

Clinical Trial Protocol

Iranian Registry of Clinical Trials

03 Jun 2026

A phase 3, randomized, multicenter, double-blind, two-armed, parallel, active-controlled, equivalency clinical trial to compare efficacy and safety of Temziva (Tocilizumab produced by AryoGen Pharmed) versus Actemra® (Tocilizumab produced by Genentech-Roche co.) in patients with active moderate to severe rheumatoid arthritis

Protocol summary

Study aim

To assess efficacy and safety of Temziva (AryoGen) versus Actemra® (Genentech-Roche) in patients with active moderate to severe rheumatoid arthritis

Design

A phase 3, randomized, multicenter, double-blind, two-armed, parallel, active-controlled, equivalency clinical trial on 272 patients

Settings and conduct

12 cities and 22 centers will be in this study. If patients hold specific criteria they will be given a randomization code and will be allocated randomly to one of two intervention groups which either receive the brand drug or Iranian drug. All the drugs in the study will be used in exactly identical boxes and syringes so the investigator, the patient, and data analyzer will be completely unaware of the drug. The patient will be injected 13 drugs in 14 visits every other week and will be monitored for 6 months after the first injection.

Participants/Inclusion and exclusion criteria

The patients with active moderate to severe rheumatoid arthritis and 4 painful joints and swollen joints, 18-65 years old with no adequate response to non-biological Disease-modifying anti-rheumatoid drugs for 12 weeks according to physician, and have discontinued biological disease-modifying anti-rheumatoid drugs for 8 weeks and declared their informed consent. The patient should not suffer from the Advanced persistent limitation in usual self-care, vocational, and avocational activities according to ACR functional status guideline. Patients should not suffer from active or latent tuberculosis, Hepatitis, and HIV infections.

Intervention groups

Tocilizumab (AryoGen) prefilled syringe with dose of 162

mg, subcutaneous (S/C) injection every other week during 24 weeks Actemra® (Genentech-Roche) prefilled syringe with dose of 162 mg, (S/C) injection every other week during 24 weeks

Main outcome variables

Percentage of Patients with an American College of Rheumatology 20 (ACR20) Response at week 24.

General information

Reason for update

Protocol update

Acronym

IRCT registration information

IRCT registration number: **IRCT20150303021315N9**

Registration date: **2018-01-18, 1396/10/28**

Registration timing: **prospective**

Last update: **2024-06-02, 1403/03/13**

Update count: **5**

Registration date

2018-01-18, 1396/10/28

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**

Aryogen Pharmed Co.

Expected recruitment start date

2022-11-01, 1401/08/10

Expected recruitment end date

2024-10-22, 1403/08/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

A phase 3, randomized, multicenter, double-blind, two-armed, parallel, active-controlled, equivalency clinical trial to compare efficacy and safety of Temziva (Tocilizumab produced by AryoGen Pharmed) versus Actemra® (Tocilizumab produced by Genentech-Roche co.) in patients with active moderate to severe rheumatoid arthritis

Public title

The comparison of the efficacy and safety between Temziva and Actemra in treatment of the patient with active Rheumatoid Arthritis

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Male or female aged 18 -65 years at the time of signing the informed consent form Participants who have been diagnosed as having rheumatoid arthritis for at least 6 months, using the 2010 American College of Rheumatology/European League Against Rheumatism (2010 ACR/EULAR) classification criteria for RA. Patients who have an inadequate response of at least 12 weeks to ≥ 1 conventional disease-modifying antirheumatic drugs (DMARDs) in which 1 of them is definitely methotrexate, according to their investigator judgment. Moderate to severe rheumatoid arthritis with ≥ 4 tender joints (of 68 joints); ≥ 4 swollen joints (of 66 joints); and an erythrocyte sedimentation rate (ESR) ≥ 30 mm/hour or a C-reactive protein level (CRP) ≥ 1.0 mg/dl at screening Patients discontinued all biological DMARD, including etanercept for 2 weeks or longer and infliximab, certolizumab, golimumab or adalimumab for 8 weeks or longer because of side effects, lack of compliance or lack of response. Ability to comprehend and willingness to sign the Informed Consent Form for this study

Exclusion criteria:

Active tuberculosis or Patients testing positive for latent tuberculosis (PPD > abnormal CXR) Have a history of serious allergies or a known hypersensitivity to Tocilizumab or any components of the formulations. Have an active hepatitis B or C or positive hepatitis B surface antigen or hepatitis C antibody. Have a known history of infection with human immunodeficiency virus (HIV). Patients who are weighing ≥ 100 kg Patients who had thrombocytopenia (platelet count < 100,000/ μ l) or Leucopenia (ANC < 2,000/ μ l or white blood cell count <

3,500/ μ l). Patients with aspartate transaminase (AST), alanine transaminase (ALT) 1.5-fold the upper limit of maximum-normal. Patients with Functional class IV as defined by the American College of Rheumatology (ACR) Classification of Functional Status in Rheumatoid Arthritis. (Class IV: Advanced persistent limitation inability to perform usual self-care, vocational, and avocational activities). Patients who have been received previous treatment with Tocilizumab Patients who had received plasmapheresis or major surgery (including joint surgery, major cardiovascular surgery except for revascularization) within 8 weeks before entering study or planned major surgery within 6 months after entering the study. Patients who had previously received Rituximab within one year before starting the study. Patients who had received oral glucocorticoids at a dosage of > 10 mg/day of prednisolone or equivalent; or had a dose increase, new administration, or intravenous, intraarticular or intramuscular injections of glucocorticoids within 4 weeks of Tocilizumab treatment. Patients who had dose changes or added-in DMARDs or immunosuppressants within 4 weeks of Tocilizumab treatment. Immunization with a live/attenuated vaccine less than 4 weeks before baseline or planning to receive a live vaccine during the study. Women who are pregnant, breastfeeding or planning to become pregnant during the study. Patients who have stopped previous MTX treatment due to hepatotoxicity. Patients with an active infection or who have had a serious infection or have been treated with intravenous antibiotics for an infection within 8 weeks or oral antibiotics within 2 weeks prior to screening. Having history of any malignancy within the previous 5 years prior to Screening. Having rheumatic disease or inflammatory joint disease other than rheumatoid arthritis Having history of demyelinating disorders including multiple sclerosis. Patients with a certain history of gastrointestinal disorders such as diverticulitis, active peptic ulcer or active duodenal ulcer which have been approved by a gastroenterologist. Patients who had GFR < 60 ml/min/1.73 m² Patients with a history of treatment with cyclosporine or tacrolimus within 1 month of receiving tocilizumab. Having any other disease or disorder which, in the opinion of the Investigator, will put the subject at risk if they are enrolled. Patients who had previously received JAK inhibitors.

Age

From **18 years** old to **65 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **272**

Randomization (investigator's opinion)

Randomized

Randomization description

The randomization plan of the patients will be carried out centrally using an R-CRAN software version 4.0.2 Blocks (with the size 2 or 4) will be made using permuted block randomization for a total of 272 patients (1:1 allocation ratio). After randomization procedure, a code will be allocated to each patient that will be used as the patient identifier throughout the study. The assigned code will be denoted by 4 initials (corresponding to the first two letters of the first name, first two letters of surname) and 3 numbers (center code). Moreover, the code described is followed by study unique identification code consisting of first two letters of the generic name of the investigational product and study phase number respectively (which is TOC) and three numbers (corresponding to the randomization number), e.g. ABCD001TOC-001. The randomization number will be assigned in a consecutive way.

Blinding (investigator's opinion)

Double blinded

Blinding description

Both products used in the study will be entirely indistinguishable for patients and health care providers since they are identical in shape, size, material and color. They don't differ in appearance. The compartments of both Tocilizumab drugs are packaged in same pack. such a way that they do not differ in appearance. Also, a suitable label is designed for pre-filled boxes and syringes. The contents of the labels are based on EMA regulation. The brand's medicine and produced medicine in the factory are completely relabeled and packaged in the same way. The blinding codes are listed on the drug label, and each drug is linked to the patient through the specific code. The patient, medical staff, and other staff are not disclosed to the type of medication that being taken. The group of patients and the type of medication they receive are not disclosed to the researchers and are kept in opaque sealed envelopes with the researcher at each center. In addition, people who review the results and analyze the data are unaware of the type of grouping of patients and they cannot distinguish the type of brand of a drug by its appearance.

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Shahid Beheshti University of Medical Sciences

Street address

3th floor, school of medicine, Evin, Chamran Highway, Tehran, Iran

City

Tehran

Province

Tehran

Postal code

19839-63113

Approval date

2017-11-07, 1396/08/16

Ethics committee reference number

IR.SBMU.REC.1396.229

2

Ethics committee

Name of ethics committee

Ethics committee of Tehran University of Medical Sciences

Street address

Tehran University of Medical Sciences, Ghods street, Keshavarz boulevard

City

Tehran

Province

Tehran

Postal code

1417653761

Approval date

2018-01-13, 1396/10/23

Ethics committee reference number

IR.TUMS.VCR.REC.1396.4203

Health conditions studied

1

Description of health condition studied

Rheumatoid Arthritis

ICD-10 code

M05.8, M06

ICD-10 code description

Other seropositive rheumatoid arthritis ,Seronegative rheumatoid arthritis

Primary outcomes

1

Description

The patients response

Timepoint

Prior to, and 24 weeks after first intervention

Method of measurement

ACR 20 response criteria

Secondary outcomes

1

Description

The patients response

Timepoint

Prior to intervention and 12 weeks after the first intervention

Method of measurement

ACR20 response criteria

2

Description

The patients response

Timepoint

12 and 24 weeks after the first intervention

Method of measurement

ACR50 and ACR70 response criteria

3

Description

Change in patients disability

Timepoint

Prior to intervention, 12 and 24 weeks after the first intervention

Method of measurement

HAQ Questionnaire

4

Description

Change in Disease Activity

Timepoint

12 and 24 weeks after the first intervention

Method of measurement

DAS-28 index

5

Description

Percentage of the patients at remission

Timepoint

12 and 24 weeks after the first intervention

Method of measurement

DAS-28 index score below 2.6

6

Description

Adverse events (AEs), Adverse drug reactions (ADR)

Timepoint

at screening visit and at each visit including day 0 and weeks 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22 and 24 after the first injection

Method of measurement

Medical examination

7

Description

Changes in physical examination findings

Timepoint

at screening visit, and 12 and 24 weeks after the first

intervention

Method of measurement

Medical examination

8

Description

Changes in vital signs (blood pressure)

Timepoint

at screening visit and prior to intervention, and weeks 12 and 24 after the first intervention

Method of measurement

Medical examination

9

Description

Immunogenicity of the drug

Timepoint

Prior to intervention, and 12 and 24 weeks after the first intervention

Method of measurement

laboratory tests

Intervention groups

1

Description

Temziva (produced by AryoGen Pharmed) prefilled syringe for patients with dose of 162 mg, subcutaneous (S/C) injection every other week during 24 weeks of study

Category

Treatment - Drugs

2

Description

Actemra® (produced by Genentech-Roche Company)prefilled syringe for patients with dose of 162 mg, subcutaneous (S/C) injection every other week during 24 weeks of study.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Rheumatism center of Iran

Full name of responsible person

Dr. Mahdi Vojdaniyan, Dr. Farhad Gharibdoost, Dr. Susan Soroush, Dr. Mohsen Soroush, Dr. Bayat

Street address

Rheumatism center of Iran, Shahid Khosravi alley, North Kargar St.

City

Tehran

Province

Tehran
Postal code
1458796508
Phone
+98 21 8800 5141
Email
info@rcr.ir

2

Recruitment center

Name of recruitment center
Golestan Hospital
Full name of responsible person
Dr. Karim Mowla Howeizeh, Dr. Elham Rajaei
Street address
Golestan hospital, Golestan Ave, Ahwaz, Iran
City
Ahwaz
Province
Khouzestan
Postal code
61357-15794
Phone
+98 61 3374 3001
Email
info@ajums.ac.ir

3

Recruitment center

Name of recruitment center
Loghmane Hakim Hospital
Full name of responsible person
Dr. Arman Ahmadzadeh. Dr. Faraneh Farsad
Street address
Loghmane Hakim Hospital, Kamali St. South Kargar St.
City
Tehran
Province
Tehran
Postal code
1258769574
Phone
+98 21 5541 9005
Email
loghman.hospital@sbmu.ac.ir

4

Recruitment center

Name of recruitment center
Hafez Hospital
Full name of responsible person
Dr. Mohammad Ali Nazarinia- Dr Mansour Hosseini
Street address
Hafez Hospital, Chamran Blvd, Shiraz, Iran
City
Shiraz
Province
Fars
Postal code

5896142823
Phone
+98 71 3647 9531
Email
info.hafez@sums.ac.ir
Web page address
<http://hafez.sums.ac.ir/>

5

Recruitment center

Name of recruitment center
Alzahra Hospital
Full name of responsible person
Dr. Hadi Karimizadeh, Dr.Peyman Motaghi
Street address
Alzahra hospital, Sofeh, Shahid Keshvari Blvd, Isfahan, Tehran.
City
Isfahan
Province
Isfahan
Postal code
8174675731
Phone
+98 31 3620 2020
Email
alzahra@mui.ac.ir
Web page address
<http://alzahra.mui.ac.ir/>

6

Recruitment center

Name of recruitment center
Razi Hospital
Full name of responsible person
Dr. Asghar Hajiabbasi
Street address
Rheumatology Department, Razi Hospital, Sardar Jangal St., Rasht, Iran.
City
Rasht
Province
Guilan
Postal code
41448
Phone
+98 13 3355 0028
Email
razi.hospital@yahoo.com
Web page address
<http://www.gums.ac.ir/razi>

7

Recruitment center

Name of recruitment center
Imam Reza Hospital
Full name of responsible person
Dr. Alireza Khabazi Oskuei
Street address
Imam Reza Hospital, Golgasht St, Tabriz

City
Tabriz
Province
East Azarbaijan
Postal code
6584965725
Phone
+98 41 3334 7054
Email
imamreza@tbzmed.ac.ir

8

Recruitment center

Name of recruitment center
Shahid Sadoghi Hospital
Full name of responsible person
Dr. Hossein Soleyman Saleh Abadi, Dr. Ali Dehghan
Street address
Sadoghi Hospital, Ibn Sina St., Shahid Qandi St., Yazd, Iran.
City
Yazd
Province
Yazd
Postal code
3571598246
Phone
+98 35 3822 4000
Email
yazd_cdc@ssu.ac.ir
Web page address
<http://ssu.ac.ir/cms/index.php?id=587>

9

Recruitment center

Name of recruitment center
Imam Reza Hospital
Full name of responsible person
Dr. Shirin Assar, Dr. Mehran Pournazari
Street address
Imam Reza hospital, Parastar St., Kermanshah, Iran.
City
Kermanshah
Province
Kermanshah
Postal code
6416516410
Phone
+98 83 3427 6300
Fax
Email
admin@irhk.ir
Web page address
<http://www.irhk.ir/>

10

Recruitment center

Name of recruitment center
Imam Reza Hospital
Full name of responsible person

Dr. Seyede Zahra Mirfeyzi, Dr. Maryam Sahebri
Street address
Imam Reza Hospital, Imam Reza Hospital SQ.
Mashhad
City
Mashhad
Province
Razavi Khorasan
Postal code
9137913316
Phone
+98 51 3854 3031
Email
emamreza@mums.ac.ir

11

Recruitment center

Name of recruitment center
Dr. Miramir Aghdashi office
Full name of responsible person
Dr. Miramir Aghdashi
Street address
Varzesh St., Soltani St., Nikan building., Level 4
City
Urmia
Province
West Azarbaijan
Postal code
6516546666
Phone
+98 914 347 8635
Email
aghdashia@gmail.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity
AryoGen Pharmed Co.
Full name of responsible person
Dr. Nassim Anjidani
Street address
Cross Tajbakhsh Street, 24th Kilometer Makhsous.
City
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 Co.
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

City
Tehran
Province
Tehran
Postal code
1411713137
Phone
+98 21 8822 0065
Fax
Email
Jamshida@sina.tums.ac.ir
Web page address

Person responsible for general inquiries

Contact

Name of organization / entity
OrchidPharmed Co
Full name of responsible person
Dr. Nassim Anjidani
Position
Pharm.D./ Medical department manager
Latest degree
Medical doctor
Other areas of specialty/work
Medical Pharmacy
Street address
No 42, Attar St., Vanak Sq.
City
Tehran
Province
Tehran
Postal code
1994766411
Phone
+98 21 4347 3000
Fax
Email
anjidani.n@orchidpharmed.com
Web page address

Person responsible for scientific inquiries

Contact

Name of organization / entity
Tehran University of Medical Sciences
Full name of responsible person
Dr. Ahmadreza Jamshidi
Position
PhD. MD of Rheumatology
Latest degree
Ph.D.
Other areas of specialty/work
Internal Medicine
Street address
Rheumatology research Center, Dr. Shariati Hospital,
North Kargar St, Tehran, Iran.

Person responsible for updating data

Contact

Name of organization / entity
OrchidPharmed Co.
Full name of responsible person
Dr. Nassim Anjidani
Position
Pharm.D./Medical Department Manager
Latest degree
Medical doctor
Other areas of specialty/work
Medical Pharmacy
Street address
No 42, Attar St., Vanak Sq.
City
Tehran
Province
Tehran
Postal code
1994766411
Phone
+98 21 4347 3000
Fax
Email
anjidani.n@orchidpharmed.com
Web page address

Sharing plan

Deidentified Individual Participant Data Set (IPD)

No - There is not a plan to make this available

Justification/reason for indecision/not sharing IPD

There is no plan for this purpose

Study Protocol

No - There is not a plan to make this available

Statistical Analysis Plan

No - There is not a plan to make this available

Informed Consent Form

No - There is not a plan to make this available

Clinical Study Report

No - There is not a plan to make this available

Analytic Code

No - There is not a plan to make this available

Data Dictionary

No - There is not a plan to make this available