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Investigating a vaccine against plague in Uganda (PlaVac Uganda)

Submission date
19/07/2022

Recruitment status
No longer recruiting

Registration date
05/08/2022

Overall study status
Completed

Last Edited
04/12/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Plague is a disease caused by an infection by 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. A person can be infected with Plague by getting a bite from a flea that carries plague, by touching an animal that is sick with plague, or by breathing in the cough of a person who is sick with plague. Plague disease can make people sick in different ways, and can be very serious. People sick with plague may have swollen and painful lymph nodes that look like very large lumps, usually in the groins, armpits and neck. If a person breathes in the plague infection, they may be sick with coughing, breathlessness and coughing up blood. A person who is sick with plague has a high chance of dying, especially if they are not given antibiotics as soon as they are sick.

Plague is present in Uganda, and the number of cases varies each year – sometimes a small number, and sometimes more than one hundred. The most recent outbreaks have been in the West Nile sub-region region in Arua and Zombo districts. Other countries in the world and in Africa also get plague, and every year people die from plague.

Plague can be cured if antibiotics are given very soon after catching the infection. The reason we want to develop a plague vaccine is that most people who get sick with plague do not have a doctor who can give the right antibiotics near to them, and often they die before they can get medical help. A vaccine that prevented plague would be much more effective and would save lives. There is no licenced plague vaccine currently available.

The University of Oxford has developed a plague vaccine that is injected into the arm. The vaccine was first tested in mice and is now being tested in people living in the UK. Forty-five people have already received the vaccine in the UK. This is the first step to see if the vaccine is safe and to check what happens in the immune system after the vaccine is given. The reason for doing this study in Uganda is to find out if the vaccine is safe and stimulates an immune response in people who live in countries that get outbreaks of plague.

Who can participate?
Adults aged between 18-49 years.

What does the study Involve?
The study will consist of two groups of volunteers, each of 18 people. Both groups will receive two doses of vaccines at different time points. The number of visits, blood tests and duration of the study are the same for both groups.
Group 1: This group will consist of up to 18 people who will receive a dose of vaccine at the beginning of the study, and then a second dose after two months.
Group 2: This group will consist of up to 18 people, who will receive a dose of vaccine at the beginning of the study, and then a second dose after six months.
Each study participant will have eight study visits including screening. Blood samples will be taken at each study visit.

What are the possible benefits and risks of participating?
There is no direct benefit to study participants from participating in the study or receiving the study vaccine, as plague outbreaks are not common in Masaka and we do not know whether the study vaccine works yet. The information from this study will be used to support further studies in Africa, to work towards developing a safe and effective vaccine, and to help prevent plague infection and outbreaks.
There may be an indirect benefit to study participants as study participants will receive free routine medical care from the study site whilst in the study.
The risks of participating are possible side effects of vaccination usually lasting less than two days:
1. Common side effects after vaccination:
1.1. Pain, redness or swelling of your arm around the spot where the vaccine was injected
1.2. General reactions such as fatigue, headache, fever, nausea, vomiting, diarrhoea, and general body pains

2. Serious, rare side effects:
2.1. Allergic reactions
With all injected vaccines, in very rare cases (approximately 1 in 1 million doses), severe allergic reactions can happen. If such reactions occur, they usually start very soon after vaccination. That is why it is important that study participants stay at the study site for at least 30 minutes after vaccination, where doctors and equipment are available to treat an allergic reaction.

2.2. Guillain-Barre syndrome:
Reactions in the nervous system (brain and nerves) are also extremely rare after vaccinations (1 in 100,000-1,000,000 vaccine doses) but can cause an illness called Guillain-Barré syndrome. This is a condition in which people can develop severe weakness and can be fatal. This reaction has been reported very rarely in people who had the Oxford/AstraZeneca COVID-19 vaccine.

3. Unknown-risk side-effects:
3.1. Blood clots
A very rare blood clotting condition that can cause clots in the brain and gut, and has caused death in some cases, is listed as a side effect of the Oxford/AstraZeneca COVID-19 vaccine.
The overall risk of these blood clots from the Oxford/AstraZeneca COVID-19 vaccine is estimated to be about 1 in 50,000 after the first dose for people aged under 40, and 1 in 100,000 after the first dose for people aged over 40.
At the moment, it is not known why these clots happen in some people. All medical regulators are collecting and analysing further data on them.
It is not yet known whether these rare clotting problems might be related to the ChAdOx1 part of the vaccine or to the COVID-19 virus part of the vaccine. This means that we don’t know whether serious blood clots could be a risk of the ChAdOx1 Plague vaccine.

Other ChAdOx1-based vaccines have been used since 2012 in research studies targeting other diseases including influenza, tuberculosis, prostate cancer, malaria, meningitis B, chikungunya, Zika and HIV. These rare blood clotting problems have not been seen in participants in these studies. However, the number of people in these studies has been small. These events have not occurred in the UK ChAdOx1 Plague study.

Where is the study run from?
Oxford Vaccine Group at the University of Oxford (United Kingdom)

When is the study starting and how long it is expected to run for?
November 2021 to June 2024

Who is funding the study?
Innovate UK, a part of UK Research and Innovation (United Kingdom)

Who is the main contact:
Professor Sir Andrew Pollard (United Kingdom)
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Contact information

Type(s)
Scientific

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
OVG2022/01

Study information

Scientific Title
A phase Ib study to assess the safety and immunogenicity of a recombinant adenovirus-based vaccine against plague in Uganda (PlaVac Uganda)

Acronym
PlaVac Uganda

Study objectives
Plague is a disease caused by infection with Yersinia pestis. The University of Oxford has developed a novel plague vaccine, which can be given intramuscularly. This novel vaccine is currently being tested in healthy adult volunteers based in the UK, and so far has shown to be safe and well tolerated(ISRCTN: 41077863). The vaccine requires further testing in people who live in the countries where a plague vaccine would be used. This is to determine if it is safe and if protective responses from the immune system are not affected by people being genetically different, or having been exposed to different diseases.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1 Submitted 13/04/2022, The Oxford Tropical Research Ethics Committee (OxTREC), (Research Services, University of Oxford, Boundary Brook House, Churchill Drive, Headington, Oxford, OX3 7GB, United Kingdom; +44 1865 282585; oxtrec@admin.ox.ac.uk), ref: OxTREC 10-22
2. Submitted 06/06/2022, UVRI Research Ethics Committee (UVRI REC), (Uganda Virus Research Institute, Plot 51-59, Nakiwogo road, Entebbe, P.O. Box 49, Entebbe-Uganda; telephone not provided; directoruvri@uvri.go.ug), ref: GC/127/917

Study design
Phase Ib non-blinded uncontrolled non-randomized study

Primary study design

Interventional

Secondary study design
Non randomised study

Study setting(s)
Community

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Prevention of plague caused by the intracellular bacterium Yersinia pestis

Interventions
The study is a phase Ib, non-blinded, non-randomised study to assess the safety and immunogenicity of one or two doses at different prime-boost intervals of the recombinant adenovirus plague vaccine candidate ChAdOx1 Plague in healthy African adults residing in Uganda. There is no placebo control.

The participants will be divided into two groups. Allocation to each arm will be decided in order of recruitment. The first recruited participant will be allocated to Group 1, and subsequent participants allocated to Group 1 or 2 on an approximately alternating basis to ensure even distribution. The total number of participants required to reach the primary endpoint will be 20 (10 per group). Group 1 participants will receive two doses of vaccine intramuscularly on day 0 and day 56. Group 2 participants will receive two doses of vaccine intramuscularly on day 0 and day 182.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
ChAdox1 Plague vaccine

Primary outcome measure
Local, systemic, and laboratory adverse events were recorded using ediaries, participant reporting to the study team, and routine laboratory haematology and biochemistry tests:
1. Local and systemic solicited adverse events from Day 0 to Day 7 post-vaccination
2. Unsolicited adverse events recorded for 28 days following each vaccination
3. Laboratory adverse events (safety blood tests) on Day 7 and day 28 following each vaccination
4. Serious adverse events (SAEs) collected throughout the study period

Secondary outcome measures

1. Antibody responses to the vaccine antigens as measured by ELISA on Day 28 post each vaccination
2. Immune responses to vaccines measured by immunological assays potentially including:
2.1. Antibody concentration against vaccine antigens before and after vaccination
2.2. Antibody functional capacity in vitro assays (serum bactericidal, phagocytosis, invasion)
2.3. Antibody functional capacity in vivo challenge assay (by serum transfer)
in blood samples from visits Day 0 to Day 210 inclusive

Overall study start date
10/11/2021

Completion date
30/06/2024

Eligibility

Key inclusion criteria
1. Willing and able to give informed consent for participation in the trial
2. Male or female aged between 18-49 years old inclusive at enrolment (first vaccination visit)
3. In good health as determined by:
3.1. Medical history (as determined by verbal medical history)
3.2. Physical examination
3.3. Clinical judgment of the investigators
4. Female participants of childbearing potential must be willing to ensure that they use effective contraception during the trial and for 3 months after the last vaccination
5. Female participants of childbearing potential must have a negative pregnancy test on the day (s) of screening and vaccination
6. Able to attend the scheduled visits and comply with all study procedures
7. Agrees to refrain from donating blood for the duration of the trial
8. Clinically acceptable baseline screening results (includes vital signs, physical examination, urinalysis, and laboratory results)
9. In the Investigator’s opinion, is able and willing to comply with all trial requirements

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
49 Years

Sex
Both

Target number of participants

36

Total final enrolment

36

Key exclusion criteria

1. Pregnancy, lactating or planning pregnancy during the course of the trial
2 History of significant organ/system disease that could interfere with trial conduct or completion, including known history of significant disease in the following:
2.1. 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
2.2. Respiratory diseases such as uncontrolled asthma and chronic obstructive pulmonary disease
2.3. Endocrine disorders such as diabetes mellitus and Addison's disease
2.4. Significant renal or bladder disease
2.5. Biliary tract disease
2.6. Gastro-intestinal diseases such as inflammatory bowel disease, major abdominal surgery within the last two years, coeliac disease and liver disease (including hepatitis B or C infection)
2.7. Neurological diseases such as seizures and myasthenia gravis
2.8. Haematological problems such as coagulation problems or anaemia (haemoglobin < 12.5g/dl for females and < 13.5 g/dl and for males)
2.9. Metabolic diseases such as glucose-6-phosphate dehydrogenase deficiency
2.10. Psychiatric illness requiring hospitalisation or depression if the severity is deemed clinically significant by the Study Investigators
2.11. Known or suspected drug and/or alcohol misuse
2.12. Non-benign cancer, except squamous cell or basal cell carcinoma of the skin and cervical carcinoma in situ
3 Any other significant disease or disorder which, in the opinion of the Investigator, could:
3.1. Put the participant at risk because of participation in the trial
3.2. Influence the result of the trial
3.3. Impair the participant's ability to participate in the trial
4. History of allergy to a vaccine or any component of the vaccines used in this study
5. History of anaphylaxis
6. Have any known or suspected impairment or alteration of immune function, resulting from, for example:
6.1. Congenital or acquired immunodeficiency
6.2. Human Immunodeficiency Virus infection or symptoms/signs suggestive of an HIV-associated condition
6.3. Autoimmune disease
6.4. 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)
7. Receipt of immunoglobulins or any blood product transfusion within 3 months prior to enrolment
8. Scheduled elective surgery or other procedures requiring general anaesthesia during the trial
9. Weight <50kg or a body mass index (BMI)greater than 35kg/m2
10. Previous occurrence of disease caused by Y pestis receipt of a vaccine against plague
11. Current active participation in another research study involving an investigational product (including receipt of an IMP within last 30 days) or where involvement in this study could impact the results

12. It is not in the best interest of the volunteer to participate in the trial, in the opinion of the Investigator

Date of first enrolment
15/02/2023

Date of final enrolment
31/03/2023

Locations

Countries of recruitment
Uganda

Study participating centre
MRC/UVRI and LSHTM Uganda Research Unit
Plot 2-5 Ntikko road
Masaka
Uganda
N/A

Sponsor information

Organisation
University of Oxford

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Sponsor type
University/education

Website
https://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
The University of Oxford and MRC/UVRI and LSHTM Uganda Research Unit will collaborate to publish the study results in a high-impact peer-reviewed journal.

Intention to publish date
30/09/2025

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication