

Clinical Trial Protocol

Iranian Registry of Clinical Trials

23 Feb 2026

Evaluation of the safety and efficacy of tocilizumab (AryoGen Pharmed Co., Iran) in patients with severe COVID-19

Protocol summary

Study aim

The evaluation of efficacy and safety of Tocilizumab (AryoGen Pharmed Co.) in patients with severe COVID-19.

Design

This is a phase III, open-label, and single-arm study with the sample size of 85 patients.

Settings and conduct

This phase-III, single-arm, open-label, multi-center (8 cities of Iran) clinical trial will be conducted in patients with COVID-19 with a follow-up duration of 14 days. Tocilizumab will be administered to the eligible patients on day 1, and the outcomes will be investigated with the 14-day monitoring of the patients.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Ability to comprehend and willingness to sign the Informed Consent Form for this study by the patient or his/her guardian; Patients aged ≥ 18 years old; Patients with any of the following symptoms: fever (body temperature $> 37.8^{\circ}\text{C}$), shortness of breath, cough, or respiratory rate higher than 30 breaths/min and $\text{SpO}_2 \leq 93\%$, with the confirmed diagnosis of SARS-CoV-2 infection based on PCR and/or radiography; Serum Interleukin-6 level ≥ 3 times upper limit of normal. Exclusion criteria include hypersensitivity to Tocilizumab or any components of the formulation, hepatic or renal disorders, bone marrow suppression, patients with a high risk of GI perforation, history of tuberculosis, hepatitis B or C, HIV, pregnancy and breastfeeding, and any other active infection.

Intervention groups

Intervention group: Subcutaneous (two PFS injections of 162 mg Tocilizumab for patients < 100 kg and three PFS injections of 162 mg Tocilizumab for patients > 100 kg) in addition to the standard treatment. In case of inadequate response, Tocilizumab would be re-administered with a 12-hour interval between injections.

Main outcome variables

All-cause mortality rate during the study (date and cause

of death, if applicable)

General information

Reason for update

To amend the study design (interventions, study endpoints, inclusion criteria, and sample size): based on the state-of-the-art studies in the field of COVID-19 and the fact that improving patient survival is the ultimate goal in these patients, the primary endpoint is changed to the all-cause mortality rate during the study. Secondary endpoints are updated accordingly. Due to the unavailability of the intravenous form, subcutaneous injection was used for all patients. As a result, the interventions section is updated. According to the definition of severe COVID-19 by WHO, respiratory rate higher than 30 breaths/min is added to the inclusion criteria number 3. Based on the significantly elevated IL-6 levels in patients with severe COVID-19 and the mechanism of action of tocilizumab, the inclusion criteria number 4 is changed to serum Interleukin-6 level ≥ 3 times upper limit of normal. Based on the first version of the protocol, the trial was going to be conducted in 500 patients with the aim of increasing the patient access to the treatment. Yet, in the current version and due to the increased concern on the safety of tocilizumab treatment in patients with COVID-19, the sample size is calculated to be 85, using Fleming's method (single-arm study) with the statistical power of 90%, alpha level of 5%, and the goal of decreasing the mortality rate by 15% (with the assumption of 60% survival rate with the standard treatment and an increase to 75% by the addition of tocilizumab to the treatment). Moreover, since only severe COVID-19 patients are included in the study, the term "severe" is added to the title. Following the addition of a study center in Semnan and the removal of the centers in Shiraz and Rasht, the total number of cities is changed to 8 in the Summary section.

Acronym

IRCT registration information

IRCT registration number: **IRCT20150303021315N17**

Registration date: **2020-04-12, 1399/01/24**
Registration timing: **registered_while_recruiting**

Last update: **2020-05-04, 1399/02/15**
Update count: **1**

Registration date
2020-04-12, 1399/01/24

Registrant information

Name

Nassim Anjidani

Name of organization / entity

Orchid Pharmed

Country

Iran (Islamic Republic of)

Phone

+98 21 4347 3000

Email address

amini@orchidpharmed.com

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-03-15, 1398/12/25

Expected recruitment end date

2020-07-21, 1399/04/31

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluation of the safety and efficacy of tocilizumab (AryoGen Pharmed Co., Iran) in patients with severe COVID-19

Public title

Tocilizumab in severe COVID-19

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Ability to comprehend and willingness to sign the informed consent form for this study by the patient or his/her guardian Patients above 18 years old Patients with fever higher than 37.8 °C, cough, shortness of breath, or respiratory rate higher than 30 breaths/min accompanied by SpO₂ ≤ %93, who have a confirmed diagnosis of SARS-CoV-2 infection using PCR and/or radiography. Serum Interleukin-6 level ≥ 3 times upper limit of normal

Exclusion criteria:

History of hypersensitivity to Tocilizumab or any components of the formulation Hepatic disease (especially active hepatic diseases and hepatic impairment) Patients with bone marrow suppression (defined as Absolute Neutrophil Count (ANC) below 2000/mm³ or platelet count below 100,000/mm³) Patients with a high risk of gastrointestinal perforation or

with distinct history of GI disorders, e.g., active peptic ulcer and diverticulitis Patients with active or latent tuberculosis Patients with history of active hepatitis B, hepatitis C, HIV, or any known immunodeficiency Pregnant or lactating patients Patients with any other active infection in addition to COVID-19 Patients with any other disease or disorder, which, in the opinion of the investigator will put the subject at risk, if they are enrolled Renal impairment (GFR of below 30ml/min/1.73m²)

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

No information

Sample size

Target sample size: **85**

Randomization (investigator's opinion)

Not randomized

Randomization description

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Single

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

National Institution for Medical Research
Development

Street address

No 21, Beesat St., West Fatemi St.

City

Tehran

Province

Tehran

Postal code

1419693111

Approval date

2020-03-13, 1398/12/23

Ethics committee reference number

IR.NIMAD.REC.1398.414

Health conditions studied

1

Description of health condition studied

COVID-19

ICD-10 code

U07.1

ICD-10 code description

COVID-19

Primary outcomes

1

Description

All-cause mortality rate during the study (date and cause of death, if applicable)

Timepoint

day 1 through 14

Method of measurement

Physical Examination

Secondary outcomes

1

Description

Percent of patients with improvement in oxygenation

Timepoint

day 1 through 14

Method of measurement

Percent of patients with at least one step decrease in oxygenation supply; steps: 1. no need for supplemental oxygenation; 2. nasal catheter oxygen inhalation; 3. Mask oxygen inhalation; 4. Noninvasive ventilator oxygen supply; 5. Invasive ventilator oxygen supply.

2

Description

Duration (days) of hospitalization

Timepoint

day 1 thorough 14

Method of measurement

Clinical Evaluation

3

Description

Changes in body temperature

Timepoint

Day 1 through 14

Method of measurement

Physical Examination

4

Description

The lesions of the pulmonary segment numbers involved in pulmonary CT

Timepoint

Day 1 and 14

Method of measurement

CT scan

5

Description

Duration (days) of mechanical ventilation

Timepoint

Day 1 through 14

Method of measurement

Clinical Evaluation

6

Description

Changes in C-reactive protein blood level

Timepoint

Day 1 through 14

Method of measurement

Laboratory Test

7

Description

Changes in Interleukin-6 blood levels

Timepoint

Day 1 through 14

Method of measurement

Laboratory Test

8

Description

Changes in White Blood Cell count

Timepoint

Day 1 through 14

Method of measurement

Laboratory Test

9

Description

Changes in cholesterol level

Timepoint

Day 1 through 14

Method of measurement

Laboratory Test

10

Description

Changes in Aspartate transaminase level

Timepoint

Day 1 through 14

Method of measurement

Laboratory Test

11

Description

Changes in Alanine transaminase level

Timepoint

Day 1 through 14

Method of measurement

Laboratory Test

12

Description

Injection site reaction

Timepoint

Day 1 through 14

Method of measurement

Clinical evaluation

13

Description

Gastrointestinal perforation

Timepoint

Day 1 through 14

Method of measurement

Clinical evaluation; radiographic imaging in case of clinical symptoms

14

Description

Infection

Timepoint

Day 1 through 14

Method of measurement

Clinical evaluation, laboratory test, imaging

15

Description

Changes in Platelet level

Timepoint

Day 1 through 14

Method of measurement

Laboratory Test

16

Description

Changes in bilirubin level

Timepoint

Day 1 through 14

Method of measurement

Laboratory Test

17

Description

Blood pressure

Timepoint

Day 1 through 14

Method of measurement

Blood pressure meter

Intervention groups

1

Description

Intervention group: Subcutaneous (two PFS injections of 162 mg Tocilizumab for patients <100 kg and three PFS injections of 162 mg Tocilizumab for patients >100 kg) in

addition to the standard treatment. In case of inadequate response, Tocilizumab would be re-administered with a 12-hour interval between injections.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Masih Daneshvari Hospital

Full name of responsible person

Payam Tabarsi

Street address

Darababd St., Shahid Bahonar St., Tehran

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2

Recruitment center

Name of recruitment center

Imam Reza Hospital

Full name of responsible person

Rozita Khodashahi

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3

Recruitment center

Name of recruitment center

Milad Hospital

Full name of responsible person

Farzin Khorvash

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Milad Hospital, Janbazan St, Isfahan.

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Province
Isfahan
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Web page address

4

Recruitment center
Name of recruitment center
Imam Khomeini Hospital
Full name of responsible person
Roya Ghasemian
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5

Recruitment center
Name of recruitment center
Beesat Hospital
Full name of responsible person
Dr. Behzad Mohsenpour
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Sanandaj
Province
Kurdistan
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6

Recruitment center
Name of recruitment center
Imam Khomeini Hospital
Full name of responsible person
Dr. Mohammad Reza Salehi
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Dr. Gharib St., Keshavarz Ave.
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7

Recruitment center
Name of recruitment center
Shahid Beheshti Hospital
Full name of responsible person
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<https://bmc.muq.ac.ir/index.aspx?siteid=114&fkeyid=&siteid=114&pageid=3554>

8

Recruitment center
Name of recruitment center
Sayyad Shirazi Hospital
Full name of responsible person
Dr. Nafiseh Abdollahi
Street address
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9

Recruitment center
Name of recruitment center
Rasoul Akram Hospital
Full name of responsible person
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Mansoori-Niayesh cross road; Niayesh street;
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10

Recruitment center

Name of recruitment center
Isabn-e-Maryam Hospital
Full name of responsible person
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Isfahan
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Isfahan
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11

Recruitment center

Name of recruitment center
Kosar Hospital
Full name of responsible person
Mahboubeh Darban
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Basij street
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Semnan
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Web page address
<https://kosarhos.semums.ac.ir/>

Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Aryogen Pharmed
Full name of responsible person

Nassim Anjidani
Street address
Next to Tajbakhsh street, 24th Kilometer of Makhsous road
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Alborz
Postal code
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Phone
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Email
contact@aryogen.com

Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Aryogen Pharmed
Proportion provided by this source
100
Public or private sector
Private
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Industry

Person responsible for general inquiries

Contact

Name of organization / entity
OrchidPharmed Co.
Full name of responsible person
Nassim Anjidani
Position
Medical Department Manager
Latest degree
Medical doctor
Other areas of specialty/work
Medical Pharmacy
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No 42, Attar street, Vanak square
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Person responsible for scientific

inquiries

Contact

Name of organization / entity

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Dr. Payam Tabarsi

Position

Professor

Latest degree

Ph.D.

Other areas of specialty/work

Infectious diseases

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Person responsible for updating data

Contact

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Orchid Pharmed

Full name of responsible person

Nassim Anjidani

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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