

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

22 Jun 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 intramuscular 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 (intramuscular ) 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 including Cell immunity 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

###### **Country**

Iran (Islamic Republic of)

###### **Phone**

+98 26 3457 0038

###### **Email address**

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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/m<sup>2</sup>; 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 Zarafshan & 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 dose 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 local 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 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 Neutralization 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- $\gamma$ , TNF- $\alpha$ , 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 - 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 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 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**

Ladan Mokhberossafa

##### **Street address**

Corner of Mansouri, Niayesh, Satarkhan Av, Tehran

##### **City**

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##### **Province**

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##### **Postal code**

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##### **Phone**

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##### **Email**

lady.Katbi@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

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##### **Province**

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##### **Postal code**

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+98 26 3457 0038

##### **Email**

a.Eshaghi@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**

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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Hesarak - Shahid Beheshti street- Karaj

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mhf2480@yahoo.com

**Person responsible for scientific inquiries**

**Contact**

**Name of organization / entity**

Iran University of Medical Sciences

**Full name of responsible person**

Saeid Kalantari

**Position**

Associate Professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Infectious diseases

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Corner of Mansouri, Niayesh, Satarkhan Av, Tehran

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**Province**

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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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Beheshti Ave, Hesarak, Karaj, Alborz Province

**City**

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**Province**

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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 available after consideration and

approval by the relevant authorities from Razi Vaccine and Serum Research Institute.

**Comments**

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