Clinical Trial Protocol
Iranian Registry of Clinical Trials

06 Nov 2026

Investigation of the effect of azithromycin on disease activity in rheumatoid arthritis patients

Protocol summary

Study aim
To evaluate the effect of Azithromycin as adjuvant therapy on Rheumatoid Arthritis (RA) activity.

Design
Phase 3, single center, parallel group, double blind, randomized controlled trial. Simple 1:1 allocation.

Settings and conduct
Imam Khomeini Hospital in Tehran with 3 months follow up. Double blinded (patients, investigators, assessors) using visually identical coded placebo and sealed opaque envelopes.

Participants/Inclusion and exclusion criteria
Inclusion: Age over 18; active Rheumatoid Arthritis (RA) on standard treatment. Exclusion: Biologics use; concurrent antibiotics; macrolide contraindications; needing biologic switch.

Intervention groups
Intervention: Standard Rheumatoid Arthritis (RA) treatment plus Azithromycin 500mg thrice weekly. Control: Standard Rheumatoid Arthritis (RA) treatment plus cornstarch placebo.

Main outcome variables
Disease Activity Score 28 (DAS 28), Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI).

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20260715070199N1**
Registration date: **2026-08-12, 1405/05/21**
Registration timing: **prospective**

Last update: **2026-08-12, 1405/05/21**
Update count: **0**

Registration date
2026-08-12, 1405/05/21

Registrant information

Name
Soheil Khalaji

Name of organization / entity

Country
Iran (Islamic Republic of)

Phone
+98 912 479 9307

Email address
s-khalaji@razi.tums.ac.ir

Recruitment status
recruiting

Funding source

Expected recruitment start date
2026-08-23, 1405/06/01

Expected recruitment end date
2027-03-20, 1405/12/29

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Investigation of the effect of azithromycin on disease activity in rheumatoid arthritis patients

Public title
Effect of Azithromycin in treatment of Rheumatoid Arthritis

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Confirmed diagnosis of Rheumatoid Arthritis (RA) based on the ACR-2020 criteria Receiving standard treatment for RA Having active disease at the time of enrollment

Exclusion criteria:
Current use of biologic agents for the treatment of RA Concurrent use of antibiotics Any contraindications to the administration of macrolides Having inactive disease at the time of study entry Need to change treatment to biologic agents at the initial visit

Age
From **18 years** old

Gender
Both

Phase
3

Groups that have been masked

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

Sample size
Target sample size: **74**

Randomization (investigator's opinion)
Randomized

Randomization description
The unit of randomization in this study is the individual. Patients are assigned to the intervention and control groups using simple randomization with a 1:1 allocation ratio. The random allocation sequence is generated using computer-generated random numbers. To ensure allocation concealment, sequentially numbered, opaque, sealed envelopes are utilized. An independent researcher, who is not involved in patient enrollment or assessment, generates the sequence and prepares the envelopes. Consequently, the group allocation for each patient remains strictly concealed until the respective envelope is opened at the time of intervention.

Blinding (investigator's opinion)
Double blinded

Blinding description
This study is designed as a randomized, double-blind, placebo-controlled trial. To prevent bias and ensure the integrity of the study, the following groups will be blinded to the treatment allocation: Trial Participants: Patients will be completely unaware of their assigned group. Both the active medication (Azithromycin 500 mg) and the placebo (a cornstarch-based formulation manufactured by Exir Pharmaceutical Company) are visually identical in shape, size, and color. The medications will be provided to participants in sealed, opaque, and identically coded envelopes without any identifying labels. Principal Investigator and Healthcare Providers: The treating physicians and healthcare staff responsible for enrolling patients, providing routine care, and dispensing the study packages will be blinded to the allocation sequence. They will only have access to the predefined random codes on the envelopes. Data Collectors and Outcome Assessors: The researchers responsible for clinical evaluations, calculating disease activity scores, and recording patient data will remain blinded to the treatment assignment to ensure unbiased clinical assessments. Mechanism of Blinding: An independent third-party researcher, who has no role in patient recruitment, clinical care, or outcome assessment, will be exclusively responsible for generating the allocation sequence, preparing the identical drug/placebo packages, and labeling them with random codes. This independent individual will keep the master blinding code secure and confidential until the data collection phase is fully completed and the database is locked for analysis.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Tehran University of Medical Sciences

Street address
School of Medicine, Poursina St., Qods St., Enghelab St.

City
Tehran

Province
Tehran

Postal code
1461884513

Approval date
2024-08-06, 1403/05/16

Ethics committee reference number
IR.TUMS.IKHC.REC.1403.198

Health conditions studied

1

Description of health condition studied
Rheumatoid Arthritis

ICD-10 code
M06.9

ICD-10 code description
Rheumatoid arthritis, unspecified

Primary outcomes

1

Description
Disease Activity Score 28 based on Erythrocyte Sedimentation Rate

Timepoint
At the beginning of the study (before intervention) and twelve weeks after the start of the intervention

Method of measurement
Calculated via standard formula using the number of swollen and tender joints in clinical examination, patient global assessment of disease activity, and laboratory value of Erythrocyte Sedimentation Rate

Secondary outcomes

1

Description
Disease Activity Score 28 based on C Reactive Protein
Timepoint
At the beginning of the study (before intervention) and twelve weeks after the start of the intervention
Method of measurement
Calculated via standard formula using the number of swollen and tender joints in clinical examination, patient global assessment of disease activity, and laboratory value of C Reactive Protein

2

Description
Clinical Disease Activity Index
Timepoint
At the beginning of the study (before intervention) and twelve weeks after the start of the intervention
Method of measurement
Calculated as the sum of the number of swollen joints, number of tender joints, patient global assessment, and evaluator global assessment

3

Description
Simplified Disease Activity Index
Timepoint
At the beginning of the study (before intervention) and twelve weeks after the start of the intervention
Method of measurement
Calculated as the sum of the number of swollen joints, number of tender joints, patient global assessment, evaluator global assessment, and laboratory value of C Reactive Protein

Intervention groups

1

Description
Intervention group: Patients in this group, in addition to their standard Rheumatoid Arthritis treatment, will receive oral Azithromycin 500 mg tablets (manufactured by Exir Pharmaceutical Company) three times a week (one tablet on Saturdays, Sundays, and Mondays) for 12 weeks.
Category
Treatment - Drugs

2

Description
Control group: In addition to receiving standard treatment for Rheumatoid Arthritis (RA) based on guidelines, patients in this group receive a placebo. The placebo is administered as an oral tablet based on cornstarch, completely identical in appearance to the active medication, given three times a week (one tablet on Saturdays, Sundays, and Mondays) for a duration of 12 weeks. The placebo is manufactured by Exir Pharmaceutical Company.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Imam Khomeini Hospital Complex
Full name of responsible person
Soheil Khalaji
Street address
Rheumatology Department, Imam Khomeini Hospital Complex, Gharib St, Keshavarz Blvd, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1419733141
Phone
+98 21 6691 1294
Fax
Email
soheil.gpi@gmail.com
Web page address

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Tehran University of Medical Sciences
Full name of responsible person
Ramin Kordi
Street address
School of Medicine, Poursina St., Qods St., Enghelab St.
City
Tehran
Province
Tehran
Postal code
141765383761
Phone
+98 21 8163 3698
Fax
Email

vcr@tums.ac.ir

Web page address

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Tehran University of Medical Sciences

Proportion provided by this source

100

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

Tehran University of Medical Sciences

Full name of responsible person

Soheil Khalaji

Position

Resident

Latest degree

Medical doctor

Other areas of specialty/work

Internal Medicine

Street address

Rheumatology Department, Imam Khomeini Hospital Complex, Gharib St, Keshavarz Blvd, Tehran, Iran

City

Tehran

Province

Tehran

Postal code

1419733141

Phone

+98 21 6691 1294

Fax

Email

soheil.gpi@gmail.com

Web page address

Person responsible for scientific inquiries

Contact

Name of organization / entity

Tehran University of Medical Sciences

Full name of responsible person

Soheil Khalaji

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1461884513

Phone

+98 21 6691 1294

Fax

Email

soheil.gpi@gmail.com

Web page address

Person responsible for updating data

Contact

Name of organization / entity

Tehran University of Medical Sciences

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Soheil Khalaji

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soheil.gpi@gmail.com

Web page address

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 Individual Participant Data (IPD) for all primary and secondary outcome measures will be shared.

When the data will become available and for how long

Data will become available 6 months after the publication of the results and will remain accessible for a period of 2 years.

To whom data/document is available

The data will be available only to researchers working in academic and scientific institutions.

Under which criteria data/document could be used

Data can be used exclusively for non-commercial academic research, systematic reviews, and meta-analyses. Requests must include a formal, methodologically sound proposal approved by an independent ethics committee.

From where data/document is obtainable

Applicants should send their requests via email to the principal investigator (Soheil Khalaji) at soheil.gpi@gmail.com.

What processes are involved for a request to access data/document

Applicants must submit a formal request along with their research proposal and ethics committee approval via email. The principal investigator and the research team will review the request within 4 weeks. If approved, a data-sharing agreement must be signed before the deidentified data is transferred securely. The entire process is estimated to take up to 2 months.

Comments