Clinical Trial Protocol
Iranian Registry of Clinical Trials

31 May 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 box 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

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Name of organization / entity
Orchid Pharmed

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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/µl) or Leucopenia (ANC<2,000/µl or white blood cell count < 3,500/µl). 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
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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
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Ethics committee of Tehran University of Medical Sciences
Street address
Tehran University of Medical Sciences, Ghods street, Keshavarz boulevard
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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
Rhuematism center of Iran
Full name of responsible person
Dr. Mahdi Vojdanian, Dr. Farhad Gharibdoost, Dr. Susan Soroush, Dr. Mohsen Soroush, Dr. Bayat
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2

Recruitment center
Name of recruitment center
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3

Recruitment center
Name of recruitment center
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4

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Recruitment center
Name of recruitment center
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Recruitment center
Name of recruitment center
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9

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11

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Sponsors / Funding sources

1

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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

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

Person responsible for general inquiries

Contact

Name of organization / entity
OrchidPahrmed Co

Full name of responsible person
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Position
Pharm.D./ Medical department manager

Latest degree
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Person responsible for updating data

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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