# 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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**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
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Fakhra clinical trial center,Persian Gulf Hall, Sased Sports Complex, Shahid Fakhrizadeh Street, Sayad Shirazi Highway, Tehran, Iran
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**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
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**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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Assistant professor
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Ph.D.
**Other areas of specialty/work**
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## Person responsible for scientific inquiries

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## Person responsible for updating data

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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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