

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

09 Jun 2026

### **Safety and efficacy of “Hydroxychloroquine + Azithromycin + Naproxen + Prednisolone” and “Hydroxychloroquine + Azithromycin + Naproxen” regimens in comparison with “Hydroxychloroquine + Kaletra” on the need for intensive care unit treatment in patients with COVID-19; a randomized, multicenter, parallel groups, open label study**

#### **Protocol summary**

##### **Study aim**

Achieve an appropriate treatment protocol for COVID-19

##### **Design**

Randomized parallel, 3 groups, clinical trial, open label

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

It is a multicenter clinical trial that will be conducted in at least 4 centers all over the country

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

Inclusion criteria: Diagnosis of COVID-19 based on either ground glass appearance in chest CT scan or positive RTPCR test for COVID-19; Requiring hospitalization; Patient's age between 16 and 100 years; Signed informed consent form; Exclusion criteria: Receiving other antiviral medications such as (Hydroxychloroquine, Kaletra, Ribavirin, Oseltamivir); Uncontrolled diabetes; Asthma; Chemotherapy in the past month; Taking immunosuppressive drugs; Chronic liver or renal failure; HIV; GI bleeding; Pregnancy; Lactation; Uncontrolled bacterial infection

##### **Intervention groups**

Intervention group1: Stat dose of two 200 mg Hydroxychloroquine tablets (total 400 mg) followed by two 250 mg Azithromycin in first day and 250 mg Azithromycin a day for 5 days + five 5 mg Prednisolone tablets a day for 5 days + 250 mg Naproxen tablets two times a day for 5 days. Intervention group2: Stat dose of two 200 mg Hydroxychloroquine tablets followed by two 250 mg Azithromycin in first day and 250 mg Azithromycin a day for 5 days plus 250 mg Naproxen tablets two times a day for 5 days. Control group: Stat dose of two 200 mg Hydroxychloroquine tablets followed by Kaletra (Lopinavir/Ritonavir) 200/50 mg two times a day for 7 days.

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

Admission to ICU, In-hospital mortality, length of stay in hospital, Radiological Treatment Response (CT scan), Laboratory Treatment Response (return of blood cell count and CRP values to normal), Fever, Dyspnea, Oxygen saturation after discontinuation of supplemental oxygen for 5 minutes, Oxygen therapy maximum flow during the day (lit/min), Pulmonary function test 6 wks after discharge, and Adverse and allergic drug reactions

#### **General information**

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

##### **Acronym**

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

IRCT registration number: **IRCT20200318046812N2**

Registration date: **2020-04-08, 1399/01/20**

Registration timing: **prospective**

Last update: **2020-04-08, 1399/01/20**

Update count: **0**

##### **Registration date**

2020-04-08, 1399/01/20

##### **Registrant information**

##### **Name**

Mostafa Ghanei

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

##### **Country**

Iran (Islamic Republic of)

##### **Phone**

+98 21 8860 0067

##### **Email address**

mghaneister@gmail.com

##### **Recruitment status**

**Recruitment complete**

## Funding source

### Expected recruitment start date

2020-04-10, 1399/01/22

### Expected recruitment end date

2021-04-11, 1400/01/22

### Actual recruitment start date

empty

### Actual recruitment end date

empty

### Trial completion date

empty

## Scientific title

Safety and efficacy of "Hydroxychloroquine + Azithromycin + Naproxen + Prednisolone" and "Hydroxychloroquine + Azithromycin + Naproxen" regimens in comparison with "Hydroxychloroquine + kaletra" on the need for intensive care unit treatment in patients with COVID-19; a randomized, multicenter, parallel groups, open label study

## Public title

evaluation of Safety and efficacy of anti inflammatory regimens in COVID-19

## Purpose

Treatment

## Inclusion/Exclusion criteria

### Inclusion criteria:

Diagnosis of COVID-19 based on either ground glass appearance in chest CT scan or positive RTPCR test for COVID-19 Requiring hospitalization Patient's age between 16 and 100 years Signed informed consent form

### Exclusion criteria:

Past history of hospitalization or treatment in hospital for COVID-19 disease Receiving other antiviral medications such as (Hydroxychloroquine, Kaletra, Ribavirin, Oseltamivir) Uncontrolled diabetes Astma Chemotherapy in the past month Taking immunosuppressive drugs Chronic liver or renal failure Taking daily systemic corticosteroids HIV GI bleeding Pregnancy or Lactation Uncontrolled bacterial infection

## Age

From **16 years** old to **100 years** old

## Gender

Both

## Phase

3

## Groups that have been masked

*No information*

## Sample size

Target sample size: **906**

## Randomization (investigator's opinion)

Randomized

## Randomization description

In this study, we will use block randomization methods using variable block size of four and six stratified by center. We will use Excel software and rand() function to generate the random sequence. The master randomization list will be kept by the epidemiologist working with the research team

## Blinding (investigator's opinion)

Not blinded

## Blinding description

### Placebo

Not used

### Assignment

Parallel

## Other design features

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Baqiyatallah university of medical sciences

##### Street address

Tehran, Vanak Square, Mulla Sadra Street

##### City

Tehran

##### Province

Tehran

##### Postal code

1435916471

#### Approval date

2020-03-26, 1399/01/07

#### Ethics committee reference number

IR.BMSU.REC.1399.019

## Health conditions studied

### 1

#### Description of health condition studied

COVID-19

#### ICD-10 code

U07.1 COVI

#### ICD-10 code description

COVID-19

## Primary outcomes

### 1

#### Description

Admission to intensive care unit

#### Timepoint

Once (when admitted to intensive care unit)

#### Method of measurement

Hospital records

## Secondary outcomes

### 1

#### Description

In-hospital mortality

#### Timepoint

Once  
**Method of measurement**  
Patient medical records

**2**  
**Description**  
length of stay in hospital  
**Timepoint**  
Once at discharge  
**Method of measurement**  
Patient medical records

**3**  
**Description**  
Radiological Treatment Response (CT scan) , more than 50% reduction in the affected area  
**Timepoint**  
CT scan will be done twice (once at the time of admission and the second time 10 days after discharge).  
Assessment will be done comparing the second CT with the first one  
**Method of measurement**  
Patient CT scan

**4**  
**Description**  
Laboratory Treatment Response; return of blood cell count and CRP values to normal  
**Timepoint**  
Daily  
**Method of measurement**  
Laboratory kits

**5**  
**Description**  
Fever  
**Timepoint**  
Daily  
**Method of measurement**  
Patient medical records

**6**  
**Description**  
Dyspnea  
**Timepoint**  
Daily  
**Method of measurement**  
Patient medical records

**7**  
**Description**  
Oxygen saturation without supplemental oxygen.  
Measurement will be done after discontinuation of oxygen therapy for 5 minutes  
**Timepoint**  
4 times a day while in the wards  
**Method of measurement**

Observation

**8**  
**Description**  
Oxygen therapy maximum flow during the day (lit/min)  
**Timepoint**  
Daily  
**Method of measurement**  
Patient medical records

**9**  
**Description**  
Discharge without Intensive care need  
**Timepoint**  
Once  
**Method of measurement**  
Patient medical records

**10**  
**Description**  
Pulmonary function  
**Timepoint**  
6 weeks after discharge  
**Method of measurement**  
Spirometry and a six-minute walking test are performed.  
Pulmonary function status is divided into two groups, normal and abnormal

**11**  
**Description**  
Allergic drug reaction  
**Timepoint**  
Daily  
**Method of measurement**  
Adverse Drug Reaction forms

**12**  
**Description**  
Adverse drug reactions  
**Timepoint**  
Daily  
**Method of measurement**  
Adverse Drug Reaction forms

## Intervention groups

**1**  
**Description**  
Intervention group: Intervention group: Group 1: Patients in this group will first receive hydroxychloroquine as two 200 mg tablets with a total of 400 mg of stat; then the following regimen will be continued for 5 days - azithromycin two 250 mg tablets on the first day. And then 250 mg daily for 5 days - 5 mg prednisolone tablets in the amount of 5 tablets (25 mg) daily for 5 days - 250 mg naproxen tablets twice a day for 5 days. Also, patients in this group to prevent complications. Digestive

patients will receive 40 mg of pentoprazole tablets or capsules daily during treatment. According to the attending physician, this treatment protocol can be continued for 10 days, depending on the clinical symptoms, if necessary. The patient will be discharged from the protocol. In this case, all the patient's information will be collected until the end of the study. If treatment is needed in the intensive care unit, all treatment methods will be used according to the patient's clinical needs and the decision of the treating physician. Prednisolone in this group will continue to be cleared and gradually reduced to 5 mg each week to be discontinued. The weekly dose will be as follows: -First week after clearance: 20 mg per day -Second week after clearance: 15 mg per day- Third week after clearance: 10 mg per day -Fourth week after clearance 5 Mg per day and finally discontinued

#### **Category**

Treatment - Drugs

#### **2**

#### **Description**

Intervention group: Patients in this group will first receive hydroxychloroquine in the form of two 200 mg tablets with a total of 400 mg of stat; then the following diet will be continued for 5 days.- Azithromycin two 250 mg tablets on the first day and then 250 mg daily for 5 days- Naproxen tablets 250 mg twice daily for 5 daysIn addition, patients in this group will receive 40 mg tablets or pentoprazole capsules daily to prevent gastrointestinal side effects during treatment.According to the attending physician, this treatment protocol can be continued for 10 days, depending on the clinical symptoms, if necessary.In this group, starting antiviral or steroid therapy before the need for treatment in the intensive care unit will cause the patient to leave the protocol. In this case, all patient information will continue to be collected until the end of the study.If treatment is needed in the intensive care unit, all treatment methods will be used according to the patient's clinical needs and the decision of the treating physician.

#### **Category**

Treatment - Drugs

#### **3**

#### **Description**

Control group: Patients in this group first receive two 200 mg hydroxychloroquine stats and then receive the following diet for 7 to 10 days:- kaltra (Lupinavir / Ritonavir) twice a day and two tablets of 200/50 mg each time for 7 days.Acetaminophen and oxycodone will be used if you need painkillers and antipyretics.According to the attending physician, this treatment protocol can be continued for 14 days, depending on the clinical symptoms, if necessary.In this group, the use of steroidal and non-steroidal anti-inflammatory drugs is not allowed until the need for treatment in the intensive care unit. If treatment is needed in the intensive care unit, all treatment methods will be used according to the patient's clinical needs and the decision of the treating physician.

#### **Category**

Treatment - Drugs

### **Recruitment centers**

#### **1**

#### **Recruitment center**

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

Baqiyatallah university of medical sciences

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

Ali Qazvini

##### **Street address**

Tehran, Vanak Square, Mulla Sadra Street, Sheikh Bahai Street

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Tehran

##### **Province**

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##### **Postal code**

1435916471

##### **Phone**

+98 21 8860 0067

##### **Email**

qazvinia@gmail.com

#### **2**

#### **Recruitment center**

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

Velaiat Hospital

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

Dr Mariam Qaraati

##### **Street address**

Taavon Square

##### **City**

Qazvin

##### **Province**

Qazvin

##### **Postal code**

02833790610

##### **Phone**

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##### **Email**

a.h.ghazale@gmail.com

#### **3**

#### **Recruitment center**

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

Forghani Hospital

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

Dr Abolfazl Mozafari

##### **Street address**

Nekoei Square

##### **City**

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##### **Province**

Ghoum

##### **Postal code**

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##### **Phone**

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**4**

**Recruitment center**

**Name of recruitment center**

Shohada Tajrish Hospital

**Full name of responsible person**

Dr Mahtab Niroomand

**Street address**

Tajrish square

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1989934148

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mahtabniroomand@yahoo.com

**Sponsors / Funding sources**

**1**

**Sponsor**

**Name of organization / entity**

Bagheiat-allah University of Medical Sciences

**Full name of responsible person**

Mostafa Ghanei

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Tehran, Vanak, Mulla Sadra Street, Sheikh Bahaei Street, Nosrat Alley

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**Grant name**

**Grant code / Reference number**

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

Yes

**Title of funding source**

Bagheiat-allah University of Medical Sciences

**Proportion provided by this source**

50

**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

**2**

**Sponsor**

**Name of organization / entity**

Iran University of Medical Sciences

**Full name of responsible person**

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**Grant name**

**Grant code / Reference number**

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

Yes

**Title of funding source**

Iran University of Medical Sciences

**Proportion provided by this source**

50

**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**

Bagheiat-allah University of Medical Sciences

**Full name of responsible person**

Seyed Hassan Saadat

**Position**

Associate professor

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Psychology

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## Person responsible for scientific inquiries

### Contact

**Name of organization / entity**  
Bagheiat-allah University of Medical Sciences  
**Full name of responsible person**  
Ali Qazvini  
**Position**  
Assistant Professor  
**Latest degree**  
Specialist  
**Other areas of specialty/work**  
pulmonologist  
**Street address**  
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## Person responsible for updating data

### Contact

**Name of organization / entity**  
Bagheiat-allah University of Medical Sciences  
**Full name of responsible person**  
Amir Hossein Ghazale  
**Position**  
Medical student  
**Latest degree**  
Medical doctor  
**Other areas of specialty/work**  
Internal Medicine  
**Street address**

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Nosrat Alley

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**Province**  
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## 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

Yes - There is a plan to make this available

### Data Dictionary

Yes - There is a plan to make this available

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

Deidentified IPD related to outcome will be shared.

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

The access period will begin 6 months after publication of the paper

### To whom data/document is available

The data will be available only for academic researchers.

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

Only meta-analysis in collaboration with the current study research team will be permitted.

### From where data/document is obtainable

From where data/document is obtainable Researchers can request data by emailing Dr. Mustafa Qanei (mghaneister@gmail.com) or Dr.Ali Qazvini(qazvinia@gmail.com)

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

Requested data will be sent by email after consideration and approval by the relevant authorities from Baghiattallah university.

### Comments