

Clinical Trial Protocol

Iranian Registry of Clinical Trials

24 Sep 2021

A double-blind, randomized, placebo-controlled Phase II/III Clinical trial to evaluate the safety and efficacy of COVID-19 inactivated vaccine (Shifa-Pharmed) in a population aged 18 to 75 years

Protocol summary

Study aim

To determine the efficacy and immunogenicity of COVID-19 inactivated vaccine (Shifa-pharmed)

Design

Phase 2/3, randomized, double-blind, parallel arms, placebo-controlled clinical trial on 20000 volunteers

Settings and conduct

This double-blind (volunteers and outcome assessors) placebo-controlled trial will be conducted on 280 healthy volunteers in phase 2 at Eram Hotel in Tehran. In phase 3, 20000 volunteers in six cities will be included. After random assignment to 5 micrograms or placebo group, they will receive the intervention twice on days 0 and 28 and be followed up for efficacy, immunogenicity, any adverse events, and COVID-19 incidence.

Participants/Inclusion and exclusion criteria

Main inclusion criteria: Healthy 18-75 years, willing to participate, the ability to understand the study, signing the informed consent, using effective contraception during the study. Main exclusion criteria: Positive PCR test, previous history of infection (positive antibody) in phase 2, symptoms consistent with COVID-19, history of close contact with COVID-19 patient in the last 14 days, history of allergy to the vaccine, immunodeficiency, coagulopathy, severe psychiatric and other chronic diseases, Receiving live vaccine in one month or other vaccines in 14 days before inoculation, Receiving immunoglobulins or blood products in 3 months before inoculation or investigational products in 6 months before inoculation, willing to pregnancy or lactation, History of recent travel abroad.

Intervention groups

5 µg antigen protein (28 days of doses interval), placebo groups (28 days of doses interval)

Main outcome variables

Vaccine efficacy in prevention of COVID-19 incidence, severe disease, and COVID-19 related death,

immunogenicity, and adverse events

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20201202049567N3**

Registration date: **2021-03-13, 1399/12/23**

Registration timing: **prospective**

Last update: **2021-03-13, 1399/12/23**

Update count: **0**

Registration date

2021-03-13, 1399/12/23

Registrant information

Name

Mohammadreza Hosseinpour

Name of organization / entity

Shifa Pharmed Industrial Co

Country

Iran (Islamic Republic of)

Phone

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2021-03-14, 1399/12/24

Expected recruitment end date

2021-05-21, 1400/02/31

Actual recruitment start date

empty

Actual recruitment end date

empty
Trial completion date
empty

Scientific title

A double-blind, randomized, placebo-controlled Phase II/III Clinical trial to evaluate the safety and efficacy of COVID-19 inactivated vaccine (Shifa-Pharmed) in a population aged 18 to 75 years

Public title

Evaluate the safety and efficacy of COVID-19 inactivated vaccine

Purpose

Prevention

Inclusion/Exclusion criteria

Inclusion criteria:

Aged 18 to 75 years Being able to fully understand the study processes and understand the explanations of the facilitators correctly Being able to fully understand the study processes and understand the explanations of the facilitators correctly Being able to understand the contents of the informed consent form and sign it before entering the study Allowing the researchers to access medical records and test results if hospitalized due to suspected, or confirmed COVID-19 Using effective methods of contraception during the study at least two months after the second dose of vaccine Volunteers who agree not to donate blood, blood products, or bone marrow from the start of the vaccine until 21 days after receiving the last dose of the vaccine

Exclusion criteria:

Confirmed, suspected, or asymptomatic COVID-19 detected by PCR at baseline History of contact with a person with SARS-CoV-2 infection (positive PCR test) during the last 14 days History of SARS-CoV-2 infection (Only in immunogenicity subsample Fever or at least two of these symptoms: Dry cough, severe fatigue, nasal congestion, runny nose, sore throat, myalgia, diarrhea, dyspnea, and shortness of breath during the 14 days prior to vaccination History of severe allergic reaction to vaccination or allergic reactions to Inactivated vaccine components Known case of tuberculosis, hepatitis B or hepatitis C History of coagulopathy History of splenectomy Uncontrolled hypertension, uncontrolled diabetes, uncontrolled chronic cardiac, renal, neurologic, or severe pulmonary disease Acute diseases or an exacerbation of a chronic disease in the last 7 days Any malignancy, immunodeficiency, HIV, lymphoma, leukemia, or other autoimmune diseases Receiving immunomodulators or immunosuppressors at least 14 days in the past 3 months or planning to use in the next year Receiving live vaccine in one month or other vaccines in 14 days before inoculation History of drug or alcohol abuse in the last 12 months caused medical, familial or occupational problems Receiving immunoglobulins or blood products in 3 months before inoculation or planning to use in the next year Receiving any other investigational drug in 6 months before inoculation Having a plan to participate in a drug trial during the study period Planning to receive any vaccination in on month after inoculation History of severe mental disorders affecting the participation in the

study Pregnant or lactating women or those who intend to become pregnant during the study period History of travel abroad in the last 14 days Any other condition that makes a person inappropriate for participation based on the investigator opinion

Age

From **18 years** old to **75 years** old

Gender

Both

Phase

2-3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size

Target sample size: **20000**

Randomization (investigator's opinion)

Randomized

Randomization description

Phase 2: For less than 50 years participants, a randomized list with a length of 200 will be produced. Each sequence has a ratio of 4:1 vaccine to placebo and 160 participants will receive the active vaccine and 40 participants will receive a placebo. Sequences are generated using sealedenvelope.com by the block size of 5 (40 blocks) which has four interventions and one placebo in each block. For 51 to 75 years participants, the randomization sequence will be separately generated for 80 participants (64 active intervention and 16 placebos) in a similar way. Phase 3: in this stage, stratified block randomization will be performed based on six cities and two age groups (<50 years and 51-75 years). Each stratum consists of blocks of size of 3 and a ratio of 2:1 (vaccine to placebo). All random allocation processes will be performed by an interactive web response system (IWRS).

Blinding (investigator's opinion)

Double blinded

Blinding description

Every dose of vaccine is packaged separately and has a unique identification number. Vials and boxes of vaccine and placebo have a similar shape and packaging that results in blinding for participants, investigators, and outcome assessors.

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

13th floor, Block A, Ministry of health, Simaye Iran street, Shahrake ghods

City

Tehran

Province

Tehran

Postal code

1417993337

Approval date

2021-03-10, 1399/12/20

Ethics committee reference number

IR.NREC.1399.008

Health conditions studied

1

Description of health condition studied

COVID-19 disease

ICD-10 code

U07.1

ICD-10 code description

COVID-19, virus identified

Primary outcomes

1

Description

Vaccine efficacy of Shifa-pharmed inactivated SARS-COV-2 vaccine

Timepoint

14 to 180 days after the last dose of intervention

Method of measurement

Comparing confirmed COVID-19 cases

2

Description

Neutralizing antibody (phase 2)

Timepoint

Day 0 of vaccination and 14, 28, 42, 90,180 and 360 days after the second dose

Method of measurement

Virus neutralization test

3

Description

Anti SARS-COV-2 antibody titer (IgG, IgM) (Geometric mean titer) (phase 2)

Timepoint

Day 0 of vaccination and 14, 28, 42, 90,180 and 360 days after the second dose

Method of measurement

ELISA

4

Description

Severe COVID-19 cases

Timepoint

Days 14 to 180 after second dose

Method of measurement

Comparing confirmed severe COVID-19 cases

Secondary outcomes

1

Description

Vaccine efficacy of Shifa-pharmed inactivated SARS-COV-2 vaccine

Timepoint

From 181 to 360 days after receiving the last dose of intervention

Method of measurement

comparing confirmed COVID-19 case

2

Description

Severe COVID-19 cases

Timepoint

181 to 360 days after second dose

Method of measurement

Comparing confirmed severe COVID-19 cases

3

Description

Any immediate reaction after inoculation

Timepoint

0-30 minute after inoculation

Method of measurement

Close observation

4

Description

Local reactions (pain, redness, swelling,) in injection site

Timepoint

Days 0 to 28 after each inoculation

Method of measurement

Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

5

Description

Systemic events (fever, headache, chills, vomiting, diarrhea, fatigues, muscle pain, joint pain,)

Timepoint

Days 0 to 28 after each inoculation

Method of measurement

Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

6

Description

Occurrence of any serious adverse event

Timepoint

Days 0 to day 360 after second dose

Method of measurement

Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

7

Description

Single dose efficacy of Shifa-pharmed inactivated SARS-COV-2 vaccine

Timepoint

day 1 after first dose to second dose

Method of measurement

Confirmed COVID-19 cases

Intervention groups

1

Description

Intervention group 2: 5 micrograms of antigen protein (Shifa Pharmed Co.) on days 0 and 28, which is received intramuscularly (deltoid muscle).

Category

Prevention

2

Description

Control group: The placebo group will receive only aluminum hydroxide adjuvant in the form of deltoid intramuscular injection on days 0 and 28. Placebo is similar to the active vaccine in shape and volume.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Eram Hotel

Full name of responsible person

Minoo Mohraz- Mohamadreza Salehi- Payam Tabarsi

Street address

Near West Hemmat Highway- Haghani Highway- Vanak square

City

Tehran

Province

Tehran

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Phone

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Fax

Email

lkafami@gmail.com

Web page address

<http://tehraneramhotel.com/home-page/>

2

Recruitment center

Name of recruitment center

Imam Khomeini hospital, Infectious diseases clinic

Full name of responsible person

Minoo Mohraz- Mohamadreza Salehi- Payam Tabarsi

Street address

Imam Khomeini hospital complex, Gharib street

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Phone

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Email

Imamhospital@tums.ac.ir

Web page address

<http://ikhc.tums.ac.ir>

3

Recruitment center

Name of recruitment center

Selected 16-hour COVID-19 center in Tehran

Full name of responsible person

Minoo Mohraz

Street address

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City

Tehran

Province

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Postal code

1417993337

Phone

+98 21 9109 0245

Email

minoomohraz@gmail.com

4

Recruitment center

Name of recruitment center

Selected 16-hour COVID-19 center in Karaj

Full name of responsible person

Mojtaba Hedayat Yaghoobi

Street address

Karaj

City

تهران

Province

Alborz

Postal code

1417993337

Phone

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Email

minoomohraz@gmail.com

5**Recruitment center****Name of recruitment center**

Selected 16-hour COVID-19 center in Mashhad

Full name of responsible person

Rosita Khodashahi

Street address

Mashhad

City

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Province

Razavi Khorasan

Postal code

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Phone

+98 21 9109 0245

Email

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6**Recruitment center****Name of recruitment center**

Selected 16-hour COVID-19 center in Shiraz

Full name of responsible person

Mohsen Moghadami

Street address

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Shiraz

Province

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Postal code

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Phone

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Email

moghadami@sums.ac.ir

7**Recruitment center****Name of recruitment center**

Selected 16-hour COVID-19 center in Isfahan

Full name of responsible person

Farzin Khorvash

Street address

Isfahan

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Province

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Postal code

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Phone

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Email

khovash@med.mui.ac.ir

8**Recruitment center****Name of recruitment center**

Selected 16-hour COVID-19 center in Booshehr

Full name of responsible person

Katayoon Vahdat

Street address

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City

Bushehr

Province

Boushehr

Postal code

1417993337

Phone

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Email

vahdatk@gmail.com

Sponsors / Funding sources**1****Sponsor****Name of organization / entity**

Shifa Pharmed Industrial Co.

Full name of responsible person

Mohammadreza Hosseinpour

Street address

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City

Kordan

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Postal code

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Phone

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Email

mr.hosseinpour@shifapharmed.com

Web page address

<https://en.bpharmed.com/>

Grant name**Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Shifa Pharmed Industrial Co.

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**

Industry

Person responsible for general inquiries

Contact

Name of organization / entity

Shifa Pharmed Industrial Co.

Full name of responsible person

Mohammadreza Hosseinpour

Position

Managing Director

Latest degree

Ph.D.

Other areas of specialty/work

Medical Pharmacy

Street address

Soha St., Shifa St.,Mapna Blv

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Fax**Email**

mr.hosseinpour@shifapharmed.com

Web page address

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Person responsible for scientific inquiries

Contact

Name of organization / entity

Tehran University of Medical Sciences

Full name of responsible person

Minoo Mohraz

Position

Professor

Latest degree

Specialist

Other areas of specialty/work

Infectious diseases

Street address

AIDS research center, Tehran University of Medical Sciences

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Person responsible for updating data

Contact

Name of organization / entity

Tehran University of Medical Sciences

Full name of responsible person

Kazem Heidari

Position

Epidemiologist

Latest degree

Ph.D.

Other areas of specialty/work

Epidemiology

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Unit 23, 4th floor, No. 1547, North Kargar Street

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Postal code

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Web page address

<http://ctc.tums.ac.ir>

Sharing plan

Deidentified Individual Participant Data Set (IPD)

Undecided - It is not yet known if there will be 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

Not applicable

Data Dictionary

Not applicable

Title and more details about the data/document

Participants' data will be available for regulatory and ethics committee for decisions.

When the data will become available and for how long

Documents including study protocol and the results will be available to the public after the study ends.

To whom data/document is available

The regulatory body and the ethics committee will have access to the study data. The monitoring team will have access to the study data during the conduct. DSMB will have access to the study data and results in predefined timelines and decides about the continuation of the study.

Under which criteria data/document could be used

With the permission of the sponsor and the approval of regulatory

From where data/document is obtainable

The study sponsor is responding to this request

What processes are involved for a request to access

data/document

After contacting the principal investigator and obtaining

permission from the sponsor

Comments