Footnote 13

History of Changes for Study: NCT04324606

A Study of a Candidate COVID-19 Vaccine (COV001)

Latest version (submitted May 22, 2020) on ClinicalTrials.gov

- A study version is represented by a row in the table.
- Select two study versions to compare. One each from columns A and B.
- Choose either the "Merged" or "Side-by-Side" comparison format to specify how the two study versions are to be displayed. The Side-by-Side format only applies to the Protocol section of the study.
- Click "Compare" to do the comparison and show the differences.
- Select a version's Submitted Date link to see a rendering of the study for that version.
- The yellow A/B choices in the table indicate the study versions currently compared below. A yellow table row indicates the study version currently being viewed.
- Hover over the "Recruitment Status" to see how the study's recruitment status changed.
- Study edits or deletions are displayed in ~~red~~.
- Study additions are displayed in *green*.

Study Record Versions

Version	A	B	Submitted Date	Changes
1	◉	○	March 26, 2020	None (earliest Version on record)
2	○	○	April 2, 2020	Arms and Interventions, Study Status, Eligibility and Oversight
3	○	○	April 14, 2020	Recruitment Status, Contacts/Locations and Study Status

Version	A	B	Submitted Date	Changes
4	○	○	April 17, 2020	Arms and Interventions, Study Description and Study Status
5	○	○	April 22, 2020	Arms and Interventions, Contacts/Locations, Eligibility, Outcome Measures, Study Design, Study Description and Study Status
6	○	○	May 7, 2020	Contacts/Locations, Arms and Interventions, Study Status, Eligibility, Outcome Measures and Study Design
7	○	○	May 15, 2020	Recruitment Status, Contacts/Locations, Study Status, Eligibility, Study Design and Study Description
8	○	◉	May 22, 2020	Arms and Interventions and Study Status

Compare

Comparison Format: ◉ Merged ○ Side-by-Side

Scroll up to access the controls

Changes (Merged) for Study: NCT04324606
March 26, 2020 (v1) -- May 22, 2020 (v8)

Changes in: Arms and Interventions, Study Status, Contacts/Locations, Outcome Measures, Study Design, Study Description, Eligibility and Oversight

☐ **Show only changed modules**

Study Identification

Unique Protocol ID: COV001

Brief Title: A Study of a Candidate COVID-19 Vaccine (COV001)

Official Title: A Phase I/II Study to Determine Efficacy, Safety and Immunogenicity of the Candidate Coronavirus Disease (COVID-19) Vaccine ChAdOx1 nCoV-19 in UK Healthy Adult Volunteers

Secondary IDs:

Study Status

Record Verification:	March 2020
Overall Status:	*Active,* not ~~yet~~ recruiting
Study Start:	~~March 2020~~ *April 23, 2020*
Primary Completion:	May 2021 [Anticipated]
Study Completion:	May 2021 [Anticipated]
First Submitted:	March 20, 2020
First Submitted that Met QC Criteria:	March 26, 2020
First Posted:	March 27, 2020 [Actual]
Last Update Submitted that Met QC Criteria:	~~March 26~~ *May 22*, 2020
Last Update Posted:	~~March~~ *May* 27, 2020 [Actual]

Sponsor/Collaborators

Sponsor:	University of Oxford
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	No
U.S. FDA-regulated Device:	No
Data Monitoring:	Yes

Study Description

Brief Summary: A phase I/II single-blinded, randomised, ~~placebo controlled,~~ multi-centre study to determine efficacy, safety and immunogenicity of the candidate Coronavirus Disease (COVID-19) vaccine ChAdOx1 nCoV-

19 in UK healthy adult volunteers aged 18-55 years. The vaccine will be administered intramuscularly (IM).

Detailed Description: There will be ~~5~~ *4* study groups and it is anticipated that a total of ~~510~~ *1090* volunteers will be enrolled. Volunteers will participate in the study for approximately 6 months, with the option to come for an additional follow up visit at Day 364.

Conditions

Conditions: Coronavirus

Keywords: COVID-19, Vaccine

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 1/Phase 2

Interventional Study Model: Sequential Assignment

Number of Arms: ~~5~~ *9*

Masking: Single (Participant)

Allocation: Randomized

Enrollment: ~~510 [Anticipated]~~ *1090 [Actual]*

Arms and Interventions

Arms	Assigned Interventions
Experimental: Group 1a Volunteers will receive a single dose of 5x10^10vp ChAdOx1 nCoV-19. Volunteers will be blinded and will not know if they have received the IMP or the ~~placebo~~ *MenACWY comparator*.	Biological: ChAdOx1 nCoV-19 *A single dose of* 5x10^10vp of ChAdOx1 nCoV-19

Arms	Assigned Interventions
~~Placebo~~ *Active* Comparator: Group 1b Volunteers will receive a *standard* single ~~injection~~ *dose* of ~~saline~~ *MenACWY vaccine delivered* intramuscularly. Volunteers will be blinded and will not know if they have received the IMP or the ~~placebo~~ *MenACWY comparator*.	*Biological* ~~Saline Placebo~~ *MenACWY* ~~Saline injection delivered intramuscularly~~ *Standard single dose of MenACWY vaccine delivered intramuscularly*
Experimental: Group 2a Volunteers will receive a single dose of 5x10^10vp ChAdOx1 nCoV-19. Volunteers will be blinded and will not know if they have received the IMP or the ~~placebo~~ *MenACWY comparator*.	Biological: ChAdOx1 nCoV-19 *A single dose of* 5x10^10vp of ChAdOx1 nCoV-19
~~Placebo~~ *Active* Comparator: Group 2b Volunteers will receive a *standard* single ~~injection~~ *dose* of ~~saline~~ *MenACWY vaccine delivered* intramuscularly. Volunteers will be blinded and will not know if they have received the IMP or the ~~placebo~~ *MenACWY comparator*.	*Biological* ~~Saline Placebo~~ *MenACWY* ~~Saline injection delivered intramuscularly~~ *Standard single dose of MenACWY vaccine delivered intramuscularly*
Experimental: Group 3 Volunteers will receive ~~two~~ *one* dose of 5x10^10vp ChAdOx1 nCoV-19 at week 0 and *one dose of 5x10^10vp ChAdOx1 nCoV-19 at* week 4.	~~Biological: ChAdOx1 nCoV-19~~ ~~5x10^10vp of ChAdOx1 nCoV-19~~ *Biological: ChAdOx1 nCoV-19 boost* *A single dose of 5x10^10vp of ChAdOx1 nCoV-19 followed by a boost dose of 5x10^10vp of ChAdOx1 nCoV-19*
Experimental: Group 4a *Volunteers will receive a single dose of 5x10^10vp ChAdOx1 nCoV-19. Volunteers will be blinded and will not know if they have received the IMP or the MenACWY comparator.*	*Biological: ChAdOx1 nCoV-19* *A single dose of 5x10^10vp of ChAdOx1 nCoV-19*
Active Comparator: Group 4b *Volunteers will receive a standard single dose of MenACWY vaccine delivered intramuscularly. Volunteers will be blinded and will not know if they have received the IMP or the MenACWY comparator.*	*Biological: MenACWY* *Standard single dose of MenACWY vaccine delivered intramuscularly*

Arms	Assigned Interventions
Experimental: Group 4c *Volunteers will receive a single dose of 5x10^10vp ChAdOx1 nCoV-19 plus Paracetamol. Volunteers will be blinded and will not know if they have received the IMP or the MenACWY comparator.*	*Biological: ChAdOx1 nCoV-19* *A single dose of 5x10^10vp of ChAdOx1 nCoV-19* *Drug: Paracetamol* *1g every 6 hours for 24 hours*
Active Comparator: Group 4d *Volunteers will receive a standard single dose of MenACWY vaccine delivered intramuscularly plus Paracetamol. Volunteers will be blinded and will not know if they have received the IMP or the MenACWY comparator.*	*Biological: MenACWY* *Standard single dose of MenACWY vaccine delivered intramuscularly* *Drug: Paracetamol* *1g every 6 hours for 24 hours*

Outcome Measures

Primary Outcome Measures:

1. Assess efficacy of the candidate ChAdOx1 nCoV-19 against COVID-19: Number of virologically confirmed (PCR positive) symptomatic cases
   Number of virologically confirmed (PCR positive) symptomatic cases of COVID-19

   [Time Frame: 6 months]
2. Assess the safety of the candidate vaccine ChAdOx1 nCoV: Occurrence of serious adverse events (SAEs)
   Occurrence of serious adverse events (SAEs) throughout the study duration

   [Time Frame: 6 months]

Secondary Outcome Measures:

3. Assess the safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV: Occurrence of solicited local reactogenicity signs and symptoms
   Occurrence of solicited local reactogenicity signs and symptoms for 7 days following vaccination

   [Time Frame: 7 days following vaccination]
4. Assess the safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV: Occurrence of solicited

systemic reactogenicity signs and symptoms
Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following vaccination

[Time Frame: 7 days following vaccination]

5. Assess the safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV: Occurrence of unsolicited adverse events (AEs)
   Occurrence of unsolicited adverse events (AEs) for 28 days following vaccination

   [Time Frame: 28 days following vaccination]
6. Assess the safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV through standard blood tests
   Change from baseline for safety laboratory measures (haematology and biochemistry blood results)

   [Time Frame: 6 months]
7. Assess the safety, tolerability and reactogenicity profile of the candidate vaccine ChAdOx1 nCoV by measuring the number of disease enhancement episodes
   Occurrence of disease enhancement episodes

   [Time Frame: 6 months]
8. Assess efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19
   Number of deaths associated with COVID-19

   [Time Frame: 6 months]
9. Assess efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19
   Number of hospital admissions associated with COVID-19

   [Time Frame: 6 months]
10. Assess efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19
    Number of intensive care unit admissions associated with COVID-19

    [Time Frame: 6 months]
11. Assess efficacy of the candidate ChAdOx1 nCoV-19 against severe and non-severe COVID-19 by measuring seroconversion

rates
Proportion of people who become seropositive for non-Spike SARS-CoV-2 antigens during the study

[Time Frame: 6 months]

12. Assess cellular and humoral immunogenicity of ChAdOx1 nCoV-19 through ELISpot assays
Interferon-gamma (IFN-γ) enzyme-linked immunospot (ELISpot) responses to SARS-CoV-2 spike protein

[Time Frame: 6 months]

13. Assess cellular and humoral immunogenicity of ChAdOx1 nCoV-19
~~Enzyme-linked immunosorbent assay (ELISA) to~~ Quantify antibodies against SARS-CoV-2 spike protein (seroconversion rates)

[Time Frame: 6 months]

Other Pre-specified Outcome Measures:

14. Assess cellular and humoral immunogenicity of ChAdOx1 nCoV-19 through Virus neutralising antibody assays
Virus neutralising antibody (NAb) assays against live and/or pseudotype SARS-CoV-2 virus

[Time Frame: 6 months]

15. *To assess safety, reactogenicity, immunogenicity and efficacy endpoints, for participants receiving prophylactic paracetamol*
All safety, reactogenicity, immunogenicity and efficacy endpoints

[Time Frame: *6 months*]

Eligibility

Minimum Age:	18 Years
Maximum Age:	55 Years
Sex:	All
Gender Based:	
Accepts Healthy Volunteers:	Yes
Criteria:	Inclusion Criteria ~~:~~

The volunteer must satisfy all the following criteria to be eligible for the study:

- Healthy adults aged 18-55 years.
- Able and willing (in the Investigator's opinion) to comply with all study requirements *(participants must not rely on public transport or taxis)*.
- 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.
- For females 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.
- Agreement to refrain from blood donation during the course of the study.
- Provide written informed consent.

Exclusion Criteria ~~:~~

The volunteer may not enter the study if any of the following apply:

- Prior receipt of any vaccines (licensed or investigational) ≤30 days before enrolment
- Planned receipt of any vaccine other than the study intervention within 30 days before and after each study vaccination .
- 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).
- Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate.
- Any confirmed or suspected immunosuppressive or immunodeficient state, including HIV infection; asplenia; recurrent severe infections and ~~chronic~~ use ~~(more than 14 days)~~ *of* immunosuppressant medication within the past 6 months ~~(inhaled and~~ *, except* topical steroids ~~are allowed~~ *or short-term oral steroids (course lasting <14 days*) .
- *Any autoimmune conditions, except mild psoriasis, well-controlled autoimmune thyroid disease, vitiligo or stable coeliac disease not requiring immunosuppressive or immunomodulatory therapy.*
- History of allergic disease or reactions likely to be exacerbated by any component of the *ChAdOx1 nCoV-19 or MenACWY* vaccines.
- Any history of ~~hereditary~~ angioedema ~~or idiopathic angioedema~~ .
- Any history of anaphylaxis ~~in relation to vaccination~~ .
- Pregnancy, lactation or willingness/intention to become pregnant during the study.

- History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ).
- *History of serious psychiatric condition likely to affect participation in the study (e.g. ongoing severe depression, history of admission to an in-patient psychiatric facility, recent suicidal ideation, history of suicide attempt, bipolar disorder, personality disorder, alcohol and drug dependency, severe eating disorder, psychosis, use of mood stabilisers or antipsychotic medication).*
- ~~History of serious psychiatric condition likely to affect participation in the study.~~
- Bleeding disorder (e.g. factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture.
- Any other serious chronic illness requiring hospital specialist supervision.
- *Chronic respiratory diseases, including mild asthma (resolved childhood asthma is allowed)*
- *Chronic cardiovascular disease (including hypertension), gastrointestinal disease, liver disease (except Gilberts Syndrome), renal disease, endocrine disorder (including diabetes) and neurological illness (excluding migraine)*
- *Seriously overweight (BMI≥40 Kg/m2) or underweight (BMI≤18 Kg/m2)*
- Suspected or known current alcohol abuse as defined by an alcohol intake of greater than 42 units every week.
- Suspected or known injecting drug abuse in the 5 years preceding enrolment.
- Any clinically significant abnormal finding on screening biochemistry, haematology blood tests or urinalysis.
- 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.
- History of laboratory confirmed COVID-19.
- ~~New onset of fever and a cough or shortness of breath in the 30 days preceding screening and/or enrolment~~ *New onset of fever or a cough or shortness of breath or anosmia/ageusia since February 2020. Should a reliable test become available, this exclusion criteria will be replaced with seropositivity for SARS-CoV-2 before enrolment.*
- *Those who have been at high risk of exposure before enrolment, including but not limited to: close contacts of confirmed COVID-19 cases, anyone who had to self-isolate as a result of a symptomatic household member, frontline healthcare professionals working in A&E, ICU and other higher risk areas. Should a reliable test become available, this exclusion criteria will be replaced with seropositivity for SARS-CoV-2 before enrolment.*

- *Living in the same household as any vulnerable groups at risk of severe COVID-19 disease (as per Public Health England guidance)*

Additional exclusion criteria (subset of participants receiving Paracetamol in group 4 only)

• History of allergic disease or reactions likely to be exacerbated by Paracetamol

Re-vaccination exclusion criteria

- Anaphylactic reaction following administration of vaccine
- Pregnancy

Contacts/Locations

Central Contact: ~~Volunteer Recruitment Co-ordinator~~
~~Telephone: 01865 611424~~
~~Email: vaccinetrials@ndm.ox.ac.uk~~

Study Officials: Andrew Pollard, Prof
Principal Investigator
University of Oxford

Locations: **United Kingdom, Hampshire**

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