Clinical Trial Protocol
Iranian Registry of Clinical Trials

02 Nov 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, 3groups, 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 Azythromycin in first day and 250 mg Azythromycin 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 Azythromycin in first day and 250 mg Azythromycin 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-hopital 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)

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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 wit 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
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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-hopital 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

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

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2

Recruitment center

Name of recruitment center

Velaiat Hospital

Full name of responsible person

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3

Recruitment center

Name of recruitment center

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Full name of responsible person

Dr Abolfazl Mozafari

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Recruitment center

Name of recruitment center

Shohada Tajrish Hospital

Full name of responsible person

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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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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

Dr Seyed Abbas Motevalian

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Hemmat Highway, next to Milad Tower, Iran University of Medical Sciences

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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

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Person responsible for scientific inquiries

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Person responsible for updating data

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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