Clinical Trial Protocol
Iranian Registry of Clinical Trials

04 Dec 2023

A phase III, Randomized, Two-armed, Double-blind, Placebo controlled trial to evaluate efficacy and safety of an adjuvanted recombinant SARS-CoV-2 spike (S) protein subunit vaccine (SpikoGen®) produced by CinnaGen Co. (Two doses of 25µg with dosing interval of 21 days)

Protocol summary

Study aim
To evaluate the incidence of COVID-19, 2 weeks after the 2nd dose

Design
A phase III, randomized, two-armed, double-blind, placebo controlled clinical trial with 16876 subjects. Stratified randomization by R-CRAN-version 4.0.1

Settings and conduct
Randomized, two-armed, double-blind, placebo controlled clinical trial in Espinas Palace Hotel, Tehran

Participants/Inclusion and exclusion criteria
50>age ≥18 years who are able to comply with study protocol. Stable medical condition. Women who are not pregnant/breastfeeding. Exclusion: Subjects with active infection with signs of COVID-19 Subjects with T≥38◦C at screening/72hr prior. Progressive/severe neurological disorder, dementia, stroke, seizures, history of GBS. High-risk subjects who are prioritized for the national vaccination program, those are treated with immunosuppressive/cytotoxic drugs/systemic corticosteroids at doses≥10mg daily of prednisolone/equivalent doses of other cortons more than 14days.People with history of SARs to the vaccine. Subjects in clinical trials within 30 days before screening until end of the study who have previously vaccinated against COVID-19. They received other authorized vaccines within 28 days prior to the screening/intend to receive vaccine up to 2 weeks after second dose. People with bleeding disorder who received/intend to receive any blood/blood products 90 days or donated ≥450ml 28 days prior to screening. Subjects given vaccination within 2 months after participating in the study, according to the national immunization/Subjects with ESRD/dawn syndrome/BMI≥40/CF/COPD/PAH/uncontrolled(asthma/HTN/DM)

Intervention groups
1IM injection of 25 ug subunit vaccine with Advax-CpG adjuvant on day 0 and 21 Placebo:1IM injection of normal saline(0.9% saline) on day 0 and 21

Main outcome variables
Evaluation of Covid-19 disease 14 days after the 2nd dose. Evaluation of severe cases of COVID-19 disease 14 days after the 2nd dose

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20150303021315N24**
Registration date: **2021-08-03, 1400/05/12**
Registration timing: **prospective**

Last update: **2021-08-03, 1400/05/12**
Update count: **0**

Registration date
2021-08-03, 1400/05/12

Registrant information

Name
Nassim Anjidani

Name of organization / entity
Orchid Pharmed

Country
Iran (Islamic Republic of)

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+98 21 4347 3000

Email address
amini@orchidpharmed.com

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2021-08-04, 1400/05/13
Expected recruitment end date
2021-09-22, 1400/06/31
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
A phase III, Randomized, Two-armed, Double-blind, Placebo controlled trial to evaluate efficacy and safety of an adjuvanted recombinant SARS-CoV-2 spike (S) protein subunit vaccine (SpikoGen®) produced by CinnaGen Co. (Two doses of 25µg with dosing interval of 21 days)

Public title
Evaluation of efficacy and safety of SpikoGen® vaccine on adults to prevent COVID-19 disease
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
Men or women 50 > age ≥ 18 Participants who are willing and able to comply with study requirements, including all scheduled visits, vaccinations and tests Healthy adults or adults with stable medical conditions Women eligible to participate in the study who are not pregnant or breastfeeding
Exclusion criteria:
Subjects with active infection with SARS-COV-2 signs at the screening visit Subjects with body temperature equal or more than 38 degrees centigrade, during 72 hours before screening visit or during the visit Subjects with any progressive or severe neurological disorder, including dementia, stroke, seizures, or a history of Guillain-Barre syndrome High-risk subjects who are prioritized for the national vaccination program, those are treated with immunosuppressive drugs or cytotoxic drugs, or systemic corticosteroids at doses ≥ 10 mg daily of prednisolone or equivalent doses of other corticosteroids more than 14 days Pregnant women, or breastfeeding mothers, or women who plan to become pregnant during the study Subjects who have a history of severe allergic reactions (e.g. anaphylaxis) to the study vaccine or any components of the vaccine or any other drugs Subjects who have received any other investigational product within 30 days prior to the screening visit or intend to participate in other clinical studies during this trial Subjects who have been vaccinated with other vaccines against the SARS-CoV-2 virus Subjects who received other authorized vaccines within 28 days prior to the screening visit in this study or intend to receive any vaccines up to 14 days after the second vaccination Subjects who have any known bleeding disorder or may have problems with the intramuscular injection according to the researcher's opinion Subjects who have received or intend to receive any blood / plasma or immunoglobulin products 90 days prior to the screening visit Subjects with special circumstances who, may increase the risk of participating in the study or interfering with the evaluation of the primary endpoints of the study according to researcher's opinion Subjects who have donated ≥450 ml of blood or blood products 28 days prior to the screening visit Subjects who are given the priority of vaccination within 2 months after participating in the study, according to the national immunization program Subjects with ESRD Subjects with dawn syndrome Subjects with BMI ≥ 40 Subjects with cystic fibrosis, COPD, PAH Subjects with uncontrolled asthma Subjects with uncontrolled hypertension Subjects with uncontrolled diabetes Mellitus
Age
From **18 years** old to **50 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size
Target sample size: **16876**
Randomization (investigator's opinion)
Randomized
Randomization description
Eligible patients will be assigned to treatment using a stratified randomization by R-CRAN-version 4.0.1. Randomization will be stratified according to two factors: Age (Below the age of 40– equal or above the age of 40 - below 50) After randomization procedure, a code will be allocated to each patient that will be used as patient identifier throughout the study. The assigned code will be denoted by 4 initials (corresponding to the first two letters of first name, first two letters of surname) and 3 numbers (center code). Moreover, the described code is followed by study unique identification code consisting of first three letters of the generic name of the investigational product, i.e. VAC and five numbers (corresponding to the randomization number), e.g. ABCD001VAC-00001. Each vaccine syringe has a unique code that differs from the rest of the vaccines. The CRO is responsible for preparing the unique codes. Therefore, only the CRO knows each code for the vaccine (manufactured by CinnaGen) or placebo (0.9% normal saline). In case of enrollment, each subject will be given a randomization code and will be assigned to one of the groups. During each visit, a vaccine with a specific code will be given to the subject. The CRO will monitor how subjects are assigned to the treatment groups
Blinding (investigator's opinion)
Double blinded
Blinding description
The vaccine and the placebo have the same research label and are suitable for the vaccine boxes and syringes. The contents of the labels are based on EMA regulation. The SpikoGen® vaccine or placebo are packaged in the same way. Unique codes are printed on

the vaccine and placebo labels, and each vaccine is linked to the participant through this unique code Participants and medical staff are not aware of the vaccine or placebo. The type of participants group and the type of vaccine they received will not be known for investigators and will be stored in opaque sealed envelopes at the center. Decoding or blind breaking, under special circumstances, is the responsibility of the DSMB Committee. Decoding for a participant is done by the investigator of the center, when all of the possibilities in the occurrence of the event are evaluated and rejected. The vaccine or the placebo is recognized as the most important factor in the occurrence of an event or management of its complications which lead to special treatment for the participant and a decision that is not possible without decoding.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Iran National Committee for Ethics in Biomedical Research.

Street address
Floor 13, Block A, Ministry of Health & Medical Education Headquarters, Between Zarafashan & South Falamak, Qods Town, Tehran, Iran.

City
Tehran

Province
Tehran

Postal code
1467664961

Approval date
2021-07-28, 1400/05/06

Ethics committee reference number
IR.NREC.1400.005

Health conditions studied

1

Description of health condition studied
COVID-19

ICD-10 code
U07.1

ICD-10 code description
COVID-19, virus identified

Primary outcomes

1

Description
Evaluation of COVID-19 incidence

Timepoint
14 days after the second dose

Method of measurement
Participants must have at least two of the following systemic symptoms: fever (38 ° C), chills, myalgia, headache, sore throat, nausea, vomiting, diarrhea, nasal discharge, new olfactory disorder, "or" the participant must have experienced at least one of the following respiratory signs and symptoms: cough, shortness of breath, clinical or radiographic evidence of pneumonia "and" at least one positive PCR test for SARS-CoV-2

2

Description
Evaluation of severe COVID-19 incidence

Timepoint
14 days after the second dose

Method of measurement
If the patient has any of the following symptoms, is classified as severe type of COVID-19: respiratory rate ≥30 per minute. Heart rate ≥125 per minute. Oxygen saturation ≤93% in ambient air. Respiratory failure or acute respiratory distress syndrome (ARDS) or (requires high-flow oxygen or non-invasive or mechanical ventilation or ECMO) Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg) or the need for vasopressors). Acute renal, hepatic or neurological dysfunction. Hospitalization in the intensive care unit or death.

Secondary outcomes

1

Description
Occurrence of solicited adverse events

Timepoint
Up to 7 days after each dose

Method of measurement
Checkup, history checking and participants reports based on adverse event reporting system

2

Description
Occurrence of unsolicited adverse events.

Timepoint
Up to 28 days after each dose.

Method of measurement
Checkup, history checking and participants reports based on adverse event reporting system

3

Description

Occurrence of serious adverse events and suspected unexpected serious adverse events

Timepoint

within 6 months after the second dose

Method of measurement

Checkup, history checking and participants reports based on adverse event reporting system

Intervention groups

1

Description

Intervention group: Injecting one dose of 1 ml solution of SpikoGen® vaccine containing recombinant SARS-CoV-2-S protein and Advax™ and CpG adjuvants in the non-dominant arm on days 0 and 21

Category

Prevention

2

Description

Control group: Injecting one dose of 1 ml placebo containing normal saline (0.9% NaCl solution) in non-dominant arm on days 0 and 21

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Espinas Palace Hotel

Full name of responsible person

Payam Tabarsi- Masoud Mardani Dashti

Street address

Espinas Palace Hotel, No.33 Alley, Abedi Street, Behroud Sq., Saadat Abad, Tehran, Iran

City

Tehran

Province

Tehran

Postal code

1981846911

Phone

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Email

reservation.p@espinashotels.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

CinnaGen Company

Full name of responsible person

Dr. Haleh Hamedifar

Street address

No.72, CinnaGen research and production Company. Simin Dasht Industrial Park, Karaj, Alborz, Iran

City

Karaj

Province

Tehran

Postal code

3165933155

Phone

+98 26 3667 0980

Email

cinnagen@cinnagen.com

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

CinnaGen Company

Proportion provided by this source

100

Public or private sector

Private

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Industry

Person responsible for general inquiries

Contact

Name of organization / entity

Orchid Pharmed

Full name of responsible person

Nassim Anjidani

Position

Medical Department Manager

Latest degree

Medical doctor

Other areas of specialty/work

Medical Pharmacy

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Person responsible for scientific inquiries

Contact

Name of organization / entity
Shahid Beheshti University of medical Sciences
Full name of responsible person
Payam Tabarsi
Position
Professor
Latest degree
Specialist
Other areas of specialty/work
Infectious diseases
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Person responsible for updating data

Contact
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Orchid Pharmed
Full name of responsible person
Nassim Anjidani
Position
Medical Department Manager
Latest degree
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available
Study Protocol
Yes - There is a plan to make this available
Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available
Informed Consent Form
Yes - There is a plan to make this available
Clinical Study Report
Yes - There is a plan to make this available
Analytic Code
Not applicable
Data Dictionary
Not applicable
Title and more details about the data/document
Participants' data will be available for regulatory and ethics committee for decisions.
When the data will become available and for how long
Documents including study protocol and the results will be available to the public after the study ends.
To whom data/document is available
The regulatory body and the ethics committee will have access to the study data. The monitoring team will have access to the study data during the conduct. DSMB will have access to the study data and results in predefined timelines and decides about the continuation of the study.
Under which criteria data/document could be used
With the permission of the sponsor and the approval of regulatory
From where data/document is obtainable
The study sponsor is responding to this request
What processes are involved for a request to access data/document
The study sponsor is responding to this request
Comments