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

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Iran (Islamic Republic of)

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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 placeboes) 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 doe 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
Postal code
1417993337
Phone
+98 21 2226 6644
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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تهران
Province
Tehran
Postal code
1419733141
Phone
+98 21 6119 3011
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
Tehran
City
Tehran
Province
Tehran
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
+98 21 9109 0245

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
Mashhad
Province
Razavi Khorasan
Postal code
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Phone
+98 21 9109 0245
Email
rkhodashahi@yahoo.com

6

Recruitment center
Name of recruitment center
Selected 16-hour COVID-19 center in Shiraz
Full name of responsible person
Mohsen Moghadami
Street address
Shiraz
City
Shiraz
Province
Fars
Postal code
1417993337
Phone
+98 21 9109 0245
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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Isfahan
Province
Isfehan
Postal code
1417993337
Phone
+98 21 9109 0245
Email
khorvash@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
Bushehr
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Bushehr
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Boushehr
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1417993337
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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
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Street address
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Alborz
Postal code
1417993337
Phone
+98 21 9109 0245
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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Kordan

Province
Alborz

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+98 21 9109 0245

Fax

Email
mr.hosseinpour@shifapharmed.com

Web page address
https://en.bpharmed.com/

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

City
Tehran

Province
Tehran

Postal code
1417993337

Phone
+98 21 6658 1583

Email
minoomohraz@gmail.com

Web page address
https://ircha.tums.ac.ir/

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

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

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Tehran

Province
Tehran

Postal code
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Phone
+98 21 8896 3546

Email
k_heidari@razi.tums.ac.ir

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