

Investigating a vaccine against plague

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| Submission date 19/03/2021 | Recruitment status No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol |
| Registration date 20/04/2021 | Overall study status Completed | <input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results |
| Last Edited 09/01/2025 | Condition category Infections and Infestations | <input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year |

Plain English Summary

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

Contact name

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Contact details

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Additional identifiers**EudraCT/CTIS number**

2020-000710-15

IRAS number

279095

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

OVG 2019/05, IRAS 279095, CPMS 47549

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 hypothesis

1. To investigate the safety and tolerability of 5×10^{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 5×10^{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 5×10^{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

Study design

Open-label non-randomized safety and immunogenicity interventional study

Primary study design

Interventional

Secondary study design

Non randomised study

Study setting(s)

Other

Study type(s)

Prevention

Participant information sheet

No participant information sheet is currently available

Condition

Plague

Interventions

Group 1: 10-15 participants will receive a single dose of 5×10^{10} vp of ChAdOx1 Plague via an intramuscular route.

Group 2: 15 participants will receive two doses of 5×10^{10} vp ChAdOx1 Plague (intramuscular), 2 months apart.

Group 3: 15 participants will receive two doses of 5×10^{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 measure

The safety and tolerability of 5 x 10¹⁰ 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

Secondary outcome measures

1. The immunogenicity of 5 x 10¹⁰ 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 10¹⁰ 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

Overall study start date

11/12/2020

Overall study end date

31/05/2024

Eligibility

Participant 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

Age group

Adult

Lower age limit

18 Years

Upper age limit

55 Years

Sex

Both

Target number of participants

36

Total final enrolment

45

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

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

Recruitment start date

03/05/2021

Recruitment end date

09/11/2021

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Centre for Clinical Vaccinology & Tropical Medicine

University of Oxford

Churchill Hospital

Oxford

United Kingdom

OX3 7LA

Sponsor information

Organisation

University of Oxford

Sponsor details

Clinical Trials Research Governance

Joint Research Office

1st floor

Boundary Brook House

Churchill Drive

Headington

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England

United Kingdom

OX3 7GB

+44 (0)1865 289885

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Sponsor type

University/education

Website

<http://www.ox.ac.uk/>

ROR

<https://ror.org/052gg0110>

Funder(s)

Funder type

Government

Funder Name

Innovate UK

Alternative Name(s)

innovateuk

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

There are no plans currently to have any additional documents be available. Planned publication in a high-impact peer-reviewed journal.

Intention to publish date

31/05/2025

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? |
|--------------------------------------|-------------|--------------|------------|----------------|-----------------|
| 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 |
| HRA research summary | | | 28/06/2023 | No | No |