Clinical Trial Protocol
Iranian Registry of Clinical Trials

14 Jun 2021

Phase 1, safety, immunogenicity and dose finding for two strengths of 0.5 × 10^6 and 2.5 × 10^6 (TCID50) inactivated SARS-CoV-2 vaccine FAKHRAVAC (MIVAC) injected in two schedules of two doses, 2 and 3 weeks apart in healthy adults aged 18-55 years: a randomized, double blind, placebo controlled, clinical trial

Protocol summary

Study aim

Dose finding, safety and immunogenicity of Covid 19 FAKHRAVAC (MIVAC) inactivated vaccine in healthy population 18-55 years

Design

Randomized, double blind, controlled trial with factorial design on 135 volunteers. Fifteen sentinels without blinding and 120 in five groups of 24, double blind and randomized

Settings and conduct

Fakhra clinical trial center, Persian Gulf Hall, Sased Sports Complex, Shahid Fakhrizadeh Street, Sayad Shirazi Highway, Tehran, Iran

Participants/Inclusion and exclusion criteria

Inclusion criteria: Age 18 to 55 years; Body mass index between 18 to 35; no abnormal clinical and laboratory findings; No current or previous infection with COVID-19; Use of safe methods of contraception; Signing informed consent form Exclusion criteria: Current acute or chronic illness requiring regular medical or surgical attention; High-risk occupations exposed with Covid-19; serving in obligatory military service; Breastfeeding; Pregnancy;

Intervention groups

Group 1: vaccine strength of 0.5*10^6 (TCID50), two doses at 14-day intervals Group 2: vaccine strength of 2.5*10^6, two doses at 14-day intervals Group 3: placebo, two doses at 14-day intervals Group 4: vaccine strength of 0.5*10^6, two doses at 21-day intervals Group 5: vaccine strength of 2.5*10^6, two doses at 21-day intervals Group 6: placebo two doses at 21-day intervals

Main outcome variables

Primary outcomes: Reactogenicity (vital signs and anaphylactic reactions 3 hours post-vaccination; Local and systemic adverse events within the first week post-vaccination; Abnormal laboratory findings one week after Secondary outcomes: SAEs, SUSARs, MAAEs up to six months after the last dose of the vaccine; Occurrence of Covid-19 disease two weeks after the second dose of the vaccine onward; Serum IgG level for SARS-CoV-2 to N and S antigens; Neutralizing antibody activity; Cell medicated immunity and safety of cell mediated immune response

General information

Reason for update

Acronym

FAKHRAVAC

IRCT registration information

IRCT registration number: **IRCT20210206050259N1**
Registration date: **2021-03-08, 1399/12/18**
Registration timing: **prospective**

Last update: **2021-03-08, 1399/12/18**
Update count: **0**

Registration date

2021-03-08, 1399/12/18

Registrant information

Name

Ahmad Karimi Rahjerdi

Name of organization / entity

Stem Cell Technology Research Center

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Iran (Islamic Republic of)

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Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2021-03-10, 1399/12/20
Expected recruitment end date
2021-04-09, 1400/01/20
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Phase 1, safety, immunogenicity and dose finding for two strengths of 0.5 × 10^6 and 2.5 × 10^6 (TCID50) inactivated SARS-CoV-2 vaccine FAKHRAVAC (MIVAC) injected in two schedules of two doses, 2 and 3 weeks apart in healthy adults aged 18-55 years: a randomized, double blind, placebo controlled, clinical trial

Public title
trial of safety, immunogenicity and dose finding for inactivated SARS-CoV-2 vaccine FAKHRAVAC (MIVAC)
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Age 18 to 55 years Body mass index between 18 and 35 kg per square meter Having complete health based on clinical and laboratory criteria No current or previous COVID-19 disease No pregnancy Useing safe methods of contraception Signing the informed consent form Having Iranian citizenship Participants should be able to read and understand informed consent, preferably with a diploma or higher certificate Temperatures less than or equal to 37.2 ° C sublingually measured by an electronic thermometer Negative IgG and IgM antibody titers against COVID-19 N antigen Negative RT-PCR -test for SARS-CoV-2 IgG ELISA negative blood test against HIV Heart rate between 60 and 100 Systolic blood pressure (between 90 and 140 mm Hg), diastolic blood pressure (between 60 and 90 mm Hg) Accept commitments to reduce the risk of COVID-19 Negative pregnancy test for β-hCG on the day of screening and the day of vaccination Clinical trial participants should refrain from donating blood or plasma from the first vaccination until 3 months after the last vaccination. Participants should not enter any other trial while in this study Expressing a person's readiness to remain among the people monitored in the study for the entire study period until the research process is completed within 14 months Use one of a safe method of contraception in men and women up to 3 months after the last dose of the vaccine
Exclusion criteria:
Current acute or chronic symptomatic illness that requires ongoing medical or surgical care high-risk occupations regarding risk of COVID-19, including medical staff, occupations with close contact with many client Serving in compulsory military service (soldiers) in the subdivisions of the Armed Forces Breastfeeding History of receiving any research vaccine during the 30 days prior to the day of screening History of transfusion of any blood product or immunoglobulin within the 3 months before the screening day History of long-term use of immunosuppressive drugs or systemic corticosteroids in the last 4 months leading up to screening day History of allergic diseases such as angioedema or anaphylactic reactions History of any allergy to drugs or vaccines History of cancer or chemotherapy in the last 5 years History of serious psychiatric illnesses History of blood disorders (Blood Dyscrasias, coagulation, platelet deficiency or disorder, etc) Having chronic obstructive pulmonary disease such as asthma and COPD, ischemic cardiovascular disease diagnosed and treated by a specialist. high blood pressure that is being treated by a doctor. diabetes that is being treated by a doctor. History of chronic neurological diseases (including seizures and epilepsy) Any history of drug abuse (addiction) or alcohol consumption during the last 2 years Any grade 1 toxicity in the hematology or biochemistry test results performed at the time of screening History of confirmed COVID-19 Acute or chronic hepatitis B and C Receiving prophylactic drug against tuberculosis History of syncope with injection or blood observation having a splenectomy for any reason Any close contact with a definitively infected person with COVID-19 for a maximum of two weeks before the day of receiving the first dose
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: **135**
Randomization (investigator's opinion)
Randomized
Randomization description
In this study, the Block Randomization method with different block sizes was used to assign each participant to the intervention groups. The rand() function of Excel software will be used to generate random sequence within each block. After determining the allocated intervention, a non-repetitive four-digit random code was assigned to each participant. Assigned codes will be delivered to the eligible participants via a software.
Blinding (investigator's opinion)
Double blinded
Blinding description
In this study, placebo will be used. Adjunct only IMP will be used as placebo. All people involved in the study will be blind to the type of IMP received except the

epidemiologist responsible for unblinding. In cases of any serious adverse event or any trend in the occurrence of adverse events towards one of the groups, unblinding will occur by DSMB request. In other clinical occasions unblinding could occur by the principle investigators' approval

Placebo

Used

Assignment

Factorial

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

7334144696

Approval date

2021-02-28, 1399/12/10

Ethics committee reference number

IR.NREC.1399.006

Health conditions studied

1

Description of health condition studied

SARS-CoV-2

ICD-10 code

U07.1 COVI

ICD-10 code description

U07.1 COVID-19, virus identified

Primary outcomes

1

Description

Abnormal vital signs and anaphylactic reactions immediately after vaccination. Vital signs include body temperature, Respiratory rate, heart rate, systolic and diastolic blood pressure before and immediately after vaccination.

Timepoint

In the first three hours after each vaccination

Method of measurement

Temperature is measured using a digital thermometer under the tongue. Heart rate and respiratory rate will be counted by the research staff in one minute. Blood pressure will be measured by a digital sphygmomanometer while sitting.

2

Description

Local adverse events within the first week post-vaccination including pain, tenderness, erythema and redness, and swelling and stiffness

Timepoint

For the first 7 days after each vaccination

Method of measurement

Study staff will contact participants daily for seven days and complete a local adverse event form.

3

Description

Systemic adverse event within the first week post-vaccination including nausea and vomiting, diarrhea, headache, fatigue, muscle pain, and other illnesses or clinical complications

Timepoint

For the first 7 days after each vaccination and then monthly for up to six months

Method of measurement

Study staff will contact participants daily for seven days and complete a systemic adverse event form.

4

Description

Abnormal laboratory findings including Hemoglobin, WBC, Lymphocytes cell, Neutrophils, Eosinophils, Platelets, ESR, CRP, LDH,CPK, RT-PCR for SARS-CoV-2, 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 vaccination

Method of measurement

Each test will be performed using the appropriate kit

Secondary outcomes

1

Description

Serious Adverse Event/Reaction(SAEs) , Suspected Unexpected Serious Adverse Reaction (SUSARs), Medically Attended Adverse Events (MAAEs)

Timepoint

Up to six months after the last dose of the vaccine

Method of measurement

Complications will be assessed by telephone each month

2

Description

Occurrence of Covid-19 disease

Timepoint
Two weeks after the second dose of the vaccine
Method of measurement
PCR test

3

Description
Serum IgG level for SARS-CoV-2 N and S antigens
Timepoint
In the vaccination program 0-14: on days zero, 7, 14, 28, 42, 72 and months 3, 6, 9, 12 and in the vaccination program 21-0: on days zero, 7, 14, 21, 35, 49 and months 3, 6, 9, 12.
Method of measurement
ELISA method

4

Description
Neutralizing antibody activity
Timepoint
In the vaccination program 0-14: on days zero, 14, 28, 42 and months 3, 6, 9, 12 and in the vaccination program 21-0: on days zero, 21, 35, 49 and months 3, 6, 9, 12.
Method of measurement
SARS-CoV-2 virus neutralizing antibody titer

5

Description
Cell-mediated immunity and cell immunogenicity safety
Timepoint
In the vaccination program 0-14: on days zero, 14, 28, 42 and months 3, 6, 9, 12 and in the vaccination program 21-0: on days zero, 21, 35, 49 and months 3, 6, 9, 12.This outcome will be measured on day 0 and 2 weeks after the second injection for all volunteers and at other time points for 20% of participants.
Method of measurement
Absolute measurement of lymphocyte cell subpopulations (B, T, NK) and their ratio, measurement of T cell subpopulations (CD3 + CD4 +, CD3 + CD8 +), measurement of TNF-a and interleukins 4, 5, 2, 17, 6, 12, 17A, 17F, 21, 8 and 10. Cell proliferation using CFSE method. Measurement of intracellular gamma interferon (interleukin-4 and TNF-alpha) in antigen-exposed CD4 and CD8 cells

Intervention groups

1

Description
Intervention group 1: Two times vaccines in the deltoid muscle (IM) with a dose of 0.5*10^6 (TCID50) at 14-day intervals
Category
Prevention

2

Description
Intervention group 2: Two times vaccines in the deltoid muscle (IM) with a dose of 2.5*10^6 (TCID50) at 14-day intervals
Category
Prevention

3

Description
Control group 1: Two times placebo in the deltoid muscle (IM) at 14-day intervals
Category
Placebo

4

Description
Intervention group 3: Two times vaccines in the deltoid muscle (IM) with a dose of 0.5*10^6 (TCID50) at 21-day intervals
Category
Prevention

5

Description
Intervention group 4: Two times vaccines in the deltoid muscle (IM) with a dose of 2.5*10^6 (TCID50) at 21-day intervals
Category
Prevention

6

Description
Control group 2: Two times placebo in the deltoid muscle (IM) at 21-day intervals
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Fakhra clinical trial center
Full name of responsible person
Mohsen Forughizadeh Moghadam
Street address
Fakhra clinical trial center,Persian Gulf Hall, Sased Sports Complex, Shahid Fakhrizadeh Street, Sayad Shirazi Highway, Tehran, Iran
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Phone
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Email
Foroughizadeh@modares.ac.ir

Web page address
http://www.fakhravac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Organization of Defensive Innovation and Research
Full name of responsible person
Ahmad Karimi Rahjerdi
Street address
NO.9, Unit 3, Mirsharifi, Valiasr St.
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Tehran
Postal code
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Phone
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Fax
+98 21 2265 8404
Email
Rahjerdi@strc.ac.ir
Web page address
http://miladpharmaceuticsco.ir
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Organization of Defensive Innovation and Research
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
Other

Person responsible for general inquiries

Contact
Name of organization / entity
Malek Ashtar University
Full name of responsible person
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Position
Assistant professor
Latest degree
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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 on study outcomes could be shared.
When the data will become available and for how long
After completion of the study and publication of the results, data could be shared for 2 years
To whom data/document is available
Data is available only to members of academic institutions within joint projects with MILAD Daru Nour Co.
Under which criteria data/document could be used
Proposal should be presented to MILAD Daru Nour Co and its necessity and scientific validity should be approved by the company
From where data/document is obtainable
You can contact Ms Kousar Naderi at k.naderi@strc.ac.ir
What processes are involved for a request to access data/document
Request for data will be made available within the approved joint projects
Comments
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