ISRCTN46336916 https://doi.org/10.1186/ISRCTN46336916

Investigating a new Vaccine Against Meningitis B (in Oxford)

Submission date
22/01/2018

Recruitment status
No longer recruiting

Registration date
23/01/2018

Overall study status
Completed

Last Edited
19/05/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Meningococcus Group B is a type of bacteria that causes significant morbidity (illness) and mortality (death) by causing meningococcal meningitis or sepsis. Currently, there are two licensed vaccines against Meningitis B available in the UK, Bexsero® and Trumenba®. Bexsero® is included in the UK routine immunisation schedule, but it has a significant rate of side effects, requires up to four doses to be efficient and is expensive. There has recently been development in vaccine technology using an adenovirus as a vector (as a way to deliver material into cells). Administration of this vaccine will lead to the virus entering human cells and producing the protein, but not replicating itself. The production of this protein produces an immune response to meningococcus group B in mice that is as good as Bexsero® and potentially longer lasting. This vaccine candidate is expected to be safe, with previously trials using a similar adenovirus vector proving safe for equivalents vectors for vaccines for malaria, TB, Ebola etc. It is also relatively inexpensive and produces little side-effects. Therefore, we believe this vaccine can improve on the current available vaccine for meningococcus B. We would therefore like to test this vaccine candidate in a Phase 1 trial, primarily to assess the safety of the vaccine in humans. This study also aims to gauge the immunogenicity (the ability to provoke an immune response) as a secondary outcome to inform further potential efficacy trials. In this regard, this study is testing combinations of low single dose, high single dose, high single dose with later high booster dose and high booster dose following a primary Bexsero® dose. These are compared to the two licensed meningococcal vaccines, Bexsero® and Trumenba®, as controls. In addition, the study will enable the development of antibody reference “serum standards” against Bexsero® & Trumenba®.

Who can participate?
Adults aged 18 to 50 years old who are in good health.

What does the study involve?
Participants are allocated to one of eight sub-groups. Those in Group 1 receive a single low dose of 2.5 x10^10 VP of ChAdOx1 MenB.1. Those in Group 2 receive a single high dose 5x10^10 VP of ChAdOx1 MenB.1. Group 3 participants receive a high dose of ChAdOx1 MenB.1 plus a repeat booster dose at six months. Group 4 participants receive a dose of Bexsero® at baseline with a high dose booster of ChAdOx1 MenB.1 at six months. Those in Group 5 receive two doses of

Bexsero® at baseline and 28 days later. Those in Groups 6 and 7 receive Bexsero® at baseline and six months. Participants in Group 8 receive two doses of Trumenba® at baseline and six months. Participants in Groups 6, 7 and 8 will be asked to consent to a blood donation for making serum standards. Symptoms of the shots are recorded in participant diaries.

What are the possible benefits and risks of participating?
Information from this study may help doctors learn more about this study meningitis B vaccine. This information may help us to make a vaccine that can protect babies, children and adults against meningitis B. Participants may experience side effects of the vaccination or blood tests as a part of this study. The team will observe everyone in the study for any side effects, particularly in the first seven days after receiving a vaccine with a diary that they fill in. Side effects may be mild or serious. Most effects will stop shortly after receiving the vaccine. In rare cases, side effects can be serious or prolonged, although no serious concerns have been raised in human trials for other similar virus-based vaccines. In general, the known risks following vaccination are minor and brief (lasting a few days). As with any vaccination, the following events could occur: Pain, redness or swelling of your arm around the spot where the vaccine was injected; General: fatigue, headache, fever, gastrointestinal symptoms such as nausea (feeling sick), vomiting, diarrhoea or abdominal pain. As with all injected vaccines, unexpected, severe allergic reactions may very rarely occur. An allergic reaction can be recognised by itchy skin rash, swelling of the face, difficulties in breathing and swallowing or by a sudden drop in blood pressure. If such reactions occur, they usually start very soon after vaccination. That is why it is important that participants stay at the study site for at least 60 minutes after vaccination, where all medical equipment and personnel are available to treat an allergic reaction. Adenovirus vaccines have previously been trialled in human volunteers, protecting against diseases other than meningitis B. These were not associated with serious side effects. Animal studies conducted to date have shown this vaccine to be capable of stimulating the immune system against meningitis B. There were some minor changes in routine blood results one month after injection, but were not associated with any clinical problems. As it is the first time that the study vaccine will be tested in humans there might be side effects that we don’t yet know about. If any new side effects are identified, from this study or from animal studies, we will tell the participants. Some participants may experience mild pain or discomfort during venepuncture (the blood test) and bruising at the site. In rare cases, participants may feel faint during the blood test. Study staff are trained to deal with these rare occurrences.

Where is the study run from?
Oxford Vaccine Group, University of Oxford (UK)

When is the study starting and how long is it expected to run for?
April 2017 to June 2022

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
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Study website
http://trials.ovg.ox.ac.uk/trials/vambox

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Public

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Additional identifiers

EudraCT/CTIS number
2017-000965-61

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2017/04

Study information

Scientific Title

A Phase I/IIa, single centre, dose-escalation study to assess the safety and immunogenicity of the recombinant adenovirus Meningitis B vaccine candidate ChAdOx1 MenB.1

Acronym
VAMBOX

Study objectives
Study hypothesis as of 31/10/2018:
The aim of this study is to investigate safety and tolerability of 2.5 x 10^10 viral particles (VP) or 5x10^10 VP of the proposed ChAdOx1 MenB.1 vaccine against meningococcus capsular group B in healthy adults aged 18 to 50 years of age, when given one dose +/- one booster dose; and when given as a booster following primary Bexsero® vaccination, in comparison to two dose Bexsero® (the current standard of care) or two dose Trumenba® vaccination.

Previous study hypothesis:
The aim of this study is to investigate safety and tolerability of 2.5 x 10^10 viral particles (VP) or 5x10^10 VP of the proposed ChAdOx1 MenB.1 vaccine against meningococcus serotype B in healthy adults aged 18 to 50 years of age, when given one dose +/- one booster dose; and when given as a booster following primary Bexsero vaccination, in comparison to standard two dose Bexsero vaccination (the current standard of care).

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford A Research Ethics Committee, 21/12/2017, ref: 17/SC/0470

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

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
http://trials.ovg.ox.ac.uk/trials/vambox

Health condition(s) or problem(s) studied
Meningitis B

Interventions
Interventions as of 31/10/2018:
The study is a phase I/IIa, single centre, dose-escalation study to assess the safety and

immunogenicity of a single dose +/- booster dose of the recombinant adenovirus Meningitis B vaccine candidate ChAdOx1 MenB.1 in healthy adults. The participants are divided into 8 sub-groups as described below. The total number of participants required to reach the primary endpoint is between 79 to 90.

Group 1: Low dose arm – This group consists of three to six individuals who receive a single dose of 2.5 x10^10 VP of ChAdOx1 MenB.1 according to a 3+3 study plan. A favourable Data Safety Monitoring Committee review of the safety data from this arm is required before commencement of group 2.

Group 2: High dose arm – This group will only proceed after DSMC review of Group 1 and approval. This group consists of 10 participants assigned to receive a single dose of the higher dose 5x10^10 VP of ChAdOx1 MenB.1. A favourable DSMC review of the safety data from this arm is required before the commencement of group 3.

Group 3: High dose ChAdOx1 MenB.1 plus booster arm – this group consists of eight participants who receive the high dose 5x10^10 VP of ChAdOx1 MenB.1, with a repeat booster dose at six months. Administration of the booster dose are subject to favourable interim review of the safety data of group 2 by the DSMC.

Group 4: Bexsero with high dose ChAdOx1 MenB.1 booster arm – this group consists of eight participants who receives a dose of Bexsero® at baseline with a booster high dose of ChAdOx1 MenB.1 at six months.

Group 5: Bexsero® Control arm – This group consists of 10 individuals who receive two doses of Bexsero® at Day 0 and Day 28 as per adult licensing. This group acts as a control to groups 1 and 2.

Group 6: Bexsero® 6 month boost control arm – This group consists of 8 individuals who receive Bexsero® doses at Day 0 and 6 months. This group acts as a control for groups 3 and 4. If participants choose to be a part of the serum standard, they would have a large blood donation at 7 months.
Group 7: Bexsero® 6 month boost control arm – This group mirrors group 6. Serum standard blood donation at 7 months. It consists of 12 to 20 individuals, depending on the number of group 6 participants consenting to serum standard.
Group 8: Trumenba® 6 month boost control arm – This group consists of 20 individuals who receive Trumenba® doses at Day 0 and 6 months. This group also acts as a control for groups 3 and 4. Serum standard blood donation at 7 months.

Previous interventions:
The study is a phase I/IIa, single centre, dose-escalation study to assess the safety and immunogenicity of a single dose +/- booster dose of the recombinant adenovirus Meningitis B vaccine candidate ChAdOx1 MenB.1 in healthy adults. The participants are divided into six subgroups as described below. The total number of participants required to reach the primary endpoint is 47.

Group 1: Low dose arm – This group consists of three-six individuals who receive a single dose of 2.5 x10^10 VP of ChAdOx1 MenB.1 according to a 3+3 study plan. A favourable Data Safety Monitoring Committee review of the safety data from this arm is required before commencement of group 2.

Group 2: High dose arm – This group will only proceed after DSMC review of Group 1 and approval. This group consists of 10 participants assigned to receive a single dose of the higher dose 5x10^10 VP of ChAdOx1 MenB.1. A favourable DSMC review of the safety data from this arm is required before the commencement of group 3.

Group 3: High dose ChAdOx1 MenB.1 plus booster arm – this group consists of eight participants who receive the high dose 5x10^10 VP of ChAdOx1 MenB.1, with a repeat booster dose at six months. Administration of the booster dose are subject to favourable interim review of the safety data of group 2 by the DSMC.

Group 4: Bexsero with high dose ChAdOx1 MenB.1 booster arm – this group consists of eight participants who receives a dose of Bexsero at baseline with a booster high dose of ChAdOx1 MenB.1 at six months.

Group 5: Bexsero Control arm – This group consists of 10 individuals who receive two doses of Bexsero at Day 0 and Day 28 as per adult licensing. This group acts as a control to groups 1 and 2.

Group 6: Bexsero 6 month boost control arm – This group consist of 8 individuals who receive Bexsero doses at Day 0 and 6 months. This group acts as a control for groups 3 and 4.

Intervention Type
Biological/Vaccine

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Not provided at time of registration

Primary outcome measure
1. Solicited symptoms the participants record following each vaccination in a diary records from Day 0 (day of vaccination) to Day 7 (plus later if any persisting symptoms). The recording and assessment of local and systemic adverse events following administration of each vaccine dose:
1.1. Tenderness and pain at the injection site
1.2. Induration
1.3. Redness
1.4. Swelling
1.5. Headache
1.6. Malaise
1.7. Myalgia
1.8. Nausea and/or vomiting
1.9. Anorexia
1.10. Fever
1.11. Arthralgia
1.12. Blood parameters
2. Unsolicited adverse events up until and including 28 days following the last vaccine
3. Serious adverse events (SAEs) during the entire study
4. Safety is measured using blood tests at all study visits

Secondary outcome measures

Secondary outcome measures as of 31/10/2018:
The immunogenicity of 2.5 x 10^10 VP or 5x10^10 VP of the proposed ChAdOx1 MenB.1 vaccine against meningococcus capsular group B in healthy adults aged 18 to 50 years of age when given one dose +/- one booster dose; and when given as a booster following primary Bexsero vaccination in comparison to two dose Bexsero® (the current standard of care) or two dose Trumenba®, is measured using the serum bactericidal antibody (SBA) assay against homologous strains at different time points.

Previous secondary outcome measures:
The immunogenicity of 2.5 x 10^10 VP or 5x10^10 VP of the proposed ChAdOx1 MenB.1 vaccine against meningococcus serotype B in healthy adults aged 18 to 50 years of age when given one dose +/- one booster dose; and when given as a booster following primary Bexsero vaccination in comparison to standard two dose Bexsero vaccination (the current standard of care) is measured using of the Serum bactericidal antibody (SBA) assay against homologous strains from D0, D14 and D28 time points.

Overall study start date
01/04/2017

Completion date
09/06/2022

Eligibility

Key inclusion criteria
1. Willing and able to give written informed consent for participation in the study
2. Aged between 18 and 50 years inclusive at the time of first vaccination
3. In good health as determined by
3.1. Medical history
3.2. Physical examination
3.3. Clinical judgment of the investigators
4. (Females of childbearing potential) Willing to use effective contraception (such as the oral contraceptive pill, contraceptive implant, barrier methods or complete abstinence from heterosexual sexual intercourse) from one month prior to first vaccination and for three months following last vaccine
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. Confirmation from the participants GP that they are satisfied from their knowledge of the volunteer that they are suitable to enrol and/or the provision of a detailed medical summary is provided to the study team to assess participant eligibility
8. Agrees to refrain from donating blood for the duration of the trial
9. 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
10. Agree to provide National Insurance number and Bank details for reimbursement purposes

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
Both

Target number of participants
Planned Sample Size: 90; UK Sample Size: 90

Total final enrolment
88

Key exclusion criteria
Participant exclusion criteria as of 31/10/2018:
1. History of significant organ/system disease that could interfere with trial conduct or completion. This includes any history of significant disease in the following;
1.1. Cardiovascular disease including congenital heart disease, previous myocardial infarction, valvular heart disease (or history of rheumatic fever), previous bacterial endocarditis, history of cardiac surgery (including pacemaker insertion), personal or family history of cardiomyopathy or sudden adult death
1.2. Respiratory disease such as uncontrolled asthma and chronic obstructive pulmonary disease
1.3. Endocrine disorders such as diabetes mellitus and Addison's disease
1.4. Significant renal or bladder disease, including history of renal calculi
1.5. Biliary tract disease
1.6. Gastro-intestinal disease such as inflammatory bowel disease, abdominal surgery within the last two years, coeliac disease and liver disease (including hepatitis B or C infection)
1.7. Neurological disease such as seizures and myasthenia gravis
1.8. Haematological problems such as anaemia or coagulation problems
1.9. Metabolic disease such as glucose-6-phosphate dehydrogenase deficiency
1.10. Psychiatric illness requiring hospitalisation or depression whose severity is deemed clinically significant by the study Investigators and/or GP
1.11. Known or suspected drug and/or alcohol misuse (alcohol misuse defined as an intake exceeding 42 units per week)
1.12. Non-benign cancer, except squamous cell or basal cell carcinoma of the skin and cervical carcinoma in situ
2. History of allergy or anaphylaxis to a vaccine or any component within the vaccines used in this study
3. Have any known or suspected impairment or alteration of immune function, resulting from, for example:
3.1. Congenital or acquired immunodeficiency
3.2. Human Immunodeficiency Virus infection or symptoms/signs suggestive of an HIV-associated condition
3.3. Autoimmune disease
3.4. Receipt of immunosuppressive therapy such as anti-cancer chemotherapy or radiation therapy within the preceding 12 months or long-term systemic corticosteroid therapy
4. Study significant abnormalities on screening investigations at the discretion of an Investigator

5. Weight < 50 kg
6. Donation of blood within the last 3 (male) or 4 (female) months) or plans on giving blood within the next year
7. Receipt of a live vaccine within 4 weeks prior to vaccination, an inactivated influenza vaccine within 14 days of vaccination or another inactivated vaccine within 7 days prior to vaccination
8. Plan to receive any vaccine other than the study vaccine within 4 weeks following vaccination
9. Scheduled procedures requiring general anaesthesia during the study
10. Receipt of immunoglobulin or any blood product transfusion within 3 months of study start
11. Current active participation in another research study involving an investigational product or where involvement in this study could impact the results
12. Donation of blood in the past 12 weeks (if male) or 16 weeks (if female), or are planning to do so within the 52 weeks of vaccination in this study
13. Previously having received a meningococcal B vaccine of any kind
14. Previously having received a meningococcal ACWY vaccine in the last 10 years (groups 7 and 8)
15. Previously having received a meningococcal C vaccine in the last 10 years (groups 7 and 8)
16. Previously received any adenovirus based vaccine of any kind (usually as part of a trial) (Groups 1,2,3,and 4 only)
17. Previous occurrence of disease caused by N. meningitidis
18. Inability, in the opinion of the Investigator, to comply with all study requirements
19. Female participants who are pregnant, lactating or planning pregnancy during the course of the study
20. Participant unwilling to allow contact with their GP, is not registered with a GP; or if GP is not contactable.
21. Any other significant disease or disorder which, in the opinion of the Investigator, may
22.1. Put the participants at risk because of participation in the study;
22.2. Influence the result of the study; and/or
22.3. Impair the participant's ability to participate in the study

Previous participant exclusion criteria:
1. History of significant organ/system disease that could interfere with trial conduct or completion. This includes any history of significant disease in the following;
1.1. Cardiovascular disease including congenital heart disease, previous myocardial infarction, valvular heart disease (or history of rheumatic fever), previous bacterial endocarditis, history of cardiac surgery (including pacemaker insertion), personal or family history of cardiomyopathy or sudden adult death
1.2. Respiratory disease such as uncontrolled asthma and chronic obstructive pulmonary disease
1.3. Endocrine disorders such as diabetes mellitus and Addison's disease
1.4. Significant renal or bladder disease, including history of renal calculi
1.5. Biliary tract disease
1.6. Gastro-intestinal disease such as inflammatory bowel disease, abdominal surgery within the last two years, coeliac disease and liver disease (including hepatitis B or C infection)
1.7. Neurological disease such as seizures and myasthenia gravis
1.8. Haematological problems such as anaemia or coagulation problems
1.9. Metabolic disease such as glucose-6-phosphate dehydrogenase deficiency
1.10. Psychiatric illness requiring hospitalisation or depression whose severity is deemed clinically significant by the study Investigators and/or GP
1.11. Known or suspected drug and/or alcohol misuse (alcohol misuse defined as an intake exceeding 42 units per week)
1.12. Non-benign cancer, except squamous cell or basal cell carcinoma of the skin and cervical carcinoma in situ
2. History of allergy or anaphylaxis to a vaccine or any component within the vaccines used in

this study
3. Have any known or suspected impairment or alteration of immune function, resulting from, for example:
3.1. Congenital or acquired immunodeficiency
3.2. Human Immunodeficiency Virus infection or symptoms/signs suggestive of an HIV-associated condition
3.3. Autoimmune disease
3.4. Receipt of immunosuppressive therapy such as anti-cancer chemotherapy or radiation therapy within the preceding 12 months or long-term systemic corticosteroid therapy
4. Study significant abnormalities on screening investigations at the discretion of an Investigator
5. Weight < 50 kg
6. Donation of blood within the last 3 (male) or 4 (female) months) or plans on giving blood within the next year
7. Receipt of a live vaccine within 4 weeks prior to vaccination, an inactivated influenza vaccine within 14 days of vaccination or another inactivated vaccine within 7 days prior to vaccination
8. Plan to receive any vaccine other than the study vaccine within 4 weeks following vaccination
9. Scheduled procedures requiring general anaesthesia during the study
10. Receipt of immunoglobulin or any blood product transfusion within 3 months of study start
11. Current active participation in another research study involving an investigational product or where involvement in this study could impact the results
12. Donation of blood in the past 12 weeks (if male) or 16 weeks (if female), or are planning to do so within the 52 weeks of vaccination in this study
13. Previously having received a meningococcal B vaccine of any kind
14. Previously received any adenovirus based vaccine of any kind (usually as part of a trial)
15. Previous occurrence of disease caused by N. meningitidis
16. Inability, in the opinion of the Investigator, to comply with all study requirements
17. Female participants who are pregnant, lactating or planning pregnancy during the course of the study
18. Participant unwilling to allow contact with their GP, is not registered with a GP; or if GP is not contactable.
19. Any other significant disease or disorder which, in the opinion of the Investigator, may
19.1. Put the participants at risk because of participation in the study;
19.2. Influence the result of the study; and/or
19.3. Impair the participant’s ability to participate in the study

Date of first enrolment
05/02/2018

Date of final enrolment
16/12/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
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ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The Investigator will co-ordinate dissemination of data from this study. All publications (e.g., manuscripts, abstracts, oral/slide presentations, book chapters) based on this study will be reviewed by each sub-investigator prior to submission. The intent is to publish in a scientific peer-reviewed, open access journal. The link to the publication and a synopsis will be available to participants and public on the Oxford Vaccine Group website.

Participants will receive a letter containing these results. The individual participant results would not be identifiable nor would they be identified in any report or publication.

The results of the research will also potentially be used for future academic research within the Oxford Vaccine Group.

Intention to publish date
30/11/2023

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 3.3	12/11/2021	02/09/2022	No	No
HRA research summary			28/06/2023	No	No
Results article		07/05/2025	19/05/2025	Yes	No