Clinical Trial Protocol
Iranian Registry of Clinical Trials

30 Jun 2022

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 and14, 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