

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

23 Feb 2026

### Comparison of the effect of bosentan with routine protocol on clinical outcomes of hospitalized patients with COVID-19 infection.

#### Protocol summary

##### Study aim

Determining the effect of bosentan on clinical outcomes of hospitalized patients with COVID-19 infection in comparison with routine protocol

##### Design

Double-blind randomized controlled clinical trial

##### Settings and conduct

In this study, COVID-19 patients, hospitalized in Shahid Mostafa Khomeini and Imam Khomeini hospitals with the mentioned inclusion and exclusion criteria will be studied. Bosentan and placebo tablets are similar, and patients and researchers are unaware of labeling. Bosentan 62.5 mg tablets will be given twice daily. Patients are followed up daily. After discharge, they will be followed up for 30 days from the time of intervention.

##### Participants/Inclusion and exclusion criteria

Inclusion Criteria: • Written informed consent; Age over 18 years; Laboratory-confirmed SARS-CoV-2 infection;  
Exclusion Criteria: • Pregnancy; Lactation; Glibenclamide Consumption; Cyclosporine Consumption;  
Aminotransferases > 3 times normal; Allergy to bosentan

##### Intervention groups

Oral Bosentan 62.5 mg, twice daily, for 30 days.

##### Main outcome variables

The time to clinical improvement, defined as the time from randomization to an improvement of two points (from the status at randomization) on a WHO 11 point clinical progression scale or live discharge from the hospital, whichever came first.

#### General information

##### Reason for update

Start recruitment process

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20211203053263N2**

Registration date: **2022-02-26, 1400/12/07**

Registration timing: **prospective**

Last update: **2022-07-19, 1401/04/28**

Update count: **2**

##### Registration date

2022-02-26, 1400/12/07

##### Registrant information

###### Name

Shaahin Shahbazi

###### Name of organization / entity

###### Country

Iran (Islamic Republic of)

###### Phone

+98 21 8821 3960

###### Email address

mdkabe@gmail.com

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2022-02-27, 1400/12/08

##### Expected recruitment end date

2022-05-29, 1401/03/08

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty

##### Trial completion date

empty

##### Scientific title

Comparison of the effect of bosentan with routine protocol on clinical outcomes of hospitalized patients with COVID-19 infection.

##### Public title

Bosentan in hospitalized patients with COVID-19 infection

##### Purpose

Treatment

##### Inclusion/Exclusion criteria

**Inclusion criteria:**

Written informed consent prior to initiation of study. Age over 18 years. Laboratory-confirmed SARS-CoV-2 infection determined by PCR less than 72 hours before randomization. Illness of any duration, and at least one of the following: Radiographic infiltrates by imaging, OR Clinical assessment (evidence of rales/crackles on exam) AND SpO<sub>2</sub> ≤ 94% on room air, OR Requiring mechanical ventilation and/or supplemental oxygen. Women of childbearing potential must agree to use at least one primary form of contraception for the duration of the study.

**Exclusion criteria:**

Pregnancy or Lactation  
Glibenclamide Consumption  
Cyclosporine Consumption  
Aminotransferases > 3 times normal  
Allergy to bosentan

**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: **200**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Permuted Block Randomization will be used for random allocation. The size of the blocks will randomly selected. There are 4, random blocks, each has an equal number of interventions and controls. In the 4 blocks, two allocations are considered for the intervention group and two allocations for the control group. Random Allocation Software will be used for this purpose. The concealment will be done using sequentially numbered, sealed envelopes.

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

Blinding in this study is double blind that the drug and placebo are labeled as "Group A" and "Group B". They are quite similar in appearance and the person participating in the study and the person distributing the medicine does not know about this labeling.

**Placebo**

Used

**Assignment**

Parallel

**Other design features**

This study is an adaptive and add on trial.

**Secondary Ids**

empty

## Ethics committees

1

**Ethics committee**

**Name of ethics committee**

Research Ethics Committees of Ilam University of Medical Sciences

**Street address**

Banghanjab Blv.

**City**

Ilam

**Province**

Ilam

**Postal code**

1639393939

**Approval date**

2022-02-21, 1400/12/02

**Ethics committee reference number**

IR.MEDILAM.REC.1400.220

## Health conditions studied

1

**Description of health condition studied**

COVID-19

**ICD-10 code**

U07.1

**ICD-10 code description**

COVID-19, virus identified

## Primary outcomes

1

**Description**

The time to clinical improvement, defined as the time from randomization to an improvement of two points (from the status at randomization) on a WHO 11 point clinical progression scale or live discharge from the hospital, whichever came first.

**Timepoint**

During hospitalization

**Method of measurement**

WHO 11 point clinical progression scale

## Secondary outcomes

1

**Description**

Proportion of patients in each category of the WHO 11 point clinical progression scale on day 30 after randomization

**Timepoint**

Day 30

**Method of measurement**

WHO 11 point clinical progression scale

## 2

### **Description**

Duration of mechanical ventilation

### **Timepoint**

During hospitalization

### **Method of measurement**

Mechanical ventilation, Observation

## 3

### **Description**

Duration of hospitalization in survivors

### **Timepoint**

During intervention

### **Method of measurement**

Observation, Medical report

## 4

### **Description**

The composite of symptomatic deep venous thrombosis; pulmonary embolism; arterial thromboembolism; myocardial infarction; ischemic stroke, up to 30 days after treatment initiation

### **Timepoint**

30 days from intervention

### **Method of measurement**

Observation

## 5

### **Description**

30 days mortality

### **Timepoint**

30 days from intervention

### **Method of measurement**

Observation, Medical report

## 6

### **Description**

Sarcopenia

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

EWGSOP2 criteria

## 7

### **Description**

Functional status

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

Post-Covid Functional Scale

## 8

### **Description**

dyspnea

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

MMRC dyspnea scale

## 9

### **Description**

fatigability

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

chalder fatigue scale

## 10

### **Description**

Sleep disorders

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

Pittsburgh Sleep Questionnaire

## 11

### **Description**

Brain fog

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

Visual Analog Scale

## 12

### **Description**

Loss of taste and smell

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

Visual Analog Scale

## 13

### **Description**

thromboembolic events

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

clinical and paraclinical exam

## 14

### **Description**

Changes in serum level of CMP

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

Serum measurement

## 15

### **Description**

Change in Weight

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

Weight scale

## 16

### **Description**

Changes in Subject's quality of life

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

Health Survey Questionnaire

## 17

### **Description**

Assessment of sexual function

### **Timepoint**

Change from baseline at 3-12 months

### **Method of measurement**

questionnaire

## **Intervention groups**

### 1

#### **Description**

Intervention group: The study group in addition to the drugs used in the treatment of COVID-19 (approved by the National Committee), is treated with oral Bosentan 62.5 mg twice a day for 30 days. Patients will be followed for 30 days for recovery or discharge, duration of mechanical ventilation dependency, length of hospital stay, mortality, and thromboembolic events.

#### **Category**

Treatment - Drugs

### 2

#### **Description**

Control group: The control group, in addition to the drugs used in the treatment of COVID-19 (approved by the National Committee), receive a placebo twice a day for 30 days. Patients will be followed for 30 days for recovery or discharge, duration of mechanical ventilation dependency, length of hospital stay, mortality, and thromboembolic events.

#### **Category**

Placebo

## **Recruitment centers**

### 1

#### **Recruitment center**

##### **Name of recruitment center**

Mostafa Khomainsi hospital of Ilam

##### **Full name of responsible person**

Shaahin Shahbazi

##### **Street address**

Tapeh Khargooshan St

##### **City**

Ilam

##### **Province**

Ilam

##### **Postal code**

1639393939

#### **Phone**

+98 84 3333 8228

#### **Email**

mdkabe@gmail.com

#### **Web page address**

<http://mostafahospital.medilam.ac.ir>

### 2

#### **Recruitment center**

##### **Name of recruitment center**

Imam Khomeini Hospital of Ilam

##### **Full name of responsible person**

Shaahin Shahbazi

##### **Street address**

Heidari street.

##### **City**

ilam

##### **Province**

Ilam

##### **Postal code**

6931975397

##### **Phone**

+98 84 3333 4500

##### **Email**

mdkabe@gmail.com

##### **Web page address**

<http://emamhospital.medilam.ac.ir>

## **Sponsors / Funding sources**

### 1

#### **Sponsor**

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

Ilam University of Medical Sciences

##### **Full name of responsible person**

Shaahin Shahbazi

##### **Street address**

Banghanjab Blv.

##### **City**

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##### **Province**

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##### **Phone**

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mdkabe@gmail.com

#### **Grant name**

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

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

Yes

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

Ilam 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**  
Ilam University of Medical Sciences  
**Full name of responsible person**  
Ilam University of Medical Sciences  
**Position**  
Associate Professor  
**Latest degree**  
Subspecialist  
**Other areas of specialty/work**  
Internal Medicine  
**Street address**  
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## Person responsible for scientific inquiries

### Contact

**Name of organization / entity**  
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**Full name of responsible person**  
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**Position**  
Associate Professor  
**Latest degree**  
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## Person responsible for updating data

### Contact

**Name of organization / entity**  
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**Full name of responsible person**  
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**Position**  
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**Other areas of specialty/work**  
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## 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