Clinical Trial Protocol
Iranian Registry of Clinical Trials

26 Oct 2021

Efficacy, safety, and immunogenicity of Soberana recombinant vaccine (product of Finlay Institute) based on RBD protein subunit of Sars-Cov-2 in a 2-dose regimen with and without a booster dose: a double-blind, randomized, placebo-controlled phase III clinical trial in the Iranian population of 18-80 years

Protocol summary

Study aim

Evaluation of efficacy, safety and immunogenicity of recombinant protein vaccine in the prevention of symptomatic infection, severe disease and death due to SARS - CoV-2, in the population aged 18-80 years

Design

In a double blind randomized trial, 24,000 adults, aged between 18 and 80 years old (in 8 cities) will assign to the vaccine and placebo groups (4:1 ratio). The intervention in 6 cities, will be performed with two doses of vaccine and in 2 cities with three doses of vaccine.

Settings and conduct

This study will be conducted in 8 centers from 7 provinces. During the study, efficacy, safety and immunogenicity of two doses of Soberana 02 vaccine and two doses of Soberana 02 with one dose of Soberana plus will evaluate in comparison with the control group. Researchers and volunteers are not aware of the product prescription for each individuals.

Participants/Inclusion and exclusion criteria

Inclusion informed consent, 18-80 years, male and female, Iranian citizens, healthy adults/adults with controlled underlying diseases, able to comply with schedule, subjects from 8 cities Exclusion Fever or infectious disease (recently),mental diseases, sever allergies, complicated diseases (asthma, hypertension, renal, liver and hart diseases), application of tetanus vaccines (recently), vaccination against SARS-CoV-2, use of immunomodulators, tattoos on arms, participation in COVID-19 vaccine trials, Blood transfusion and its products (recently), Coagulation problems, heavy smoker-First priority groups for vaccination

Intervention groups

Cohort 1: 25 µg of RBD-TT, IM, 0 - 28 Cohort 2: 25 µg of RBD-TT, IM, 0 - 28 + a booster dose (Soberana Plus), 56 Placebo groups (in each cohort):Aluminum hydroxide, IM, 0.5 mL, 0 - 28

Main outcome variables

PCR-confirmed of Covid-19 starting 14 days after the last dose of each scheme in the population

General information

Reason for update

Due to the small number of volunteers who were above 65 years (as they have had access to COVID-19 vaccine from the national health system), the 10% limit for recruitment of the above 65 years age group was removed from the protocol upon approval of the DSMB. As per the request of the DSMB committee, new sample size is estimated for the cellular immunity assessment. Accordingly, the following fields in the IRCT were updated: - Secondary outcome variable section> description of the third outcome variable> the sample size for cellular immunity assessment is changed to 130 people. - Abstract section > Study Design section: e 10% limit for recruitment of the above 65 years age group is removed.

Acronym

IRCT registration information

IRCT registration number: **IRCT20210303050558N1**
Registration date: **2021-04-24, 1400/02/04**
Registration timing: **prospective**

Last update: **2021-06-23, 1400/04/02**
Update count: **1**

Registration date

2021-04-24, 1400/02/04

Registrant information

Name
Ehsan Mostafavi
Name of organization / entity
Country
Iran (Islamic Republic of)
Phone
+98 21 6411 2121
Email address
mostafaviehsan@gmail.com

Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2021-04-25, 1400/02/05
Expected recruitment end date
2021-05-20, 1400/02/30
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Efficacy, safety, and immunogenicity of Soberana recombinant vaccine (product of Finlay Institute) based on RBD protein subunit of Sars-Cov-2 in a 2-dose regimen with and without a booster dose: a double-blind, randomized, placebo-controlled phase III clinical trial in the Iranian population of 18-80 years

Public title
Efficacy, safety and immunogenicity of Soberana 02 vaccine (product of Finlay Institute): a double-blind, randomized, placebo-controlled phase III clinical trial
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
Giving written informed consent Ability to comply with the vaccination plan, scheduled visits and lab tests Having general health and controlled underlying diseases Iranian citizenship Residing in the studied cities (Isfahan, Babol, Bandar Abbas, Zanjan, Kerman, Hamedan, Yazd and Sari) Both Genders Aged 18 to 80 years
Exclusion criteria:
Pregnant or lactating women or those who plan to become pregnant up to 3 months after the last dose of the vaccine Application of vaccines containing tetanus toxoid in the last 3 months History of blood /blood products transfusions such as immunoglobulin in the last three months Type 2 diabetes (HbA1c higher than 7.5) Chronic liver disease (liver enzymes more than 5 times normal: ALT≥150, AST≥100) Subjects previously vaccinated against SARS-CoV-2. History of psychiatric disorders Uncontrolled asthma (having an asthma attack in the last three months). History of severe allergic reaction (anaphylaxis) to the vaccine throughout life History of smoking more than 20 cigarettes a day for more than twenty years Coagulation problems that contraindicate IM injection Previous vaccination with any coronavirus vaccine or participation in other COVID-19 vaccine trials Treatment with immunomodulators in the last 30 days Uncontrolled hypertension (cytological pressure more than 140, diastolic pressure more than 90 mm Hg) Fever or acute illness for 7 days before the injection or on the day of the injection Chronic kidney disease (GFR less than 30) All individuals who are in phase one priority of vaccination based on the National COVID-19 Vaccination Program Subjects with tattoos in the deltoid region on both arms Individuals in priority of the first phase of national vaccination (health workers can participate if they give consent)
Age
From **18 years** old to **80 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size
Target sample size: **24000**
Randomization (investigator's opinion)
Randomized
Randomization description
The random chain will be defined in the system before the start of the study and the list of randomized treatment groups and the corresponding codes will be delivered to the Food and Drug Administration. Random codes and the type of intervention will be assigned to the candidates based on this list, the details of which are given in the following sections. The random chain in this study will be based on the stratified block randomization method. Stratified randomization will be based on studied cities and the randomization unit is individual participants. Random blocks are a common method for constructing and allocating interventions in clinical trials in which the sample size is divided into a number of blocks of a certain size and in each block the ratio of intervention and control groups in the study is observed. Using this method, it is possible to ensure that the ratio of the intervention group to the control is observed at any time during the study. In the present study, the sample size of 24,000 people in 8 study centres (3000 people in each centre) has been determined. Each centre also has 500 codes in excess of the study size to meet the extraordinary needs of the study (for example, the decision to increase the sample size in one of the centres). The size of the blocks is 25. Therefore, for each centre, 3500 codes in 140 random blocks will be considered, in each of which there are 20 intervention codes and 5 control codes. Each intervention or control code has a unique block ID in the form of a UUID, a 1-digit code for the study centre, a block code from 1 to 140 for labeling vial-holding blocks, and a volunteer

code. The volunteer code consists of 5 digits, the first digit of which is the code of the study centre and 4 digits after 1 to 3000 and is therefore unique in the study. Random chain construction is done through a program written specifically for this study. Random chain construction will be performed through a randomization program using the Python 3.8.2 programming language, which was written specifically for this study. In this program, first the total sample size, number of centers, block size, number and ratio of interventions as well as the intervention label are defined. The program then calculates the required number of blocks for each center based on its sample size and block size and creates random chains for each block. In summary, in this method, first a list of intervention and control codes in a block will be made by observing the ratio of the groups. The ordering of the indices is done using a random process in which one of the indices is selected at each stage using a uniform distribution, added in the final order and removed from the unselected indices. This process is repeated for each block.

Blinding (investigator's opinion)
Double blinded

Blinding description
The unique codes of the volunteers are delivered to the preparation group and a label with the volunteer code is inserted on each vial. None of the people working in the preparation department will be in contact with those are involved in the site. Therefore, at the time of delivery of the vial block to the centres, the study colleagues will not be able to distinguish between the drug vial and the placebo. The suspensions in the vaccine and placebo vials are milky white and are similar in color and clarity. Moreover, vaccine and placebo vials are offered in similar appearance, they are inseparable, and packaging and are placed in boxes of 25. Each box will contain the block number and serial numbers of the vaccine/placebo inside. According to this process, participants, vaccinators, researchers, and outcome assessors will be blind. Vaccinators check the unique code information assigned to the candidate with the code on the vaccine/placebo vial before injection. During the study, all consumed vials will be archived and maintained.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
National Committee for Ethics in Biomedical Research

Street address
Sima-Ye-Iran St, Shahrak Gharb, Ministry o Health, Treatment and Medical Education

City
Tehran

Province
Tehran

Postal code
1467664961

Approval date
2021-04-17, 1400/01/28

Ethics committee reference number
IR.NREC.1400.001

Health conditions studied

1

Description of health condition studied
Coronavirus Disease (COVID-19)

ICD-10 code
U11

ICD-10 code description
Need for immunization against COVID-19

Primary outcomes

1

Description
The effectiveness of the vaccine in preventing symptomatic Covid-19 infection

Timepoint
The incidence of symptomatic Covid-19 that occurs from day 14 after the second injection will be compared in the vaccine and placebo groups. Positive cases will be evaluated before this time period and will be evaluated in stratification analyzes.

Method of measurement
PCR test results for COVID-19

2

Description
The effectiveness of the vaccine in preventing severe form of Covid-19

Timepoint
All cases of severe infection will be detected from day 14 after injection of the last dose to 4 and 6 months from start of the injection (respectively in 2-dose and 2-dose + booster regimens).

Method of measurement
Positive results of Covid-19 PCR test and clinical condition of the patient that the hospitalized patient will need to receive oxygen through non-invasive respiratory ventilation (NIV) or high oxygen flow or the patient will need intubation.

3

Description
The effectiveness of the vaccine in death from Covid-19

Timepoint
All cases of death due to COVID-19 will be detected from

day 14 after injection of the last dose to 4 and 6 months from start of the injection (respectively in 2-dose and 2-dose + booster regimens).

Method of measurement

Positive results of Covid-19 PCR test and according to the diagnosis of the research physician and the DSMB team and based on the definition of the World Health Organization

Secondary outcomes

1

Description

Humoral safety will be studied on a subset of the population of Babol, Sari (under 2-dose regimen) and Zanjan (under 2-dose + booster regimen).

Timepoint

The Humoral test will be done before and 1 month after receiving the last dose. Also, in Babol and Sari, an additional assessment will be done on days 5 and 28 of a 30% sample of subjects (900 people in each city).

Method of measurement

Anti-S-RBD antibody test

2

Description

The frequency of local and systemic events and mild, moderate , severe, critical adverse events and death will be recorded by the participants in the forms.

Timepoint

The occurrence of side effects and adverse events will be monitored from Zero day to 5 months after the injection of the last dose.

Method of measurement

Active and inactive monitoring from Zero day to 5 months after the injection of the last dose with the registration of adverse events in CIFs

3

Description

Evaluation of Cellular safety will be performed on 130 people in one of the cities of Babol or Sari (depending of logistic status).

Timepoint

Cell immunoassay will be performed at the same time as the humoral tests.

Method of measurement

Interferon Gamma Release Assay

Intervention groups

1

Description

Intervention group in the first cohort: In 6 cities (Isfahan, Babol, Bandar Abbas, Sari, Kerman and Hamedan) 80% of people (14,400 people) receive the intervention (vaccine) after random allocation. Intervention is included intramuscular injection of vaccine candidates with conjugation of 25 µg RBD to tetanus toxin in a 2-dose program (days 0 and 28). This vaccine is made by the Finlay Institute of Vaccines.

Category

Prevention

2

Description

Control group in the first cohort: In 6 cities (Isfahan, Babol, Bandar Abbas, Sari, Kerman and Hamedan) 20% of people (3600 people) receive a placebo after random allocation. The intervention involves an intramuscular injection of a dose of aluminum hydroxide on days 0 and 28. This placebo is made by the Finlay Institute of Vaccines.

Category

Placebo

3

Description

Intervention group in the second cohort: In two cities (Zanjan and Yazd) 80% of people (4800 people) receive the intervention (vaccine) after random allocation. The intervention includes: a 2-dose program + a booster dose (days 0, 28, 56). The booster dose of the candidate vaccine is Sobrana Plus (50 micrograms d-RBD +, IM 0.5 ml). This vaccine is made by the Finlay Institute of Vaccines.

Category

Prevention

4

Description

Control group in the second cohort: In 2 cities (Zanjan and Yazd) 20% of people (1200 people) receive a placebo after random allocation. The intervention involves an intramuscular injection of a dose of aluminum hydroxide on days 0, 28 and 56. This placebo is made by the Finlay Institute of Vaccines.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Shahid Nilforuzadeh Hall, on the campus of Isfahan University of Medical Sciences

Full name of responsible person

Dr. Morteza Pourahmad

Street address

Hezar Jerib St., Isfahan University of Medical Sciences and Health Services

City

Isfahan

Province

Isfehan

Postal code

۷۳۴۶۱-۸۱۷۴۶

Phone
+98 31 3668 0048

Email
mortezapourahmad@yahoo.com

2

Recruitment center

Name of recruitment center
Sport Hall of Babol University of Medical Sciences and Health Services

Full name of responsible person
Dr. Mostafa Javanian

Street address
Ganj Afrooz St., Babol University of Medical Sciences, Babol, Mazandaran

City
Babol

Province
Mazandaran

Postal code
۴۷۷۴۵-۴۷۱۷۶

Phone
+98 11 3219 9592

Email
sfjalali42@yahoo.com

3

Recruitment center

Name of recruitment center
Behvarz Training Center

Full name of responsible person
Dr.Hossein Farshidi

Street address
Payambar Azam Town, Hormoz Boulevard, Green Tree Site Phase 2

City
Bandar Abass

Province
Hormozgan

Postal code
7919693116

Phone
+98 76 3371 0371

Email
Traznahan@yahoo.com

4

Recruitment center

Name of recruitment center
School of Nursing and Midwifery, Mazandaran University of Medical Sciences

Full name of responsible person
Dr. Roya Ghasemian

Street address
Imam Square, Joybar Three Ways, beginning of Valiasr Highway, Mazandaran University of Medical Sciences, Sari

City
Mazandaran

Province
Mazandaran

Postal code
4815733971

Phone
+98 11 3304 4000

Email
roya31gh@gmail.com

5

Recruitment center

Name of recruitment center
Corona Vaccine Clinical Trial Center, Zanjan University of Medical Sciences

Full name of responsible person
Dr. Samad Ghodrati

Street address
Amirkabir crossroads, next to Zanjan county health center

City
Zanjan

Province
Zanjan

Postal code
4513956184

Phone
+98 24 3315 6201

Email
ghodrati@zums.ac.ir

6

Recruitment center

Name of recruitment center
Health Technology Incubator of Kerman University of Medical Sciences

Full name of responsible person
Dr. Iman Ghasemzadeh

Street address
Kerman Health Technology, between Farhangian interchange & Amirkabir interchange, Jomhouri blvd

City
Kerman

Province
Kerman

Postal code
76188-66749

Phone
+98 34 3211 4534

Email
imanaten@gmail.com

7

Recruitment center

Name of recruitment center
Shahid Soleimani Sports Hall, Hamadan University of Medical Sciences and Health Services

Full name of responsible person
Dr. Fariba Keramat

Street address
Palestine Square, Shahid Soleimani Sports Hall

City
Hamedan
Province
Hamadan
Postal code
6517838678
Phone
+98 81 3525 0182
Email
faribakeramat@yahoo.com

8

Recruitment center
Name of recruitment center
Akbari Health Center
Full name of responsible person
Dr. Mohammadreza Mirjalili
Street address
Safaieh, Imam Hassan Square, Shahid Karimi Street, in front of Safaieh Hotel
City
Yazd
Province
Yazd
Postal code
8916978477
Phone
+98 35 3725 8474
Email
Dr.mirjalili@ssu.ac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Pasture Institute of Iran
Full name of responsible person
Dr Alireza Biglari
Street address
No. 69, 12 Farvardin St., Tehran
City
Tehran
Province
Tehran
Postal code
1316943551
Phone
+98 21 6695 4321
Email
biglari63@hotmail.com
Web page address
http://fa.pasteur.ac.ir/
Grant name
Pasteur institute of Iran
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Pasture Institute of Iran
Proportion provided by this source
100
Public or private sector
Public
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact
Name of organization / entity
Pasture Institute of Iran
Full name of responsible person
Dr. Ehsan Mostafavi
Position
Professor
Latest degree
Specialist
Other areas of specialty/work
Epidemiology
Street address
No. 69, 12 Farvardin St., Tehran
City
Tehran
Province
Tehran
Postal code
1316943551
Phone
+98 21 6411 2121
Email
mostafaviehsan@gmail.com

Person responsible for scientific inquiries

Contact
Name of organization / entity
Tehran University of Medical Sciences
Full name of responsible person
Dr. Hamid Emadi Kuchak
Position
Professor
Latest degree
Specialist
Other areas of specialty/work
Infectious diseases
Street address
Enghela street, Tehran University of Medical Sciences
City
Tehran
Province
Tehran
Postal code
1467664961
Phone

+98 21 8897 3372

Email

emadiham@tums.ac.ir

Person responsible for updating data

Contact

Name of organization / entity

Pasture Institute of Iran

Full name of responsible person

Dr. Sana Eybpoosh

Position

Assistant Professor

Latest degree

Specialist

Other areas of specialty/work

Epidemiology

Street address

No. 69, 12 Farvardin St., Tehran

City

Tehran

Province

Tehran

Postal code

1316943551

Phone

+98 21 6411 2121

Email

mostafaviehsan@gmail.com

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