

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### **A Randomized, Multi-centric, Double-blind, Placebo-controlled study to Evaluate the Efficacy and Safety of Bromhexine, a serine protease (TMPRSS2) blocker, to prevent COVID-19**

#### **Protocol summary**

##### **Study aim**

To evaluate the safety and efficacy of bromhexine in post exposure prophylaxis against COVID-19

##### **Design**

Clinical trial with controlled group, parallel design, double-blinded, multi-centric, randomized; phase 3 on 1050 patients. Randomization of the patients will be conducted using block randomization method via Rand function in Excel software.

##### **Settings and conduct**

The present study will be conducted at Imam Hossein, Shahid Labafinejad, Shohadaye Gomnam Medical Centers affiliated to Shahid Beheshti University of Medical Sciences, Tehran. The study designed as double blinded in which the participants and outcome assessors will be masked to their assignment.

##### **Participants/Inclusion and exclusion criteria**

Inclusion criteria: Individuals who have the ability to understand and desire to sign the informed consent; Age of 18 years or more; Exposure and close contact with a COVID-19 patients within 4 days before entering the study; must agree not to enroll in another study prior to completion of Day 14 of study. Non inclusion criteria: individuals with low risk of exposure (wearing a face mask and an eye shield); individuals with exposure time of less than 15 minutes; patients who receive medication for prophylaxis or treatment if COVID-19; patients with any sign and symptoms of COVID-19; Taking the medication for less than 3 days; COVID-19 compatible symptoms on day 1.

##### **Intervention groups**

Intervention group: patients will receive Bromhexine 8mg 3 times a day for 14 days. Control group: patients will receive placebo 3 times a day for 14 days.

##### **Main outcome variables**

Incidence of COVID-19 disease; COVID-19 disease severity

#### **General information**

##### **Reason for update**

In this update, we considered adding exclusion criteria to the record. based on the blinding of the statistical analyzers and outcome assessors, these two changes have been made. an interim analysis has been considered. considering the blinding strategy in this study, we blinded the outcome assessors and statistical analyzers from the study allocation. because of the incidence of the COVID-19 compatible symptoms in the 1st day in some patients and also some patients didn't take the medications as ordered, these two exclusion criteria have been considered. an interim analysis to assess the outcome occurrence is considered.

##### **Acronym**

##### **IRCT registration information**

IRCT registration number: **IRCT20120703010178N22**

Registration date: **2020-12-07, 1399/09/17**

Registration timing: **registered\_while\_recruiting**

Last update: **2021-07-06, 1400/04/15**

Update count: **1**

##### **Registration date**

2020-12-07, 1399/09/17

##### **Registrant information**

###### **Name**

Mohammad Sistanizad

###### **Name of organization / entity**

###### **Country**

Iran (Islamic Republic of)

###### **Phone**

+98 21 8820 0087

###### **Email address**

sistanizadm@sbmu.ac.ir

##### **Recruitment status**

**Recruitment complete**

## Funding source

### Expected recruitment start date

2020-08-22, 1399/06/01

### Expected recruitment end date

2020-12-21, 1399/10/01

### Actual recruitment start date

empty

### Actual recruitment end date

empty

### Trial completion date

empty

## Scientific title

A Randomized, Multi-centric, Double-blind, Placebo-controlled study to Evaluate the Efficacy and Safety of Bromhexine, a serine protease (TMPRSS2) blocker, to prevent COVID-19

## Public title

Bromhexine hydrochloride for prophylaxis against COVID-19

## Purpose

Prevention

## Inclusion/Exclusion criteria

### Inclusion criteria:

Exposure and close contact (defined as being within 6 feet for a period of 15 minutes or more in a 24 hour period or 5 minutes or more for healthcare associated exposure) to a COVID-19 case within 4 days before entering the study must agree not to enroll in another investigational study prior to completion of Day 14 of study Individuals who have the ability to understand and desire to sign the informed consent Age of 18 years or more

### Exclusion criteria:

Current Hospitalization Receipt of any experimental treatment for 2019-nCoV (off-label, compassionate use, or trial related) within the 30 days prior to the time of the screening evaluation Hypersensitivity to bromhexine or any component of the formulation Low risk in individuals in close contact (wearing face mask and eye shield) Individuals with exposure of less than 15 minutes Receipt of any medication for prophylaxis and treatment of 2019-nCoV Patients with any related sign and symptoms of COVID-19

## Age

From **18 years** old

## Gender

Both

## Phase

3

## Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

## Sample size

Target sample size: **1050**

## Randomization (investigator's opinion)

Randomized

## Randomization description

Randomization will be recorded on an Excel file by the principal investigator. Participants will be randomized via permuted block randomization. Each block will be consistent of variable sizes of 4 or 6 or 8 patients. For assignment of each patient to the drug or placebo group, for each patients a unique code consistent of 2 letters and a digit will be assigned. the code will be unique for each patient ( for example code AB1 for first patient). Only the principle investigator will be informed of the assignment of each code to the medication or placebo group.

## Blinding (investigator's opinion)

Double blinded

## Blinding description

Participants will be provided masked study medicine, directly in research centers or shipped by courier service. The intervention vs. placebo will not be identical; however, participants and outcome assessors will be masked to their assignment.

## Placebo

Used

## Assignment

Parallel

## Other design features

In this clinical trial an interim analysis in the sample size if 50% is allowed

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Ethics committee of School of Pharmacy and Nursing & Midwifery; Shahid Beheshti University of Medica

##### Street address

Niayesh complex; No 2660; Valiasr street; Tehran

##### City

Tehran

##### Province

Tehran

##### Postal code

6153- 14155

#### Approval date

2020-11-01, 1399/08/11

#### Ethics committee reference number

IR.SBMU.PHARMACY.REC.1399.247

## Health conditions studied

### 1

#### Description of health condition studied

COVID-19

#### ICD-10 code

U07.1

**ICD-10 code description**  
COVID-19, virus identified

**2**

**Description of health condition studied**  
COVID-19

**ICD-10 code**  
U07.2

**ICD-10 code description**  
COVID-19, virus not identified

## Primary outcomes

**1**

**Description**  
Incidence of COVID-19 disease

**Timepoint**  
At day 14

**Method of measurement**  
Clinical assessment

**2**

**Description**  
Ordinal Scale of COVID-19 disease severity

**Timepoint**  
Censored at Day 14

**Method of measurement**  
Clinical assessment

## Secondary outcomes

**1**

**Description**  
Hospitalization or death

**Timepoint**  
Day 14

**Method of measurement**  
Phone call

**2**

**Description**  
Confirmed COVID-19 diagnosis

**Timepoint**  
Day 14

**Method of measurement**  
Self report

**3**

**Description**  
Sign and Symptoms compatible with COVID-19

**Timepoint**  
day 14

**Method of measurement**  
Self report

**4**

**Description**  
Treatment withdrawal or discontinuation

**Timepoint**  
day 14

**Method of measurement**  
self report

## Intervention groups

**1**

**Description**  
Intervention group: Receiving Bromhexine 8 mg 3 times a day for 14 days in patients with history of close contact to confirmed COVID-19 in past 4 days

**Category**  
Treatment - Drugs

**2**

**Description**  
Control group: Receiving placebo 3 times a day for 14 days in patients with history of close contact to confirmed COVID-19 in past 4 days

**Category**  
Placebo

## Recruitment centers

**1**

### Recruitment center

**Name of recruitment center**  
Imam Hossein medical and educational center

**Full name of responsible person**  
Mohammad Sistanizad

**Street address**  
Madani street

**City**  
Tehran

**Province**  
Tehran

**Postal code**  
1617763141

**Phone**  
+98 21 8887 3704

**Email**  
Sistanizadm@sbmu.ac.ir

**2**

### Recruitment center

**Name of recruitment center**  
Labbafinejad Medical and Educational Center

**Full name of responsible person**  
Shadi Ziaie

**Street address**  
9th Boostan street, Pasdaran avenue

**City**  
Tehran

**Province**

Tehran  
**Postal code**  
1666663111  
**Phone**  
+98 21 2360 2280  
**Email**  
Shadi\_z73@yahoo.com

### 3

#### **Recruitment center**

**Name of recruitment center**  
Shohadaye Gomnam hospital  
**Full name of responsible person**  
Mohammad Sistanizad  
**Street address**  
Shahid Mohammad Reza Aazami street, Khavaran street, khorasan square, Tehran  
**City**  
Tehran  
**Province**  
Tehran  
**Postal code**  
1794694616  
**Phone**  
+98 21 3631 2001  
**Email**  
Sistanizadm@sbmu.ac.ir

### **Sponsors / Funding sources**

#### 1

#### **Sponsor**

**Name of organization / entity**  
Shahid Beheshti University of Medical Sciences  
**Full name of responsible person**  
Hassan Yazdan Panah  
**Street address**  
Shahid Beheshti School of Pharmacy, after Niayesh intersection; Valiasr street  
**City**  
Tehran  
**Province**  
Tehran  
**Postal code**  
1991953381  
**Phone**  
+98 21 8820 0118  
**Email**  
yazdanpanah@sbmu.ac.ir

#### **Grant name**

#### **Grant code / Reference number**

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

Yes

#### **Title of funding source**

Shahid Beheshti University of Medical Sciences

#### **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**  
Shahid Beheshti University of Medical Sciences  
**Full name of responsible person**  
Mohammad Sistanizad  
**Position**  
Associated Professor / Clinical Pharmacy Specialist  
**Latest degree**  
Specialist  
**Other areas of specialty/work**  
Medical Pharmacy  
**Street address**  
Department of Clinical Pharmacy, Shahid Beheshti School of Pharmacy, after Niayesh intersection; Valiasr street  
**City**  
Tehran  
**Province**  
Tehran  
**Postal code**  
6153- 14155  
**Phone**  
+98 218800087  
**Fax**  
**Email**  
sistanizadm@sbmu.ac.ir  
**Web page address**

### **Person responsible for scientific inquiries**

#### **Contact**

**Name of organization / entity**  
Shahid Beheshti University of Medical Sciences  
**Full name of responsible person**  
Mohammad Sistanizad  
**Position**  
Associated Professor / Clinical Pharmacy Specialist  
**Latest degree**  
Specialist  
**Other areas of specialty/work**  
Medical Pharmacy  
**Street address**  
Department of Clinical Pharmacy, Shahid Beheshti School of Pharmacy, after Niayesh intersection; Valiasr street  
**City**  
Tehran  
**Province**  
Tehran  
**Postal code**  
6153- 14155

**Phone**  
+98 218800087  
**Fax**  
**Email**  
sistanizadm@sbmu.ac.ir  
**Web page address**

## Person responsible for updating data

### Contact

**Name of organization / entity**  
Shahid Beheshti University of Medical Sciences  
**Full name of responsible person**  
Omid Moradi  
**Position**  
Clinical resident  
**Latest degree**  
Medical doctor  
**Other areas of specialty/work**  
Medical Pharmacy  
**Street address**  
Shahid Beheshti School of Pharmacy, after Niayesh  
intersection; Valiasr street  
**City**  
Tehran  
**Province**  
Tehran  
**Postal code**  
1991953381  
**Phone**  
009 21 88200118  
**Email**  
O\_moradi@sbmu.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

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

### Title and more details about the data/document

Primary and secondary outcome data after making participants unrecognizable will be released

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

6 months after publishing the results of primary outcome

### To whom data/document is available

Any researchers will have access to the data after allowance of corresponding author

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

Performing any analysis to any data resulted from this study will be allowed only with the permission of corresponding author

### From where data/document is obtainable

Correspondance author

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

After requesting for data, correspondence will check the authorization and then they will be informed about it

### Comments