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A study of the Ad26.COV2.S vaccine candidate for the prevention of SARS-CoV-2-mediated COVID-19 in adults

Submission date
04/11/2020

Recruitment status
No longer recruiting

Registration date
04/11/2020

Overall study status
Completed

Last Edited
25/06/2024

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
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 April 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.
This study is being done to test the new experimental vaccine called Ad26.COV2.S. A vaccine may help to prevent disease by allowing the human body to form an immune response against what causes the disease, in this case a virus. This defensive response is a way the body fights infections. Doctors and scientists hope Ad26.COV2.S will prevent or lessen the severity of COVID-19. The main aims of this study are to see how well Ad26.COV2.S works to prevent COVID-19, if the Ad26.COV2.S vaccine is safe, and if it causes any unwanted side effects.

Who can participate?
Participants of any gender from two age groups: one group aged 18 to 59 years, and another group aged 60 years and older. Participants can be healthy or have some existing health conditions that may make them more vulnerable to progress to severe COVID-19.

What does the study involve?
In this study all participants will receive two injections, about 2 months apart. Some participants

will receive two injections of Ad26.COV2.S and others will receive two injections of placebo. The placebo looks just like the Ad26.COV2.S vaccine and is given in the same way, by injection (shot). The placebo injection in this study will be sodium chloride, also known as sterile saltwater. It has no active vaccine in it. Using a placebo in the study enables researchers to see potential differences between the vaccine and the placebo. All participants will have two injections of the study vaccine or placebo, blood draws, saliva samples, swabs of the back of the nose. All participants will be asked every day to answer questions about how they are feeling via an electronic device. If participants get COVID-19 symptoms, the study staff will monitor them and their symptoms daily via an electronic device and ask them for nasal swabs and saliva samples.

What are the possible benefits and risks of participating?
The most common risks of taking part in the study are getting symptoms such as pain and/or swelling at the injection site, muscle aches, headaches, or fever after getting the study vaccine or placebo. There are other, less frequent risks. It is not known whether getting the study vaccine will benefit participants in any way, since it is not known whether the vaccine will work. During the study, the sponsor may learn new information about the study vaccine. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks. There is a small chance that participants may have a bad reaction to the vaccine, or it may make them sicker if they get COVID-19. There are no costs to participants to be in the study. The sponsor will pay for the study vaccines and tests that are part of the study. The participant will receive reasonable reimbursement for study-related costs (e.g., travel/parking costs). There will be no payment for doctor visits, treatments, or tests that are not part of this study.

Where is the study run from?
Janssen Vaccines & Prevention B.V. is the sponsor for this study and has partnered with IQVIA for study delivery. The study will be run at multiple healthcare locations both within the UK and around the world.

When is the study starting and how long is it expected to run for?
July 2020 to June 2023 (recruitment starts in November 2020)

Who is funding the study?
Janssen Vaccines & Prevention B.V. (USA)

Who is the main contact?
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Contact information

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Scientific

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Clinical Trials Information System (CTIS)
2020-003643-29

Integrated Research Application System (IRAS)
288552

ClinicalTrials.gov (NCT)
NCT04614948

Protocol serial number
Protocol-ID VAC31518COV3009, IRAS 288552, CPMS 46804

Study information

Scientific Title

A randomized, double-blind, controlled Phase 3 study to assess the efficacy and safety of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older

Acronym
ENSEMBLE 2

Study objectives
Ad26.COV2.S is better than placebo in the prevention of molecularly confirmed moderate to severe/critical coronavirus disease-2019 (COVID-19) in adult participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/11/2020, Yorkshire & The Humber - Sheffield Research Ethics Committee (NHS Blood and Transplant Blood Donor Centre, Holland Drive, Newcastle upon Tyne, Tyne and Wear, NE2 4NQ, UK; +44 (0)207 104 8029; sheffield.rec@hra.nhs.uk), REC ref: 20/YH/0317

Study design
Multi-centre randomized double-blind placebo-controlled parallel-group study with staggered enrollment strategy

Primary study design
Interventional

Study type(s)
Prevention

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

Interventions
Participants will be randomized in parallel in a 1:1 ratio to receive experimental treatment or placebo using the interactive web response system (IWRS). The randomization will be stratified for vaccination unit, age group, and absence/presence of comorbidities.

Participants in the experimental treatment arm will receive an intramuscular (IM) injection of Ad26.COV2.S vaccine on Day 1 and Day 57.
Participants in the placebo comparator arm will receive an IM injection of placebo on Day 1 and Day 57.

The study will consist of: a screening phase (up to 28 days), double-blind study period (60 weeks), and a long-term follow-up period (1 additional year). The total study duration will be a maximum of 2 years and 3 months for the participants. Assessments like efficacy (COVID-19-like signs and symptoms, etc), immunogenicity (such as humoral immune responses), and safety (such as AEs monitoring) will be performed throughout the study.

Added 18/11/2021:
All ongoing participants who only received a single vaccination with Ad26.COV2.S in the study will be offered to receive single booster dose of Ad26.COV2.S in the open label phase, preferably within 6 to 12 months after the participant's first Ad26.COV2.S vaccination

Intervention Type
Biological/Vaccine

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ad26.COV2.S, JNJ-78436735, VAC31518

Primary outcome(s)
Number of participants who were seronegative at baseline with first occurrence of molecularly confirmed moderate to severe/critical COVID-19, with onset at least 14 days after the 2nd vaccination, monitored from 14 days after 2nd vaccination (Day 71) to end of study (2 years and 3 months). Moderate defined as one sign or symptom form a list of signs and symptoms, such as respiratory rate >= 20 breaths per minute and symptoms such as shortness of breath or two signs or symptoms from a list of signs and symptoms or severe COVID-19 defined in US Food and Drug Administration (FDA) guidance.

Key secondary outcome(s))
1. Number of participants, regardless of their serostatus, with first occurrence of molecularly confirmed moderate to severe/critical COVID-19, monitored from 1 day after the 1st vaccination (Day 2) to end of study (2 years and 3 months). Moderate defined as one sign or symptom form a list of signs and symptoms, such as respiratory rate >= 20 breaths per minute and symptoms such as shortness of breath or two signs or symptoms from a list of signs and symptoms or severe COVID-19 defined in USA Food and Drug Administration (FDA) guidance.
2. Number of participants, regardless of their serostatus, with first occurrence of molecularly confirmed moderate to severe/critical COVID-19, with onset at least 14 days after 2nd vaccination, monitored from 14 days after the 2nd vaccination (Day 71) to end of study (2 years and 3 months). Moderate defined as one sign or symptom form a list of signs and symptoms, such as respiratory rate >= 20 breaths per minute and symptoms such as shortness of breath or two signs or symptoms from a list of signs and symptoms or severe COVID-19 defined in USA Food and Drug Administration (FDA) guidance.
3. Number of participants who were seronegative at baseline with first occurrence of molecularly confirmed moderate to severe/critical COVID-19, monitored from 1 day after the 1st vaccination (Day 2) to end of study (2 years and 3 months). Moderate defined as one sign or symptom form a list of signs and symptoms, such as respiratory rate >= 20 breaths per minute and symptoms such as shortness of breath or two signs or symptoms from a list of signs and symptoms or severe COVID-19 defined in US Food and Drug Administration (FDA) guidance.
4. Number of participants who were seronegative at baseline with first occurrence of molecularly confirmed moderate to severe/critical COVID-19, with onset at least 14 days after 1st vaccination, monitored from 14 days after the 1st vaccination (Day 15) to end of study (2 years and 3 months). Moderate defined as one sign or symptom form a list of signs and symptoms, such as respiratory rate >= 20 breaths per minute and symptoms such as shortness of breath or two signs or symptoms from a list of signs and symptoms or severe COVID-19 defined in USA Food and Drug Administration (FDA) guidance.

5. Number of participants with first occurrence of COVID-19 requiring medical intervention (such as a composite endpoint of hospitalization, intensive care unit (ICU) admission, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO), linked to objective measures such as decreased oxygenation, X-ray or computed tomographic [CT] findings) linked to any molecularly confirmed, COVID-19, with onset at least 14 days after the 2nd vaccination, monitored from 14 days after the 2nd vaccination (Day 71) to end of study (2 years and 3 months)
6. SARS-CoV-2 viral load assessed by quantitative reverse-transcriptase polymerase chain reaction (RT-PCR) in participants with molecularly confirmed, moderate to severe/critical COVID-19, measured during the course of a COVID-19 episode, from 14 days after the 2nd vaccination (Day 71) to end of study (2 years and 3 months). Nasal swabs will be used to detect and/or quantify SARS-CoV-2.
7. Number of participants with first occurrence of molecularly confirmed mild COVID-19, with onset at least 14 days after 2nd vaccination, monitored from 14 days after the 2nd vaccination (Day 71) to end of study (2 years and 3 months. Molecularly confirmed mild COVID-19 is defined as a SARS-CoV-2 positive RT-PCR or molecular test result from any available respiratory tract sample (for example, nasal swab sample, sputum sample, throat swab sample, saliva sample) or other sample. Mild COVID-19 includes: fever, sore throat, malaise, headache, muscle pain, gastrointestinal symptoms, cough, chest congestion, runny nose, wheezing, skin rash, eye irritation or discharge, or chills, without shortness of breath or dyspnea.
8. Number of participants with first occurrence of molecularly confirmed COVID-19 defined by the US FDA harmonized case definition, with onset at least 14 days after 2nd vaccination, monitored from 14 days after the 2nd vaccination (Day 71) to end of study (2 years and 3 months). Molecularly confirmed moderate and severe/critical COVID-19 defined as a positive SARS-CoV-2 positive RT-PCR or molecular test result from any available respiratory tract sample (for example, nasal swab sample, sputum sample, throat swab sample, saliva sample) or other sample; and COVID-19 symptoms consistent with those defined by the US FDA harmonized case definition at the time of finalization of this protocol: fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea.
9. Burden of Disease (BOD) based on first occurrence of molecularly confirmed symptomatic COVID-19 (including mild, moderate, or severe/critical COVID-19) with onset at least 14 days after 2nd vaccination, monitored from 14 days after the 2nd vaccination (Day 71) to end of study (2 years and 3 months).
10. Number of participants with serologic conversion, determined by Enzyme-Linked Immunosorbent Assay (ELISA) and/or SARS-CoV-2 immunoglobulin assay that is dependent on the SARS-CoV-2 nucleocapsid (N) protein, between baseline (Day 1) and 14 days, 6 months, and 1 year after the 2nd vaccination
11. Number of participants with first occurrence of SARS-CoV-2 infection that is either serologically and/or molecularly confirmed, with onset at least 14 days after 2nd vaccination, monitored from 14 days after the 2nd vaccination (Day 71) to end of study (2 years and 3 months).
12. Number of participants with serious adverse events (SAEs) monitored from Day 1 to end of study (2 years and 3 months). An SAE is any untoward medical occurrence that at any dose may result in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly /birth defect, is a suspected transmission of any infectious agent via a medicinal product.
13. Number of participants with medically-attended adverse events (MAAEs), monitored from Day 1 to 6 months after 2nd vaccination (up to 34 weeks). MAAEs are defined as AEs with medically-attended visits including hospital, emergency room, urgent care clinic, or other visits to or from medical personnel for any reason. Routine study visits will not be considered medically-attended visits. New onset of chronic diseases will be collected as part of MAAEs.

14. Number of participants with medically-attended adverse events (MAAEs) leading to study discontinuation, monitored from Day 1 to end of study (2 years and 3 months). MAAEs are defined as AEs with medically-attended visits including hospital, emergency room, urgent care clinic, or other visits to or from medical personnel for any reason. Routine study visits will not be considered medically-attended visits. New onset of chronic diseases will be collected as part of MAAEs.
15. Number of participants with solicited local adverse events (AEs) with onset in the 7 day-period after the first or second vaccination, assessed up to day 8 (7 days after first vaccination on Day 1) and up to Day 64 (7 days after second vaccination on Day 57). Participants will be asked to note in the e-Diary occurrences of injection site pain/tenderness, erythema, and swelling at the study vaccine injection site daily for 7 days post each vaccination (day of each vaccination and the subsequent 7 days).
16. Number of participants with solicited systemic AEs with onset in the 7-day period after the first or second vaccination, measured up to Day 8 (7 days after first vaccination on Day 1) and up to Day 64 (7 days after second vaccination on Day 57). Participants will be instructed on how to record daily temperature using a thermometer provided for home use. Participants should record the temperature in the e-Diary in the evening of the day of each vaccination, and then daily for the next 7 days approximately at the same time each day. If more than 1 measurement is made on any given day, the highest temperature of that day will be recorded in the e-Diary. Fever is defined as endogenous elevation of body temperature >= 38.0 degrees Celsius or >= 100.4 degrees Fahrenheit, as recorded in at least one measurement. Participants will also be instructed on how to note signs and symptoms in the e-Diary on a daily basis for 7 days post each vaccination (day of each vaccination and the subsequent 7 days), for the following events: fatigue, headache, nausea, myalgia.
17. Number of participants with unsolicited local adverse events (AEs) with onset in the 28-day period after the first or second vaccination, measured up to Day 29 (28 days after first vaccination on Day 1), and up to Day 85 (28 days after second vaccination on Day 58). Unsolicited AEs are all AEs for which the participant is not specifically questioned in the participant diary.
18. SARS-CoV-2 binding antibodies assessed by ELISA (as a measure for humoral immune response) for up to 2 years and 3 months.

Removed 01/02/2021:
19. SARS-CoV-2 neutralizing antibody titers assessed by Virus Neutralization Assay (VNA) (as a measure for humoral immune response) for up to 2 years and 3 months.

Added 20/04/2021:
19. Number of participants with first occurrence of Molecularly confirmed Moderate to Severe /Critical COVID-19 and who were Seronegative at baseline, monitored from 28 days after the first vaccination (day 29) to end of study (2 years and 3 months). Moderate defined as one sign or symptom from a list of signs and symptoms, such as respiratory rate >= 20 breaths per minute and symptoms such as shortness of breath or two signs or symptoms from a list of sign and symptoms or severe COVID-19 defined in FDA guidance.
20. Number of participants with Asymptomatic infection detected by reverse Transcriptase-Polymerase chain reaction (RT-PCR) for up to 2 years and 3 months. Number of participants with asymptomatic infection as assessed by RT-PCR will be reported.

Completion date
18/06/2023

Eligibility

Key inclusion criteria
1. Adult men or women of 18 years or older
2. Contraceptive (birth control) use should be consistent with local regulations regarding the acceptable methods of contraception for those participating in clinical studies
3. All participants of childbearing potential must: have a negative highly sensitive urine pregnancy test at screening; and have a negative highly sensitive urine pregnancy test immediately prior to each study vaccine administration
4. Participant agrees to not donate bone marrow, blood, and blood products from the first study vaccine administration until 3 months after receiving the last dose of study vaccine
5. Must be willing to provide verifiable identification, has means to be contacted and to contact the investigator during the study
6. Must be able to read, understand, and complete questionnaires in the electronic clinical outcome assessment (eCOA) (that is, the coronavirus disease-2019 [COVID-19] signs and symptoms surveillance question, the e-Diary, and the electronic patient-reported outcomes (ePROs)

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Sex
All

Total final enrolment
31705

Key exclusion criteria
1. Participant has a clinically significant acute illness (this does not include minor illnesses such as diarrhea or mild upper respiratory tract infection) or temperature greater than or equal to (>=) 38.0 degrees Celsius (100.4 degrees Fahrenheit) within 24 hours prior to the planned first dose of study vaccine; randomization at a later date is permitted at the discretion of the investigator and after consultation with the sponsor
2. Participant has a known or suspected allergy or history of anaphylaxis or other serious adverse reactions to vaccines or their excipients
3. Participant received or plans to receive: (a) licensed live attenuated vaccines - within 28 days before or after planned administration of study vaccine; and (b) other licensed (not live) vaccines - within 14 days before or after planned administration of study vaccine
4. Participant previously received a coronavirus vaccine
5. Participant received an investigational drug (including investigational drugs for prophylaxis of COVID-19) or used an invasive investigational medical device within 30 days or received an investigational vaccine (including investigational Adenoviral-vectored vaccines) within 6 months before the planned administration of the first dose of study vaccine or is currently enrolled or plans to participate in another investigational study during the course of this study

Date of first enrolment
15/11/2020

Date of final enrolment
12/03/2021

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Belgium

Colombia

France

Germany

Philippines

South Africa

Spain

United States of America

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Sponsor information

Organisation
Janssen (Netherlands)

ROR
https://ror.org/04cxegr21

Funder(s)

Funder type
Industry

Funder Name
Janssen Pharmaceuticals

Alternative Name(s)
Janssen Pharmaceutica NV, JANSSEN-CILAG NV, Janssen Belgium, Janssen, Janssen Pharmaceuticals

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Belgium

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing policy of the Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access (YODA) Project site at yoda.yale.edu.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			25/06/2024	No	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes