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A first-in-human study to assess the safety of an MVA-based vaccine for Crimean-Congo Haemorrhagic Fever (MVA-CCHF) and the vaccine's ability to generate an immune response

Submission date
03/02/2020

Recruitment status
No longer recruiting

Registration date
10/11/2021

Overall study status
Completed

Last Edited
11/06/2025

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
The Crimean-Congo Haemorrhagic Fever (CCHF) Virus is a fatal disease that has spread across many countries in Africa, Middle East, Asia and Eastern Europe. This infection is spread by ticks and has a fatality rate of up to 80% with symptoms causing bruising, bleeding and organ failure. Currently there are no approved treatments for this disease. As a result of this we are proposing to conduct a Phase I study with a primary objective to assess the safety and immune response of a new vaccine for CCHF (MVA-CCHF).

Who can participate?
Healthy adults aged 18 to 45 years. Female volunteers of childbearing potential are required to use an effective form of contraception for the duration of their participation in the study.

What does the study involve?
Healthy volunteers will each receive 2 vaccinations (on Day 0 and Day 28). Participants will be in the study for 12 months with approximately 13 scheduled visits; these will include screening, vaccination and follow up visits.

What are the possible benefits and risks of participating?
Possible benefits: Volunteers will not benefit directly from participation in this study. It is hoped that the information gained from this study will contribute to the development of a safe, effective and versatile vaccine programme against Crimean Congo Haemorrhagic Fever.
Possible risks: Localised bruising and discomfort at the site of venepuncture. Allergic reaction to the vaccine

Where is the study run from?
Southampton General Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2020 to June 2025

Who is funding the study?
1. Innovate UK
2. National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Lisa Crumpler, Lisa.crumpler@uhs.nhs.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2019-004724-38

Integrated Research Application System (IRAS)
268347

Protocol serial number
CPMS 44608, IRAS 268347

Study information

Scientific Title
A phase I study to assess the safety and immunogenicity of an MVA-based vaccine for Crimean-Congo Haemorrhagic Fever (MVA-CCHF)

Study objectives
1. To assess the humeral and cellular immunogenicity of the candidate vaccine MVA-CCHF in humans
2. To assess the safety, tolerability and reactogenicity profile of the candidate vaccine MVA-CCHF in humans

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/03/2020, South Central - Oxford A Research Ethics Committee (Whitefriars Level 3 Block B, Lewins Mead, Bristol, Greater Bristol, United Kingdom, BS1 2NT, UK; +44 (0)207 104 8290; oxforda.rec@hra.nhs.uk), ref: 20/FC/0038

Study design
Interventional non-randomized study

Primary study design
Interventional

Study type(s)
Treatment, Safety, Efficacy

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

Interventions
Current intervention as of 09/05/2025:
Study design:
Open label, single-centre, first-in-human, dose escalation Phase I Crimean-Congo Haemorrhagic Fever (CCHF) vaccine trial.

Rationale for the study:
Currently there are no licensed vaccines to CCHF. The study intends to generate data regarding the safety, reactogenicity (study of the property of a vaccine being able to produce expected adverse events such as bruising, redness, swelling) and immunogenicity (i.e. ability of the vaccine to stimulate immune response) of the MVA-CCHF vaccine.

Study presence and duration:
18 healthy volunteers (male and female) aged 18-45 years old will take part in the study. Single centre – UK Southampton. The study will last 24 months, and the participants will be enrolled in the study for 12 months after their Day 0 visit – after being consented and screened. Volunteers will be vaccinated twice (on Day 0 and Day 28) and will be in the study for a total of 12 months with 13 scheduled visits.

Before a participant takes part in the study:
The study information sheet will be made available to the volunteer at least 24 hours prior to the screening visit.

Screening visit:
- At the screening visit, the investigator will go through the inclusion and exclusion criteria and ensure that the volunteer is eligible to proceed.
- The volunteer will be fully informed of all aspects of the trial, the potential risks and their obligations. The aims of the study and all tests to be carried out will be explained. The volunteer will be given the opportunity to ask any questions that they have and will then have time to consider whether or not to participate.
- If they do decide to participate, they will sign and date the consent form and will be given a copy to take away. The original will kept and stored as source documentation. These forms will also be signed and dated by the Investigator.
- the investigator will then collect the medical history, concomitant medications and review contraindications.
- the investigator will then carry out physical examination, observations, ECG, blood and urine tests.
- female volunteers will have a pregnancy test

After the screening visit:
- The volunteer's GP will be contacted to corroborate their medical history. Volunteers will only be enrolled in the study if written or verbal information regarding the volunteer's medical history is obtained from the GP. In cases where verbal information is provided, the investigator conducting the telephone call will document the discussion in the volunteer's medical notes.
- any abnormal clinical findings from the medical history, physical examination and all tests at screening will be assessed by a clinician referring to site-specific laboratory adverse event grading tables. Any abnormal test result deemed clinically significant may be repeated to ensure it is not a single occurrence. If an abnormal finding is deemed to be clinically significant, the volunteer will be informed, and appropriate medical care arranged with the permission of the volunteer.
- the eligibility of the volunteer will be reviewed by the study clinician at the end of the screening visit and again when all results from the screening visit have been considered and a copy of the volunteer's medical history has been received from the GP. Decisions to exclude the volunteer from enrolling in the trial or to withdraw a volunteer from the trial will be at the discretion of the Investigator. If eligible, a day 0 visit will be scheduled for the volunteer to receive the vaccine.
- Volunteers will be allocated a 3-digit subject identifier code (SIC). This will be allocated by the site reflecting the order of consent to the study within the site.

Day 0 – Vaccination:
- the volunteer is enrolled into a study group for vaccination
(Volunteers will be enrolled into each group or subgroup sequentially, there is no randomisation on this trial).
- volunteers will be informed of which group they are enrolled into.

Day 0 and day 28 – Vaccination visits:
- the investigator will re-check inclusion and exclusion criteria, an abbreviated physical examination (at the investigator's discretion) and measurement of physical observations.
- if medical status and/or physical examination suggest significant changes have occurred since screening, the Day 0 visit can be re-scheduled, or the subject excluded from the study if he/she fails to meet the inclusion and exclusion criteria.
- the study team will advise the volunteer prior to the dosing visit that receipt of licensed vaccines e.g. (FLU vaccine) is not permitted within the month preceding vaccination or the month following each vaccination. Should a volunteer have received a licensed vaccine in the month prior to MVA-CCHF vaccination the Day 0 visit will be rescheduled to an acceptable time-point.
- before vaccination, the investigator must check for any symptoms of an acute illness or body temperature >37.5°C. In such a situation, the subject may be vaccinated at a later date within the screening window or be withdrawn at the discretion of the investigator.
- if the second vaccine is administered at a later date due to an interim positive test for COVID-19, all subsequent visit windows will be adjusted according to the time of delay of the second dose of vaccine.
- female volunteers will have a pregnancy test
- the volunteer is vaccinated
- after the vaccine administration, volunteers will be observed for a minimum of 60 minutes to monitor for the development of any acute reactions, or longer if deemed necessary.
- volunteers will be provided with a diary card, thermometer, and ruler to measure and record body temperature, solicited local and systemic AEs.
- If the volunteer has remained well during this observation period, they may go home and will return to the study site the next day.
- If at any point following vaccination, the CI or local safety monitor identifies any acute clinical concern requiring urgent medical intervention, an acute admission for further clinical management will be arranged.

Subsequent visits: Days: 1, 3, 7, 14, 29, 31, weeks: 5, 6, 8, 12, 26, 52
Volunteers will return to the study site for follow up visits.
- Diary cards will be reviewed for details of solicited and unsolicited AEs for 28 days after each vaccination, and any new or undocumented medical issues or symptoms that have arisen will be assessed.
- Physical observations and venepuncture for immunology and safety bloods will be undertaken as per the applicable schedule of events. Information on medications administered will be recorded.
- On Day 3 and Day 31, volunteers that have been enrolled in Group 1 will be contacted via telephone to collect safety information (solicited and unsolicited AEs, SAEs and concomitant medications).

Dose escalation methodology and group allocation:
Volunteers will be enrolled into each group or subgroup sequentially, there is no randomisation on this trial.

Group 1 has 4 subgroups:
Subgroup 1A: 6 volunteers; 2 doses of MVA-CCHF at ≤1 x 107 pfu intramuscularly
Subgroup 1Bi – 2 volunteers, 2 doses of MVA-CCHF at ≤1.5 x 107 pfu, intramuscularly
Subgroup 1Bii: 4 volunteers; 2 doses of MVA-CCHF at ≤1x108pfu intramuscularly
Subgroup 1C: 6 volunteers; 2 doses of MVA-CCHF at ≤2x108 pfu intramuscularly

An independent safety review will be carried out by the local safety committee once all volunteers in each subgroup have received the first and second dose of MVA-CCHF and have attended the week 5 (7 days post second vaccine dose) follow up visit.
Safety data will be reviewed by the local safety committee prior to a decision being made on whether it is safe to dose escalate. This will include review of adverse events, safety blood results, physical observations, concomitant medications, diary card review and any other findings deemed relevant by the investigator or local safety committee.
Confirmation that the local safety committee have deemed it is safe to dose escalate is required prior to dosing volunteers in subsequent subgroups.
This strategy allows independent scrutiny of the data prior to dose escalation. As the MVA component of this vaccine has been used in previous clinical studies six volunteers in each dose group is considered to be sufficient to determine the safety of this vaccine.

Establishment of dose safety:
The first volunteer to receive each dose will be vaccinated alone and then reviewed on the day following vaccination and contacted (by the site team) via telephone on Day 3.
An interim safety review will then take place where the local safety monitor will review adverse event, safety data and diary completion prior to making a decision on further enrolment.
Providing there are no safety concerns, as assessed by the local safety monitor and Principal investigator, a further two volunteers may be vaccinated 3 days after the first volunteer, at least one hour apart. This will be repeated once the additional two volunteers have received a dose of the vaccine and have attended the day 3 telephone follow up. Providing that there are no safety concerns, as assessed by the local safety monitor and chief investigator, a further three volunteers may be vaccinated 3 days after the first volunteer, at least one hour apart.

The above steps will be repeated once the first volunteer in each subgroup has received the second dose of MVA-CCHF, prior to proceeding with administering a second dose to the following volunteers. Should data become available during the telephone call with a volunteer on Day 3 or Day 31 that may adversely impact the decision to enrol further volunteers, the volunteer will be invited to the study site for an unscheduled visit for further review.

Volunteer withdrawal:
In accordance with the principles of the current revision of the Declaration of Helsinki and any other applicable regulations, a volunteer has the right to withdraw from the study at any time and for any reason, and is not obliged to give his or her reasons for doing so. The Investigator may withdraw the volunteer at any time in the interests of the volunteer's health and well-being.
In addition, the volunteer may withdraw/be withdrawn for any of the following reasons:
- Administrative decision by the Investigator
- Ineligibility (either arising during the study or retrospectively, having been overlooked at screening)
- Significant protocol deviation.
- Volunteer non-compliance with study requirements.
- An AE, which requires discontinuation of the study involvement or results in inability to continue to comply with study procedures.
- Pregnancy

The reason for withdrawal will be recorded in the eCRF. If withdrawal is due to an AE, appropriate follow-up visits or medical care will be arranged, with the agreement of the volunteer, until the AE has resolved, stabilised or a non-trial related causality has been assigned.

If a volunteer withdraws from the study, blood samples collected before their withdrawal from the trial will be used/ stored unless the volunteer specifically requests otherwise.

In all cases of subject withdrawal, except for those of complete consent withdrawal, long-term safety data collection including some procedures such as safety bloods, may continue as appropriate if subjects have received one or more vaccine doses and have indicated willingness to attend a relevant follow-up time point.

Should a volunteer decide that they do not want to proceed with receiving a second dose of MVA-CCHF after receiving the first dose but agree to continue attending follow up visits they will be asked to attend at Day 1, Day 3 (telephone call), Day 7, Day 14, Day 28, Month 3, Month 6 and Month 12.

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Previous intervention from 22/06/2023 to 09/05/2025:
Study design:
Open label, single-centre, first-in-human, dose escalation Phase I Crimean-Congo Haemorrhagic Fever (CCHF) vaccine trial.

Rationale for the study:
Currently there are no licensed vaccines to CCHF. The study intends to generate data regarding the safety, reactogenicity (study of the property of a vaccine being able to produce expected adverse events such as bruising, redness, swelling) and immunogenicity (i.e. ability of the vaccine to stimulate immune response) of the MVA-CCHF vaccine.

Study presence and duration:
18 healthy volunteers (male and female) aged 18-45 years old will take part in the study. Single centre – UK Southampton. The study will last 24 months, and the participants will be enrolled in the study for 12 months after their Day 0 visit – after being consented and screened. Volunteers will be vaccinated twice (on Day 0 and Day 28) and will be in the study for a total of 12 months with 13 scheduled visits.

Before a participant takes part in the study:
The study information sheet will be made available to the volunteer at least 24 hours prior to the screening visit.

Screening visit:
- At the screening visit, the investigator will go through the inclusion and exclusion criteria and ensure that the volunteer is eligible to proceed.
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- If they do decide to participate, they will sign and date the consent form and will be given a copy to take away. The original will kept and stored as source documentation. These forms will also be signed and dated by the Investigator.
- the investigator will then collect the medical history, concomitant medications and review contraindications.

- the investigator will then carry out physical examination, observations, ECG, blood and urine tests.
- female volunteers will have a pregnancy test

After the screening visit:
- The volunteer's GP will be contacted to corroborate their medical history. Volunteers will only be enrolled in the study if written or verbal information regarding the volunteer's medical history is obtained from the GP. In cases where verbal information is provided, the investigator conducting the telephone call will document the discussion in the volunteer's medical notes.
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Dose escalation methodology and group allocation:
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Group 1 has 3 subgroups:
Group 1A – 6 volunteers will receive 2 doses of MVA-CCHF vaccine at a concentration of 1 x 10^7 pfu
Group 1B – 6 volunteers will receive 2 doses of MVA-CCHF vaccine at a concentration of 1.5 x 10^7 pfu
Group 1C – 6 volunteers will receive 2 doses of MVA-CCHF vaccine at a concentration of 3 x 10^7 pfu

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Safety data will be reviewed by the local safety committee prior to a decision being made on whether it is safe to dose escalate. This will include review of adverse events, safety blood results, physical observations, concomitant medications, diary card review and any other findings deemed relevant by the investigator or local safety committee.
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Dose escalation methodology and group allocation:
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An independent safety review will be carried out by the local safety committee once all volunteers in each subgroup have received the first and second dose of MVA-CCHF and have attended the week 5 (7 days post second vaccine dose) follow up visit.
Safety data will be reviewed by the local safety committee prior to a decision being made on whether it is safe to dose escalate. This will include review of adverse events, safety blood results, physical observations, concomitant medications, diary card review and any other findings deemed relevant by the investigator or local safety committee.
Confirmation that the local safety committee have deemed it is safe to dose escalate is required prior to dosing volunteers in subsequent subgroups.
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In accordance with the principles of the current revision of the Declaration of Helsinki and any other applicable regulations, a volunteer has the right to withdraw from the study at any time and for any reason, and is not obliged to give his or her reasons for doing so. The Investigator may withdraw the volunteer at any time in the interests of the volunteer's health and well-being.
In addition, the volunteer may withdraw/be withdrawn for any of the following reasons:
- Administrative decision by the Investigator
- Ineligibility (either arising during the study or retrospectively, having been overlooked at screening)
- Significant protocol deviation.
- Volunteer non-compliance with study requirements.

- An AE, which requires discontinuation of the study involvement or results in inability to continue to comply with study procedures.
- Pregnancy

The reason for withdrawal will be recorded in the eCRF. If withdrawal is due to an AE, appropriate follow-up visits or medical care will be arranged, with the agreement of the volunteer, until the AE has resolved, stabilised or a non-trial related causality has been assigned.

If a volunteer withdraws from the study, blood samples collected before their withdrawal from the trial will be used/ stored unless the volunteer specifically requests otherwise.

In all cases of subject withdrawal, except for those of complete consent withdrawal, long-term safety data collection including some procedures such as safety bloods, may continue as appropriate if subjects have received one or more vaccine doses and have indicated willingness to attend a relevant follow-up time point.

Should a volunteer decide that they do not want to proceed with receiving a second dose of MVA-CCHF after receiving the first dose but agree to continue attending follow up visits they will be asked to attend at Day 1, Day 3 (telephone call), Day 7, Day 14, Day 28, Month 3, Month 6 and Month 12.

Previous intervention:
Study design:
Open label, single-centre, first-in-human, dose escalation Phase I Crimean-Congo Haemorrhagic Fever (CCHF) vaccine trial.

Rationale for the study:
Currently there are no licensed vaccines to CCHF. The study intends to generate data regarding the safety, reactogenicity (study of the property of a vaccine being able to produce expected adverse events such as bruising, redness, swelling) and immunogenicity (i.e. ability of the vaccine to stimulate immune response) of the MVA-CCHF vaccine.

Study presence and duration:
24 healthy volunteers (male and female) aged 18-45 years old will take part in the study. Single centre – UK Southampton. The study will last 24 months, and the participants will be enrolled in the study for 12 months after their Day 0 visit – after being consented and screened. Volunteers will be vaccinated twice (on Day 0 and Day 28) and will be in the study for a total of 12 months with 13 scheduled visits.

Before a participant takes part in the study:
The study information sheet will be made available to the volunteer at least 24 hours prior to the screening visit.

Screening visit:
- At the screening visit, the investigator will go through the inclusion and exclusion criteria and ensure that the volunteer is eligible to proceed.
- The volunteer will be fully informed of all aspects of the trial, the potential risks and their obligations. The aims of the study and all tests to be carried out will be explained. The volunteer will be given the opportunity to ask any questions that they have and will then have time to consider whether or not to participate.
- If they do decide to participate, they will sign and date the consent form and will be given a

copy to take away. The original will kept and stored as source documentation. These forms will also be signed and dated by the Investigator.
- the investigator will then collect the medical history, concomitant medications and review contraindications.
- the investigator will then carry out physical examination, observations, ECG, blood and urine tests.
- female volunteers will have a pregnancy test

After the screening visit:
- The volunteer's GP will be contacted to corroborate their medical history. Volunteers will only be enrolled in the study if written or verbal information regarding the volunteer's medical history is obtained from the GP. In cases where verbal information is provided, the investigator conducting the telephone call will document the discussion in the volunteer's medical notes.
- any abnormal clinical findings from the medical history, physical examination and all tests at screening will be assessed by a clinician referring to site-specific laboratory adverse event grading tables. Any abnormal test result deemed clinically significant may be repeated to ensure it is not a single occurrence. If an abnormal finding is deemed to be clinically significant, the volunteer will be informed, and appropriate medical care arranged with the permission of the volunteer.
- the eligibility of the volunteer will be reviewed by the study clinician at the end of the screening visit and again when all results from the screening visit have been considered and a copy of the volunteer's medical history has been received from the GP. Decisions to exclude the volunteer from enrolling in the trial or to withdraw a volunteer from the trial will be at the discretion of the Investigator. If eligible, a day 0 visit will be scheduled for the volunteer to receive the vaccine.
- Volunteers will be allocated a 3-digit subject identifier code (SIC). This will be allocated by the site reflecting the order of consent to the study within the site.

Day 0 – Vaccination:
- the volunteer is enrolled into a study group for vaccination
(Volunteers will be enrolled into each group or subgroup sequentially, there is no randomisation on this trial).
- volunteers will be informed of which group they are enrolled into.

Day 0 and day 28 – Vaccination visits:
- the investigator will re-check inclusion and exclusion criteria, an abbreviated physical examination (at the investigator's discretion) and measurement of physical observations.
- if medical status and/or physical examination suggest significant changes have occurred since screening, the Day 0 visit can be re-scheduled, or the subject excluded from the study if he/she fails to meet the inclusion and exclusion criteria.
- the study team will advise the volunteer prior to the dosing visit that receipt of licensed vaccines e.g. (FLU vaccine) is not permitted within the month preceding vaccination or the month following each vaccination. Should a volunteer have received a licensed vaccine in the month prior to MVA-CCHF vaccination the Day 0 visit will be rescheduled to an acceptable time-point.
- before vaccination, the investigator must check for any symptoms of an acute illness or body temperature >37.5°C. In such a situation, the subject may be vaccinated at a later date within the screening window or be withdrawn at the discretion of the investigator.
- if the second vaccine is administered at a later date due to an interim positive test for COVID-19, all subsequent visit windows will be adjusted according to the time of delay of the second dose of vaccine.
- female volunteers will have a pregnancy test

- the volunteer is vaccinated
- after the vaccine administration, volunteers will be observed for a minimum of 60 minutes to monitor for the development of any acute reactions, or longer if deemed necessary.
- volunteers will be provided with a diary card, thermometer, and ruler to measure and record body temperature, solicited local and systemic AEs.
- If the volunteer has remained well during this observation period, they may go home and will return to the study site the next day.
- If at any point following vaccination, the CI or local safety monitor identifies any acute clinical concern requiring urgent medical intervention, an acute admission for further clinical management will be arranged.

Subsequent visits: Days: 1, 3, 7, 14, 29, 31, weeks: 5, 6, 8, 12, 26, 52
Volunteers will return to the study site for follow up visits.
- Diary cards will be reviewed for details of solicited and unsolicited AEs for 28 days after each vaccination, and any new or undocumented medical issues or symptoms that have arisen will be assessed.
- Physical observations and venepuncture for immunology and safety bloods will be undertaken as per the applicable schedule of events. Information on medications administered will be recorded.
- On Day 3 and Day 31, volunteers that have been enrolled in Group 1 will be contacted via telephone to collect safety information (solicited and unsolicited AEs, SAEs and concomitant medications).

Dose escalation methodology and group allocation:
Volunteers will be enrolled into each group or subgroup sequentially, there is no randomisation on this trial.

Group 1 has 3 subgroups:
Group 1A – 6 volunteers will receive 2 doses of MVA-CCHF vaccine at a concentration of 1 x 10^7 pfu
Group 1B – 6 volunteers will receive 2 doses of MVA-CCHF vaccine at a concentration of 5 x 10^7 pfu
Group 1C – 6 volunteers will receive 2 doses of MVA-CCHF vaccine at a concentration of 1 x 10^8 pfu

Group 2 – 6 volunteers will receive 2 doses of MVA-CCHF vaccine at the most tolerated and immunogenic dose from Group 1.

An independent safety review will be carried out by the local safety committee once all volunteers in each subgroup have received the first and second dose of MVA-CCHF and have attended the week 5 (7 days post second vaccine dose) follow up visit.
Safety data will be reviewed by the local safety committee prior to a decision being made on whether it is safe to dose escalate. This will include review of adverse events, safety blood results, physical observations, concomitant medications, diary card review and any other findings deemed relevant by the investigator or local safety committee.
Confirmation that the local safety committee have deemed it is safe to dose escalate is required prior to dosing volunteers in subsequent subgroups.
Enrolment in the dose expansion phase of the study (Group 2) can only commence once the dose of MVA-CCHF to be used has been confirmed by the local safety committee.
This strategy allows independent scrutiny of the data prior to dose escalation. As the MVA component of this vaccine has been used in previous clinical studies six volunteers in each dose group is considered to be sufficient to determine the safety of this vaccine.

Establishment of dose safety:
The first volunteer to receive each dose will be vaccinated alone and then reviewed on the day following vaccination and contacted (by the site team) via telephone on Day 3.
An interim safety review will then take place where the local safety monitor will review adverse event, safety data and diary completion prior to making a decision on further enrolment.
Providing there are no safety concerns, as assessed by the local safety monitor and Principal investigator, a further two volunteers may be vaccinated 3 days after the first volunteer, at least one hour apart. This will be repeated once the additional two volunteers have received a dose of the vaccine and have attended the day 3 telephone follow up. Providing that there are no safety concerns, as assessed by the local safety monitor and chief investigator, a further three volunteers may be vaccinated 3 days after the first volunteer, at least one hour apart.

The above steps will be repeated once the first volunteer in each subgroup has received the second dose of MVA-CCHF, prior to proceeding with administering a second dose to the following volunteers. Should data become available during the telephone call with a volunteer on Day 3 or Day 31 that may adversely impact the decision to enrol further volunteers, the volunteer will be invited to the study site for an unscheduled visit for further review.

Volunteer withdrawal:
In accordance with the principles of the current revision of the Declaration of Helsinki and any other applicable regulations, a volunteer has the right to withdraw from the study at any time and for any reason, and is not obliged to give his or her reasons for doing so. The Investigator may withdraw the volunteer at any time in the interests of the volunteer's health and well-being. In addition, the volunteer may withdraw/be withdrawn for any of the following reasons:
- Administrative decision by the Investigator
- Ineligibility (either arising during the study or retrospectively, having been overlooked at screening)
- Significant protocol deviation.
- Volunteer non-compliance with study requirements.
- An AE, which requires discontinuation of the study involvement or results in inability to continue to comply with study procedures.
- Pregnancy

The reason for withdrawal will be recorded in the eCRF. If withdrawal is due to an AE, appropriate follow-up visits or medical care will be arranged, with the agreement of the volunteer, until the AE has resolved, stabilised or a non-trial related causality has been assigned.

If a volunteer withdraws from the study, blood samples collected before their withdrawal from the trial will be used/ stored unless the volunteer specifically requests otherwise.

In all cases of subject withdrawal, except for those of complete consent withdrawal, long-term safety data collection including some procedures such as safety bloods, may continue as appropriate if subjects have received one or more vaccine doses and have indicated willingness to attend a relevant follow-up time point.

Should a volunteer decide that they do not want to proceed with receiving a second dose of MVA-CCHF after receiving the first dose but agree to continue attending follow up visits they will be asked to attend at Day 1, Day 3 (telephone call), Day 7, Day 14, Day 28, Month 3, Month 6 and Month 12.

Intervention Type

Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
MVA-CCHF vaccine

Primary outcome(s)
Safety, reactogenicity, and adverse events measured using patient records:
1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following each vaccination
2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following vaccination
3. Occurrence of unsolicited adverse events for 28 days following the first vaccination and for subsequent vaccinations from time of vaccination through the following 28 days
4. Change from baseline for safety laboratory measures for 28 days following each vaccination
5. Occurrence of serious adverse events within 28 days (day of vaccination and 27 subsequent days) after each vaccination and over the whole study duration. Solicited and unsolicited AE data will be collected at each clinic visit. It will be collected from diary cards, clinical review, clinical examination (including observations) and laboratory results. This AE data will be tabulated and frequency, duration and severity of AEs compared between groups. Haematological and biochemical laboratory values will be presented according to toxicity grading scales and tabulated by group. SAEs, AEs of special interest and withdrawal due to AE(s)/SAE(s) will be described in detail.

Key secondary outcome(s))
Current secondary outcome measures as of 06/04/2023:
The cellular and humoral immunogenicity of MVA-CCHF measured by Enzyme Linked ImmunoSpot (ELISpot) and relative quantities of IgG specific to the CCHF glycoprotein and vaccinia virus antigens will be measured by Enzyme Linked Immunosorbant Assay (ELISA) for 1 year following first dose of vaccination

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Previous secondary outcome measures:
The cellular and humoral immunogenicity of MVA-CCHF measured by Enzyme Linked ImmunoSpot (ELISpot) and relative quantities of IgG specific to the CCHF glycoprotein will be measured by Enzyme Linked Immunosorbant Assay (ELISA) for 1 year following first dose of vaccination

Completion date
30/06/2025

Eligibility

Key inclusion criteria
1. Healthy adults aged 18 to 45 years
2. Able and willing (in the Investigator’s opinion) to comply with all study requirements
3. Willing to allow the Investigators to discuss the volunteer’s medical history with their General Practitioner (GP)
4. Willingness to practice continuous effective contraception (see below) during the study and

(for females only) a negative pregnancy test on the day(s) of screening and vaccination
5. Agreement to refrain from blood donation during the course of the study
6. Provide written informed consent
7. Female volunteers of childbearing potential are required to use an effective form of contraception for the duration of their participation in the study. Acceptable forms of contraception for female volunteers are as follows:
7.1.Established use of oral, injected or implanted hormonal methods of contraception
7.2. Placement of an intrauterine device or intrauterine system
7.3. Total abdominal hysterectomy or surgical sterilisation
7.4. Barrier methods of contraception (condom or occlusive cap with spermicide)
7.5. Male sterilisation if the vasectomised partner is the sole partner for the subject
7.6. True abstinence when this is in line with the preferred and usual lifestyle of the subject

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
18

Key exclusion criteria
Current exclusion criteria as of 06/04/2023:
1. Participation in another research study involving receipt of an investigational product in the 30 days preceding receipt of MVA-CCHF, or planned use during the study period
2. Prior receipt of an MVA based vaccine or other investigational vaccine likely to impact on interpretation of the trial data, as assessed by the investigator
3. Any medical condition that in the judgment of the investigator would make intramuscular (IM) injection unsafe
4. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate
5. Confirmed or under investigation for immunosuppressive or immunodeficient state, including HIV infection; asplenia; recurrent, severe infections and chronic (more than 14 days) immunosuppressant medication during the period starting six months prior to the first vaccine dose. For corticosteroids, this will mean prednisone 20 mg/day (for adult subjects), or equivalent. Inhaled and topical steroids are allowed
6. Administration of long-acting immune-modifying drugs at any time during the study period (e. g. infliximab)
7. History of CCHF anti-viral treatment within 60 days prior to vaccination
8. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine

9. Any history of anaphylaxis in relation to vaccination
10. Pregnancy, lactation or willingness/intention to become pregnant during the study
11. History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ)
12. History of serious psychiatric condition likely to affect participation in the study
13. Any other serious, chronic illness requiring hospital specialist supervision
14. Suspected or known current alcohol abuse as defined by an alcohol intake of greater than 42 units every week
15. Suspected or known injecting drug abuse in the 5 years preceding enrolment
16. Seropositive for hepatitis B surface antigen (HBsAg)
17. Seropositive for hepatitis C virus (antibodies to HCV)
18. Known positive HIV test
19. History of clinical CCHF
20. Any clinically significant abnormal finding on screening biochemistry or haematology blood tests or urinalysis
21. Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study/comply with study requirements or impair interpretation of the study data
22. Inability of the study team to contact the volunteer's GP to confirm medical history and safety to participate

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Previous exclusion criteria:
1. Participation in another research study involving receipt of an investigational product in the 30 days preceding receipt of MVA-CCHF, or planned use during the study period
2. Prior receipt of an MVA based vaccine or other investigational vaccine likely to impact on interpretation of the trial data, as assessed by the investigator
3. Any medical condition that in the judgment of the investigator would make intramuscular (IM) injection unsafe
4. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate
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15. Suspected or known injecting drug abuse in the 5 years preceding enrolment
16. Seropositive for hepatitis B surface antigen (HBsAg)
17. Seropositive for hepatitis C virus (antibodies to HCV)
18. Known positive HIV test

19. History of clinical CCHF
20. Travel to a CCHF endemic region during the study period or within the previous six months
21. Any clinically significant abnormal finding on screening biochemistry or haematology blood tests or urinalysis
22. Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study/comply with study requirements or impair interpretation of the study data
23. Inability of the study team to contact the volunteer's GP to confirm medical history and safety to participate

Date of first enrolment
15/11/2021

Date of final enrolment
30/04/2023

Locations

Countries of recruitment
United Kingdom

Study participating centre
Southampton General Hospital
University of Southampton and University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR
https://ror.org/0485axj58

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

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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 during and/or analysed during the current study will be available upon request from the chief investigator. At a later date they will be made available in a publicly accessible repository. All details will be confirmed in due course.

IPD sharing plan summary
Stored in publicly available repository, Available on request