Clinical Trial Protocol
Iranian Registry of Clinical Trials

24 Oct 2026

Phase II, Safety and Immunogenicity of RAZI SARS-CoV-2 recombinant Spike protein vaccine (RAZI Cov Pars) in adults aged 18-70 years; a Randomised, double blind, parallel 2 arms clinical trial

Protocol summary

Study aim

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

Design

Phase II, two parallel groups, randomized, double blind, placebo controlled trial will be conducted on 500 volunteers.

Settings and conduct

Tehran Rasoul Akram Hospital

Participants/Inclusion and exclusion criteria

Important inclusion criteria: Iranian nationals; Able to read and write; 18 - 70 years old; Negative RT-PCR tests for COVID, Negative S antibody titer; Signed informed consent, Non pregnant or lactating (women); Important exclusion criteria: Any ongoing, symptomatic, uncontrolled, acute or chronic illness requiring medication or surgery (including respiratory/cardiac diseases, uncontrolled hypertension, uncontrolled 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 two study groups consists of one vaccine group receiving a selected vaccine dose from phase I, and a placebo group receiving adjuvant only. They will receive an injection of IMP on day 0 and 21 followed by intranasal spray on day 51.

Main outcome variables

Primary outcomes: Immediate abnormal vital signs & anaphylactic reactions after vaccination: Local & Systemic adverse events within the first week post vaccination; Serum ELISA IgG level for SARS CoV- 2 antigens S، S1, N, S2, NTC، RBD. Secondary outcomes: Abnormal lab findings within one week of vaccination, Occurrence of COVID-19 disease 2 weeks after 2nd vaccine dose: SAEs, SUSARs, MAAEs, up to 6 months after last vaccine dose; Neutralizing antibody activity VNT; and Cell-mediated immunity by exposing extracted PBMC to viral antigen up to 1 year after start of vaccination.

General information

Reason for update

End of follow-up of volunteers up to sixth month, due to COVID-19 pandemic conditions and the need for access to vaccines or boosters

Acronym

IRCT registration information

IRCT registration number: **IRCT20201214049709N2**
Registration date: **2021-04-13, 1400/01/24**
Registration timing: **prospective**

Last update: **2021-12-25, 1400/10/04**
Update count: **2**

Registration date

2021-04-13, 1400/01/24

Registrant information

Name

Ali Eshaghi

Name of organization / entity

Razi Vaccine and Serum Research Institute

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date
2021-04-21, 1400/02/01
Expected recruitment end date
2021-06-15, 1400/03/25
Actual recruitment start date
2021-05-27, 1400/03/06
Actual recruitment end date
2021-07-15, 1400/04/24
Trial completion date
2022-01-14, 1400/10/24

Scientific title
Phase II, Safety and Immunogenicity of RAZI SARS-CoV-2 recombinant Spike protein vaccine (RAZI Cov Pars) in adults aged 18-70 years; a Randomised, double blind, parallel 2 arms clinical trial

Public title
Phase II, Safety and Immunogenicity of recombinant vaccine for COVID-19
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
Having Iranian citizenship; Able to read and write preferably having Diploma; Adults aged 18 - 70 years; Body mass index 17 to 35kg/m2; Having sublingual temperature less than or equal to 37.2 ° C in the morning based on electronic thermometer; Negative IgG and IgM antibody titers for COVID-19 N antigen; Negative RT-PCR test forCOVID-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 ofCOVID-19; For females of childbearing age 18 to 49years: not being pregnant based on the first day of the last menstrual period; For females of childbearing age 18to 49 years: negative pregnancy test based on bHCG on the day of screening and the day of vaccination if deemed necessary by principle investigator; 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 continuous 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 uncontrolled hypertension (systolic blood pressure > 140 and diastolic blood pressure > 90); Suffering from uncontrolled diabetes (HbA1c >7) or requiring insulin treatment; 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 **70 years** old
Gender
Both

Phase
2
Groups that have been masked

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

Sample size
Target sample size: **500**
Actual sample size reached: **500**
Randomization (investigator's opinion)
Randomized
Randomization description
In this study, we will use Block Randomization method

with various block sizes. The sequence within each block will be randomized using Excel software and rand() function. A unique four-digit code will be assigned to each participant for the purpose of concealment and s/he will be identified with this number until the end of the study (randomization code).

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, placebo will be used. The adjuvant used in the vaccine will be used as placebo. All study staff will be blinded to the type of intervention received by the participant. Randomization codes will be kept by the study epidemiologist and will be used for unblinding if necessary.

Placebo

Used

Assignment

Parallel

Other design features

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

۸۱۴۵۵۶۱۸

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

U07.1

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 two 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 two hours after each vaccination.

Timepoint

Before vaccination and every 40 minutes up to two hours after vaccination at each dose

Method of measurement

Clinical examination

2

Description

The number and percentage of local adverse reactions 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 and21-27) daily assessment

Method of measurement

They will be assessed through daily telephone calls. Furthermore symptom registration cards will be given to each patient at the time of vaccination and they will be asked to bring them back on the next visit.

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 intensity.

Timepoint

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

Method of measurement

They will be assessed through daily telephone calls. Furthermore symptom registration cards will be given to each patient at the time of vaccination and they will be asked to bring them back on the next visit.

4

Description

Serum levels of specific IgG antibodies against S, S1, S2,NTC, RBD components of SARS-CoV-2 spike protein antigen(s). Changes in these factors as well as showing

no response against N antigen will be explored.

Timepoint

Days zero, 21, 35, 51, and months 3, 6

Method of measurement

Will be measured using ELISA method.

Secondary outcomes

1

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, Sodium, Potassium, BUN, Creatinine, 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.

2

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 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

3

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.

4

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.

5

Description

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

Timepoint

Añy 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

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 10% 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 and months 3 and 6, and comparisons will be done with day 0.

Method of measurement

Virus Nutralization Test (VNT)

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 10% 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 - Assessment 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 Eli spot and ELISA kit.

Timepoint

Cell mediated immunity will be assessed on days 0, 35 and months 3 and 6 and comparison will be made between day 0 and other time points.

Method of measurement

Immunologic lab tests

Intervention groups

1

Description
Intervention group: Participants in this group will receive two doses (IM) of RAZI recombinant spike protein vaccine 21 days apart followed by a nasal spray 51 days after the first dose (day 0).
Category
Prevention

2

Description
Control group: Participants in this group will receive two doses (IM) of placebo (Adjuvant only) by 50% v/v concentration 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
Arash Mohazzab
Street address
Corner of Mansouri, Niayesh, Satarkhan Av, Tehran
City
Tehran
Province
Tehran
Postal code
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Phone
+98 21 6653 8539
Email
amohazzab@yahoo.com

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Razi Vaccine and Serum Research Institute
Full name of responsible person
Ali Eshaghi
Street address
Beheshti Ave, Hesarak, Karaj, Alborz Province
City
Karaj
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Alborz
Postal code
3197619751
Phone
+98 26 3457 0038
Email
a.Eshahghi@rvsri.ac.ir
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
Industry

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

Contact
Name of organization / entity
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Full name of responsible person
Saeid Kalantari
Position
Associate Professor

Latest degree
Specialist
Other areas of specialty/work
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Person responsible for updating data

Contact
Name of organization / entity
Razi Vaccine and Serum Research Institute
Full name of responsible person
Ladan Mokhberossaf
Position
Assistant Professor
Latest degree
Specialist
Other areas of specialty/work
Public Health/Community Medicine
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City
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Province
Alborz
Postal code
3197619751
Phone
00982634570038-46
Email
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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