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# A study of a new vaccine against Crimean-Congo Haemorrhagic Fever (a life-threatening tick-borne viral disease)

**Submission date**
21/04/2023

**Recruitment status**
No longer recruiting

**Registration date**
04/08/2023

**Overall study status**
Completed

**Last Edited**
04/09/2025

**Condition category**
Infections and Infestations

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

## Plain English summary of protocol

Background and study aims
Crimean-Congo haemorrhagic fever (CCHF) is caused by a virus which can result in severe illness and death. Cases occur in many parts of the world, including southern Europe, the Middle East, Africa and southwest Asia. The World Health Organisation estimates that 3 billion people live in areas at risk, and the CCHF virus infects up to 15,000 people per year, causing 500 deaths.
The virus is transmitted by ticks, which can live on many domestic and wild animals, including cattle, sheep and goats. Humans usually become infected after a tick bite, although the virus can also be caught from close contact with infected animals or humans. In some people Infection causes no symptoms, but in others it can cause very serious illness with impaired blood clotting, which can lead to severe bleeding. Up to 40% of people admitted to hospital with the infection die. There are currently no specific, effective treatments and there is no approved vaccine. The only vaccine for humans was developed in the early 1970s in Russia; it is not suitable for widespread use.

Who can participate?
Healthy volunteers aged 18 to 55 years.

What does the study involve?
All participants will attend a screening visit, to decide their eligibility obtain their consent to take part. At the next visit the first study vaccination will be given; the second will be given 12 weeks later. Any symptoms after the vaccinations will be recorded in an electronic diary. All participants will be followed up for one year after the first vaccination.
The first six participants will attend a total of 15 study visits (1 screening, 2 vaccination and 11 follow-up visits). The remaining participants will attend a total of 11 study visits (1 screening, 2 vaccination and 8 follow-up visits). All visits will include a blood test.

What are the possible benefits and risks of participating?
There are no benefits to participation. The most likely side effects that recipients of ChAdOx2 CCHF may experience are short-lived local (primarily injection site tenderness or pain) and systemic vaccine reactions (fatigue, headache, malaise, feverishness) that resolve completely

within days.
However, this is a first-in-human vaccine trial and there is a chance that participants could experience an unexpectedly severe side effect or a new, previously unseen, side effect.
As with any vaccine, the participants may experience some discomfort at the injection site. Usually this is mild but sometimes individuals experience more significant pain which might interfere with their usual activities. Post-vaccination arm pain usually resolves within a few days but may occasionally persist for up to a week or longer. Other less common symptoms around the injection site might include redness, swelling, itchiness or a feeling of warmth. In the first 24-48 hours after vaccination the participants may experience flu-like symptoms (muscle aches, joint aches, feverishness, chills, headache, nausea, tiredness and/or feeling generally unwell), which are expected to resolve within a few days.
ChAdOx1 and ChAdOx2 are closely related vectors, and vaccines based on these two platforms are likely to have similar safety profiles. Vaccine reaction symptoms were measured in the large ChAdOx1 COVID-19 vaccine trials involving over 10,000 volunteers.
Symptoms were mostly described as mild, although a minority described temporary moderate or severe-intensity symptoms. The dose given was equivalent to the dose in this trial. Individuals tend to have fewer and milder symptoms after their second dose.
The following conditions have been listed as extremely rare serious reactions following the ChAdOx1 COVID-19 vaccine: serious rare blood clot disorders, Guillain-Barré syndrome (rare neurological illness), inflammation of the spinal cord, anaphylaxis / serious allergic reactions, capillary leak syndrome, risk of bleeding with intramuscular administration. It is currently unknown whether these rare reactions may occur with other ChAdOx vaccines but investigators using ChAdOx2 CCHF should be alert to them.
With any new medicine or vaccine that is in early development, there is always a possibility of an unpredicted or unexpected side effect occurring. If the participants experience concerning or unexpected symptoms, they should seek urgent medical advice or phone the 24hr study contact number and speak to a study doctor.
When people are vaccinated with ChAdOx2 CCHF they should make the intended immune response against the CCHF virus. However, they may also make an immune response against the ChAdOx vector. There is a theoretical risk that receipt of a ChAdOx-based vaccine (such as the ChAdOx2 CCHF vaccine in this trial) might impair the response to future doses of ChAdOx-based (or other adenovirus-based) vaccines. Whether this effect occurs in practice is one of the questions that this study will investigate.
Before each vaccination, the on-going eligibility of the volunteer will be reviewed. ChAdOx2 CCHF will be administered intramuscularly according to vaccine administration SOPs. The injection site will be covered with a sterile dressing and the volunteer will stay at the trial site for observation, in case of immediate adverse events. After 30 min the sterile dressing will be removed, the injection site inspected and vital signs checked.
An oral thermometer, tape measure and electronic diary access will be given to each volunteer, with instructions on use, along with a contact card including the emergency 24-hour telephone number to contact the on-call study physician if needed.
Blood sampling may cause slight pain and occasionally bruising. Occasionally, people feel light-headed, nauseous or faint. The amounts of blood taken are fairly small and should be well tolerated by healthy adults.
As we carry out medical tests throughout the trial it is possible that we pick up previously unknown health issues. If abnormal results or undiagnosed conditions are found during the study, these would be discussed with the participants and, if they agree, their GP would be informed. The GP might carry out further investigations (blood tests, scans or referral to specialists).
The possible adverse effects of the ChAdOx2 CCHF vaccine on the outcome of pregnancy are unknown and pregnant women will be excluded from the study. Participants of childbearing potential will be required to use an effective contraceptive measure during the study. If a

volunteer becomes pregnant during the trial, she/they will be followed up for clinical safety assessment until the pregnancy outcome is determined with her/their ongoing consent. The baby will be followed up for up to 3 months after delivery. Male participants with female partners are not required to use barrier methods for contraception.
The study will be overseen by an independent Data Safety Monitoring Committee.

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

When is the study starting and how long is it expected to run for?
April 2023 to April 2025

Who is funding the study?
UK Research and Innovation

Who is the main contact?
1. Katrina Pollock, katrina.pollock@paediatrics.ox.ac.uk
2. Kavyashri Kashojhala, kavyashri.kashojhala@paediatrics.ox.ac.uk

# Contact information

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## Additional identifiers

### Clinical Trials Information System (CTIS)
2022-003889-20

### Integrated Research Application System (IRAS)
1007128

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
OVG2022/05, IRAS 1007128, CPMS 56015

## Study information

### Scientific Title
A phase 1 safety and immunogenicity study of a Crimean-Congo haemorrhagic fever virus vaccine, ChAdOx2 CCHF, in healthy adult volunteers in the UK

### Acronym
CCHF01

### Study objectives
Primary objective:
To assess the safety and tolerability of ChAdOx2 CCHF in healthy adult volunteers

Secondary objectives:
1. To assess the immunogenicity of ChAdOx2 CCHF vaccine in healthy adult volunteers
2. To compare the immunogenicity of ChAdOx2 CCHF vaccine in individuals previously vaccinated with a ChAdOx vaccine compared with ChAdOx naïve individuals

### Ethics approval required
Old ethics approval format

## Ethics approval(s)
1. Approved 16/01/2024, London - Harrow Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8357; harrow.rec@hra.nhs.uk), ref: 23/LO/0420
2. Approved 02/08/2023, London - Harrow Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8154, +44 (0)207 104 8357; harrow.rec@hra.nhs.uk), ref: 23/LO/0420

## Study design
Interventional non-randomized Phase I safety and immunogenicity study

## Primary study design
Interventional

## Study type(s)
Safety

## Health condition(s) or problem(s) studied
Crimean Congo Haemorrhagic Fever (CCHF)

## Interventions
Following completion of an online questionnaire volunteers will be invited for screening visit, consent and eligibility check. Eligible participants will be assigned to cohort 1 or cohort 2 based on cohort and participant availability until each cohort is complete. There will be an initial lead-in cohort (Cohort 1) of 6 participants, followed by a cohort of 40 participants (Cohort 2), divided into two groups according to whether the participant has previously received a ChAdOx vaccine (Group A) or is ChAdOx vaccine naïve (Group B). All participants will receive two doses of ChAdOx2 CCHF, 12 weeks apart. Blood samples will be collected at every visit for safety and immunology. The study is open-label and will not involve randomisation. Follow-up will be for 1 year.

## Intervention Type
Biological/Vaccine

## Phase
Phase I

## Drug/device/biological/vaccine name(s)
ChAdOx2 CCHF

## Primary outcome(s)
Current primary outcome measures as of 30/01/2024:
1. Occurrence of solicited local reactogenicity signs and symptoms as recorded in the e-diary, self-reported or investigator observed from D0 to D7 post-vaccination. Timepoints: 7 days following each vaccination (D0 to D7; V2 to V2+7)
2. Occurrence of solicited systemic reactogenicity signs and symptoms as recorded in the e-diary, self-reported or investigator observed from D0 to D7 post-vaccination; Timepoints: 7 days following each vaccination (D0 to D7; V2 to V2+7)
3. Occurrence of unsolicited adverse events (AEs) as recorded in the e-diary, self-reported or investigator observed from D0 to D28 post-vaccination; Timepoints: 28 days following each vaccination (D0 to D28; V2 to V2+28)

4. Occurrence of abnormal safety laboratory measures as recorded and graded in the eCRF by manual entry is specified time periods; Timepoints: Cohort 1: D0, D2, D7, D14, D28, D56, V2, V2+2, V2+7, V2+14, V2+28, V1 + 180, V1+365; Timepoints: Cohort 2: D0, D1, D14, D28, V2, V2+1, V2+14, V2+28, V1+180, V1+365
5. Occurrence of serious adverse events (SAEs) and adverse events of special interest (AESIs) throughout the study as recorded in eCRF; Timepoints: Whole duration of the study (D0 to V1 +365)

Previous primary outcome measures:
1. Occurrence of solicited local reactogenicity signs and symptoms as recorded in the e-diary, self-reported or investigator observed from D0 to D7 post-vaccination. Timepoints: 7 days following each vaccination (D0 to D7; V2 to V2+7)
2. Occurrence of solicited systemic reactogenicity signs and symptoms as recorded in the e-diary, self-reported or investigator observed from D0 to D7 post-vaccination; Timepoints: 7 days following each vaccination (D0 to D7; V2 to V2+7)
3. Occurrence of unsolicited adverse events (AEs) as recorded in the e-diary, self-reported or investigator observed from D0 to D28 post-vaccination; Timepoints: 28 days following each vaccination (D0 to D28; V2 to V2+28)
4. Occurrence of abnormal safety laboratory measures as recorded and graded in the eCRF by manual entry is specified time periods; Timepoints: Cohort 1: D0, D2, D7, D14, D28, D56, V2, V2+2, V2+7, V2+14, V2+28, V2+56, V2+140, V2+280; Timepoints: Cohort 2: D0, D1, D14, D28, V2, V2+1, V2+14, V2+28, V2+140, V2+280
5. Occurrence of serious adverse events (SAEs) and adverse events of special interest (AESIs) throughout the study as recorded in eCRF; Timepoints: Whole duration of the study (D0 to V2+280)

### Key secondary outcome(s))
Anti-CCHF glycoprotein-specific serological response as measured by the laboratory for cohorts 1 and 2 on D0, D28, V2, V2+28

### Completion date
10/04/2025

## Eligibility

### Key inclusion criteria
1. Adults aged between 18 to 55 years (inclusive).
2. In good health as determined by:
2.1. Medical history
2.2. Physical examination
2.3. Clinical judgement of the Investigators
3. Able to attend the scheduled visits and to comply with all study procedures, including internet access for the recording of electronic diary cards.
4. Willing and able to give informed consent for participation in the study.
5. Willing to allow confirmation of past medical history either through provision of a GP medical record summary, allowing investigators to obtain a copy of their medical history from their GP practice, or by providing an alternative acceptable means of confirming their past medical history.
6. Willing to allow their GP and/or consultant, if appropriate, to be notified of participation in the study.
7. Willing to provide their national insurance number or passport number to be registered on

The Over-Volunteering Prevention System (TOPS).
8. Agree to refrain from blood donation during the course of the study.
9. For participants of childbearing potential only (as defined by protocol section 8.3): willing to use effective contraception from one month prior to receiving the first dose of vaccine and for the duration of enrolment in the study (and for a minimum of 18 weeks after final study vaccination) AND have a negative high-sensitivity urine pregnancy test on the days of screening and vaccination.

### 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
46

### Key exclusion criteria
1. Participation in another research study involving an investigational product, or which includes procedures that could compromise the integrity of this study (such as significant volumes of blood already taken), within the 12 weeks prior to enrollment, or planned participation in such a study within the trial period.
2. History of previous confirmed or suspected CCHF infection.
3. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate.
4. Any confirmed or suspected immunosuppressive or immunodeficient state, including HIV infection; asplenia; severe infection(s); 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 consecutive days within the previous 3 months).
5. History of anaphylaxis in relation to vaccination.
6. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine including hypersensitivity to the active substance or to any of the excipients of the IMP.
7. History of hereditary angioedema, acquired angioedema, or idiopathic angioedema.
8. History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ).
9. History of any serious psychiatric condition likely to affect participation in the study.
10. For participants of childbearing potential only: participants who are pregnant, breastfeeding or lactating, or are planning pregnancy during the study.
11. History of a bleeding disorder (e.g., factor deficiency, coagulopathy or platelet disorder), or

prior history of significant bleeding or bruising following IM injections or venepuncture.
12. History of confirmed major thrombotic event (including cerebral venous sinus thrombosis, deep vein thrombosis, pulmonary embolism); history of antiphospholipid syndrome, or history of heparin induced thrombocytopenia.
13. History of episodes of capillary leak syndrome.
14. Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder, or neurological illness, as judged by the Investigator (note, mild/moderate well-controlled co-morbidities are acceptable)
15. Suspected or known current alcohol abuse as defined by an alcohol intake of greater than 14 units per week, or an abnormal GGT
16. Suspected or known injecting drug use within the 5 years preceding enrolment.
17. Detectable circulating hepatitis B surface antigen (HBsAg).
18. Seropositive for hepatitis C virus (antibodies to HCV).
19. Seropositive for HIV.
20. Any clinically significant finding 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.
21. Member of the study team. This is deliberately loosely defined, but at a minimum will include: anyone on the delegation log; anyone who might be anticipated to be placed onto the delegation log in the course of the study; anyone who has access to personal data on study participants (beyond name, contact details, DOB); and anyone who attends meetings where details of the study are discussed, for example safety updates.

Temporary exclusion criteria:
1. Receipt of any systemic corticosteroid (or equivalent) treatment within 14 days prior to vaccination, or for more than 7 days consecutively within the previous 3 months.
2. Febrile illness (oral temperature ≥37.5°C) or systemically unwell on the day of vaccination.
3. Receipt of systemic antibiotics will result in vaccination being postponed until 7 days after the last antibiotic dose. This does not apply to topical antibiotic preparations.
4. Use of antipyretics in the 4 hours prior to vaccination.
5. Occurrence of a laboratory adverse event, which in the opinion of the Investigator, requires further time and/or investigation to resolve or stabilize prior to a dose of vaccine being administered.
6. Occurrence of any illness or adverse event, which in the opinion of the investigator, requires of further time and/or investigation to resolve or stabilize prior to a dose of vaccine being administered.
7. Receipt of any vaccines administered within 30 days of study vaccines (before or after) EXCEPT for influenza and COVID-19 vaccines*, which must not be given within 14 days of the study vaccines (before or after).
8. Immunisation with a ChAdOx1- or ChAdOx2-vectored vaccine less than 6 months before the first study vaccination visit.
9. Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer if included in the study, affect the ability of the volunteer to to participate in the study, or impair interpretation of the study data.

## Date of first enrolment
15/08/2023

## Date of final enrolment
31/12/2023

# Locations

**Countries of recruitment**
United Kingdom

**Study participating centre**
**Not provided at time of registration**
United Kingdom
-

# Sponsor information

**Organisation**
University of Oxford

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

# Funder(s)

**Funder type**
Government

**Funder Name**
UK Research and Innovation

**Alternative Name(s)**
UKRI

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

# Results and Publications

## 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

Other, Data sharing statement to be made available at a later date

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |
| Protocol file | version 2.0 | 14/07/2023 | 03/08/2023 | No | No |
| Protocol file | version 3.0 | 22/09/2023 | 30/01/2024 | No | No |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |