Clinical Trial Protocol
Iranian Registry of Clinical Trials

06 Nov 2026

Phase I, Safety and Immunogenicity of Razi SARS-CoV-2 recombinant Spike protein vaccine (Razi Cov Pars), in healthy adults aged 18-55 years; parallel 4 arms design (adjuvant only and three vaccine doses of 5, 10, and 20 µg/200µl); a Randomised, double blind, clinical trial

Protocol summary

Study aim

Dose finding, safety and immunogenicity of recombinant protein sub-unit Covid vaccine developed by RAZI institute (Razi Cov Pars)

Design

Phase I, randomized, double blind, placebo controlled trial will be conducted on 133 healthy volunteers including 13 sentinel and 120 participants randomly allocated to 4 study groups.

Settings and conduct

Terhan Rasoul Akram Hospital

Participants/Inclusion and exclusion criteria

Important inclusion criteria: Iranian nationals; Diploma and above; 18 - 55 years old; healthy based on clinical & laboratory criteria; Negative RT-PCR tests for COVID, Negative S antibody titer; Signed informed consent, Non pregnant or lactating (women); Important exclusion criteria: Any ongoing, symptomatic acute or chronic illness requiring medication or surgery (including respiratory/cardiac diseases, hypertension, diabetes, neurological diseases, serious psychiatric disorder & blood disorders that diagnosed by a physician); Breastfeeding; History of allergic diseases or reaction to the drug/vaccine

Intervention groups

The four study groups consists of three vaccine groups receiving 5, 10, 20 µg/200µL intramascular doses on day 0 and 21 followed by 10 µg/200µl intranasal spray on day 51. The fourth group receives adjuvant only on day 0, and 21 (intramascular) and 51 (intranasal spray).

Main outcome variables

Primary outcomes: Immediate abnormal vital signs & anaphylactic reactions after vaccination: Local & Systemic adverse events within the first week post-vaccination: Abnormal lab. findings Secondary outcomes: Occurrence of COVID-19 disease 2 weeks after 2nd vaccine dose: SAEs, SUSARs, MAAEs, up to 6 months after last vaccine dose: Serum ELISA IgG level for SARS-CoV-2 antigens S، S1, N, S2, NTD، RBD; Serum ELISA IgA level for RBD; Neutralizing antibody activity cVNT; Cell-mediated immunity up to 5 months after start of vaccination.

General information

Reason for update

Revision of to lab variables incluсding Cell immunitiy and IgG serum level

Acronym

IRCT registration information

IRCT registration number: **IRCT20201214049709N1**
Registration date: **2021-01-21, 1399/11/02**
Registration timing: **prospective**

Last update: **2022-05-25, 1401/03/04**
Update count: **4**

Registration date

2021-01-21, 1399/11/02

Registrant information

Name
Ali Eshaghi

Name of organization / entity
Razi Vaccine and Serum Research Institute

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Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date
2021-01-29, 1399/11/10
Expected recruitment end date
2021-03-10, 1399/12/20
Actual recruitment start date
2021-02-28, 1399/12/10
Actual recruitment end date
2021-04-10, 1400/01/21
Trial completion date
2021-10-13, 1400/07/21

Scientific title
Phase I, Safety and Immunogenicity of Razi SARS-CoV-2 recombinant Spike protein vaccine (Razi Cov Pars), in healthy adults aged 18-55 years; parallel 4 arms design (adjuvant only and three vaccine doses of 5, 10, and 20 µg/200µl); a Randomised, double blind, clinical trial

Public title
Phase I, Safety and Immunogenicity of Razi SARS-CoV-2 recombinant Spike protein vaccine (Razi Cov Pars)
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
Having Iranian citizenship; Diploma or higher degree; Adults aged 18 - 55 years; Body mass index 17 to 35 kg/m2; Having good health based on clinical and laboratory criteria; Having sublingual temperature less than or equal to 37.2 ° C in the morning based on mercury thermometer; Negative IgG and IgM antibody titers for COVID-19 S antigen; Negative RT-PCR test for COVID-19; Negative IgG ELISA for HIV; Having heart rate between 60 and 100; Signed the informed consent form; The participant agrees to reduce the risk of developing of COVID-19; For females of childbearing age 18 to 49 years: not being pregnant based on the first day of the last menstrual period; For females of childbearing age 18 to 49 years: negative pregnancy test based on bHCG on the day of screening and the day of vaccination; For females of childbearing age 18 to 49 years: use at least one effective method of contraception (condoms, oral contraceptive pills, intrauterine device, Norplant capsule) and willing to continue using it up to three month after last vaccine dose; Unwillingness to have children and use effective methods of contraception up to three months after completion of vaccination (all participants). Confirmation by a psychiatrist that the participant's mental health and capacity allows him/her to make a decision regarding his/her participation in the trial.
Exclusion criteria:
Any ongoing, symptomatic acute or chronic illness requiring medical or surgical care on the day of vaccination; Working in an occupation with a high risk of exposure to COVID-19 including medical staff, occupations with close contact with the client; Breastfeeding; Receipt any vaccine during the 30 days before the screening day; Received blood and/or any blood products and/or immunoglobulins within three months preceding the screening day; Any confirmed or suspected immunodeficient state; History of long-term use of immunosuppressive medication (defined as more than 14 continuous days) in the last 4 months leading up to screening day; Long-term use (defined as more than 14 continuous days) of systemic corticosteroids (equivalent to 10 mg or more daily prednisolone) within the past 4 months, except topical steroids; History of allergic diseases such as angioedema or anaphylactic reactions; History of any allergy to the drug or vaccine (defined as any clinical signs or symptom of itching at the injection site, urticaria in the body after injection, excessive redness at the injection site); History of autoimmune diseases (other than controlled autoimmune thyroid disease, stable celiac disease, mild psoriasis, vitiligo that does not require corticosteroid or immunosuppressive therapy); History of chemotherapy in the last 5 years; History of cancer in the last 5 years; History of serious psychiatric illnesses; History of blood disorders (dyscrasia, coagulopathy, platelet deficiency or disorder, deficiency of blood factors); Suffering from chronic obstructive pulmonary disease such as asthma and COPD that diagnosed by a specialist and is/was under medication; Suffering from ischemic heart disease that is/was under medication by a specialist , history of cardiac interventions; Suffering from hypertension that is/was under medication by a specialist ; Suffering from diabetes that is/was under medication by a specialist ; History of chronic neurological diseases (including seizures and epilepsy); Any history of substance or alcohol abuse within the last 2 years; Any abnormality in the hematology or biochemical laboratory tests based on FDA toxicity score (grade >1) on the screening day; History of confirmed COVID-19; Acute febrile illness at the time of vaccination; History of acetaminophen allergy; Acute or chronic hepatitis B and C; Receiving prophylactic drug against tuberculosis; History of syncope with blood transfusion or blood observation; Splenectomy for any reason; Any close contact with a confirmed COVID-19 case within two weeks before the first dose of vaccine; History of SARS or MERS; Participate in any clinical trials (research) study other than this study.
Age
From **18 years** old to **55 years** old
Gender
Both

Phase
1
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size
Target sample size: **153**
Actual sample size reached: **153**
Randomization (investigator's opinion)
Randomized
Randomization description
In this study, we will use Block Randomization method

with various block sizes. Excel software and rand() function will be used to prepare random order inside each block. When the intervention of each participant is determined, then a unique four-digit code will be assigned to the person (concealment). This number is the randomization code of the participant and the person will be identified with this number until the end of the study. A chain of 133 random allocations for use in the first phase of the study will be kept by the study epidemiologist.

Blinding (investigator's opinion)
Double blinded

Blinding description
In this study, a placebo will be used. The adjuvant used in the vaccine will be used as placebo. In this way, all study staff will be blinded to the type of intervention received by the participant.

Placebo
Used

Assignment
Parallel

Other design features
When the results of the first interim analysis was known on the selected vaccine strength to enter the phase II trial, an additional group of open labeled and non-randomized subjects were recruited to assess mucosal protection and received either selected intranasal vaccine or placebo for the third dose (third step).

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
National Research Ethics Committee

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
7334144696

Approval date
2021-01-16, 1399/10/27

Ethics committee reference number
IR.NREC.1399.005

Health conditions studied

1

Description of health condition studied
SARS-CoV-2

ICD-10 code
U07.1

ICD-10 code description
COVID-19

Primary outcomes

1

Description
Abnormal vital signs and anaphylactic reactions before and immediately after vaccination: number and percentages of participants who develop abnormal vital signs within three hours of receiving the vaccine at each doses will be recorded. Abnormal vital signs include temperature, respiratory rate, heart rate, systolic and diastolic blood pressure. Anaphylaxis is defined as an immediate systemic hypersensitivity simultaneously involving two systems. Anaphylactic reactions include: erythema, pruritus, urticaria and angioedema, bronchospasm, laryngeal edema, dizziness, hypotension, nausea, shortness of breath, wheezing, arrhythmia, cyanosis, vomiting, diarrhea, abdominal pain and will be checked up to three hours after each vaccination.

Timepoint
Before vaccination and hourly for three hours after vaccination at each dose

Method of measurement
Clinical examination

2

Description
The number and percentage of ocal adverse events within the first week post-vaccination (including pain, tenderness, erythema / redness, swelling and stiffness, itching) that will be assessed based on the severity score, duration and peak intensity.

Timepoint
Seven days after 1st and 2nd vaccination(Days 0-7 and 21-27)daily assessment

Method of measurement
Daily symptom registration cards will be given to patients at the time of vaccination and they will be asked to bring them with themselves on the next visit. These patients will be contacted daily during these seven days and the study staff will ensure that the cards are completed.

3

Description
The number and percentage of systemic adverse event within the first week post-vaccination (including nausea and vomiting, diarrhea, headache, fatigue, muscle pain) that will be assessed based on the severity score, duration and peak intensity.

Timepoint
Seven days after each vaccination step (Days 0-7 and 21-27 and 51-57) daily assessment

Method of measurement
Daily symptom registration cards will be given to patients at the time of vaccination and they will be asked

to bring them with themselves on the next visit. These patients will be contacted daily during these seven days and the study staff will ensure that the cards are completed.

4

Description

The number and percentage of people who shows abnormal laboratory findings, including biochemistry, hematology, and urine tests. These tests include: Hemoglobin, WBC, Lymphocytes cell, Neutrophils, Eosinophils, Platelets, ESR, CRP, LDH, Sodium, Potassium, HbA1c, BUN, Creatinine, Calcium, Alkaline phosphatase, ALT, AST, Bilirubin (total), Uric Acid, U/A, Urine protein, Urine glucose, Urine RBC

Timepoint

7 Days after each vaccine dose (Days 7, 28, 58)

Method of measurement

Each test will be performed using the appropriate kit.

Secondary outcomes

1

Description

Number and percentage of Severe Adverse event (SAEs)

Timepoint

Monthly until sixth month after last vaccine dose

Method of measurement

These events will be collected monthly from the participants through face to face or telephone contacts. In case of Severe Adverse event identification in the participants, more information about the event will be collected and discussed at the DSMB meeting.

2

Description

Number and percentage of Suspected Unexpected Serious Adverse Reaction(SUSAR)

Timepoint

Monthly until sixth month after last vaccine dose

Method of measurement

These events will be collected monthly from the participants through face to face or telephone contacts. In case of Suspected Unexpected Serious Adverse Reaction identification in the participants, more information about the event will be collected and discussed at the DSMB meeting.

3

Description

Number and percentage of Medically Attended Adverse Events (MAAEs)

Timepoint

Monthly until sixth month after last vaccine dose

Method of measurement

These events will be collected monthly from the participants through face to face or telephone contacts. In case of medically attended events identification in the participants, more information about the event will be collected and discussed at the DSMB meeting.

4

Description

Number and percentage of Covid-19 disease occurrence two weeks after second vaccine dose

Timepoint

Any time between the 14 days after second vaccine dose and the end of study

Method of measurement

Diagnosis of Covid-19 disease will be based on Iran's Ministry of Health's guideline and a positive positive PCR test

5

Description

Serum levels of specific IgG antibodies against S, S1, S2, NTD, RBD components of SARS-CoV-2 spike protein antigen(s). "serum antibody level" will be assessed using geometric mean, as well as "serum fold rise" and "seroconversion rate " and will be compared between the two groups. Seroconversion rate is defined as the the proportion of the individuals whose serum IgG levels have two fold or more using the ELISA method. Changes in these factors as well as showing no response against N antigen will be explored.

Timepoint

Days zero, 7, 14, 21, 28, 35, 51, 58, 65 and month 5

Method of measurement

Will be measured using ELISA method.

6

Description

Neutralizing antibody activity: Neutralizing antibody titers will be measured on day zero and day 35 (2 weeks after the second dose) in all participants. Measurements in other times will only be performed on 20% of participants. The following tasks will be performed during the conduct of this test. 1- In vitro assessment of inhibitory effect of antibody on the binding of Spike antigen with human ACE2 receptor and 2- Assessing VNT titer

Timepoint

Humoral immunity will be assessed based on the neutralizing antibody titers on days 0, 35, 65, and month 5 and comparisons will be done with day 0.

Method of measurement

Conventional Virus Nutralization Test (cVNT)

7

Description

The cell-mediated immunity will be evaluated by counting the number of CD3, CD4 and CD8 cells and joint calculation of CD3 and CD4 and CD3 and CD8 . IFN-γ, TNF-α, and interleukins 2, 4, 6, and 17 will also be measured. Evaluation of cell mediated immunity will be performed only in 20% of participants in each group. Cell mediated immunity will be measured in all participants on day 35 (2 weeks after the second dose). Summary of

the measures performed in this section are as follows: 1- Assessment of CD4 to CD8 cell proportions after stimulation of PBMC (Peripheral Blood Mononuclear Cells) by inactivated virus and recombinant spike protein using flow cytometry 2- Assessment of specific proliferation of PBMC cells stimulated by inactivated virus and recombinant spike protein using flow cytometry 3 - Assesment of TH1 and TH2 specific cellular immunity after PBMC stimulation in vaccinated individuals with recombinant spike protein to determine the levels of interferon-gamma, interleukin-4, tumor necrosis factor-alpha and interleukin 6 using ELISA kit and flow cytometry.

Timepoint

Cell mediated immunity will be assessed on days 0, 35 and 65 and month 5 and comparison will be made between day 0 and other time points.

Method of measurement

Immunologic lab tests

8

Description

IgA Secretory activity levels

Timepoint

IgA Secretory activity levels on days 0, 65, 120 and 150

Method of measurement

Immunologic lab tests

Intervention groups

1

Description

Intervention group 1: Vaccine at 5 µg/200µl dose; Participants in this group will receive two doses (IM) of RAZI recombinant spike protein vaccine 21 days apart followed by a 10 µg/200µl nasal spray 51 days after the first dose (day 0)

Category

Treatment - Drugs

2

Description

Intervention group 2: Vaccine at 10 µg/200µl dose; Participants in this group will receive two doses (IM) of RAZI recombinant spike protein vaccine 21 days apart followed by a 10 µg/200µl nasal spray 51 days after the first dose (day 0)

Category

Treatment - Drugs

3

Description

Intervention group 3: Vaccine at 20 µg/200µl dose; Participants in this group will receive two doses (IM) of RAZI recombinant spike protein vaccine 21 days apart followed by a 10 µg/200µl nasal spray 51 days after the first dose (day 0)

Category

Treatment - Drugs

4

Description

Control group: Adjuvant; Participants in this group will receive two doses (IM) of Adjuvant by 50% v/v concentation produced in RAZI institute 21 days apart followed by another dose in the form of nasal spray at day 51 (counted from day 0)

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Rasoul Akram Hospital

Full name of responsible person

Ladan Mokhberossafa

Street address

Corner of Mansouri, Niayesh, Satarkhan Av, Tehran

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Razi Vaccine and Serum Research Institute

Full name of responsible person

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Email

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Grant name

Grant code / Reference number

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

Yes

Title of funding source

Razi Vaccine and Serum Research Institute

Proportion provided by this source

100

Public or private sector
Public

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact

Name of organization / entity
Razi Vaccine and Serum Research Institute

Full name of responsible person
Mohammad Hossein Fallah Mehrabadi

Position
Faculty member

Latest degree
Ph.D.

Other areas of specialty/work
Epidemiology

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Person responsible for scientific inquiries

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Name of organization / entity
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Full name of responsible person
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Person responsible for updating data

Contact

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Full name of responsible person
Ladan Mokhberossaf

Position
Assistant Professor

Latest degree
Specialist

Other areas of specialty/work
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available

Study Protocol
Yes - There is a plan to make this available

Statistical Analysis Plan
Yes - There is 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
Yes - There is a plan to make this available

Data Dictionary
Yes - There is a plan to make this available

Title and more details about the data/document
Deidentified IPD related to outcome will be shared.

When the data will become available and for how long
The access period will begin once the study is complete and the main results have been published in peer reviewed journals.

To whom data/document is available
The data that have been published in peer reviewed journals, will be available just for academic researchers.

Under which criteria data/document could be used
The proposed study protocol should be submitted to RAZI vaccine and serum research institute and approved by its scientific and technical committee.

From where data/document is obtainable
After publishing the article researchers can submit their request to Dr. Mohammad Hossein Fallah at the following

email address (mhf2480@yahoo.com)

What processes are involved for a request to access data/document

Data will be made availabe after consideration and approval by the relevant authorities from Razi Vaccine and Serum Research Institute.

Comments

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