Clinical Trial Protocol
Iranian Registry of Clinical Trials

03 Feb 2023

Safety and Immunogenicity of Razi Cov-2 recombinant Spike protein vaccine (RAZI Cov Pars) in healthy children and adolescents aged 5-17 years; single group, open label study

Protocol summary

Study aim
Evaluation of safety and immunogenicity of recombinant protein sub-unit COVID-19 vaccine (Razi Cov Pars) in healthy children and adolescents aged 5-17

Design
Single group, open label study will be conducted on 420 volunteers

Settings and conduct
Recruitment centers: Razi Vaccine and Serum Research Institute, Hesarak, Karaj

Participants/Inclusion and exclusion criteria
Important inclusion criteria: participants legal guardian should be able to read and write; Age between 5-17 years; Negative RT-PCR tests for COVID-19; 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); History of allergic diseases or reactions to any drug/vaccine.

Intervention groups
Participants in the 12-17 years age group will receive two intramuscular doses of 10µg/200µl vaccine strengths on days 0 and 21, followed by an intranasal dose on day 51. Participants in the 5-11 years age group will receive half the dose of 12-17 years old's with the same administration schedule.

Main outcome variables
Primary outcomes: abnormal vital signs & anaphylactic reactions following vaccination: Local & Systemic adverse events within the first week post vaccination; abnormal lab findings within one week of vaccination; Neutralizing antibody activity VNT on days 0, 35, 90, and 180. Secondary outcomes: SAEs, SUSARs, MAAEs, up to 6 months after the second vaccine dose; Serum ELISA IgG level for SARS CoV- 2 antigens S1, RBD and cell-mediated immunity on days 0, 35, 90, and 180.

General information

Reason for update
change in participant age range

Acronym

IRCT registration information
IRCT registration number: **IRCT20201214049709N5**
Registration date: **2022-02-09, 1400/11/20**
Registration timing: **prospective**

Last update: **2022-06-20, 1401/03/30**
Update count: **1**

Registration date
2022-02-09, 1400/11/20

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
2022-06-25, 1401/04/04

Expected recruitment end date
2022-10-23, 1401/08/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Safety and Immunogenicity of Razi Cov-2 recombinant Spike protein vaccine (RAZI Cov Pars) in healthy children and adolescents aged 5-17 years; single group, open label study

Public title

Safety and Immunogenicity of Razi Cov-2 recombinant Spike protein vaccine (RAZI Cov Pars) in healthy children and adolescents aged 5-17 years

Purpose

Prevention

Inclusion/Exclusion criteria

Inclusion criteria:

Participants legal guardian should be able to read and write Age between 5-17 years Having good health based on clinical and laboratory criteria Negative RT-PCR test for COVID-19 Signed the informed consent form Not pregnant Negative beta HCG pregnancy test on screening and vaccination day Use of at least one effective method of contraception (condoms, oral contraceptive pills, intrauterine device, Norplant capsule) and willing to continue using it in female couples

Exclusion criteria:

Any ongoing, symptomatic acute or chronic illness requiring continuous medical or surgical care on the day of vaccination Breastfeeding Received any Covid Vaccine Received any vaccine during the 14-days period prior to the screening day Received blood and/or any blood products and/or immunoglobulins within three months preceding the screening day History of long-term use of immunosuppressive medication (defined as more than 14 consecutive days) in the last 6 months leading up to screening day Long-term use (defined as more than 14 consecutive days) of systemic corticosteroids within the past 6 months leading up to screening day History of severe allergic diseases (such as Dyspnea, angioedema, anaphylactic reactions, urticaria and eczema) History of allergy to any 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 immunological disorder (congenital or acquired) History of chemotherapy in the last 5 years History of cancer in the last 5 years History of acute and serious psychiatric illnesses History of blood disorders (dyscrasia, coagulopathy, platelet deficiency or disorder, deficiency of blood factors) Severe acute or chronic renal or hepatic failure based on laboratory parameters Suffering from chronic obstructive pulmonary disease such as asthma, or severe renal/hepatic diseases requiring continuous treatment by a specialist Uncontrolled hypertension Uncontrolled Diabetes History of chronic neurological diseases (including seizures and epilepsy) Any history of substance or alcohol abuse Grade 1 or higher abnormal laboratory (hematology or biochemistry) tests based on toxicity score on the screening day History of confirmed COVID-19 diseases during the 6-months period before the screening day (positive PCR test or clinical diagnosis) Acute febrile illness at the time of vaccination History of allergy to acetaminophen Receiving prophylactic drug against tuberculosis History of faint when see blood Splenectomy for any reason Any close contact with a confirmed COVID-19 case within two weeks before the first dose of vaccine Congenital disorders, developmental disorders, severe malnutrition or genetic diseases Participating in any clinical trials (research) other than this study

Age

From **5 years** old to **17 years** old

Gender

Both

Phase

1-2

Groups that have been masked

No information

Sample size

Target sample size: **420**

Randomization (investigator's opinion)

N/A

Randomization description

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Single

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

2022-02-06, 1400/11/17

Ethics committee reference number

IR.NREC.1400.019

2

Ethics committee

Name of ethics committee

National Research Ethics Committee

Street address

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Province

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Approval date

2022-06-08, 1401/03/18

Ethics committee reference number

IR.NREC.1401.001

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 immediately after vaccination: Number and percentages of participants who develop abnormal vital signs within half an hour of receiving the vaccine at each doses will be recorded. Abnormal vital signs include temperature, respiratory rate, heart rate, systolic and diastolic blood pressure before and after vaccination. 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 after each vaccination.

Timepoint

Before vaccination and 30 minutes after vaccination at each dose

Method of measurement

Temperature is measured using a digital thermometer. Blood pressure will be measured using a digital sphygmomanometer

2

Description

Local adverse reactions: The number and percentage of local adverse reactions within the first week post-vaccination (including pain, tenderness, erythema/redness, swelling and stiffness, itching)

Timepoint

The first seven days after 1st and 2nd vaccine dose (Days 0-7 and 21-28)

Method of measurement

The required information will be collected using the application installed on the mobile phones of the volunteer or their legal guardian. Volunteer will be contacted if they do not complete the relevant forms on their application.

3

Description

Systemic adverse event: The number and percentage of systemic adverse event within the first week post-vaccination (including nausea and vomiting, diarrhea, headache, fatigue, muscle pain)

Timepoint

The first seven days after each vaccine dose (Days 0-7, 21-28, 51-58)

Method of measurement

The required information will be collected using the application installed on the mobile phones of the volunteer or their legal guardian. Volunteer will be contacted if they do not complete the relevant forms on their application.

4

Description

Abnormal laboratory findings: The number and percentage of people who show abnormal laboratory findings one week after vaccination (Based on toxicity scores), including biochemistry, hematology, and urine tests. These tests include: Hemoglobin, WBC, Lymphocytes, Neutrophils, Eosinophils, Platelets ESR, CRP, Sodium, Potassium, BUN, Creatinine, Alkaline phosphatase, ALT, AST, and U/A, Urine protein, Urine glucose, Urine RBC

Timepoint

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

Method of measurement

Each test will be performed using the appropriate kit.

5

Description

Measurement of neutralizing antibody titers to assess humoral immunity

Timepoint

Neutralizing antibody titers will be assessed on days 0, 35, 90 and 180 and comparison will be made between day 0 and other time points.

Method of measurement

Conventional Virus Neutralization Test (cVNT)

Secondary outcomes

1

Description

Severe Adverse event (SAEs), Suspected Unexpected Serious Adverse Reaction (SUSAR) and Medically Attended Adverse Events (MAAEs)

Timepoint
Weekly until sixth month after second vaccine dose
Method of measurement
The required information will be collected using a weekly questionnaire delivered through the installed application on the volunteer mobile phone or their legal guardian. Volunteer will be contacted if they do not complete the relevant forms on their application.

2

Description
Measurement of serum levels of specific IgG antibodies against S1 and RBD components of SARS-CoV-2 spike protein antigen (s)
Timepoint
Measurement will be done on days zero, 35, 90 and 180 and comparison will be made between day 0 and other time points.
Method of measurement
Will be measured using ELISA method

3

Description
Evaluation of cell-mediated immunity by counting CD3, CD4 and CD8 cells number. IFN-γ, TNF-α, and interleukin 2, 4, 6, and 17 will also be measured following the stimulation of peripheral blood mono nuclear cells by covid 19 s antigen. Evaluation of cell mediated immunity will be performed only in 10% of participants.
Timepoint
Cell mediated immunity will be assessed on days 0, 35, 90 and 180 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 the 12-17 years age group will receive two intramuscular doses of 10µg/200µl vaccine strengths on days 0 and 21, followed by an intranasal dose on day 51. Participants in the 5-11 years age group will receive half the dose of 12-17 years old's with the same administration schedule.
Category
Prevention

Recruitment centers

1

Recruitment center
Name of recruitment center
Razi Vaccine and Serum Research Institute
Full name of responsible person
Dr Mojtaba Noofeli
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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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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

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Full name of responsible person
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Associate Professor

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Person responsible for updating data

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Province
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Postal code
3197619751

Phone
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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
De-identified 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