

Clinical Trial Protocol

Iranian Registry of Clinical Trials

26 Oct 2021

A double-blinded, randomized, placebo-controlled Phase I Clinical trial to evaluate the safety and immunogenicity of COVID-19 inactivated vaccine (Shif-Pharmed) in a healthy population

Protocol summary

Study aim

To determine the safety and immunogenicity of COVID-19 inactivated vaccine in a healthy population

Design

Phase I, randomized, double-blind, parallel arms, placebo-control clinical trial on 56 healthy volunteers

Settings and conduct

This double-blind (volunteers and outcome assessors) placebo control study will be conducted on 56 healthy volunteers at Eram Hotel in Tehran. After random assignment to 3 micrograms, 5 micrograms, or placebo group (based on two stages random allocation), they will receive the intervention twice on days 0 and 14 and following-up until day 28 for any adverse events and measuring humoral and cellular immunity. All participants will be followed up for 360 days to identifying any potential late side effects.

Participants/Inclusion and exclusion criteria

Main inclusion criteria: Healthy 18-50 years, willing to participate, the ability to understand the study, signing the informed consent, not being pregnant, using effective contraception during the study. Main exclusion criteria: Positive PCR test, previous history of infection (positive antibody), symptoms consistent with COVID-19, history of close contact with COVID-19 patient in the last 14 days, abnormal paraclinical findings, history of allergy to the vaccine, neurologic disease, immunodeficiency, coagulopathy, 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, the high-risk job for SARS-CoV2 exposure

Intervention groups

Group 1: 3 µg antigen protein (24), Group 2: 5 µg antigen protein (24), Placebo (8)

Main outcome variables

The occurrence of adverse events, Seroconversion rate, Neutralizing antibody, incidence of SARS-COV-2 infection, cytokines assay, Lymphocyte count

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20201202049567N1**

Registration date: **2020-12-15, 1399/09/25**

Registration timing: **prospective**

Last update: **2020-12-15, 1399/09/25**

Update count: **0**

Registration date

2020-12-15, 1399/09/25

Registrant information

Name

Mohammadreza Hosseinpour

Name of organization / entity

Shifa Pharmed Industrial Co

Country

Iran (Islamic Republic of)

Phone

+98 21 9109 0245

Email address

mr.hosseinpour@shifapharmed.com

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-12-21, 1399/10/01

Expected recruitment end date

2021-02-18, 1399/11/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

A double-blinded, randomized, placebo-controlled Phase I Clinical trial to evaluate the safety and immunogenicity of COVID-19 inactivated vaccine (Shif-Pharmed) in a healthy population

Public title

Phase 1 clinical trial of an inactivated COVID-19 vaccine (Shifa-Pharmed) in healthy individuals

Purpose

Prevention

Inclusion/Exclusion criteria**Inclusion criteria:**

Aged 18 to 50 years Healthy general condition according to medical history and initial medical examinations Willing and able to cooperate throughout the study period according to the study protocol 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 researchers access to medical records, test results if hospitalized due to suspicion, or approval of COVID-19 A negative pregnancy test at screening or vaccination (women only) Using effective methods of contraception during the study (male and female) Volunteers who agree not to donate blood, blood products, or bone marrow from the start of the vaccine until three months after receiving the last dose

Exclusion criteria:

Confirmed, suspected, or asymptomatic COVID-19 detected by PCR at baseline. COVID-19 positive antibody History of SARS-CoV-2 infection History of contact with a person with SARS-CoV-2 infection (positive PCR test) during the last 14 days People in the home quarantine period due to Covid (suspicion of exposure or suspicious symptoms) Fever (axillary temperature greater than 37 ° C) Dry cough, extreme tiredness, nasal congestion, runny nose, sore throat, muscle aches, diarrhea, dyspnea, and shortness of breath during the 14 days prior to vaccination Abnormality in biochemistry, blood and urine laboratory tests History of severe allergy or allergic reactions to Inactivated vaccine components Personal or family history of seizure, epilepsy, encephalopathy or mental disorders Congenital malformations History of neurologic disorders or seizure or Guillain-Barre syndrome (excluding childhood febrile seizure) Growth disorders Any Genetic disorder History or signs of malnutrition Hepatorenal diseases Uncontrolled hypertension Diabetes complications BMI > 40 Any malignancy Acute diseases or an exacerbation of a chronic disease in the last 7 days Known case of immunodeficiency, HIV, lymphoma, leukemia, or other autoimmune diseases Thyroid disease or history of thyroidectomy Splenectomy or history of any organ removal History of coagulopathy Receiving Anti-TB

treatment Positive HBSAg Positive HIV test Positive HCV antibody Receiving immunomodulators or immunosuppressors at least 14 days in the past 3 months Receiving live vaccine in one month or other vaccines in 14 days before inoculation History of drug or alcohol abuse Receiving immunoglobulins or blood products in 3 months before inoculation Receiving any other investigational drug in 6 months before inoculation 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 Having a high-risk job of being exposed to the SARS-CoV-2 virus or having a high risk of exposure according to the investigator evaluation Any other condition that makes a person inappropriate for participation based on the investigator opinion

Age

From **18 years** old to **50 years** old

Gender

Both

Phase

1

Groups that have been masked

- Participant
- Investigator
- Outcome assessor

Sample size

Target sample size: **56**

Randomization (investigator's opinion)

Randomized

Randomization description

A two-stage individual permuted block randomization is planned for the study. At the first stage, 14 participants randomly receive a low dose of 3 micrograms (12 candidates) or placebo (2 volunteers). For this purpose, two random block sequences with size 7 are produced, including 6 vaccines and one placebo code. After getting approval for the safety of the low-dose vaccine, in the second stage, 42 volunteers are randomly assigned to the intervention group of 3 micrograms (12 participants), 5 micrograms (24 participants), and the placebo (6 participants). For this purpose, 6 blocks with size 7 (2 people in the group of 3 micrograms, 4 people in the group of 5 micrograms, one person in the placebo group) will be generated. 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

The Data and Safety Monitoring Board (DSMB) oversees the safety of participants throughout the study. The committee consists of seven independent members (including infectious disease specialist, immunologist, virologist, epidemiologist, vaccinologist, etc.). The DSMB is held at intervals of 7 days after the recruitment of first 3, 7, 14, 21 volunteers and then 14 days after the enrolment of 35th and 28 days after the 56th participant. The safety profile of the candidates is reviewed individually and the result of the committee is submitted to the regulatory body. The progress of the trial to next stage occurs only with the DSMB approval and the national regulatory authorities.

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

2020-12-02, 1399/09/12

Ethics committee reference number

IR.NREC.1399.003

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

Any immediate reaction after inoculation

Timepoint

0-30 minute after inoculation

Method of measurement

Close observation

2

Description

Percentage of local reactions (pain, redness, swelling,in injection site)

Timepoint

Days 0 to 7 after each inoculation

Method of measurement

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

3

Description

Percentage of systemic events (fever, headache, chills, vomiting, diarrhea, fatigues, muscle pain, joint pain,)

Timepoint

Days 0 to 7 after each inoculation

Method of measurement

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

4

Description

Incidence of any adverse event (AE)

Timepoint

Days 0 to 7 after each inoculation

Method of measurement

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

5

Description

Incidence of any serious adverse event (SAE)

Timepoint

Days 0 to 7 after each inoculation

Method of measurement

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

Secondary outcomes

1

Description

Any adverse events (AEs or SAEs)

Timepoint

From Days 7 to 28 after inoculation

Method of measurement

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

2

Description

Percentage of seroconversion occurrence

Timepoint

Days 0, 7, 14, 21, 28, 90, 180, 360

Method of measurement

At least a 4-fold increase in antibody titer (IgG and IgM) above baseline : ELISA assay

3

Description

Antibody- IgG and IgM titer (The geometric mean titer of antibody)

Timepoint

Days 0, 7, 14, 21, 28 and 90, 180, 360 (follow up period)

Method of measurement

ELISA

4

Description

Neutralizing antibody activity

Timepoint

Days 0, 7, 14, 21, 28 and 90, 180, 360 (follow up period)

Method of measurement

ELISA

5

Description

Lymphocytes subset count (Including CD3+, 4+, 8+, NK cell, B cell, ...)

Timepoint

Days 0, 14 and 28 after inoculation

Method of measurement

Flow Cytometry

6

Description

Cytokine assay (including IL 1, 2,4,5,6,8,10,12,17A,17F,21IFN- gamma, TNF - alpha)

Timepoint

Days 0, 14 and 28 after inoculation

Method of measurement

ELISA

7

Description

The severity of SARS-COV-2 infection (if present)

Timepoint

Any time after inoculation: days 0 to 28

Method of measurement

Clinical grading

Intervention groups

1

Description

Intervention group 1: 3 micrograms of antigen protein (Shifa Pharmed Co.) on days 0 and 14, which is received intramuscularly (deltoid muscle).

Category

Prevention

2

Description

Intervention group 2: 5 micrograms of antigen protein

(Shifa Pharmed Co.) on days 0 and 14, which is received intramuscularly (deltoid muscle).

Category

Prevention

3

Description

Control group: The placebo group will receive only aluminum hydroxide adjuvant in the form of deltoid intramuscular injection on days 0 and 14. 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

Email

info@tehraneramhotel.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

City

Tehran

Province

Tehran

Postal code

1419733141

Phone

+98 21 6119 3011

Email

Imamhospital@tums.ac.ir

Web page address

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

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Shifa Pharmed Industrial Co.

Full name of responsible person

Mohammadreza Hosseinpour

Street address

Soha St., Shifa St.,Mapna Blv

City

Kordan

Province

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

City

Kordan

Province

Alborz

Postal code

1417993337

Phone

+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

City

Tehran

Province

Tehran

Postal code

1417993337

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