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Investigating a vaccine against COVID-19

Submission date
04/05/2020

Recruitment status
No longer recruiting

Registration date
07/05/2020

Overall study status
Completed

Last Edited
24/04/2024

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

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.
In 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. There are no currently licensed vaccines or specific treatments for COVID-19. 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 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. The researchers will do this by randomly allocating participants to receive the investigational vaccine or a MenACWY vaccine in addition to doing blood tests and collecting information about any symptoms that occur after vaccination.

Who can participate?
Healthy adults aged 18 years and older. Participation in this study is voluntary but the researchers are only accepting volunteers from the local area around the study sites.

What does the study involve?
Participants will be randomly allocated to receive the investigational vaccine or a MenACWY vaccine. The researchers will then do blood tests and collect information about any symptoms

that occur after vaccination. Dependent on the group, there will be between six and twelve study visits over a 12-month period. Participants will be asked to complete a diary for up to 28 days after the vaccination and will be closely monitored by the study team.

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, participants will receive a full medical examination as part of the study. 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?
Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2020 to December 2024

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Emma Plested, covid19@ndm.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2020-001228-32

Integrated Research Application System (IRAS)
281904

ClinicalTrials.gov (NCT)
NCT04400838

Protocol serial number
CPMS 45551, IRAS 281904

Study information

Scientific Title
A phase II/III study to determine the efficacy, safety and immunogenicity of the candidate coronavirus disease (COVID-19) vaccine ChAdOx1 nCoV-19

Acronym
COV002

Study objectives
Current objectives as of 28/09/2020:
1. To assess the efficacy of the candidate ChAdOx1 nCoV-19 against COVID-19 in adults aged 18 years and older
2. To assess the safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV-19
3. To assess the efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19
4. To assess the humoral immunogenicity of ChAdOx1 nCoV-19
5. To assess the cellular immunity of ChAdOx1 nCoV-19 in older adults and in children (groups 1, 2, 3, 7 and 8 only)
6. To assess the safety and immunogenicity of a booster dose of ChAdOx1 nCoV-19 in older adults aged 56 years or older (two-dose schedules for groups 1, 2, 7 and 8 only)

Previous objectives:
1. To assess the efficacy of the candidate ChAdOx1 nCoV-19 against COVID-19 in adults aged 18 years and older
2. To assess the safety of the candidate vaccine ChAdOx1 nCoV-19 in adults and children

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/04/2020, South Central - Berkshire Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)2071048046; berkshire.rec@hra.nhs.uk), REC ref: 20/SC/0179

Study design
Single-blind randomized safety and efficacy study, with immunogenicity sub-studies in older and younger age groups

Primary study design

Interventional

Study type(s)
Prevention

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

Interventions
Current intervention as of 21/04/2021 (see additional files for previous interventions prior to 04/12/2020):
Group 1
80 participants aged 56-69 years will receive either single-dose ChAdOx1 nCoV-19 5x10(10) virus particles (vp) (Abs 260) or MenACWY at day 0, or two-dose ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) prime followed by 2.2x10(10) (qPCR) boost or two-dose MenACWY (4-6 weeks apart), then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at days 31, 35 and 42. All group 1 volunteers that were originally randomised to single-dose subgroups will now be offered a booster vaccination. Once boosted, these remaining volunteers will instead be followed up on a schedule relative to the boost dose which will be POST BOOST+28 days, POST BOOST +90, POST BOOST +182 and POST BOOST +364 days.

Group 2
120 participants aged 70 years or older will receive ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) or MenACWY at day 0, or two-dose ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) prime followed by 2.2 x10(10) (qPCR) boost or two-dose MenACWY (4-6 weeks apart), then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at days 31, 35 and 42. All group 2 volunteers that were originally randomised to single-dose subgroups will now be offered a booster vaccination. Once boosted, these remaining volunteers will instead be followed up on a schedule relative to the boost dose which will be POST BOOST+28 days, POST BOOST +90, POST BOOST +182 and POST BOOST +364 days.

Group 4
Up to 3550 participants aged 18-55 years will receive either single-dose ChAdOx1 nCoV-19 5x10 (10) virus particles (vp) (Abs 260) or MenACWY at day 0, or two-dose ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) prime followed by 2.2x10(10) (qPCR) boost or two-dose MenACWY (4-12 weeks apart, +2 weeks), then followed up at days 28, 90, 182 and 364. Two dose subgroups will have additional visits at day 42 and 56. A further prime/boost subgroup will receive a two-dose ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) prime and 3.5 – 6.5 × 10(10) vp (Abs 260, corrected for PS80) boost or ChAdOx1 nCoV-19 5x10(10) vp (qPCR) boost at day 0 and day 28, respectively, or two-dose MenACWY, (4-12 weeks apart, +2 weeks). The booster subgroup will be further followed up at days 28, 90, 182 and 365 after booster.

Group 5
Up to 230 participants aged 18-55 will receive ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) or ChAdOx1 nCoV-19 5x10(10) vp (qPCR) or MenACWY at day 0 or two-dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp (Abs 260, corrected for PS80) or ChAdOx1 nCoV-19 (Covishield 0.9x1011 vp/ml, 0.25ml prime and 0.5ml boost), or two-dose MenACWY, (4-6 weeks apart) then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at day 31, 35 and 42. All group 5a volunteers that were originally randomised to single-dose subgroups will

now be offered a booster vaccination. Once boosted, these remaining volunteers will instead be followed up on a schedule relative to the boost dose which will be POST BOOST+28 days, POST BOOST +90, POST BOOST +182 and POST BOOST +364 days.

Group 6
Up to 6000 participants aged 18-55 years will receive ChAdOx1 nCoV-19 5x10(10) vp (qPCR) or MenACWY at day 0 or two dose ChAdOx1 nCoV-19 5x10(10) vp (qPCR) prime and 3.5 – 6.5 × 10 (10) vp (Abs 260, corrected for PS80) boost or ChAdOx1 nCoV-19 5x10(10) vp (qPCR) boost or two-dose MenACWY, (4-12 weeks apart, +2 weeks), then followed up at days 28, 90, 182 and 364. Two dose subgroups will have additional visits at day 42 and 56. Booster subgroup will be further followed up at days 28, 90, 182 and 365 after booster.

Group 7
80 participants aged 56-69 years will receive either single dose ChAdOx1 nCoV-19 5x10(10) virus particles (vp) (qPCR) or single dose MenACWY at day 0, or two dose ChAdOx1 nCoV-19 5x10(10) vp (qPCR) or MenACWY (4-6 weeks apart), then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at days 31, 35 and 42.

Group 8
120 participants aged 70 years or older will receive single dose ChAdOx1 nCoV-19 5x10(10) vp (qPCR) or single dose MenACWY at day 0, or two dose ChAdOx1 nCoV-19 5x10(10) vp (qPCR) prime and (3.5 – 6.5 × 1010 vp, Abs 260, corrected for PS80) boost OR ChAdOx1 nCoV-19 5x1010vp (qPCR) boost (4-6 weeks apart), OR two-dose MenACWY (4-6 weeks apart) then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at days 31, 35 and 42.

Group 9
Approximately 1000 participants aged 56-69 will receive two-dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp, (Abs 260, corrected for PS80) or two-dose MenACWY (4-6 weeks apart), then followed up at days 28, 56, 118, 210 and 364.

Group 10
Approximately 1000 participants aged 70 years and over will receive two-dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp, (Abs 260, corrected for PS80) or two-dose MenACWY (4-6 weeks apart), then followed up at days 28, 56, 118, 210 and 364.

Group 11
Up to 60 participants aged 18-55 who previously received a ChAdOx1 vectored vaccine will receive two-dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp (Abs 260, corrected for PS80) (4-6 weeks apart), then followed up at days 14, 28, 56, 118, 210 and 364.

Group 12
Up to 60 HIV infected individuals aged 18-55 will receive two dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp (Abs 260, corrected for PS80) at day 0 and day 28, then followed up at days 3, 7, 14, 28, 31, 35, 42, 56, 182 and 364.

Volunteers will stay in the trial site for observation for a minimum of 15 minutes (+15 minutes), in case of immediate adverse events.
In groups 1-3, 5, 7, 8, 11 and 12 and in a subset of volunteers in groups 4,6, 9 and 10 (n=1000, each groups 4 and 6 and up to 500 in each of groups 9 and 10), participants will be given an oral

thermometer, tape measure and diary card (paper or electronic), with instructions on use. All participants will be given the emergency 24-hour telephone number to contact the on-call study physician if needed.

Safety will be assessed in real time. The DSMB will periodically assess safety and efficacy data every 4-8 weeks and/or as required.

Participants will be followed over the duration of the study to record adverse events and episodes of virologically confirmed symptomatic COVID-19 cases. Participants will be tested for COVID-19 if they present with a new onset of fever OR cough OR shortness of breath.

All study participants (that remain blinded) will be unblinded. Following this, control participants aged 30 and above will be offered ChAdOx1 nCoV-19 in the approved MHRA 4-to-12 week, 2-dose schedule. Participants will remain enrolled in the study and continue the follow up visit schedule listed for their sub-group concurrently with the provision of treatment prime and boost visits. Due to the updated guidance relating to the emerging association of thrombosis with thrombocytopenia and ChAdOx1 nCoV-19, trial participants aged 29 and under will not be offered (prime) vaccinations with ChAdOx1 nCoV-19. These individuals will instead be advised to await vaccination under the national rollout program.

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Previous intervention as of 04/12/2020 (see additional files for previous interventions):
Group 1
80 participants aged 56-69 years will receive either single-dose ChAdOx1 nCoV-19 5x10(10) virus particles (vp) (Abs 260) or MenACWY at day 0, or two-dose ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) prime followed by 2.2x10(10) (qPCR) boost or two-dose MenACWY (4-6 weeks apart), then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at days 31, 35 and 42. All group 1 volunteers that were originally randomised to single-dose subgroups will now be offered a booster vaccination. Once boosted, these remaining volunteers will instead be followed up on a schedule relative to the boost dose which will be POST BOOST+28 days, POST BOOST +90, POST BOOST +182 and POST BOOST +364 days.

Group 2
120 participants aged 70 years or older will receive ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) or MenACWY at day 0, or two-dose ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) prime followed by 2.2 x10(10) (qPCR) boost or two-dose MenACWY (4-6 weeks apart), then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at days 31, 35 and 42. All group 2 volunteers that were originally randomised to single-dose subgroups will now be offered a booster vaccination. Once boosted, these remaining volunteers will instead be followed up on a schedule relative to the boost dose which will be POST BOOST+28 days, POST BOOST +90, POST BOOST +182 and POST BOOST +364 days.

Group 4
Up to 3550 participants aged 18-55 years will receive either single-dose ChAdOx1 nCoV-19 5x10 (10) virus particles (vp) (Abs 260) or MenACWY at day 0, or two-dose ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) prime followed by 2.2x10(10) (qPCR) boost or two-dose MenACWY (4-12 weeks apart, +2 weeks), then followed up at days 28, 90, 182 and 364. Two dose subgroups will have additional visits at day 42 and 56. A further prime/boost subgroup will receive a two-dose ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) prime and 3.5 – 6.5 × 10(10) vp (Abs 260, corrected for

PS80) boost or ChAdOx1 nCoV-19 5x10(10) vp (qPCR) boost at day 0 and day 28, respectively, or two-dose MenACWY, (4-12 weeks apart, +2 weeks). The booster subgroup will be further followed up at days 28, 90, 182 and 365 after booster.

Group 5
Up to 230 participants aged 18-55 will receive ChAdOx1 nCoV-19 5x10(10) vp (Abs 260) or ChAdOx1 nCoV-19 5x10(10) vp (qPCR) or MenACWY at day 0 or two-dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp (Abs 260, corrected for PS80) or ChAdOx1 nCoV-19 (Covishield 0.9x1011 vp/ml, 0.25ml prime and 0.5ml boost), or two-dose MenACWY, (4-6 weeks apart) then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at day 31, 35 and 42. All group 5a volunteers that were originally randomised to single-dose subgroups will now be offered a booster vaccination. Once boosted, these remaining volunteers will instead be followed up on a schedule relative to the boost dose which will be POST BOOST+28 days, POST BOOST +90, POST BOOST +182 and POST BOOST +364 days.

Group 6
Up to 6000 participants aged 18-55 years will receive ChAdOx1 nCoV-19 5x10(10) vp (qPCR) or MenACWY at day 0 or two dose ChAdOx1 nCoV-19 5x10(10) vp (qPCR) prime and 3.5 – 6.5 × 10 (10) vp (Abs 260, corrected for PS80) boost or ChAdOx1 nCoV-19 5x10(10) vp (qPCR) boost or two-dose MenACWY, (4-12 weeks apart, +2 weeks), then followed up at days 28, 90, 182 and 364. Two dose subgroups will have additional visits at day 42 and 56. Booster subgroup will be further followed up at days 28, 90, 182 and 365 after booster.

Group 7
80 participants aged 56-69 years will receive either single dose ChAdOx1 nCoV-19 5x10(10) virus particles (vp) (qPCR) or single dose MenACWY at day 0, or two dose ChAdOx1 nCoV-19 5x10(10) vp (qPCR) or MenACWY (4-6 weeks apart), then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at days 31, 35 and 42.

Group 8
120 participants aged 70 years or older will receive single dose ChAdOx1 nCoV-19 5x10(10) vp (qPCR) or single dose MenACWY at day 0, or two dose ChAdOx1 nCoV-19 5x10(10) vp (qPCR) prime and (3.5 – 6.5 × 1010 vp, Abs 260, corrected for PS80) boost OR ChAdOx1 nCoV-19 5x1010vp (qPCR) boost (4-6 weeks apart), OR two-dose MenACWY (4-6 weeks apart) then followed up at days 3, 7, 14, 28, 56, 182 and 364. Two dose subgroups will have additional visits at days 31, 35 and 42.

Group 9
Approximately 1000 participants aged 56-69 will receive two-dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp, (Abs 260, corrected for PS80) or two-dose MenACWY (4-6 weeks apart), then followed up at days 28, 56, 118, 210 and 364.

Group 10
Approximately 1000 participants aged 70 years and over will receive two-dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp, (Abs 260, corrected for PS80) or two-dose MenACWY (4-6 weeks apart), then followed up at days 28, 56, 118, 210 and 364.

Group 11
Up to 60 participants aged 18-55 who previously received a ChAdOx1 vectored vaccine will receive two-dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp (Abs 260, corrected for PS80) (4-6 weeks apart), then followed up at days 14, 28, 56, 118, 210 and 364.

Group 12
Up to 60 HIV infected individuals aged 18-55 will receive two dose ChAdOx1 nCoV-19 3.5 – 6.5 × 10(10) vp (Abs 260, corrected for PS80) at day 0 and day 28, then followed up at days 3, 7, 14, 28, 31, 35, 42, 56, 182 and 364.

Volunteers will stay in the trial site for observation for a minimum of 15 minutes (+15 minutes), in case of immediate adverse events.
In groups 1-3, 5, 7, 8, 11 and 12 and in a subset of volunteers in groups 4,6, 9 and 10 (n=1000, each groups 4 and 6 and up to 500 in each of groups 9 and 10), participants will be given an oral thermometer, tape measure and diary card (paper or electronic), with instructions on use. All participants will be given the emergency 24-hour telephone number to contact the on-call study physician if needed.

Safety will be assessed in real time. The DSMB will periodically assess safety and efficacy data every 4-8 weeks and/or as required.

Participants will be followed over the duration of the study to record adverse events and episodes of virologically confirmed symptomatic COVID-19 cases. Participants will be tested for COVID-19 if they present with a new onset of fever OR cough OR shortness of breath.

Intervention Type
Biological/Vaccine

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
ChAdOx1-nCoV19, MenACWY

Primary outcome(s)
Current primary outcome measure as of 17/11/2020:

1. Efficacy of the candidate ChAdOx1 nCoV-19 against COVID-19 in adults aged 18 years and older measured by virologically confirmed (PCR* positive) symptomatic cases of COVID-19.

2. Safety of the candidate vaccine ChAdOx1 nCoV-19 in adults and children measured by recording the occurrence of serious adverse events (SAEs) throughout the study duration.

* Or other nucleic acid amplification test (NAAT)

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Previous primary outcome measure as of 30/07/2020:

1. Efficacy of the candidate ChAdOx1 nCoV-19 against COVID-19 in adults aged 18 years and older measured by virologically confirmed (PCR positive) symptomatic cases of COVID-19
2. Safety of the candidate vaccine ChAdOx1 nCoV-19 in adults and children measured by recording the occurrence of serious adverse events (SAEs) over the course of 6 months

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Previous primary outcome measure:
1. Efficacy of the candidate ChAdOx1 nCoV-19 against COVID-19 in adults aged 18 years and older measured by virologically confirmed (PCR positive) symptomatic cases of COVID-19 over the course of 6 months
2. Safety of the candidate vaccine ChAdOx1 nCoV-19 in adults and children measured by recording the occurrence of serious adverse events (SAEs) over the course of 6 months

Key secondary outcome(s))

Current secondary outcome measures as of 28/09/2020:

1. Safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV-19:
1.1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following vaccination
1.2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following vaccination
1.3. Occurrence of unsolicited adverse events (AEs) for 28 days following vaccination
1.4. Change from baseline for safety laboratory measures (except groups 4, 6, 9 and 10)
1.5. Occurrence of disease enhancement episodes
2. Efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19 over the course of 6 months:
2.1. Hospital admissions associated with COVID-19
2.2. Intensive care unit (ICU) admissions associated with COVID-19
2.3. Deaths associated with COVID-19
2.4. Seroconversion against non-Spike SARS-CoV-2 antigens
2.5. Severe COVID-19 disease (defined according to clinical severity scales)
3. Cellular and humoral immunogenicity of ChAdOx1 nCoV-19 over the course of 6 months:
3.1. Antibodies against SARS-CoV-2 spike protein (seroconversion rates) at Day 28 post-vaccination
3.2. Proportion of seroconversion to antibodies against SARS-CoV-2 spike protein at Day 28 post-vaccination
3.3. Cellular immunity of ChAdOx1 nCoV-19 in older adults and in children (groups 1, 2, 3, 7 and 8 only)
3.4. Interferon-gamma (IFN-γ) enzyme-linked immunospot (ELISpot) responses to SARS-CoV-2 spike protein
4. Safety and immunogenicity of a booster dose of ChAdOx1 nCoV-19 in older adults aged 56 years or older (two-dose schedules for groups 1, 2, 7 and 8 only):
4.1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following booster vaccination
4.2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following booster vaccination
4.3. Occurrence of unsolicited adverse events (AEs) for 28 days following booster vaccination
4.4. Change from baseline and change from pre-booster for safety laboratory measures
4.5. Occurrence of disease enhancement episodes over the course of 6 months
4.6. Antibodies against SARS-CoV-2 spike protein at Day 56 post-vaccination
4.7. Proportion of seroconversion to antibodies against SARS-CoV-2 spike protein at Day 56 post-vaccination

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Previous secondary outcome measures from 15/06/2020 to 28/09/2020:

1. Safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV-19:
1.1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following vaccination
1.2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following vaccination
1.3. Occurrence of unsolicited adverse events (AEs) for 28 days following vaccination (except group 4 and 6)
1.4. Change from baseline for safety laboratory measures (except group 4 and 6)
1.5. Occurrence of disease enhancement episodes
2. Efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19 over the course of 6 months:
2.1. Hospital admissions associated with COVID-19
2.2. Intensive care unit (ICU) admissions associated with COVID-19
2.3. Deaths associated with COVID-19
2.4. Seroconversion against non-Spike SARS-CoV-2 antigens
3. Cellular and humoral immunogenicity of ChAdOx1 nCoV-19 over the course of 6 months:
3.1. Antibodies against SARS-CoV-2 spike protein (seroconversion rates) at Day 28 post-vaccination
3.2. Proportion of seroconversion to antibodies against SARS-CoV-2 spike protein at Day 28 post-vaccination
3.3. Cellular immunity of ChAdOx1 nCoV-19 in older adults and in children (groups 1, 2 and 3 only)
3.4. Interferon-gamma (IFN-γ) enzyme-linked immunospot (ELISpot) responses to SARS-CoV-2 spike protein
4. Safety and immunogenicity of a booster dose of ChAdOx1 nCoV-19 in older adults aged 56 years or older (two-dose schedules for groups 1 and 2 only):
4.1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following booster vaccination
4.2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following booster vaccination
4.3. Occurrence of unsolicited adverse events (AEs) for 28 days following booster vaccination
4.4. Change from baseline and change from pre-booster for safety laboratory measures
4.5. Occurrence of disease enhancement episodes over the course of 6 months
4.6. Antibodies against SARS-CoV-2 spike protein at Day 56 post-vaccination
4.7. Proportion of seroconversion to antibodies against SARS-CoV-2 spike protein at Day 56 post-vaccination

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Previous secondary outcome measures as of 22/05/2020:

1. Safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV-19:
1.1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following vaccination
1.2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following vaccination
1.3. Occurrence of unsolicited adverse events (AEs) for 28 days following vaccination (except group 4)
1.4. Change from baseline for safety laboratory measures (except group 4)
1.5. Occurrence of disease enhancement episodes
2. Efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19 over the course of 6 months:

2.1. Hospital admissions associated with COVID-19
2.2. Intensive care unit (ICU) admissions associated with COVID-19
2.3. Deaths associated with COVID-19
2.4. Seroconversion against non-Spike SARS-CoV-2 antigens
3. Cellular and humoral immunogenicity of ChAdOx1 nCoV-19 over the course of 6 months:
3.1. Antibodies against SARS-CoV-2 spike protein (seroconversion rates) at Day 28 post-vaccination
3.2. Proportion of seroconversion to antibodies against SARS-CoV-2 spike protein at Day 28 post-vaccination
3.3. Cellular immunity of ChAdOx1 nCoV-19 in older adults and in children (groups 1, 2 and 3 only)
3.4. Interferon-gamma (IFN-γ) enzyme-linked immunospot (ELISpot) responses to SARS-CoV-2 spike protein
4. Safety and immunogenicity of a booster dose of ChAdOx1 nCoV-19 in older adults aged 56 years or older (two-dose schedules for groups 1 and 2 only):
4.1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following booster vaccination
4.2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following booster vaccination
4.3. Occurrence of unsolicited adverse events (AEs) for 28 days following booster vaccination
4.4. Change from baseline and change from pre-booster for safety laboratory measures
4.5. Occurrence of disease enhancement episodes over the course of 6 months
4.6. Antibodies against SARS-CoV-2 spike protein at Day 56 post-vaccination
4.7. Proportion of seroconversion to antibodies against SARS-CoV-2 spike protein at Day 56 post-vaccination

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Previous secondary outcome measures:

1. Safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV-19:
1.1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following vaccination
1.2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following vaccination
1.3. Occurrence of unsolicited adverse events (AEs) for 28 days following vaccination
1.4. Change from baseline for safety laboratory measures over the course of 6 months
1.5. Occurrence of disease enhancement episodes
2. Efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19 over the course of 6 months:
2.1. Hospital admissions associated with COVID-19
2.2. Intensive care unit (ICU) admissions associated with COVID-19
2.3. Deaths associated with COVID-19
2.4. Seroconversion against non-Spike SARS-CoV-2 antigens
3. Cellular and humoral immunogenicity of ChAdOx1 nCoV-19 over the course of 6 months:
3.1. Antibodies against SARS-CoV-2 spike protein (seroconversion rates) at Day 28 post-vaccination
3.2. Proportion of seroconversion to antibodies against SARS-CoV-2 spike protein at Day 28 post-vaccination
3.3. Cellular immunity of ChAdOx1 nCoV-19 in older adults and in children (groups 1, 2 and 3 only)
3.4. Interferon-gamma (IFN-γ) enzyme-linked immunospot (ELISpot) responses to SARS-CoV-2

spike protein
4. Safety and immunogenicity of a booster dose of ChAdOx1 nCoV-19 in older adults aged 56 years or older (two-dose schedules for groups 1 and 2 only):
4.1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following booster vaccination
4.2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following booster vaccination
4.3. Occurrence of unsolicited adverse events (AEs) for 28 days following booster vaccination
4.4. Change from pre-booster for safety laboratory measures
4.5. Occurrence of disease enhancement episodes over the course of 6 months
4.6. Antibodies against SARS-CoV-2 spike protein at Day 56 post-vaccination
4.7. Proportion of seroconversion to antibodies against SARS-CoV-2 spike protein at Day 56 post-vaccination

Completion date
31/12/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/12/2020 (see additional files for previous interventions):
1. Adults aged 18-55 years (groups 4, 5, 6 and 11)
2. Adults aged 56-69 years (groups 1, 7 and 9)
3. Adults aged 70 years and older (groups 2, 8 and 10)
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 and access all medical records when relevant to study procedures
6. 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
7. Agreement to refrain from blood donation during the course of the study
8. Provide written informed consent

Additional Inclusion criteria for Group 12 (HIV sub-study):
1. HIV positive
2. Receiving antiretroviral therapy
3. Undetectable HIV viral load
4. CD4 >350 cells/ml

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
55 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 21/10/2020 (see additional files for previous interventions):
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 COV002 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 accidently unblind participants to group allocation. Participation in COV002 can only be allowed if volunteers are kept blinded to their serology results from local/national serological surveys
3. Receipt of any vaccine (licensed or investigational) other than the study intervention within 30 days before and after each study vaccination, with the exception of the licensed seasonal influenza vaccination and the licensed pneumococcal vaccination. Participants will be encouraged to receive these vaccinations at least 7 days before or after their study vaccine
4. Prior or planned receipt of an investigational or licensed vaccine or product likely to impact on interpretation of the trial data (e.g. Adenovirus vectored vaccines, any coronavirus vaccines). This exclusion criteria will not apply to group 11, as recruitment will be targeted at those volunteers who previously received a ChAdOx1 vectored vaccine.
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 (except group 12, where HIV infected participants are allowed); asplenia; recurrent severe infections and use 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
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: Continuous use of anticoagulants, such as coumarins and related anticoagulants (i.e. warfarin) or novel oral anticoagulants (i.e. apixaban, rivaroxaban, dabigatran and edoxaban)
15. Suspected or known current alcohol or drug dependency
16. 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
17. 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)
18. History of laboratory-confirmed COVID-19 (except groups 5d, 9, 10 and 11).
18.1 Seropositivity to SARS-CoV-2 before enrolment (except groups 5d, 9 and,10 and 11)

Additional exclusion criteria for Groups 4, 6, 9 and 10:
19. History of allergic disease or reactions likely to be exacerbated by paracetamol. Note: Caution should be taken when recommending paracetamol to adults who already take paracetamol chronically

Additional exclusion criteria for Group 3:
20. Chronic medical conditions such as chronic lung disease, chronic liver disease, chronic renal failure, chronic heart disease, congenital genetic syndromes (e.g. Trisomy 21)
21. Fulfil any of the contraindications to vaccination as specified in The Green Book

NB: volunteers with previous PCR-positive results are also allowed in groups 9, 10 and 11

Date of first enrolment
28/05/2020

Date of final enrolment
30/09/2020

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Centre for Clinical Vaccinology & Tropical Medicine
University of Oxford
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
NIHR WTCRF
University Hospital Southampton NHS Foundation Trust
Southampton
United Kingdom
SO16 6YD

Study participating centre

NIHR Imperial CRF
NIHR Imperial Clinical Research Facility Imperial College
Hammersmith Hospital, Imperial College NHS Trust
150 Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
St Georges University Hospital NHS Foundation Trust
Blackshaw Road
Tooting
London
United Kingdom
SW17 0TQ

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Southmead Road
Westbury-on-Trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
University of Nottingham Health Service
Cripps Health Centre
University Park
Nottingham
United Kingdom
NG7 2QW

Study participating centre

Sheffield Teaching Hospitals
Royal Hallamshire Hospital
Glossop Road
Sheffield
United Kingdom
S10 2RX

Study participating centre
University Hospitals Birmingham NHS Foundation Trust (UHB)
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
Wales (Public Health Wales)
Aneurin Bevan Local Health Board of Aneurin Bevan Local Health Board Headquarters,
St. Cadoc's Hospital, Lodge Road, Caerleon,
Newport
United Kingdom
NP18 3XQ

Study participating centre
Greater Glasgow and Clyde NHS Board
NHS Greater Glasgow and Clyde Corporate HQ
J B Russell House Gartnavel Royal Hospital Campus
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Department of Infection
St Thomas Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Liverpool School of Tropical Medicine
Accelerator Research Clinic Clinical Sciences Accelerator
1 Daulby Street
Liverpool
United Kingdom
L7 8XZ

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Royal Victoria Infirmary
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
UCLH
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
NHS Lothian
Western General Hospital
Crewe Rd
Edinburgh
United Kingdom
EH4 2XU

Study participating centre
NIHR Cambridge Clinical Research Facility
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Oxford University Hospital Foundation Trust
John Radcliffe Hospital

Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Nottingham University Hospitals NHS Trust
C Floor
South Block
Queen's Medical Centre Campus
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Hull University Teaching Hospitals NHS Trust (HUTH)
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
Northwick Park Hospital
London North West University Healthcare Trust
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

Sponsor information

Organisation
University of Oxford

Funder(s)

Funder type
Research organisation

Funder Name
National Institute for Health Research

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 current data sharing plans for this study are unknown and will be 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	results	19/12/2021	19/11/2020	Yes	No
Results article	results	06/03/2021	23/02/2021	Yes	No
Results article		29/06/2022	04/07/2022	Yes	No
HRA research summary			28/06/2023	No	No
Interim results article	interim results	09/01/2021	09/12/2020	Yes	No
Interim results article	Reactogenicity and immunogenicity after a late second dose or a third dose of ChAdOx1 nCoV-19 in the UK	01/09/2021	06/09/2021	Yes	No
Other files	Previous inclusion and exclusion criteria		28/09/2020	No	No
Other files	Previous inclusion and exclusion criteria		04/12/2020	No	No
Participant information sheet	version v2.0	14/04/2020	07/05/2020	No	Yes

Participant information sheet	version v2.0	14/04/2020	07/05/2020	No	Yes
Participant information sheet	version v2.0	14/04/2020	07/05/2020	No	Yes
Participant information sheet	version v3.0	13/05/2020	22/05/2020	No	Yes
Participant information sheet	version V4.0	26/05/2020	04/06/2020	No	Yes
Participant information sheet	version V2.0	26/05/2020	04/06/2020	No	Yes
Participant information sheet	version V2.0	26/05/2020	04/06/2020	No	Yes
Participant information sheet	version V2.0	26/05/2020	04/06/2020	No	Yes
Participant information sheet	version V4.0	08/06/2020	15/06/2020	No	Yes
Participant information sheet	version V4.0	08/06/2020	15/06/2020	No	Yes
Participant information sheet	version V4.0	08/06/2020	15/06/2020	No	Yes
Participant information sheet	version V4.0	08/06/2020	15/06/2020	No	Yes
Participant information sheet	version V6.0	18/06/2020	24/06/2020	No	Yes
Participant information sheet	version V5.0	18/06/2020	24/06/2020	No	Yes
Participant information sheet	version V5.0	18/06/2020	24/06/2020	No	Yes
Participant information sheet	version V5.0	18/06/2020	24/06/2020	No	Yes
Participant information sheet	version V8.0	12/07/2020	17/07/2020	No	Yes
Participant information sheet	version V8.0	12/07/2020	17/07/2020	No	Yes
Participant information sheet	version V8.0	12/07/2020	17/07/2020	No	Yes
Participant information sheet	version V9.0	20/07/2020	30/07/2020	No	Yes
Participant information sheet	version V9.0	20/07/2020	30/07/2020	No	Yes
Participant information sheet	version V9.0	20/07/2020	30/07/2020	No	Yes
Participant information sheet	version V10.0	05/08/2020	25/08/2020	No	Yes
Participant information sheet	version V10.0	05/08/2020	25/08/2020	No	Yes
Participant information sheet	version V10.0	05/08/2020	25/08/2020	No	Yes
Participant information sheet	version V11.0	11/09/2020	15/09/2020	No	Yes
Participant information sheet	version V11.0	11/09/2020	15/09/2020	No	Yes
Participant information sheet	version V11.0	11/09/2020	15/09/2020	No	Yes
Participant information sheet	version V12.0	15/09/2020	28/09/2020	No	Yes
Participant	version V12.0	15/09	28/09		

information sheet		/2020	/2020	No	Yes
Participant information sheet	version V12.0	15/09 /2020	28/09 /2020	No	Yes
Participant information sheet	version V13.0	14/10 /2020	21/10 /2020	No	Yes
Participant information sheet	version V13.0	14/10 /2020	21/10 /2020	No	Yes
Participant information sheet	version V13.0	14/10 /2020	21/10 /2020	No	Yes
Participant information sheet	version V14.0	02/12 /2020	04/12 /2020	No	Yes
Participant information sheet	version V14.0	02/12 /2020	04/12 /2020	No	Yes
Participant information sheet	version V14.0	02/12 /2020	04/12 /2020	No	Yes
Participant information sheet	version V15.0	10/12 /2020	14/12 /2020	No	Yes
Participant information sheet	version V15.0	10/12 /2020	14/12 /2020	No	Yes
Participant information sheet	version V15.0	10/12 /2020	14/12 /2020	No	Yes
Participant information sheet	version V16.0	01/03 /2021	10/03 /2021	No	Yes
Participant information sheet	version V16.0	01/03 /2021	10/03 /2021	No	Yes
Participant information sheet	version V16.0	01/03 /2021	10/03 /2021	No	Yes
Participant information sheet	version 17.0	09/04 /2021	21/04 /2021	No	Yes
Participant information sheet	version 17.0	09/04 /2021	21/04 /2021	No	Yes
Participant information sheet	version 4.0	09/04 /2021	21/04 /2021	No	Yes
Participant information sheet	version 17.0	09/04 /2021	21/04 /2021	No	Yes
Participant information sheet	version 4.1	14/05 /2021	24/05 /2021	No	Yes
Participant information sheet	version 17.1	14/05 /2021	24/05 /2021	No	Yes
Participant information sheet	version 17.1	14/05 /2021	24/05 /2021	No	Yes
Participant information sheet	version 17.1	14/05 /2021	24/05 /2021	No	Yes
Participant information sheet	version 5	12/08 /2021	02/09 /2021	No	Yes
Participant information sheet	version 18	12/08 /2021	02/09 /2021	No	Yes
Participant information sheet	version 18	12/08 /2021	02/09 /2021	No	Yes
Participant information sheet	version 18	12/08 /2021	02/09 /2021	No	Yes
Participant information sheet	Group 12 version 6.0		14/10 /2021	No	Yes
Participant information sheet	Participant information sheet	11/11 /2025	11/11 /2025	No	Yes
	version 22.2	26/06	01/08		

Protocol file		/2023	/2023	No	No
Protocol file	version 22.3	27/03 /2024	24/04 /2024	No	No
Study website	Study website	11/11 /2025	11/11 /2025	No	Yes