

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

23 Feb 2026

### Evaluating the efficacy and safety of bromhexine in hospitalized COVID-19 patients

#### Protocol summary

##### Study aim

Evaluating the efficacy and safety of bromhexine as a treatment option for patients with COVID-19

##### Design

Prospective clinical trial with parallel randomized control and treatment, double blinded groups, phase 2 trial on 100 patients. Block randomization will be done using online website ([www.sealedenvelope.com/simple-randomiser/v1/lists](http://www.sealedenvelope.com/simple-randomiser/v1/lists)).

##### Settings and conduct

Masih Daneshvari Hospital. How to do the study: 100 patients with COVID-19, using block randomization will be divided in to intervention and control group (placebo). This is a double blind study. In this study patient and physician will be blinded. For blinding, treatment and placebo group will be named group A and B, respectively.

##### Participants/Inclusion and exclusion criteria

Patients who are  $\geq 18$  years old at time of signing Informed Consent Form with laboratory (RT-PCR) confirmed infection with COVID-19 and lung involvement confirmed with chest imaging will be included in the study. Furthermore, patients who are hospitalized with a  $SaO_2/SPO_2 \leq 94\%$  on room air or  $PaO_2/FiO_2$  ratio  $< 300$  mgHg and it is  $\leq 12$  days since illness onset are included in the study. Study exclusion criteria is as follows: Severe liver disease (e.g. Child Pugh score  $\geq C$ ,  $AST > 5$  times upper limit), pregnant or breastfeeding, or positive pregnancy test, patients with known severe renal impairment (estimated glomerular filtration rate  $\leq 30$  mL/min/1.73 m<sup>2</sup>) or receiving continuous renal replacement therapy, hemodialysis, peritoneal dialysis.

##### Intervention groups

Patients allocated to treatment group were given 8 mg bromhexine tablet (Tolid Daroo), four times a day, orally for 28 days in conjugation with supporting treatment. Furthermore, patients in the control group received placebo (Tolid Daroo) plus supportive treatment according to national guidelines.

#### Main outcome variables

Time to Clinical Improvement (TTCI), need for invasive mechanical ventilation, and death.

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20151227025726N24**

Registration date: **2020-11-25, 1399/09/05**

Registration timing: **retrospective**

Last update: **2020-11-25, 1399/09/05**

Update count: **0**

##### Registration date

2020-11-25, 1399/09/05

##### Registrant information

##### Name

Farzaneh Dastan

##### Name of organization / entity

Shahid Beheshti University of Medical Sciences

##### Country

Iran (Islamic Republic of)

##### Phone

+98 912 270 5933

##### Email address

f\_dastan@sbm.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2020-07-10, 1399/04/20

##### Expected recruitment end date

2020-09-10, 1399/06/20

##### Actual recruitment start date

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

Evaluating the efficacy and safety of bromhexine in hospitalized COVID-19 patients

**Public title**

Evaluation of the efficacy and safety of bromhexine administration in COVID-19

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Age  $\geq 18$  years at time of signing Informed Consent Form  
Laboratory (RT-PCR) confirmed infection with COVID-19  
Lung involvement confirmed with chest imaging  
Hospitalized with a SaO<sub>2</sub>/SPO<sub>2</sub>  $\leq 94\%$  on room air or PaO<sub>2</sub>/FiO<sub>2</sub> ratio  $< 300$  mmHg  $\leq 12$  days since illness onset  
Willingness of study participant to accept randomization to any assigned treatment arm  
Must agree not to enroll in another study of an investigational agent prior to completion of Day 28 of study

**Exclusion criteria:**

Physician makes a decision that trial involvement is not in patients' best interest, or any condition that does not allow the protocol to be followed safely  
Severe liver disease (e.g. Child Pugh score  $\geq C$ , AST  $> 5$  times upper limit)  
Pregnant or breastfeeding, or positive pregnancy test  
Patients with known severe renal impairment (estimated glomerular filtration rate  $\leq 30$  mL/min/1.73 m<sup>2</sup>) or receiving continuous renal replacement therapy, hemodialysis, peritoneal dialysis  
Will be transferred to another hospital which is not the study site within 72 hours  
Receipt of any experimental treatment for 2019-nCoV (off-label, or trial related) within the 30 days prior to the time of the screening evaluation  
Allergic to the Bromhexine

**Age**

From **18 years** old

**Gender**

Both

**Phase**

2-3

**Groups that have been masked**

- Participant
- Investigator

**Sample size**

Target sample size: **100**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

We randomize patients at a 1:1 ratio to receive either oral Bromhexine or placebo. Participants will be enrolled by the local principle investigators at site. Consecutively patients will receive a trial number by the principal investigator. Before the trial commences, each trial number will be randomized to a treatment arm by computer (randomization will be done using online

website

[www.sealedenvelope.com/simple-randomiser/v1/lists](http://www.sealedenvelope.com/simple-randomiser/v1/lists))

The intervention assignment communicates to the principle investigators. The study is double blinded and the trial monitor throughout by the data monitoring committee. Trial recruitment stops after the target study population is reached and will close when all patients complete their follow-up.

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

In this double blind study, patients who received the drug or placebo and physician (researcher) are blinded to the study groups (drug or placebo). Similar labeling will be used for the drug and placebo and only the randomizer will be aware of the study groups.

**Placebo**

Used

**Assignment**

Parallel

**Other design features****Secondary Ids**

empty

**Ethics committees****1****Ethics committee****Name of ethics committee**

Ethics Committee of Shahid Beheshti University of Medical Sciences

**Street address**

3 rd floor, School of Medicine, Evin St, Shahid Chamran Highway

**City**

Tehran

**Province**

Tehran

**Postal code**

1983963113

**Approval date**

2020-06-30, 1399/04/10

**Ethics committee reference number**

IR.SBMU.NRITLD.REC.1399.142

**Health conditions studied****1****Description of health condition studied**

COVID-19 pneumonia

**ICD-10 code**

U07.1

**ICD-10 code description**

COVID-19, virus identified

**Primary outcomes**

## 1

### **Description**

Time to Clinical Improvement (TTCI)

### **Timepoint**

Daily

### **Method of measurement**

TTCI is defined as the time (in days) from initiation of the study treatment (active or placebo) until a decline of two categories from admission status occur. 1. Hospital discharge or meeting discharge criteria; 2. Non-ICU hospitalization, not requiring supplemental oxygen; 3. Non-ICU hospitalization, requiring supplemental oxygen (but not NIV/ HFNC); 4. ICU/non-ICU hospitalization, requiring NIV/ HFNC therapy; 5. ICU hospitalization, requiring IMV; 6. Death.

## 2

### **Description**

Need for invasive mechanical ventilation

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## 3

### **Description**

Death

### **Timepoint**

At the end of the study

### **Method of measurement**

Medical record

## **Secondary outcomes**

## 1

### **Description**

Clinical status

### **Timepoint**

Days 7, 14, 21, 28

### **Method of measurement**

Medical record

## 2

### **Description**

Time to hospital discharge

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## 3

### **Description**

All-cause mortality

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## 4

### **Description**

Duration of mechanical ventilation

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## 5

### **Description**

Duration of extracorporeal membrane oxygenation (ECMO)

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## 6

### **Description**

Duration of supplemental oxygen

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## 7

### **Description**

Duration of hospitalization

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## 8

### **Description**

Time to RT-PCR negativity in upper and lower respiratory tract specimen

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## 9

### **Description**

Change (reduction) in viral load in upper and lower respiratory tract specimen

### **Timepoint**

Daily

### **Method of measurement**

Medical record

## **Intervention groups**

## 1

### **Description**

Intervention group: Patients allocated to treatment group

were given 8 mg bromhexine tablet (Tolid Daroo), four times a day, orally for 28 days. Patients also received Supportive treatment includes interferon b1a (Resigen) 44 microgram every other day for 3 doses + Lopinavir/Ritonavir 200-50 mg (Hetero Labs Limited) 2 Tab twice daily for 7 days.

#### Category

Treatment - Drugs

## 2

#### Description

Control group: Control group received placebo (Tolid Daroo), four times a day, orally for 28 days. Patients also received supportive treatment includes interferon b1a (Resigen) 44 microgram every other day for 3 doses + Lopinavir/Ritonavir 200-50 mg (Hetero Labs Limited) 2 Tab twice daily for 7 days.

#### Category

Treatment - Drugs

## Recruitment centers

### 1

#### Recruitment center

##### Name of recruitment center

Masih Daneshvari Hospital

##### Full name of responsible person

Payam Tabarsi

##### Street address

Daraabad, Shahid Bahonar St. (Niavaran), Masih Daneshvari Hospital

##### City

Tehran

##### Province

Tehran

##### Postal code

1956944413

##### Phone

+98 21 2712 3000

##### Email

payamtabarsi@yahoo.com

## Sponsors / Funding sources

### 1

#### Sponsor

##### Name of organization / entity

Shahid Beheshti University of Medical Sciences

##### Full name of responsible person

Afshin Zarghi

##### Street address

3rd floor, School of Medicine, Evin St, Shahid Chamran Highway

##### City

Tehran

##### Province

Tehran

##### Postal code

1983963113

##### Phone

+98 21 23871

##### Email

mpd@sbm.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

Payam Tabarsi

##### Position

Professor

##### Latest degree

Subspecialist

##### Other areas of specialty/work

Infectious diseases

##### Street address

Shahid Bahonar St., Darabad St

##### City

Tehran

##### Province

Tehran

##### Postal code

1956944413

##### Phone

+98 21 2610 5050

##### Email

payamtabarsi@yahoo.com

## Person responsible for scientific inquiries

#### Contact

##### Name of organization / entity

Shahid Beheshti University of Medical Sciences

##### Full name of responsible person

Farzaneh Dastan

##### Position

Assistant professor

##### Latest degree

Specialist

##### Other areas of specialty/work

Medical Pharmacy  
**Street address**  
Bahonar St., Darabad St.,  
**City**  
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1956944413  
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fzh.dastan@gmail.com

## Person responsible for updating data

### Contact

**Name of organization / entity**  
Shahid Beheshti University of Medical Sciences  
**Full name of responsible person**  
Zahra Mirshafiei Langari  
**Position**  
Hospital pharmacist  
**Latest degree**  
Medical doctor  
**Other areas of specialty/work**  
Medical Pharmacy  
**Street address**  
Dr. Masih Daneshvari Hospital, Daar-Abad, Niavaran  
**City**  
Tehran  
**Province**  
Tehran  
**Postal code**  
19569-44413  
**Phone**  
+98 21 2712 2066  
**Email**  
z.mirshafei@gmail.com

## Sharing plan

### Deidentified Individual Participant Data Set (IPD)

Yes - There is 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

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

All potential data can be shared after blinding

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

Six months after publishing the results

### To whom data/document is available

Researchers working in academic institutions

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

For research purposes and meta-analysis studies

### From where data/document is obtainable

Dr. farzaneh Dastan, Dr. Masih Daneshvari Hospital, Daar-Abad, Niavaran

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

Official letter to the researchers through Email (fzh.dastan@gmail.com).

### Comments