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Investigating a vaccine against plague

Submission date
19/03/2021

Recruitment status
No longer recruiting

Registration date
20/04/2021

Overall study status
Completed

Last Edited
26/05/2026

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
Plague is a disease caused by infection with Yersinia pestis, which is a type of bacteria. In humans, this infection can cause high fevers, swollen lymph nodes, shortness of breath, coughing up blood, bloodstream infection and, if left untreated, death. It is spread by the bite of an infected flea, the handling of an animal infected with plague, or from inhaling respiratory droplets from an infected person.
There are three different forms of plague infection; bubonic, pneumonic and septicaemic. Bubonic plague is characterised by swollen and painful lymph nodes near to where the bacteria entered through the skin. Pneumonic plague is where the bacteria is breathed into the lungs and results in shortness of breath, fever and coughing up blood. If pneumonic plague is not treated with antibiotics within 24 hours there is almost a 100% chance of death. Both bubonic and pneumonic plague can develop into septicaemic plague, which is a life-threatening infection of the blood.
Plague is found across the world, but the biggest burden is in very remote and poor parts of Africa and Asia. During 1998-2016, a total of 13,234 suspected cases of plague were recorded in Madagascar alone. Plague can be treated effectively with antibiotics, if treated early, however, this is often not possible in rural areas, where a vaccine would be much more effective.
Some effective vaccines against plague are available in some parts of the world, however, they are not ideal for various reasons. The University of Oxford has developed a new plague vaccine, which can be given by injection into the arm. The vaccine is made with a virus that has been modified to make it harmless, and this virus vaccine carrier has already been tested in humans (most recently with a vaccine against COVID-19 and also Meningitis B) and shown to be safe. This new plague vaccine needs testing to see if it is safe and produces an effective response from the immune system in healthy participants. All participants will be monitored closely throughout the trial, with blood and nose-fluid samples taken to see what is happening in the immune system.

Who can participate?
Male or female volunteers aged 18-55 inclusive who are in good health and able to travel to the Centre for Clinical Vaccinology and Tropical Medicine in Oxford regularly over one year (updated 16/09/2021, previously: Male or female volunteers aged 18-55 inclusive who are in good health and live in the Thames Valley or surrounding area).

What does the study involve?
Participants will receive either one or two doses of the investigational vaccine, ChAdOx1 Plague.

The researchers will then take blood and nose-fluid samples at follow-up visits and record any symptoms that occur after vaccination. There will be up to 14 study visits (depending on which group a participant is in) over a 12-month duration

What are the possible risks and benefits of participating?
Recipients of ChAdOx1 Plague do not receive any guaranteed benefit. However, it is hoped that the information gained from this study will contribute to the development of a safe and effective vaccine against plague. The only benefits for participants would be information about their general health status.
The main potential risks are those associated with phlebotomy (blood taking) and vaccination. Localised bruising and discomfort can occur at the site of blood taking. Sometimes people can faint when having their blood taken. The total volume of blood drawn over a 12-month period will be up to 630 ml. This should not have any bad effect on healthy people. In the UK, volunteers are permitted to donate 470 ml during a single blood donation for the National Blood Transfusion Service over a 3-4 month period. Volunteers will be asked to refrain from blood donation for the duration of their involvement in the trial.
Allergic reactions from mild to severe may occur in response to any constituent of a medicinal product's preparation. Anaphylaxis is extremely rare (about 1 in 1,000,000 vaccine doses) but can occur in response to any vaccine or medication.
The typical reaction where a vaccine is given is temporary pain, tenderness, redness, and swelling at the site of the injection. People can also have "flu-like" symptoms after any vaccination, such as feverishness and achiness, and this can last for 2- 3 days. Sometimes people feel faint when they see a needle or have an injection. As with any other vaccine, temporary ascending paralysis (Guillain-Barré syndrome, GBS) or immune-mediated reactions that can lead to organ damage may occur, but this should be extremely rare (100,000-1,000,000 vaccine doses).
Synthetic absorptive matrix (SAM) strips are used to sample the nasal fluid from inside the nostril. Sometimes this can make people sneeze or have a runny nose. Rarely, this can cause nosebleeds. These SAM strips are made of soft cotton-like material and insertion should not be painful.

Where is the study run from?
Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital (UK)

When is the study starting and how long is it expected to run for?
December 2020 to May 2024

Who is funding the study?
Innovate UK

Who is the main contact?
Ella Morey, info@ovg.ox.ac.uk

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-000710-15

Integrated Research Application System (IRAS)
279095

Central Portfolio Management System (CPMS)
47549

Protocol serial number
OVG 2019/05

Study information

Scientific Title
A phase I study to assess the safety and immunogenicity of a recombinant adenovirus-based vaccine against plague

Acronym
PlaVac

Study objectives
1. To investigate the safety and tolerability of 5 x 10(10) vp of the proposed ChAdOx1 Plague vaccine in healthy adults aged 18 to 55 years, when given one or two doses intramuscularly.
2. To investigate the immunogenicity of 5 x 10(10) vp of the proposed ChAdOx1 Plague vaccine in healthy adults aged 18 to 55 years, when given as one or two doses intramuscularly, with different prime-boosting intervals.
3. To utilize exploratory immunogenicity assays to determine the immunogenicity of 5 x 10(10) vp of the proposed ChAdOx1 Plague vaccine, in healthy adults aged 18 to 55 years, when given one or two doses intramuscularly, with different prime-boosting intervals.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/12/2020, South Central - Berkshire B Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 0148310; berkshireb.rec@hra.nhs.uk), REC ref: 20/SC/0405

Primary study design
Interventional

Study design
Open-label non-randomized safety and immunogenicity interventional study

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Plague

Interventions
Group 1: 10-15 participants will receive a single dose of 5 x 10(10) vp of ChAdOx1 Plague via an intramuscular route.
Group 2: 15 participants will receive two doses of 5 x 10(10) vp ChAdOx1 Plague (intramuscular), 2 months apart.
Group 3: 15 participants will receive two doses of 5 x 10(10) vp of ChAdOx1 Plague (intramuscular), 6 months apart.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
ChAdOx1 Plague

Primary outcome(s)
The safety and tolerability of 5 x 10(10) vp of the proposed ChAdOx1 Plague vaccine in healthy adults aged 18 to 55 years when given as one or two doses intramuscularly, measured by

recording local and systemic adverse events in participant eDiaries for 28 days following administration of each vaccine dose

Key secondary outcome(s)
1. The immunogenicity of 5 x 10(10) vp of the proposed ChAdOx1 Plague vaccine in healthy adults aged 18 to 55 years when given as one or two doses intramuscularly with different prime-boost intervals, using ELISA to measure antibody responses to the vaccine antigens at 1-month post-vaccination
2. The safety of 5 x 10(10) vp of the proposed ChAdOx1 Plague vaccine in healthy adults aged 18 to 55 years when given as one or two doses intramuscularly with different prime-boost intervals, measured by recording local and systemic adverse events in participant eDiaries for 28 days following administration of each vaccine dose

Completion date
31/05/2024

Eligibility

Key inclusion criteria
1. Willing and able to give written informed consent for participation in the study
2. Aged between 18 and 55 years inclusive at the time of first visit
3. In good health as determined by medical history (as determined by verbal medical history), physical examination, clinical judgment of the investigators.
4. Female participants (of childbearing potential) who are willing to ensure that they or their partner use effective contraception during the vaccination period and for the months after vaccination and have a negative pregnancy test on the day(s) of screening and vaccination
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 (GP) to be notified of participation
7. Willing to allow the investigators to discuss the volunteer’s medical history with their General Practitioner or hospital consultant and access all medical records, including electronic patient records, when relevant to study procedures
8. Agrees to refrain from donating blood for the duration of the trial
9. Agrees 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. Agrees to provide National Insurance number and bank details for reimbursement purposes
11. Normal baseline/screening laboratory (blood/urine) results

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
45

Key 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
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 coagulation problems or anaemia (haemoglobin < 125g/L and < 135 g/L for females and males, respectively)
1.9. Metabolic disease such as glucose-6-phosphate dehydrogenase deficiency
1.10. Psychiatric illness requiring hospitalisation or depression if severity is deemed clinically significant by the study Investigators
1.11. Known or suspected drug and/or 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 (including for more than 7 days consecutively within the previous 3 months).
4. Any significant abnormalities on screening investigations that are either unlikely to resolve or do not resolve on repeat testing (at the discretion of an Investigator) within the recruitment timeline of the study
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
8. Plan to receive any vaccine other than the study vaccine within 2 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. Previous occurrence of disease caused by Y. pestis or vaccine against plague
13. Inability, in the opinion of the Investigator, to comply with all study requirements
14. Female participants who are pregnant, lactating or who are unwilling to ensure that they or their partner use effective contraception throughout the trial period
15. Participant unwilling to allow contact with their GP or is not registered with a GP
16. Any other significant disease or disorder which, in the opinion of the Investigator, may:
16.1. Put the participants at risk because of participation in the study;
16.2. Influence the result of the study; and/or
16.3. Impair the participant's ability to participate in the study
17. Tattoo at the injection site that would interfere with the assessment of injection site

Date of first enrolment
03/05/2021

Date of final enrolment
09/11/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Centre for Clinical Vaccinology & Tropical Medicine
University of Oxford
Churchill Hospital
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OX3 7LA

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Innovate UK

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 and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1.0	28/01/2026	04/02/2026	No	No
HRA research summary			28/06/2023	No	No
Other publications	Mixed-methods study comprising a questionnaire and semi-structured interview, as part of the PlaVac trials	08/05/2026	26/05/2026	Yes	No
Plain English results			24/06/2025	No	Yes
Protocol file	version 3.3	27/08/2021	16/09/2021	No	No
Protocol file	version 3.4	19/11/2021	25/01/2022	No	No
Protocol file	version 4.0	28/02/2022	14/07/2022	No	No
Protocol file	version 5.0	11/05/2023	19/05/2023	No	No