Clinical Trial Protocol
Iranian Registry of Clinical Trials

21 Mar 2023

Comparison of the tolerability, safety, and immunogenicity of Shifa-Pharmed COVID-19 inactivated vaccine (CovIran) and Sinopharm vaccine in the healthy population aged 12 to 18 years: a double-blind, randomized, active-controlled, Phase I-II clinical trial.

Protocol summary

Study aim
To determine the tolerability, safety, and immunogenicity of COVID-19 inactivated vaccine (CovIran-Barkat) in a healthy population aged 12-18 years compared to Sinopharm

Design
Phase 1/2 , randomized, double-blind, parallel arms, active-controlled clinical trial on 500 healthy volunteers aged 12-18 yeras

Settings and conduct
This double-blind (volunteers and outcome assessors) active-controlled trial will be conducted on 60 and 440 healthy volunteers aged 12-18 years in phases 1 and 2, respectively at Eram Hotel in Tehran. After random assignment to the CovIran or Sinopharm group, they will receive the intervention twice on days 0 and 28 and be followed up for safety, immunogenicity, any adverse events, and COVID-19 incidence.

Participants/Inclusion and exclusion criteria
Main inclusion criteria: Participants must be healthy, aged 12-18, willing to participate, able to understand, sign the informed consent, not pregnant, and using effective contraception during the study. Main exclusion criteria: Positive PCR test, Previous history of infection, symptoms consistent with COVID-19, history of close contact with COVID-19 patient in the last 14 days, any abnormal paraclinical findings, history of allergy to the vaccine, any neurologic disease, immunodeficiency, coagulopathy, psychiatric and other chronic diseases, receiving the live vaccine in 14 days before inoculation, receiving immunoglobulins or blood products in 3 months before inoculation or investigational products in 6 months before inoculation.

Intervention groups
Intervention group: Shifa-Pharmed inactivated vaccine/Control group: Sinopharm vaccine (both 0.5 ml, IM injection on days 0 and 28)

Main outcome variables
The occurrence of adverse events, humoral immunity (Seroconversion rate, Neutralizing antibody, Anti-RBD, Anti-SPIKE titer), Cellular immunity, the incidence of SARS-COV-2 infection and its severity.

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20171122037571N3**
Registration date: **2021-11-11, 1400/08/20**
Registration timing: **prospective**

Last update: **2021-11-11, 1400/08/20**
Update count: **0**

Registration date
2021-11-11, 1400/08/20

Registrant information

Name
Hamed Hosseini

Name of organization / entity

Country
Iran (Islamic Republic of)

Phone
+98 21 8670 5503

Email address
hmdhosseini@gmail.com

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date

2021-11-15, 1400/08/24

Expected recruitment end date

2022-02-13, 1400/11/24

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison of the tolerability, safety, and immunogenicity of Shifa-Pharmed COVID-19 inactivated vaccine (CovIran) and Sinopharm vaccine in the healthy population aged 12 to 18 years: a double-blind, randomized, active-controlled, Phase I-II clinical trial.

Public title

Phase I/II clinical trial of Shifa-Pharmed COVID-19 inactivated vaccine (CovIran-Barkat) among healthy adolescents aged 12 to 18 years.

Purpose

Prevention

Inclusion/Exclusion criteria

Inclusion criteria:

Aged 12 to 18 years According to the protocol, the volunteer and their legal guardian be able and willing to cooperate with the researchers throughout the study period. The volunteer and/or their legal guardian are able to fully understand the executive processes of the study and to understand the explanations of the facilitators correctly. The volunteer and/or their legal guardian are able to understand the contents of the informed consent form and sign the informed consent before interring in the study. The volunteer and/or their legal guardian allow the researchers to access medical records and test results if hospitalised for any reason including due to the suspected or confirmed COVID-19. Healthy general condition according to medical history and initial medical examinations. BMI of higher than 3rd percentile according to WHO standards for child growth at visit day (day 0). Volunteers and their legal guardians agree not to donate blood, blood products, or bone marrow from the time of vaccine inoculation until 3 months after receiving the last dose of the vaccine Women with fertility potential: Negative pregnancy test on the first day of injection (day zero) and day of the second injection (day 28). Furthermore, volunteers should use the effective contraception method 28 days before the first dose and continue to use it for at least three months after the second dose.

Exclusion criteria:

Confirmed, suspected, or asymptomatic COVID-19 detected by PCR at baseline. Positive Neutralizing antibody or COVID-19 nucleocapsid antibody (N-protein) on the day of the screening visit. History of SARS-CoV-2 infection (documented rtPCR) History of contact with a person with SARS-CoV-2 infection (positive PCR test) during the last 14 days During the period of home quarantine due to Covid-19 (suspicion of exposure or suspicious symptoms). In the 14 days prior to vaccination, fever or presence of at least two symptoms from Dry cough, severe fatigue, nasal congestion, runny nose, sore throat, myalgia, diarrhoea, dyspnea, and shortness of breath Abnormality in biochemistry, blood and urine laboratory tests prior to vaccination(biochemistry including Na, K, BUN/Urea, creatinine, FBS, Liver function tests: AST, ALT, ALP, total bilirubin, CBC: leukocyte count, Hemoglobin, platelet, neutrophil. lymphocyte, urine analysis: protein, glucose and blood cells (Microscopic examination). History of severe allergy, urticaria or allergic reactions to COVID-19 Inactivated vaccine ingredients (allergic to Aluminium). Personal or family history of seizure, epilepsy, encephalopathy or mental disorders, Congenital malformations, History of neurologic disorders or seizure (excluding febrile seizure). Any genetic disorder. History or signs of malnutrition, history of growth disorders. Uncontrolled hypertension, any hepatic or renal disease, Diabetes mellitus, chronic pulmonary disease and asthma, chronic kidney disease, serious cardiovascular disorders such as congenital heart defects, arrhythmia, heart blocks, ..., any type of malignancy, thyroid disease, history of coagulation disorders. Any acute diseases or an exacerbation of a chronic disease in the last 7 days prior to study. Known case of immunodeficiency, HIV, lymphoma, leukemia, or other autoimmune diseases. Receive immunosuppressive drugs or corticosteroids in the last 6 months Splenectomy or history of any organ removal History of dermatological disorders that can cause local complications at the injection site. History of hereditary and acquired angioedema over the past year Receiving Anti-TB treatment Positive HBsAg/ Positive HCV antibody History of any substance abuse (including alcohol, opium, etc.) / Recent history of inhaled use of substances such as tobacco, cannabis, and etc 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 Receiving any other investigational COVID-19 vaccine Receiving immunoglobulins or blood products in 3 months before inoculation Receiving any other investigational drug in 6 months before inoculation and/or planning to receive any other vaccine in one month after inoculation Participation in any interventional clinical trial within 28 days prior to receiving the first dose or willingness to participate during the present study period History of severe mental disorders affecting the participation in the study Women with a positive pregnancy test (Beta HCG in a blood sample) or breastfeeding or those who intend to become pregnant during the study period. First-degree relatives of any member of the research team (including the study sponsor) Any other circumstances are other than the above-mentioned ones that the researcher deems inappropriate for a person participating in a clinical trial. These cases are recorded as the reason for not entering.

Age

From **12 years** old to **18 years** old

Gender

Both

Phase

1-2

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size
Target sample size: **500**
Randomization (investigator's opinion)
Randomized
Randomization description
Phase one: will be conducted in 2 stages: First stage: Initially, 10 participants who meet the criteria receive a dose of vaccine (two participants aged 17-18 years, two aged 15-16 years, three aged 13-14 and finally three aged 12 years old), and are followed up for any adverse events. Second stage: if no serious adverse event was detected within 48 hours, the rest of the participants (50 cases) will receive the CovIran vaccine (20 individuals) or Sinopharm vaccine (30 individuals). For this purpose, ten permuted block random with the size of 5 is produced, each including 2 vaccines and 3 placebo codes. Permuted block randomisation for 440 participants is planned by 110 random blocks of 4, each including 2 vaccines and 2 placebos via an online system (http://sealedenvelope.com).
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
Not 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(qarb)
City
Tehran
Province
Tehran
Postal code
1417993337
Approval date
2021-11-07, 1400/08/16
Ethics committee reference number
IR.NREC.1400.010

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
Phase 1: Any immediate reaction after inoculation
Timepoint
0-30 minutes after inoculation
Method of measurement
Close observation

2

Description
Phase 1: 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
Phase 1: Percentage of systemic events (fever, headache, chills, nausea, vomiting, diarrhoea, fatigue, muscle pain, arthralgia, ...)
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
Phase 1: occurrence of any adverse event (serious or non-serious)
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
Phase 2: Percentage of seroconversion occurrence
Timepoint
Days 0, 7 , 28, 42, 90, 180, 360
Method of measurement

ELISA assay

6

Description
Phase 2: Anti-Spike, Neutralizing Antibody, Anti-RBD titres (with GMT , GMI)
Timepoint
Days 0, 7, 28, 42, 90, 180, 360
Method of measurement
ELISA assay

7

Description
Phase 2: Lymphocytes subset count and cytokines for determining cellular immunity
Timepoint
Days 0, 28
Method of measurement
ELISA assay

Secondary outcomes

1

Description
Phase 1: occurrence of any Systemic events
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

2

Description
Phase 1: Any adverse events (serious or non-serious)
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

3

Description
Phase 1: seroconversion occurrence
Timepoint
Days 0, 7 , 28, 42, 90, 180, 360
Method of measurement
ELISA assay

4

Description
Phase 1: Lymphocytes subset count and cytokines for determining cellular immunity
Timepoint
Days 0, 28
Method of measurement
ELISA assay

5

Description
Phase 1: Anti-Spike, Neutralizing antibody, Anti-RBD titres (with GMT, GMI)
Timepoint
Days 0, 7 , 28, 42, 90, 180, 360
Method of measurement
ELISA assay

6

Description
Phase 1: Occurrence and the severity of SARS-COV-2 infection
Timepoint
180 days after last inoculation
Method of measurement
Comparing confirmed COVID-19 cases, severity status is categorised as non-severe, severe, and critical based on the WHO diagnosis scheme.

7

Description
Phase 2: Any immediate reaction after inoculation
Timepoint
0-30 minutes after inoculation
Method of measurement
Close observation

8

Description
Phase 2: Local reactions in injection site (pain, redness, swelling, ...)
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

9

Description
Phase 2: Percentage of systemic reactions (fever, headache, chills, nausea, vomiting, diarrhea, fatigue, myalgia, arthralgia, ...)
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

10

Description
Phase 2: Any adverse events (serious or non-serious)
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

11

Description
Phase 2: Occurrence and the severity of SARS-COV-2 infection
Timepoint
180 days after last inoculation
Method of measurement
Comparing confirmed COVID-19 cases, severity status is categorised as non-severe, severe, and critical based on the WHO diagnosis scheme.

Intervention groups

1

Description
Intervention group: Intramuscular injection (deltoid muscle) of 0.5 ml Shifa-Pharmed inactivated vaccine (CovIran- Barkat) on days 0 and 28
Category
Prevention

2

Description
Control group: Intramuscular injection (deltoid muscle) of 0.5 ml Sinopharm vaccine on days 0 and 28
Category
Prevention

Recruitment centers

1

Recruitment center
Name of recruitment center
Eram Grand Hotel
Full name of responsible person
Minoo Mohraz- Mohamadreza Salehi- Payam Tabarsi- Hamid Eshaghi
Street address
Near West Hemmat Highway- Haghani Highway- Vanak square
City
Tehran
Province
Tehran
Postal code
1417993337
Phone
+98 21 2226 6644
Email
Ikafami@gmail.com
Web page address
https://tehraneramhotel.com/

2

Recruitment center
Name of recruitment center
Imam Khomeini hospital, Infectious diseases clinic
Full name of responsible person
Minoo Mohraz- Mohamadreza Salehi- Payam Tabarsi- Hamid Eshaghi
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
SHIFAPHARMED Industrial Group Co
Full name of responsible person
Hasan Jalili
Street address
Soha St., Shifa St.,Mapna Blv
City
Kordan
Province
Alborz
Postal code
1417993337
Phone
+98 21 9109 0245
Email
hjalili@ut.ac.ir
Web page address
http://www.shifapharmed.com/
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
SHIFAPHARMED Industrial Group 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
SHIFAPHARMED Industrial Group Co
Full name of responsible person
Hasan Jalili
Position
Managing Director
Latest degree
Ph.D.
Other areas of specialty/work
Medical Biotechnology
Street address
Soha St., Shifa St.,Mapna Blv
City
Kordan
Province
Alborz
Postal code
1417993337
Phone
+98 21 9109 0245
Email
hjalili@ut.ac.ir
Web page address
http://www.shifapharmed.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
Hamed Hosseini
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
hmdhosseini@gmail.com
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
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available
Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available
Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available
Analytic Code
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available