ISRCTN14037053 https://doi.org/10.1186/ISRCTN14037053

Dendritic cell vaccine to prevent COVID-19

Submission date
25/12/2020

Recruitment status
No longer recruiting

Registration date
31/12/2020

Overall study status
Completed

Last Edited
30/12/2020

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

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.

This study aims to test a vaccine for COVID-19 that contains a SARS-CoV-2 S-protein.

Who can participate?
Subjects eligible for treatment will be those who are not actively infected with SARS-CoV-2, have no evidence of prior infection with SARS-CoV-2, and give informed consent for a vaccination with AV-COVID-19.

What does the study involve?
Participants will first be screened for COVID-19 infection and have some blood taken. Then participants will be randomly allocated to receive the experimental vaccine at one of 9 different doses. Participants will be followed up for 28 days.

What are the possible benefits and risks of participating?
You may not benefit medically from participating in this study, but it is hoped that the AV-COVID-19 vaccine will induce your immune system to produce antibodies against SARS-CoV-2 S-

protein that may prevent a COVID-19 infection from occurring in the future.
With this investigational product and the periodic exposure to GM-CSF, the most common side effects include mild to moderate local injection site reaction (80%; e.g., irritation/pain, redness of the skin, itching), flu-like symptoms (15%; e.g., fatigue, headache, body aches, low-grade fever), and bone discomfort (10%) that resolve in 24 to 72 hours. Occasionally, patients experienced hives and/or redness or tenderness at the site of a previous injection, or elsewhere on the body. These effects typically go away over a few hours to days and seldom require medical attention.
As with taking any drug, there is a risk of an allergic reaction. Should a significant allergic reaction occur, your health care team may prescribe agents to relieve the symptoms.
There could be unanticipated toxicities or side effects from these study therapies.

Where is the study run from?
Dr Kariadi Hospital (Indonesia)

When is the study starting and how long is it expected to run for?
November 2020 to January 2022

Who is funding the study?
Indonesia Ministry of Health

Who is the main contact?
Dr Muhammad Karyana, mkaryana@gmail.com

Contact information

Type(s)
Public

Contact name
Dr Muhammad Karyana

ORCID ID
http://orcid.org/0000-0002-7785-5731

Contact details
National Institute of Health Research and Development
Ministry of Health
Jl. Percetakan Negara No. 29
Jakarta
Indonesia
10560
+62 816789817
muhammad.karyana@kemkes.go.id

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT04685603

Secondary identifying numbers
UTN U1111-1263-0568, CL-COV-P02-ID

Study information

Scientific Title
Adaptive phase I clinical trial of a preventive vaccine consisting of autologous dendritic cells previously incubated with S-protein from SARS-CoV-2, in subjects negative for COVID-19 infection and anti-SARS-CoV-2 antibodies

Study objectives
The aim of the study is to trial a preventive vaccine consisting of autologous dendritic cells previously incubated with S-protein from SARS-CoV-2

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/11/2020, Health Research Ethics Committee Central Army Hospital RSPAD Gatot Soebroto (Jl. Abdul Rahman Saleh No. 24 Jakarta Pusat 10410; +6221-3441008; kepkrspad@gmail.com), ref: 06/XI/KEPK/2020

Study design
Multicenter interventional double-blinded randomized controlled trial

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 the contact details to request a patient information sheet.

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

Interventions

Participants are randomly allocated to receive AV-COVID-19 in 9 arms:
1. 0.1 mg antigen, 0 mcg GMCSF
2. 0.33 mg antigen, 0 mcg GMCSF
3. 1.0 mg antigen, 0 mcg GMCSF
4. 0.1 mg antigen, 250 mcg GMCSF
5. 0.33 mg antigen, 250 mcg GMCSF
6. 1.0 mg antigen, 250 mcg GMCSF
7. 0.1 mg antigen, 500 mcg GMCSF
8. 0.33 mg antigen, 500 mcg GMCSF
9. 1.0 mg antigen, 500 mcg GMCSF

Randomisation will occur using a 3 x 3 matrix. Because of blocking after enrollment of each set of nine subjects, all 27 of these subjects will have received an injection of autologous AV-COVID-19 that was incubated with one of three different quantities of S-protein, 9 subjects will have received autologous AV-COVID-19 that was incubated with each of the three different quantities of S protein, and 3 subjects will have received an injection for each of the 9 separate conditions defined by the 3 x 3 matrix. The subjects and the medical personnel will not know what is being injected. The pharmacist will know whether the product has been admixed in GM-CSF or not.

After enrolling for screening, subjects will undergo a nasal swab test to exclude active COVID-19 infection and a rapid test for anti-coronavirus antibodies to exclude pre-existing anti-SARS-CoV-2 antibodies. 50 mL of blood will be collected, from which peripheral blood monocytes will be isolated and differentiated into DC before incubation with SARS-CoV-2 S-protein, during which time the protein is digested into 9 to 25 amino acid peptide sequences presented on the dendrites of DC in conjunction with histocompatibility class I and class II molecules. Safety and quality testing will be performed on a small quantity of the batch, and the remaining AV-COVID-19 will be cryopreserved for shipping to the treatment site.
Once the Study Drug is ready, if eligible, the subject will be seen at Study Week-0 for treatment. Prior to injection of the Study Drug, a nasal swab test will be collected to confirm that they are still negative for COVID-19, and blood will be drawn to determine baseline levels of anti-SARS-CoV-2 antibodies. At the treatment site, the product will be thawed and admixed with saline or (saline with GM-CSF), and within 5 hours of thawing, will be injected SC via a 25-gauge needle.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
AV-COVID-19

Primary outcome measure
Each of the following will be measured from the daily log and patient report:
1. Frequency of solicited local and systemic reactogenicity adverse events (AEs) measured as the percentage of participants with solicited AEs (local, systemic) by severity score, duration, and peak intensity measured at 7 days after each vaccination
2. Safety Laboratory Values (Serum Chemistry) measured by FDA toxicity scoring (absolute and change from baseline where identified) at 7 days after each vaccination
3. Safety Laboratory Values (Hematology) measured by FDA toxicity scoring (absolute and change from baseline where identified) at 7 days after each vaccination

4. Frequency of any serious adverse events (SAEs) measured as the percentage of participants with serious undesirable effect associated with the use of a medical product in a patient, which consist of death, life-threatening, hospitalization, disability or permanent damage, congenital anomaly/birth defect, required intervention to prevent permanent impairment or damage (devices), and other serious important medical events between baseline and 1 year
5. Frequency of any new-onset chronic medical conditions (NOCMCs) documented between the time of study vaccination and 1 year
6. Frequency of medically attended adverse events (MAAEs) defined as the percentage of participants with MAAEs (AEs that lead to an unscheduled visit to a healthcare practitioner) by MedDRA classification, severity score, and relatedness between baseline and 1 year
7. Frequency of Unsolicited AE and Adverse Events of Special Interest (AESIs) defined as the percentage of participants with unsolicited AEs (treatment-emergent, serious, suspected unexpected serious, those of special interest, and all MAAEs) or AESIs (potential immune-mediated medical conditions, or AEs relevant to COVID-19) by MedDRA classification, severity score, and relatedness between baseline and 90 days

Secondary outcome measures
1. Serum IgG antibody levels specific for the SARS-CoV-2 rS protein antigen(s) expressed as Geometric Mean Fold Rises (GMFRs) as detected by ELISA expressed as GMFRs at 28 days
2. Serum Immunoglobulin G (IgG) antibody levels expressed as Geometric Mean Titers (GMTs). Serum IgG antibody levels specific for the SARS-CoV-2 rS protein antigen(s) as detected by enzyme-linked immunosorbent assay (ELISA) expressed as GMTs at 28 days
3. Serum IgG Antibody Levels specific for the SARS-CoV-2 rS protein antigen(s) expressed as Seroconversion Rates (SCRs) as detected by ELISA expressed as SCRs at 28 days. SCR is the proportion of participants with ≥4-fold rises in ELISA units.
4. Neutralizing antibody activity expressed as GMTs as detected by microneutralization assay (MN) expressed as GMTs at multiple time points at 28 days
5. Neutralizing antibody activity expressed as GMFRs as detected by MN expressed as GMFRs at multiple time points at 28 days
6. Neutralizing antibody activity expressed as SCRs as detected by MN expressed as SCRs at multiple time points at 28 days
7. Assessment of Cell-Mediated (T helper 1 [Th1]/T helper 2 [Th2]) Pathways. Cell-mediated (Th1 /Th2) pathways as measured by whole blood (flow cytometry) and/or in vitro peripheral blood mononuclear cell (PBMC) stimulation (eg, enzyme-linked immunospot [ELISpot], cytokine staining) with SARS-CoV-2 rS protein(s) at 28 days
8. Optimal dose of SARS-CoV2 antigen and GM-CSF through measurement of IgG in subject blood at 1 month
9. Duration of detection IgG and neutralizing antibody against SARS-CoV-2in blood after vaccination through measurement of IgG and neutralizing antibody in subject blood at 12 months

Overall study start date
26/11/2020

Completion date
31/01/2022

Eligibility

Key inclusion criteria
1. 18 years or older
2. In relatively good health with adequate physical and mental function

3. Increased risk for medical complications associated with COVID-19 infection or increased risk for exposure to SARS-CoV-2

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
27 subjects (9 arms each 3 subject)

Key exclusion criteria
1. Active COVID-19 infection by PCR testing
2. Pre-existing IgG or IgM SARS-CoV-2 antibodies
3. Pregnant, Known hypersensitivity to GM-CSF
4. Known active immune deficiency disease or active HIV
5. HBV, HCV, On active treatment with corticosteroids or other immunosuppressive agent
6. Participated in previous COVID-19 vaccine study

Date of first enrolment
07/12/2020

Date of final enrolment
31/01/2021

Locations

Countries of recruitment
Indonesia

Study participating centre
Dr Kariadi Hospital
Jl. DR. Sutomo No.16
Randusari
Kec. Semarang Selatan
Semarang, Jawa Tengah
Indonesia
50244

Sponsor information

Organisation
Ministry of Health

Sponsor details
Jl. H.R. Rasuna Said Blok X.5 Kav. 4-9
Jakarta
Indonesia
12950
+62 21-5201590
kontak@kemkes.go.id

Sponsor type
Government

Website
https://www.kemkes.go.id/index.php

ROR
https://ror.org/04gq6mn61

Funder(s)

Funder type
Government

Funder Name
Ministry of Health, Republic of Indonesia

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. Data will become available beginning 9 months and ending 36 months following article publication. Individual participant data that underlie the results reported in this article will be shared after deidentification (text, tables, figures, and appendices). Data will be shared with researchers who provide a methodologically sound proposal in order to achieve the aims in the approved proposal. Proposals should be directed to

muhammad.karyana@kemkes.go.id. To gain access, data requestors will need to sign a data access agreement

IPD sharing plan summary

Available on request