Clinical Trial Protocol
Iranian Registry of Clinical Trials

30 May 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°C), shortness of breath, cough, or respiratory rate higher than 30 breaths/min and SpO2≤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
City
Tehran
Province
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Phone
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Email
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Web page address
https://nritld.sbmu.ac.ir/index.jsp?fkeyid=&siteid=200&pageid=1419

2

Recruitment center
Name of recruitment center
Imam Reza Hospital
Full name of responsible person
Rozita Khodashahi
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Mashhad
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Razavi Khorasan
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Email
Rkhodashahi@yahoo.com
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https://emamreza.mums.ac.ir/

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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Isfehan
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Email
khorvash@med.mui.ac.ir
Web page address

4

Recruitment center
Name of recruitment center
Imam Khomeini Hospital
Full name of responsible person
Roya Ghasemian
Street address
Valiasr Highway, Joybar three ways
City
Sari
Province
Mazandaran
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4815733971
Phone
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Email
ict@mazums.ac.ir

5

Recruitment center
Name of recruitment center
Beesat Hospital
Full name of responsible person
Dr. Behzad Mohsenpour
Street address
Keshavarz St.,
City
Sanandaj
Province
Kurdistan
Postal code
131651332
Phone
+98 87 3328 5912
Email
Beesat@muk.ac.ir

6

Recruitment center
Name of recruitment center
Imam Khomeini Hospital
Full name of responsible person
Dr. Mohammad Reza Salehi
Street address
Dr. Gharib St., Keshavarz Ave.
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Tehran
Postal code
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Phone
+98 21 6119 0000
Email
Imamhospital@tums.ac.ir

7

Recruitment center
Name of recruitment center
Shahid Beheshti Hospital
Full name of responsible person
Dr. Ehsan Sharifipour
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Shahid Beheshti blvd.
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Ghoum
Province
Ghoum
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3719964797
Phone
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Email
bmc@muq.ac.ir
Web page address
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
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Shahid Sayyad Shirazi blvd.
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Gorgan
Province
Golestan
Postal code
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Phone
+98 17 3220 2291
Email
infosayyad@goums.ac.ir

9

Recruitment center
Name of recruitment center
Rasoul Akram Hospital
Full name of responsible person
Dr. Ali Javad Mousavi
Street address
Mansoori-Niayesh cross road; Niayesh street; Sattarkhan street
City

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Tehran
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1445613131
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+98 21 6435 1000
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10

Recruitment center
Name of recruitment center
Isabn-e-Maryam Hospital
Full name of responsible person
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Street address
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City
Isfehan
Province
Isfehan
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Email
st-maryam@mui.ac.ir
Web page address
https://isa.mui.ac.ir/

11

Recruitment center
Name of recruitment center
Kosar Hospital
Full name of responsible person
Mahboubeh Darban
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Basij street
City
Semnan
Province
Semnan
Postal code
3519899951
Phone
+98 23 3344 1022
Email
kosarhos@semums.ac.ir
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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Garm Darreh
Province
Alborz
Postal code
56145226
Phone
+98 26 3610 6480
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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Province
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Postal code
1651655
Phone
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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
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Ph.D.
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Infectious diseases
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Province
Tehran
Postal code
1956944413
Phone
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Email
payamtabarsi@yahoo.com

Person responsible for updating data

Contact

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Orchid Pharmed
Full name of responsible person
Nassim Anjidani
Position
Medical Manager
Latest degree
Medical doctor
Other areas of specialty/work
Medical Pharmacy
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City
Tehran
Province
Tehran
Postal code
5131331565
Phone
+98 21 4347 3000
Fax
+98 21 8856 2862
Email
anjidani.n@orchidpharmed.com

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