ISRCTN17072692 https://doi.org/10.1186/ISRCTN17072692

Clinical trial to assess the safety of a coronavirus vaccine in healthy men and women

Submission date
22/05/2020

Recruitment status
No longer recruiting

Registration date
04/06/2020

Overall study status
Completed

Last Edited
09/07/2024

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The SARS-CoV-2 virus ('coronavirus') is the cause of COVID-19 – an infection spread by coughs, sneezes and contaminated surfaces that usually causes a mild or moderate illness in healthy young people, but can cause severe pneumonia and death – especially in older adults and people with other illnesses. There is currently a pandemic of SARS-CoV-2 affecting every country in the world, and the World Health Organisation estimates that without an effective vaccine almost 80% of the world population will eventually become infected by this entirely new virus. The best chance to control the pandemic and prevent recurrence of COVID-19 is likely to be the development of a vaccine that can build-up immunity within a population to block the spread of virus between people. There is currently no vaccine against SARS-CoV-2 although many are undergoing clinical testing. Researchers are testing a new SARS-CoV-2 vaccine in healthy men and women aged 18-75 but they will start in those aged 18–45 years old. The vaccine is a purified synthetic chemical called mRNA which mimics the virus gene for a spike protein on its surface. The virus uses the spike protein to attach to human cells and invade. When injected into muscle the vaccine triggers cells to manufacture copies of the spike protein, and these stimulate the body to produce antibodies. It is hoped that these antibodies in the blood of a vaccinated person will block the entry of SARS-CoV-2 viruses completely or limit it and subsequent infection. It is not yet known whether the vaccine will work, or what its side effects will be. The main aim of the study is to assess the safety of the vaccine and its effects on the immune system.

Who can participate?
Healthy adult volunteers aged 18- 45 (for the dose escalation and evaluation) and aged 18-75 (for the expanded safety evaluation)

What does the study involve?
For the dose escalation participants receive 0.1 µg of the vaccine and are invited to enter information on any local and systemic reactions into an online diary that evening and daily thereafter for 6 days. After 48 hours the team will call the first participant and go through their diary. If the reactions are Grade 1-2, or transient Grade 3 that resolve within 24 hours, three further participants will receive 0.1 µg. After 48 hours the team will call participants 2, 3 and 4 and go through their diaries. Provided there are none of the safety concerns outlined above, a fifth participant will proceed to receive the next dose (0.3 µg). The steps described above will be

repeated in order to escalate to the highest dose (1.0 µg) if there are none of the safety concerns outlined above after 48 hours. Participants will be followed up for 52 weeks in total. For the randomised dose evaluation participants are randomly allocated to the three different doses and are followed up for 52 weeks in total. For the non-randomised expanded safety evaluation participants receive the highest dose (1.0 µg).

What are the possible benefits and risks of participating?
Participants will have a health check which might be a benefit. The results will help the research effort to tackle SARS-CoV-2 whether this candidate vaccine goes forward or not. Many people feel that it is rewarding to make this very personal contribution to science. The study vaccine may provide protection against SARS-CoV-2 infection or COVID-19 disease but this is not known. There is a risk that participants will not follow all national and local guidance to avoid becoming infected with SARS-CoV-2. The vaccine has not been given to humans before and so the researchers do not know what side effects it may cause, but in animal testing it was safe. The vaccine is entirely synthetic and does not contain any SARS-CoV-2 viruses, and therefore cannot replicate to cause infection or COVID-19 disease. In some animal testing of experimental vaccines against viruses in the same 'family' as SARS-CoV-2 a rare effect was seen that instead of preventing infection the immune response to those vaccines appeared to make the disease symptoms worse after infection ('antibody-dependent enhancement'). The design of the vaccine in this study has been optimised to reduce the theoretical possibility that this could happen with COVID-19 disease in humans, but only large scale human vaccine trials will confirm whether this remains a rare risk for any SARS-CoV-2 vaccine. Fainting may occur around the time of vaccine injection or blood sampling, particularly if you strongly dislike needles. The researchers minimise the risk by asking participants to recline or lie down during those procedures. Blood tests can sometimes cause bruising and soreness of the arms or, very rarely, a blockage of a vein or a small nerve injury which can cause numbness and pain. Normally these problems disappear with time. The vaccine has not been tested for safety in pregnancy. The risks of becoming pregnant during the study are unknown, and participants must avoid pregnancy until at least 18 weeks after the second vaccination. Heterosexually active female participants of childbearing potential must use effective contraception and have pregnancy tests. Participants who become pregnant while taking part in the study must immediately tell the study team. Likewise male participants should avoid pregnancy with a female partner until at least 18 weeks after the second vaccination, and let the study team know if this happens.

Where is the study run from?
Medical Research Council Clinical Trials Unit at UCL (UK)

When is the study starting and how long is it expected to run for?
April 2020 to July 2021

Who is funding the study?
1. Medical Research Council (UK)
2. UK Research and Innovation (UK)

Who is the main contact?
Unfortunately, this study is not recruiting public volunteers at this time. This is because the research isn’t ready for volunteers yet or the researchers are directly identifying volunteers in certain areas or hospitals. Please do not contact the research team as they will not be able to respond. For more information about COVID-19 research, visit the Be Part of Research homepage.

Contact information

Type(s)
Public

Contact name
Mr James Fletcher

Contact details
MRC CTU at UCL
90 High Holborn
London
United Kingdom
WC1V 6LJ
-
imperial.recruitment.icrf@nhs.net

Type(s)
Scientific

Contact name
Prof Sheena McCormack

Contact details
MRC CTU at UCL
90 High Holborn
London
United Kingdom
WC1V 6LJ
-
mrcctu.covac@ucl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2020-001646-20

Integrated Research Application System (IRAS)
279315

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 279315

Study information

Scientific Title

A first-in-human clinical trial to assess the safety and immunogenicity of a self-amplifying ribonucleic acid (saRNA) vaccine encoding the S glycoprotein of SARS-CoV-2, the causative agent of COVID-19

Acronym
COVAC1

Study objectives
That the candidate vaccine will elicit binding and neutralising antibodies in a similar or greater proportion of individuals than natural infection, and be sufficiently safe and immunogenic to proceed to clinical efficacy testing.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/06/2020, North East - York Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 1048091; no email provided), 20/NE/0169

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
The study has three components:

1. Open-label, non-randomised dose escalation: 15 participants age 18-45 will be in the dose-escalation component. This will be carried out in a single centre.
1.1. The first participant will receive 0.1 µg and be invited to enter information on local and systemic reactions, into an online diary, that evening and daily thereafter for 6 days
1.2. At 48 hours post-vaccination the team will call the first participant and go through their diary. If the reactions are Grade 1-2, or transient Grade 3 that resolve within 24 hours, three further participants will receive 0.1 µg
1.3. At 48 hours post-vaccination the team will call participants 2, 3 and 4 and go through their diaries. Provided there are none of the safety concerns outlined above, a fifth participant will proceed to receive the next dose (0.3 µg)
1.4. The steps described above will be repeated in order to escalate to the highest dose (1.0 µg): the sentinel at 0.3 µg will be followed by three more participants at the same dose, provided there are none of the safety concerns outlined above at 48 hours post-vaccination of the sentinel; and a sentinel at 1.0 µg will follow if there are none of the safety concerns outlined above at 48 hours post-vaccination of the participants at 0.3 µg
1.5. Participants will be followed up for 52 weeks in total

2. Randomised dose evaluation: 105 individuals aged 18-45 will be enrolled through a single centre. Participants and laboratory staff will be blind to allocation.
2.1. Participants will be allocated in a 1:1:1 ratio to the three different doses based on block randomisation. They will be followed up for 52 weeks in total.

3. Non-randomised expanded safety evaluation: At least 200 individuals aged 18-75 will receive the highest dose (1 µg) enrolled through multiple centres.

The LNP-nCoVsaRNA vaccine candidate is manufactured by Polymun Scientific Immunbiologische Forschung GmbH, Klosterneuburg, Austria in accordance with European GMP on behalf of the sponsor, who is also responsible for the product development. LNP-nCoVsaRNA will be supplied to the sites free-of-charge by the sponsor's distribution partner, PCI Pharma Services. PCI will supply the IMP with COVAC1-specific labels, according to GMP. The vaccine will be supplied in glass vials at a concentration of 500 µg RNA per mL, with a 100 µl fill volume. It will be supplied with a sterile dilution buffer for reconstitution – phosphate-buffered saline in glass vials with an 18 ml fill volume. The vaccine is a solution with a slightly cloudy appearance. This vaccine candidate is not classified as a genetically modified organism (GMO). The vaccine should be administered intramuscularly in the deltoid muscle of the non-dominant upper arm using a 21-25 gauge needle. Participants will be observed for 60 minutes after the injection.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
LNP-nCoVsaRNA

Primary outcome(s)
1. Solicited local injection site reactions (pain, tenderness, erythema, swelling), collected via symptom diaries and immunisation eCRFs, within 7 days of administration of each vaccine
2. Solicited systemic and laboratory reactions (pyrexia, fatigue, myalgia, headache, chills, arthralgia) collected via symptom diaries and immunisation eCRFs, within 7 days of administration of each vaccine
3. Unsolicited adverse reactions (ARs, including serious ARs) collected via the eDC system throughout the study period (52 weeks)
4. Serious Adverse Events collected via the eDC system throughout the study period (52 weeks)
5. Unsolicited adverse events collected via the eDC system throughout the study period (52 weeks)
6. The titre of serum neutralising antibodies measured using SARS-CoV-2 pseudovirus-based neutralization assay, data received by statisticians directly from the laboratory, at 2 weeks after the second vaccination
7. The titre of vaccine-induced serum IgG binding antibody responses to the SARS-CoV-2 S glycoprotein, data received by statisticians directly from the laboratory, at 2 weeks after the first and second vaccinations

Key secondary outcome(s))
There are no secondary outcome measures

Completion date

31/07/2021

Eligibility

Key inclusion criteria
1. Healthy adults from the following age ranges:
1.1. For the dose escalation and evaluation, aged 18- 45 years on the day of screening
1.2. For the expanded safety evaluation, aged 18-75 years on the day of screening
2. At a similar risk of acquiring SARS-CoV2 infection to the general population
3. Willing and able to provide written informed consent
4. If female and of childbearing potential and not sterilised, willing to use a highly effective method of contraception from screening until 18 weeks after the last injection
5. If male and not sterilised, willing to avoid impregnating female partners from screening until 18 weeks after last injection
6. Willing to avoid all other vaccines 4 weeks after the first injection through to 4 weeks after the second injection
7. Willing and able to comply with visit schedule, complete online diaries and provide samples
8. Willing to grant authorised persons access to his/her trial-related medical record and GP records either directly or indirectly

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Total final enrolment
192

Key exclusion criteria
1. Pregnant or lactating
2. Presence of active systemic disease or pre-exisiting conditions that require investigation or a change to treatment that in the opinion of the investigator may compromise the volunteer’s safety, preclude vaccination or compromise interpretation of the immune response to vaccine
3. History of COVID-19 infection
4. History of severe or multiple allergies to drugs or pharmaceutical agents
5. History of severe local or general reaction to vaccination defined as:
5.1. Local: extensive, indurated redness and swelling involving most of the arm, not resolving

within 72 hours
5.2. General: fever >= 39.5oC within 48 hours; anaphylaxis; bronchospasm; laryngeal oedema; collapse; convulsions or encephalopathy within 72 hours
6. Ever received an experimental vaccine against COVID-19
7. Receipt of any immunosuppressive agents within 18 weeks of screening by any route other than topical
8. Detection of antibodies to hepatitis C
9. Detection of antibodies to HIV
10. Grade 1 and above abnormalities in routine laboratory parameters (see Table 4) using the FDA toxicity table Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (https://www.fda.gov/media/73679/download)
11. Participating in another clinical trial with an investigational drug or device, or treated with an investigational drug within 28 days of screening
12. Has received an immunisation within 28 days of screening

Date of first enrolment
16/06/2020

Date of final enrolment
31/10/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR Imperial Clinical Research Facility
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
Surrey Clinical Research Facility
Egerton Road
Guildford
Surrey
United Kingdom
GU2 7XP

Study participating centre

University Hospital Southampton
Tremona Road
Southampton
Hampshire
United Kingdom
SO16 6YD

Study participating centre
St. George's Hospital
Blackshaw Road
Tooting
London
United Kingdom
SW17 0QT

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		14/01/2022	20/01/2022	Yes	No
Results article		13/01/2023	24/01/2023	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Sub-study results	04/10/2022	09/07/2024	Yes	No