Clinical Trial Protocol
Iranian Registry of Clinical Trials

27 Sep 2026

A phase II, 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
Evaluating Immunogenicity and safety of recombinant SARS-COV-2-S protein

Design
A phase II, randomized, two-armed, double-blind, placebo controlled clinical trial with 400 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
inclusion:Individuals≥18 years.who are willing and able to comply with study requirements.Healthy and stable medical conditions.Women who are not pregnant/breastfeeding.exclusion:Subjects with active infection with signs of SARS-COV-2.Subjects with temperature ≥38◦C at screening or 72hrs prior.Progressive/severe neurological disorder,seizures,history of Guillain-Barre syndrome.who receive immunosuppressive medications.Pregnant/breastfeeding or women who become pregnant during the study.People with history of severe adverse reactions to the study vaccine.who participated in clinical trials within 30 days before screening until end of the study.who have previously vaccinated against SARS-CoV-2.who received other authorized vaccines within 28 days prior to the screening/intend to receive vaccine up to 14 days after second dose.People with known bleeding disorder.who received/intend to receive any blood/blood products 90 days or donated ≥450ml 28 days prior to screening

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

Main outcome variables
solicited adverse events up to 7 days after each dose. unsolicited adverse events up to 28 days after each dose Evaluation and comparison of individuals with seroconversion for IgG bAb against S protein on days 21 and 35. GMT measurement for IgG binding antibody (bAb) against protein S on days 0, 21 and 35

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20150303021315N23**
Registration date: **2021-05-24, 1400/03/03**
Registration timing: **prospective**

Last update: **2021-07-08, 1400/04/17**
Update count: **1**

Registration date
2021-05-24, 1400/03/03

Registrant information

Name
Nassim Anjidani

Name of organization / entity
Orchid Pharmed

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Iran (Islamic Republic of)

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2021-05-29, 1400/03/08
Expected recruitment end date
2021-07-22, 1400/04/31
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
A phase II, 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
evaluate efficacy and safety of SpikoGen® vaccine on healthy adults to prevent COVID-19 disease
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
Men or women ≥18 years 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 at the visit. Subjects with any progressive or severe neurological disorder, seizures, or a history of Guillain-Barre syndrome. Subjects who receive immunosuppressive or cytotoxic medications. 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.

Age
From **18 years** old
Gender
Both

Phase
2
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size
Target sample size: **400**
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: 1. Age (Below the age of 65 – 65 and above) 2. High risk and low risk adults below the age of 65 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
2021-05-22, 1400/03/01

Ethics committee reference number
IR.NREC.1400.002

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
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
Evaluation of seroconversion for IgG against S protein

Timepoint
On days 21 and 35

Method of measurement
ELISA and statistical analysis

4

Description
GMC measurement for IgG-binding antibody (bAb) against protein S

Timepoint
On days 0, 21 and 35

Method of measurement
ELISA and statistical analysis

Secondary outcomes

1

Description
Evaluation of seroconversion for nAb against SARS-CoV-2

Timepoint
Days 21 and 35

Method of measurement
sVNT (by ELISA) and statistical analysis

2

Description
Evaluation of seroconversion for IgA against RBD

Timepoint
Days 21, 35

Method of measurement
ELISA test and statistical analysis

3

Description
Evaluation of seroconversion for IgA against S protein

Timepoint
Days 21, 35

Method of measurement
ELISA test and statistical analysis

4

Description
Evaluation of seroconversion for IgG against RBD

Timepoint

Days 21, 35

Method of measurement

ELISA test and statistical analysis

5

Description

Evaluating GMC of bAb (IgG) against RBD

Timepoint

Days 0, 21, 35

Method of measurement

ELISA test and statistical analysis

6

Description

Evaluating GMFR of bAb (IgG) against S protein

Timepoint

Days 21, 35

Method of measurement

ELISA test and statistical analysis

7

Description

Evaluating GMFR of bAb IgG against RBD

Timepoint

Days 21, 35

Method of measurement

ELISA test and statistical analysis

8

Description

Evaluating GMC of nAb against SARS-COV-2

Timepoint

Days 0, 21, 35

Method of measurement

ELISA test and statistical analysis

9

Description

Evaluating GMFR of nAb against SARS-COV-2

Timepoint

Days 21, 35

Method of measurement

ELISA test and statistical analysis

10

Description

Evaluating cellular immune response by measuring proliferation percentage of CD4/CD8 lymphocytes

Timepoint

Days 0, 21, 35

Method of measurement

Flow cytometry

11

Description

incidence of SAEs and SUSARs

Timepoint

During 6 months after second dose

Method of measurement

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

12

Description

Evaluation of cell proliferation (percentage of CD4 and CD8 cells) producing interferon-gamma after exposure to specific antigen, 25% of sample size (100 patients)

Timepoint

On days 0, 21, 35

Method of measurement

Intracellular Cytokine Staining and Flow cytometry

13

Description

nAb titer measurement against SARS-CoV-2

Timepoint

Days 21 and 35

Method of measurement

cVNT and statistical analysis

14

Description

Evaluating GMC of IgA against S protein

Timepoint

Days 0, 21, 35

Method of measurement

ELISA test and statistical analysis

15

Description

Evaluating GMFR of IgA against S protein

Timepoint

Days 21, 35

Method of measurement

ELISA test and statistical analysis

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

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Tehran

Province
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Postal code
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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
Alborz

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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No 42. Attar sq, Attar st, Valiasr st, Vanak sq, Tehran, Iran

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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
Medical doctor

Other areas of specialty/work
Infectious diseases

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Person responsible for updating data

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

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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

After contacting the principal investigator and obtaining permission from the sponsor

Comments