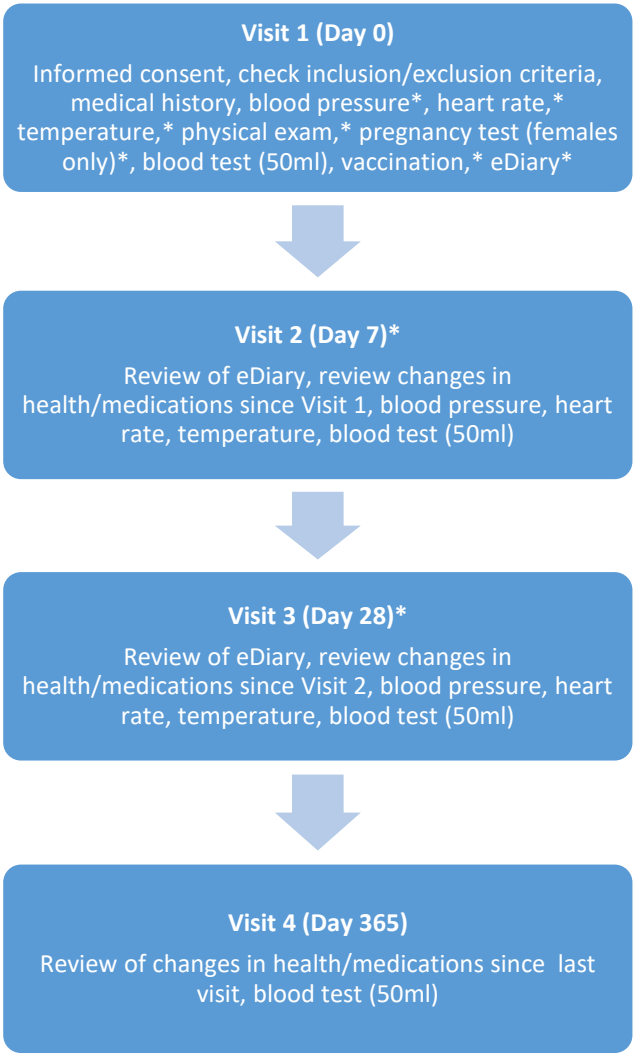

Figure 1. Study design.

Those marked * apply only if opting to receive the AD26.ZEBOV vaccine in this study.

Subsequent visits

Those participants who have opted to receive the booster vaccination will be asked to attend three further visits at the Oxford Vaccine Group. They will be seven days, one month and one year after receiving the vaccination. Those who have opted not to receive the booster will be asked to attend one further visit, one year after their first visit.

At each visit you will be asked if you have had any health problems since your last visit and a blood sample (50ml) will be taken. Each of these visits will take approximately 30 minutes.

Will my GP be informed of my participation in this study?

We will send your GP a letter informing them of your participation in the study. With your consent, we may contact your GP if you were unsure about your medical history, or if you were to experience a change in your health or medications during the study. We would also notify your GP whether you received the AD26.ZEBOV vaccine or if you withdraw from the study.

What are the side effects of the vaccine and blood tests?

The AD26.ZEBOV vaccine has been given to 3,574 participants in clinical trials.

No serious safety concerns have been observed in these studies.

One serious case of probable peripheral sensory neuropathy (nerve damage that may cause tingling, numbness, pain or loss of pain sensation) of moderate severity has occurred and has been ongoing for several months, interfering with some of the participant's daily activities.

The side effects seen in these studies were mainly local reactions such as injection site pain, tenderness, warmth, redness, swelling and/or itching mostly of mild severity. These were common, with most participants experiencing at least one of these reactions, but they were generally mild and usually resolved within 24 hours. General reactions that were common included fever, headache, aching muscles or joints, chills, tiredness, loss of appetite and nausea. These were generally mild and short-lived, resolving within 24 hours. Study participants may experience a mild fever lasting for two or three days after vaccination. A high temperature (>40°C) was seen very rarely following vaccination. A few participants in these studies have experienced 'pins and needles' in their hands or feet, or mild to moderate muscle weakness, but it is not known if they received AD26.ZEBOV or placebo. These symptoms have been observed to last no more than 24 to 48 hours in the majority of cases but can last for several weeks before going away on their own. These types of symptoms have been reported following administration of other licensed vaccines and following acute viral infections of various types.

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.

With any vaccine there is a very rare (less than 1 in 1 million) chance of having a severe allergic reaction called anaphylaxis. Including a rash, hives, or difficulty breathing. Some allergic reactions can be life-threatening. This was not seen in any of the previous studies with this vaccine. When it does occur, it is usually soon after receiving the vaccination. Hence, we would monitor you after you received the vaccine for 30 minutes, have effective treatment on hand and have trained staff with resuscitation equipment to deal with anaphylaxis in case it should occur.

Blood tests could leave you with a small bruise at the site of the needle, and sometimes some mild pain. Sometimes people faint when they have blood tests. We would ask you to ensure you have eaten and drunk plenty of fluids before any blood tests.

We give you access to a study doctor 24 hours a day via telephone if for any reason you had any concerns regarding your health or potential symptoms of the vaccination.

What would happen to any samples I give?

The blood samples collected during this study will be anonymised and labelled with a unique participant number. The samples will be analysed at the Jenner Institute laboratory, University of Oxford. We will conduct tests on your blood samples to assess your immune response to the Ebola virus vaccines. We may also send some samples to other researchers working with us on this research project, including researchers outside the European Union. These samples would be anonymised.

We will ask for your separate permission to store blood (including serum, DNA and cells), in a collection of samples called a Biobank. Details of this will be provided to you in a separate information booklet and you will be asked to sign a separate consent form. This will be done after you are enrolled into this study.

You are free to say no to this, and whether or not you agree does not influence your participation in this study. If you do not wish for your samples to be stored in the Biobank, we will destroy them 12 months after the last participant has completed the study.

Reimbursement

You will be reimbursed for your time, travel and inconvenience as follows:

	Amount per visit
Travel expenses	£15
Inconvenience of blood test	£10
Time required for visit	£20

This means you will be reimbursed up to £45 for each visit, to a total of £90 or £180 dependent on how many study visits you attend and whether or not you opt to have a booster vaccine.

Payments will be made via bank transfer in instalments during the study and usually take 4-6 weeks to be processed. You will be required to provide banking details including account name, sort code and account number. All personal banking details will be stored confidentially and stored for 7 years in line with University financial policy.

What is expected of me during the study?

We would expect you to:

- Attend all study visits.
- Give correct and accurate information about your medical history and any current medical conditions.
- Tell the study staff about any new medication or vaccine since your participation in the Ebola vaccine trial.
- Complete the eDiary following vaccination (if applicable).
- If you are a female of childbearing potential and choose to have the booster vaccination, we will ask you to use effective method of contraception as outlined above.

What are the advantages of taking part in the study?

There are no clear benefits to you if you take part in this study. By taking part you may help to establish the clinical use of the Ebola vaccines and provide important data to influence Ebola virus vaccine policy in future.

Would I be notified of the results?

At the end of the study we would seek to publish the study results in a scientific journal. We would inform you of the study results and send you a link to the study publication. You would not be identified in any way in any study publications. This can often take 2 to 3 years following your last study visit. We cannot provide you with your individual study results.

Would my taking part be kept confidential?

Yes. All information that is collected about you during the course of the study will be coded with a study number and your initials, and kept strictly confidential. Apart from the letter(s) sent to your GP, any information about you that leaves the clinic would have your personal details removed (including name, date of birth and address).

With your consent, we may also contact you to inform you of future related studies or vaccine-related research; you could say no to this and still take part in this current study. You would not be obliged to take part in any future research; we only ask for your consent to contact you. Your contact details would be held separately from this study in a password protected 'volunteer's database' at the study site.

In order to ensure that the study is being conducted correctly and complying with applicable regulations, responsible members of the Clinical Trials and Research Governance Office (CTRG), University of Oxford, may be given access to data for monitoring and/or audit of the study.

What will happen to my data?

We will be using information from you, and, if necessary and with your consent, your medical records in order to undertake this study. Research is a task that we perform in the public interest. The University of Oxford, as sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly. We will keep identifiable information about you such as contact details for a minimum of 5 years after the study has finished. The need to store this information for longer in relation to licensing of the vaccine will be subject to ongoing review. For effective vaccines that may be licensed, we may store research data securely at the University of Oxford for at least 15 years after the end of the study, subject to adjustments in clinical trials regulations. In addition to the anonymised scientific data, we will also store documents containing personal information that you provide when registering for the trial (including contact details), medical information and signed consent forms during this archiving period.

The study team will use your name and contact details, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, in relation to your health during the study and to oversee the quality of the study. At the completion of the study, unless you consent otherwise (e.g. if you request to be informed of other trials), your personal details will not be used to contact you other than exceptional circumstances concerning your safety. If you consent to take part in another study carried out by the study site, personal information and medical information including blood test results may be accessed to avoid unnecessary repetition.

Your bank details will be stored for 7 years in line with University financial policy.

Your rights to access, change, or move your personal information may be limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at:

http://www.admin.ox.ac.uk/councilsec/compliance/gdpr/individualrights/

Anonymised data may be sent to other researchers working with us on this research project, including researchers outside the European Union, as well as to collaborating partners who are organising and funding this research work. Safety data and results of the blood tests collected in the course of this study may also be shared with the vaccine manufacturers. Data from this study may be used to file patents, licence vaccines in the future or make profits in other ways. You will not be paid for any part of this. Results of the study may also be published in scientific journals and presented at conferences. It will not be possible to identify you in any reports, publications or presentations.

You can find out more about how we use your information by contacting Oxford Vaccine Group on 01865 611400 or email info@ovg.ox.ac.uk.

Where can I get advice on whether or not to take part?

We are happy to answer any questions you might have and contacting us does not commit you to taking part in the study. For independent advice you can contact **INVOLVE** (www.invo.org.uk) which is a government funded national advisory group supporting those considering involvement in NHS, public health and social care research. Please feel free to discuss this study with whoever you wish (e.g. your GP, a family member or friend) before deciding whether or not to participate.

What if I wish to withdraw from the study?

At any time during the study, and for any reason, you would be entirely free to change your mind about taking part, and to withdraw from the study. We would keep the information and samples already collected, however, all data and samples would be anonymised. This would not affect your subsequent medical care or legal rights in any way.

What if there is a problem?

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer harm as a direct consequence of your participation in this study. If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact Dr. Matthew Snape, Chief Investigator, (Tel: 01865 611400, Email: info@ovg.ox.ac.uk) or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480 or the head of CTRG, email ctrg@admin.ox.ac.uk.

Who is organising and funding the study?

The study is funded by Innovate (U.K. Government funding) and sponsored by the University of Oxford. Janssen Pharmaceuticals, the manufacturer of the AD26.ZEBOV vaccine, have provided the University of Oxford with this vaccine for use in this study.

Who has reviewed and approved this study?

This study has been reviewed and given favourable opinion by the South Central - Berkshire B Ethics Committee and the Medicines and Healthcare products Regulatory Agency (MHRA) and relevant NHS trusts.

So, in summary, what would happen if I decide to take part in the study?

- We will arrange a suitable time and date for you to attend a study visit at the Oxford Vaccine Group, CCVTM.
- At your first study visit we will discuss the study and ask you to sign a consent form and check your eligibility to take part in the study.
- We will review your medical/medication/vaccination history and obtain a blood sample.
- If you agree to receiving the AD26.ZEBOV vaccine we will
    - Administer this as an injection in your arm
    - Ask you to complete an online diary
    - Ask you to attend an appointment at 7 days and 1 month after the vaccine for another blood test.
- All participant would be asked to attend a visit at one year after their first visit.
- You will be reimbursed £45 for each visit you attend for your time, travel and inconvenience of blood tests.

What do I do now?

Thank you for considering taking part in this study. You do not need to make a final decision straight away. If you wish to take part please go to https://trials.ovg.ox.ac.uk/REVOLVE to complete the self-screening form to send us your details and check if you would potentially be eligible. Alternatively, if you would like to contact us directly please ring us on 01865 611400 or Email: info@ovg.ox.ac.uk.

Yours sincerely,

The REVOLVE Study team
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Re-evaluating Optimal Vaccine Schedules against Ebola (REVOLVE)

Informed Consent Form

Participant Name: _____ Participant Number: |___|___|___|___|

*Please **initial** in each box if you agree with the statement*.

1. I have read the *Re-evaluating Optimal Vaccine Schedules against Ebola (REVOLVE)* study information booklet (version 4.2, dated 29-Jul-2019). _____
2. I have had the opportunity to discuss the study, to ask questions about the study and I am satisfied with the answers and explanations that have been provided. _____
3. I understand that my participation is voluntary and I am free to withdraw from the study at any time, without having to give a reason for leaving and without affecting my medical care or legal rights. _____
4. I agree to donate blood as part of this study. I consider these samples a gift to the University of Oxford and I understand I will not gain any direct personal benefit from this. _____
5. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the study team, the University of Oxford (Sponsor) and/or regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. _____
6. I agree to my GP being informed of my participation in the study. I agree to my GP being approached for additional information regarding my medical and vaccination history, if required. _____
7. I understand that information collected about me may be used in an anonymous form to support other research in the future. It will not be possible for me to be identified by it. _____

If all of the applicable sentences above are initialled, meaning "yes", then please continue:

I voluntarily agree to take part in this study. _____

*Please **circle** either Yes or No for each optional question below*

Optional: I agree to receive the AD26.ZEBOV Ebola vaccine as a part of this study. **Yes / No** _____

Optional: I give permission for the study team to contact me about ethically approved research by Oxford Vaccine Group for which I may be suitable. I understand that agreeing to be contacted does not oblige me to participate. **Yes / No** _____

Name: _____

Signature: _____ Date: |___ ___| |___ ___ ___| 20|___ ___|

Investigator's/Nurse's name: _____

Signature: _____ Date: |___ ___| |___ ___ ___| 20|___ ___|

1 copy for participant (original), 1 copy for research site file


oxford vaccine group