

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

25 Oct 2020

### Investigating the Effect of BCG Vaccine on Preventing COVID-19 Infection in Healthcare Staff Exposed to SARS-CoV-2

#### Protocol summary

##### Study aim

Assessing the effect of the BCG vaccine on preventing COVID-19 infection in healthcare workers exposed to coronavirus

##### Design

Phase III double blind Placebo-controlled adaptive multi-centre randomized controlled trial. Groups are determined by block randomization to receive a BCG vaccine or normal saline in a 1: 1 ratio.

##### Settings and conduct

The study will include five hundred healthcare workers in the COVID-19 hospitals in Shiraz, Iran. Participants will be follow-up for 12 months with regular mobile phone text messages to identify COVID-19 infection and related issues. Blood samples will be collected prior to randomization and at 12 months to determine exposure to severe acute respiratory syndrome coronavirus 2.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria include HCW over 18 years of age, male or female, hospital personnel who take care of patients with SARS CoV-2 infection with a signed and dated informed consent form. Exclusion criteria include HCW with fever, skin infections at the site of vaccine injection, intercurrent respiratory infection, or those who take immunosuppressive medications, those with any serious underlying conditions such as malignancies, receiving any live vaccine, BCG vaccine injection over the past year, having a positive COVID-19 test result.

##### Intervention groups

Experimental: 0.10 mL intradermal injection of BCG Vaccine over the distal insertion of the deltoid muscle onto the humerus. Placebo Comparator: Placebo intradermal injection of 0.1ml of 0.9% NaCl solution

##### Main outcome variables

1- Confirmed COVID-19 infection 2- Hospitalization due to COVID-19 3- Death due to COVID-19.

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20200411047019N1**

Registration date: **2020-05-18, 1399/02/29**

Registration timing: **prospective**

Last update: **2020-05-18, 1399/02/29**

Update count: **0**

##### Registration date

2020-05-18, 1399/02/29

##### Registrant information

##### Name

Bahman Pourabbas

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

+98 71 3647 4304

##### Email address

pourabbasb@sums.ac.ir

##### Recruitment status

**recruiting**

##### Funding source

##### Expected recruitment start date

2020-06-04, 1399/03/15

##### Expected recruitment end date

2021-06-05, 1400/03/15

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty

##### Trial completion date

empty

##### Scientific title

Investigating the Effect of BCG Vaccine on Preventing COVID-19 Infection in Healthcare Staff Exposed to SARS-CoV-2

## Public title

Effect of BCG Vaccine on Preventing COVID-19

## Purpose

Prevention

## Inclusion/Exclusion criteria

### Inclusion criteria:

Healthcare workers potentially exposed to patient with COVID-19 infection in hospitals Over 18 years of age Complete the consent form with date and signature Male and female

### Exclusion criteria:

Allergy to the BCG vaccine or any BCG vaccine contraindication Fever (>38 C) within the past 24 hours or generalised skin diseases such as infection, eczema, dermatitis or psoriasis at or near the site of vaccination. Pregnancy Cases with active or latent Mycobacterium tuberculosis Known HIV infection Individuals with any serious underlying illness (such as malignancy) except those with cardiovascular disease, hypertension, diabetes, and/or chronic respiratory disease if they are not immunocompromised Live vaccine administered for 4 weeks prior to randomization Suspected to active viral or bacterial infections Individuals with a SARS-CoV-2 positive test result Severely immunocompromised subject or who has taken immunosuppressive therapy in the last years

## Age

From **18 years** old

## Gender

Both

## Phase

3

## Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

## Sample size

Target sample size: **500**

## Randomization (investigator's opinion)

Randomized

## Randomization description

In this study, block randomization will be used and the size of the blocks will be selected randomly (for example 8 or 6 participants in each block with an equal number of two groups). In this method, the blocks are determined based on the hospital health care workers information that is in the face of covid 19. In each block, half of the people are considered as intervention groups and the rest half as placebo. The main goal of this method is to balance the number of participants in each group.

## Blinding (investigator's opinion)

Double blinded

## Blinding description

Statistical data analyst will distribute the health care workers in randomized blocks using software in two groups including vaccine recipients and placebo.

Identical vials without specifications (vials A and B) will be given to nurses for injection. -Participants won't be aware of the injection material. Individuals who won't be aware of the grouping are as follow: -Individuals who receive feedback from participants about influenza-like illness or severe respiratory illness. -People who perform PCR tests to diagnose the coronavirus. -Personnel and researchers who complete information based on questionnaires and register in SPSS software. The final analysis will be performed by the statistical analyst who is informed of the grouping.

## Placebo

Used

## Assignment

Parallel

## Other design features

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Ethics committee of Shiraz university of medical sciences

##### Street address

Clinical Microbiology Research center, Nemazi Hospital, Zand St,Zand St.

##### City

Shiraz

##### Province

Fars

##### Postal code

7188858184

#### Approval date

2020-05-20, 1399/02/31

#### Ethics committee reference number

IR.SUMS.REC.1399.181

## Health conditions studied

### 1

#### Description of health condition studied

Coronavirus Disease 2019 (COVID-19)

#### ICD-10 code

U07.1 COVI

#### ICD-10 code description

U07.1 COVID-19, virus identified

## Primary outcomes

### 1

#### Description

COVID-19 infection

#### Timepoint

Time Frame: At the beginning and weekly for up to 12

months

**Method of measurement**

A questionnaire for assessment of fever (>38), cough, shortness of breath, respiratory failure, runny / blocked nose and PCR or serology for detection of SARS-Cov-2

**2**

**Description**

Severe COVID-19 disease

**Timepoint**

Time Frame: At the beginning and weekly for up to 12 months

**Method of measurement**

A questionnaire to assess hospitalization or death due to covid-19 infection.

**Secondary outcomes**

**1**

**Description**

Hospital admission duration due to SARS-CoV-2

**Timepoint**

At the beginning and weekly for up to 12 months

**Method of measurement**

Review of hospital records

**2**

**Description**

Hospital admission due to documented SARS-CoV-2 infection

**Timepoint**

Review of hospital records

**Method of measurement**

Incidence of hospitalization days due to documented SARS-CoV-2 infection

**3**

**Description**

Pneumonia

**Timepoint**

At the beginning and weekly for up to 12 months

**Method of measurement**

Number of pneumonia cases with abnormal chest X-rays or CT scan and evaluation the extent of lung involvement

**4**

**Description**

Mechanical ventilation duration with SARS-CoV-2

**Timepoint**

At the beginning and weekly for up to 12 months

**Method of measurement**

Review of hospital records

**5**

**Description**

ICU admission duration due to SARS-CoV-2

**Timepoint**

At the beginning and weekly for up to 12 months

**Method of measurement**

Review of hospital records

**6**

**Description**

Mechanical ventilation usage in patients with SARS-CoV-2

**Timepoint**

At the beginning and weekly for up to 12 months

**Method of measurement**

Review of hospital records

**7**

**Description**

Number of days absence at work due to febrile respiratory illness

**Timepoint**

At the beginning and weekly for up to 12 months

**Method of measurement**

self-reporting

**8**

**Description**

Seroconversion of SARS-CoV-2-specific antibodies (IgM,G)

**Timepoint**

At the beginning, during the study (if symptoms occurs) and at 12 months

**Method of measurement**

Measurement of plasma/serum SARS-CoV-2-specific antibodies (IgM,G) at vaccination time and also the end of the study period.

**9**

**Description**

Intensive care unit admission due to documented SARS-CoV-2 infection

**Timepoint**

At the beginning and weekly for up to 12 months

**Method of measurement**

Review of hospital records

**Intervention groups**

**1**

**Description**

Intervention group: Healthcare workers who are exposed to the pandemic virus (COVID-19) will be randomly assigned to receive 0.1 ml intradermal injection of BCG vaccine. All participants will be followed-up for 12 months by text messages (up to weekly). The Mantoux Tuberculin skin test (before receiving the BCG vaccine) will be performed by intradermal injection of 0.1 ml (PPD) in front of the left forearm. This test will be read after 48-72 hours, a positive tuberculin test is 10 mm or more. Blood samples will be collected at the beginning and 12 months for PCR and antibody detection.

**Category**

Prevention

**2****Description**

Control group: Healthcare workers who are exposed to the pandemic virus (COVID-19) will be randomly assigned to receive 0.1 ml intradermal injection of BCG vaccine. All participants will be followed-up for 12 months by text messages (up to weekly). The Mantoux Tuberculin skin test (before receiving the BCG vaccine) will be performed by intradermal injection of 0.1 ml (PPD) in front of the left forearm. This test will be read after 48-72 hours, a positive tuberculin test is 10 mm or more. Blood samples will be collected at the beginning and 12 months for PCR and antibody detection.

**Category**

Placebo

**Recruitment centers****1****Recruitment center****Name of recruitment center**

Ali asghar hospital

**Full name of responsible person**

Ali Akbari

**Street address**

Meshkinfam St.

**City**

Shiraz

**Province**

Fars

**Postal code**

1879671439

**Phone**

+98 71 3228 8602

**Fax**

+98 71 3228 8907

**Email**

aliasghar@sums.ac.ir

**2****Recruitment center****Name of recruitment center**

Faghihi hospital

**Full name of responsible person**

Mohsen Moghademi

**Street address**

Zand St.

**City**

Shiraz

**Province**

Fars

**Postal code**

7134844119

**Phone**

+98 71 3235 1087

**Email**

faghihihsp@sums.ac.ir

**Web page address****3****Recruitment center****Name of recruitment center**

Rajae hospital

**Full name of responsible person**

Ali Akbari

**Street address**

Chamran Blv.

**City**

Shiraz

**Province**

Fars

**Postal code**

7194815711

**Phone**

+98 71 3636 4001

**Email**

rajaeehospital@sums.ac.ir

**4****Recruitment center****Name of recruitment center**

Nemazi hospital

**Full name of responsible person**

Mohsen Moghadami

**Street address**

Zand st.

**City**

Shiraz

**Province**

Fars

**Postal code**

7193613311

**Phone**

+98 71 3647 4332

**Email**

nemazee\_inf@sums.ac.ir

**Sponsors / Funding sources****1****Sponsor****Name of organization / entity**

Professor Alborzi Clinical Microbiology Research Center, Shiraz University of Mdicl Sciences

**Full name of responsible person**

GHolamreza Pouladfar

**Street address**

Nemazi hospital. Zand street

**City**

Shiraz

**Province**

Fars

**Postal code**

71936-13311

**Phone**

+98 71 3647 4304

**Email**

alborzicmrc@sums.ac.ir

**Grant name**

covid-19 grant

**Grant code / Reference number**

99-01-106-22342

**Is the source of funding the same sponsor organization/entity?**

No

**Title of funding source**

Shiraz University of Medical Sciences

**Proportion provided by this source**

25

**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**

Shiraz University of Medical Sciences

**Full name of responsible person**

Bahman Pourabbas

**Position**

Assistant professor

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Microbiology

**Street address**

Prof. Alborzi Clinical Microbiology Research Center -  
Nemazi Hospital- Zand St.- Shiraz - Iran

**City**

شیراز

**Province**

Fars

**Postal code**

7193613311

**Phone**

+98 71 3647 4304

**Fax**

+98 71 3647 4303

**Email**

pourabbasb@sums.ac.ir

## Person responsible for scientific inquiries

**Contact**

**Name of organization / entity**

Shiraz University of Medical Sciences

**Full name of responsible person**

Gholamreza Pouladfar

**Position**

Associate professor

**Latest degree**

Subspecialist

**Other areas of specialty/work**

Infectious diseases

**Street address**

Clinical Microbiology Research Center- Nemazi  
hospital- Zand st.

**City**

Shiraz

**Province**

Fars

**Postal code**

7193613311

**Phone**

+98 71 3647 4304

**Email**

pouladfar\_ghr@hotmail.com

## Person responsible for updating data

**Contact**

**Name of organization / entity**

Shiraz University of Medical Sciences

**Full name of responsible person**

Bahman Pourabbas

**Position**

Assistant professor

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Microbiology

**Street address**

Prof. Alborzi Clinical Microbiology Research Center -  
Nemazi Hospital- Zand St.- Shiraz - Iran

**City**

Shiraz

**Province**

Fars

**Postal code**

7193613311

**Phone**

+98 71 3647 4304

**Fax**

+98 71 3647 4303

**Email**

pourabbasb@sums.ac.ir

## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**

Yes - There is 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**

All collected deidentified IPD will be shared.

**When the data will become available and for how long**

The data will become available starting 6 months after publication for 1 year.

**To whom data/document is available**

It will be available for people working in academic institutions.

**Under which criteria data/document could be used**

The data will be shared by request and the persons who

are responsible for general and scientific inequires will review the request.

**From where data/document is obtainable**

person who are responsible for general inequires:

Bahman Pourabbas bpourabbas@yahoo.com person who

are responsible for scientific inequires: Gholamreza

Pouladfar pouladfar\_ghr@hotmail.com

**What processes are involved for a request to access data/document**

The academic applicants should send their request by email. The responsible persons will answer up to 2 weeks.

**Comments**