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A phase III study to investigate a vaccine against COVID-19

Submission date
26/05/2020

Recruitment status
No longer recruiting

Registration date
11/06/2020

Overall study status
Completed

Last Edited
14/08/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Current plain English summary as of 25/11/2020:
Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.
Since early 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of March 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.
Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.
The WHO declared the COVID-19 epidemic a Public Health Emergency of International Concern on 30th January 2020. Vaccines are the most cost-effective way of controlling outbreaks and the international community have stepped-up their efforts towards developing one against COVID-19.
The aim of this study is to assess whether healthy people in Brazil can be protected from COVID-19 with a new vaccine called ChAdOx1 nCoV-19. It will also provide valuable information on the safety of the vaccine and its ability to generate good immune responses against the virus.

Who can participate?
Adults aged 18 and above

What does the study involve?
Participants are randomly allocated to receive two doses of the investigational vaccine or a well-established meningitis vaccine. Volunteers will be followed for 12 months after their final vaccine, and they will be tested for COVID-19 if they develop any symptoms which may

represent COVID-19 disease. In addition, blood tests will be done during the study to look at how the volunteers' immune systems have reacted to the virus. At the end of the study, the researchers will look at how many people had COVID-19 disease in each group and this will help them to decide if the vaccine has worked.

What are the possible benefits and risks of participating?
Knowledge gained from this study will help researchers to develop a vaccine against the newly emerging coronavirus disease COVID-19. There are no direct benefits of taking part, however, the majority of participants in this study will not have had MenACWY vaccine previously, and therefore will gain the benefit of protection against group A, C, W and Y meningococcus. Although this is the first time this vaccine has been administered to humans, similar investigational vaccines have been widely administered for many pathologies without significant safety concerns. Drawing blood may cause slight pain and occasionally bruising. Common side effects of vaccinations are some mild redness and swelling at the injection site. Participants may feel like they have flu-like symptoms within 24 hours of the vaccinations. These usually resolve within 48 hours.

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

When is the study starting and how long is it expected to run for?
May 2020 to March 2023

Who is funding the study?
University of Oxford (UK)

Who is the main contact?
Dr Peter O'Reilly
covid19@ndm.ox.ac.uk

Previous plain English summary:
Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.
Since early 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of March 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.
Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.
The WHO declared the COVID-19 epidemic a Public Health Emergency of International Concern on 30th January 2020. Vaccines are the most cost-effective way of controlling outbreaks and the international community have stepped-up their efforts towards developing one against COVID-19.
The aim of this study is to assess whether healthy people in Brazil can be protected from COVID-

19 with a new vaccine called ChAdOx1 nCoV-19. It will also provide valuable information on the safety of the vaccine and its ability to generate good immune responses against the virus.

Who can participate?
Adults aged 18 to 55

What does the study involve?
Participants are randomly allocated to receive the investigational vaccine or a well-established meningitis vaccine. Volunteers will be followed for 12 months, and they will be tested for COVID-19 if they develop any symptoms which may represent COVID-19 disease. In addition, blood tests will be done during the study to look at how the volunteers' immune systems have reacted to the virus. At the end of the study, the researchers will look at how many people had COVID-19 disease in each group and this will help them to decide if the vaccine has worked.

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

When is the study starting and how long is it expected to run for?
May 2020 to October 2021 (updated 04/08/2020, previously: July 2021)

Who is funding the study?
University of Oxford (UK)

Who is the main contact?
Dr Peter O'Reilly
covid19@ndm.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Peter O'Reilly

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University of Oxford

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
COV003

Study information

Scientific Title
A phase III randomized controlled trial to determine safety, efficacy, and immunogenicity of the non-replicating ChAdOx1 nCoV-19 vaccine

Acronym
COV003

Study objectives
The candidate ChAdOx1 nCoV-19 vaccine is efficacious against PCR-confirmed COVID-19 disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 03/06/2020, The National Commission for Research Ethics (Comissão Nacional de Ética em Pesquisa (CONEP), SRTVN 701, Via W 5 Norte, lote D - Edifício PO 700, 3º andar, Asa Norte CEP, Brasilia, 70.719-040, Brazil; +55 61 3315-5877; conep@saude.gov.br), ref: 4068113
2. Approved 12/06/2020, Oxford Tropical Research Ethics Committee (OxTREC) (University of Oxford, Research Services, University Offices, Wellington Square, Oxford, OX1 2JD, UK; +44 (0) 1865 (2)82106; oxtrec@admin.ox.ac.uk), ref: 36-20

Study design
Single-blind randomised efficacy, safety and immunogenicity study

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

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

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

Interventions
Current interventions as of 25/11/2020:
Volunteers will initially be invited for a screening visit. Prior to attending they will have received written information about the study and had time to consider it. At the screening visit, a doctor will explain the study and answer any questions they may have. If the volunteer decides to take part, they will be asked to sign a consent form. The doctor will then check whether the volunteer is eligible to take part. This will involve taking a medical history and performing a physical examination if deemed necessary, taking blood tests for SARS-CoV-2 antibodies, urinary pregnancy test for women, and measuring blood pressure and temperature.

Participants will be randomised (1:1 using block randomisation) to receive either ChAdOx1 nCoV-19 or MenACWY (licensed control vaccine). Participants will also be advised to take paracetamol for 24 hours after vaccination if there are no contraindications to doing so.

Participants will be given two doses of ChAdOx1 nCoV-19 or MenACWY, 4-12 weeks apart.
ChAdOx1 nCoV-19: 5 x 10(10) vp
Men ACWY: 0.5 ml
Two doses of ChAdOx1 nCoV-19 or MenACWY given intramuscularly.
Paracetamol 1 g taken 6 hourly for the first 24 hours after receiving vaccine.

Total follow up time 1 year for each study arm. All participants will be invited to follow-up visits at day 28, 90, 182 and 364 after their last vaccination. Participants will be asked to contact the study team if they develop symptoms suggestive of COVID-19 at any point during the trial. Symptomatic participants will be asked to present for a visit to test for SARS-CoV-2 PCR.

Previous interventions:
Volunteers will initially be invited for a screening visit. Prior to attending they will have received written information about the study and had time to consider it. At the screening visit, a doctor will explain the study and answer any questions they may have. If the volunteer decides to take part, they will be asked to sign a consent form. The doctor will then check whether the volunteer is eligible to take part. This will involve taking a medical history and performing a physical examination if deemed necessary, taking blood tests for SARS-CoV-2 antibodies, urinary pregnancy test for women, and measuring blood pressure and temperature.

Participants will be randomised (1:1 using block randomisation) to receive either ChAdOx1 nCoV-19 or MenACWY (licensed control vaccine). Participants will also be advised to take paracetamol for 24 hours after vaccination if there are no contraindications to doing so.

ChAdOx1 nCoV-19: 5 x 10(10) vp
Men ACWY: 0.5 ml
One dose of ChAdOx1 nCoV-19 or MenACWY given intramuscularly. Single intervention only.
Paracetamol 1 g taken 6 hourly for the first 24 hours after receiving vaccine.

Total follow up time 1 year for each study arm. All participants will be invited to follow-up visits at day 28, 90, 182 and 364 and participants will be asked to contact the study team if they develop symptoms suggestive of COVID-19 at any point during the trial. Symptomatic participants will be asked to present for a visit to test for SARS-CoV-2 PCR.

Intervention Type
Biological/Vaccine

Phase
Phase III

Drug/device/biological/vaccine name(s)
ChAdOx1 nCoV-19 vaccine, MenACWY vaccine

Primary outcome measure
Current primary outcome measure as of 25/11/2020:
Virologically confirmed (PCV positive) symptomatic cases of COVID-19 over the course of 12 months

Previous primary outcome measure:
Virologically confirmed (PCR positive) symptomatic cases of COVID-19 over the course of 12 months

Secondary outcome measures
1. Occurrence of solicited local and systemic reactogenicity signs and symptoms for 7 days following vaccination, recorded in an electronic diary (in a subset of 200 participants only)
2. Occurrence of serious adverse events reported by participant/documented in an electronic diary over the course of 12 months
3. Occurrence of disease enhancement episodes reported by participant/documented in hospital records over the course of 12 months
4. Hospitalization due to PCR-confirmed COVID-19 disease, reported by participants, over the course of 12 months
5. Severe PCR confirmed COVID-19 disease, parameters recorded from hospital records /participant interview, over the course of 12 months
6. Death associated with COVID-19 disease over the course of 12 months
7. Antibodies against SARS-CoV-2 non-spike protein (sero-efficacy rates) measured by ELISA over the course of 12 months
8. Antibodies against SARS-CoV-2 spike protein (sero-conversion rates) measured by ELISA at 28 days post vaccination
9. Virus neutralising antibody (NAb) assays against live and/or pseudotyped SARS-CoV-2 virus at 28 days post vaccination

All participants will be invited to follow-up visits at day 28, 90, 182 and 364 following their last vaccination. Participants will be asked to contact the study team if they develop symptoms suggestive of COVID-19 at any point during the trial. Symptomatic participants will be asked to present for a visit to test for SARS-CoV-2 PCR.

Overall study start date
01/05/2020

Completion date
31/03/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 25/11/2020:
1. Adults aged 18 to 55 years of age
2. Adults aged 56-69 years old (after review of safety data by DSMB in this age group in the UK trial)
3. Adults aged 70 and above years old (after review of safety data by DSMB in this age group in the UK trial)
4. Able and willing (in the Investigator's opinion) to comply with all study requirements
5. Willing to allow the investigators to discuss the volunteer's medical history with their General Practitioner/personal doctor and access all medical records when relevant to study procedures
4. For females of childbearing potential only, willingness to practice continuous effective contraception (see below) during the study and 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. Health professionals and/or adults at high risk of exposure to SARS-CoV-2

Previous inclusion criteria:
1. Adults aged 18 to 55 years of age. Upper age can be extended upon the availability of additional safety data in an older population
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/personal doctor and access all medical records when relevant to study procedures
4. For females of childbearing potential only, willingness to practice continuous effective contraception (see below) during the study and 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

Participant type(s)
Mixed

Age group
Mixed

Sex
Both

Target number of participants
10300 (with a 1% margin)

Key exclusion criteria
1. Participation in COVID-19 prophylactic drug trials for the duration of the study. Note: Participation in COVID-19 treatment trials is allowed in the event of hospitalisation due to COVID-19. The study team should be informed as soon as possible
2. Participation in SARS-CoV-2 serological surveys where participants are informed of their serostatus for the duration of the study. Note: Disclosure of serostatus post enrolment may accidentally unblind participants to group allocation. Participation in COV003 can only be allowed if volunteers are kept blinded to their serology results from local/national serological surveys
3. Planned receipt of any vaccine (licensed or investigational), other than the study intervention, within 30 days before and after study vaccination
4. Prior receipt of an investigational or licensed vaccine likely to impact on interpretation of the trial data (e.g. Adenovirus vectored vaccines, any coronavirus vaccines)
5. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate
6. Any confirmed or suspected immunosuppressive or immunodeficient state; asplenia; recurrent severe infections and chronic use (more than 14 days) of immunosuppressant medication within the past 6 months except topical steroids or short-term oral steroids (course lasting ≤14 days)
7. History of allergic disease or reactions likely to be exacerbated by any component of ChAdOx1 nCoV-19 or MenACWY or paracetamol
8. Any history of angioedema
9. Any history of anaphylaxis
10. Pregnancy, lactation or willingness/intention to become pregnant during the study
11. Current diagnosis of or treatment for 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. Bleeding disorder (e.g. factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture
14. Suspected or known current alcohol or drug dependency
15. Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness (mild/moderate well-controlled comorbidities are allowed)
16. History of laboratory-confirmed COVID-19
17. Seropositive for SARS-CoV-2 antibodies before enrolment
18. New onset of fever or a cough or shortness of breath or anosmia/ageusia since February 2020, unless seronegative for SARS-CoV-2 antibodies at screening
19. Continuous use of anticoagulants, such as coumarins and related anticoagulants (i.e. warfarin) or novel oral anticoagulants (i.e. apixaban, rivaroxaban, dabigatran and edoxaban)
20. 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 or impair interpretation of the study data

Date of first enrolment
15/06/2020

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
Brazil

Study participating centre
Centro de Referência Imunobiológicos Especiais- CRIE-Unifesp
Federal University of São Paulo Rua Borges Lagoa
770 Vila Clementino
São Paulo
Brazil
CEP 04038-001

Study participating centre
Instituto D'Or de Pesquisa e Ensino - I'Dor
Rua Diniz Cordeiro, 30 - Botafogo
Rio de Janeiro
Brazil
RJ, 22281-100

Study participating centre
Instituto D'Or de Pesquisa e Ensino - I'Dor
Avenida São Rafael, 2152 - São Marcos
Salvador
Brazil
BA, 41253-190

Study participating centre
Centro de Pesquisas Clinicas de Natal (CPCLIN)
Rua Dr Ponciano Barbosa, 282 – Cidade Alta
Natal
Brazil
RN, 59025-050

Study participating centre
Universidade Federal de Santa Maria (UFSM)
Av. Roraima, 1000 Cidade Universitária Bairro Camobi
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RS, 97105-900

Study participating centre
Hospital das Clinicas de Porto Alegre Universidade Federal do Rio Grande do Sul (UFRGS)
Rua Ramiro Barcelos, 2.350 Bairro Santa Cecília
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Sponsor information

Organisation
University of Oxford

Sponsor details
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+44 (0)1865 616480
ctrg@admin.ox.ac.uk

Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
University/education

Funder Name
University of Oxford

Results and Publications

Publication and dissemination plan

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Data from the study may also be used as part of a thesis for a PhD or MD. Planned publication in a high-impact peer-reviewed journal.

Intention to publish date

31/10/2023

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?
Interim results article	interim results	09/01/2021	09/12/2020	Yes	No
Results article	results	06/03/2021	23/02/2021	Yes	No
Results article	exploratory analysis of responses in males and females	29/06/2022	04/07/2022	Yes	No
Other publications	post-hoc exploratory analysis of the vaccine against the SARS-CoV-2 lineages circulating		14/08/2024	Yes	No