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The 3TR-PARTNER-RA study: Are RNA signatures (biomarkers) in the tissue which surrounds the joints (synovial tissue) from patients with early Rheumatoid Arthritis (symptoms <12 months) predictive of response to biologic drug treatments?

Submission date
03/08/2024

Recruitment status
Recruiting

Registration date
16/12/2024

Overall study status
Ongoing

Last Edited
17/06/2025

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by persistent synovitis (joint inflammation), systemic inflammation, and autoantibodies, particularly rheumatoid factor and citrullinated peptide. These autoantibodies are thought to play critical roles in initiating inflammatory responses in RA. In industrialized countries, RA affects 0.5-1% of adults, with 5-50 per 100,000 new cases annually.
Despite the clinical and radiological benefits of biological therapies, many patients fail to achieve low disease activity or remission. Almost 40% of all patients treated with biologic disease-modifying anti-rheumatic drugs (b-DMARDs) do not experience minimally acceptable improvement. Thus, treating RA patients according to their biomarker profiles would provide better care, prevent unnecessary exposure to potentially toxic drugs, and be cost-saving.
We aim to test whether RNA signatures (biomarkers) in the tissue surrounding the joints (synovial tissue) from patients with early RA are predictive of response to abatacept, a biologic disease-modifying anti-rheumatic drug (b-DMARD).

Who can participate?
Adults with early RA (symptoms for less than 12 months) who have not previously been treated with DMARD therapies.

What does the study involve?
Participants will undergo a synovial biopsy of their joint to collect tissue samples for RNA analysis. Patients will then be randomly assigned to receive either abatacept and methotrexate

or placebo and methotrexate. The randomisation will be based on biomarker profiles. Patients will attend study visits every 4 weeks for up to 16 weeks, followed by a 30-day safety follow-up visit.

What are the possible benefits and risks of participating?
Participants may experience an improvement in their arthritis symptoms, although there may be no direct benefit. However, the trial will generate essential information that could benefit future RA patients. Abatacept has evidence supporting its effectiveness in patients where conventional DMARDs have failed. This study aims to determine whether specific RNA signatures can accurately predict the best treatment for early RA patients.
Injection site reactions with abatacept and the risk of infections will be discussed with the patient before enrollment in the study. Participants would be at no greater risk than routine care within the NHS.
An ultrasound-guided synovial biopsy is a quick, safe, and well-tolerated procedure. Patients who consent to the study and the biopsy will have a longer hospital appointment and may experience discomfort from the local anaesthetic and biopsy procedure. However, published data confirm that this procedure is well-tolerated and safe, and patients are generally agreeable to multiple biopsies

Where is the study run from?
Queen Mary University of London (UK)

When is the study starting and how long is it expected to run for?
August 2024 to September 2026

Who is funding the study?
The Innovative Medicines Initiative 2 Joint Undertaking IMI2 JU (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2024-511470-79

IRAS number
1008435

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 1008435

Study information

Scientific Title
The 3TR Molecular PAthobiology and PRecision Therapy iN EaRly Rheumatoid Arthritis Study (3TR-PARTNER-RA)

Acronym
3TR-PARTNER-RA

Study objectives
The primary objective of this trial is to determine whether synovial molecular profiles can inform treatment response to abatacept in early RA.
To this aim, we will compare the change in Clinical Disease Activity Index (CDAI) score at 16 weeks between the biomarker positive and the biomarker negative patients within the abatacept group (i.e. Group 1 vs Group 3).
We hypothesise that patients with high synovial immunological infiltrate (lymphoid pathotype) will respond better to abatacept therapy.

Secondary objective:
We aim to assess patients treated according to their biomarker: comparing the biomarker-positive patients (as Groups 1 minus 2) vs the biomarker-negative patients (as Groups 3 minus 4).

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 13/12/2024, South Central - Hampshire B Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8000; contact@hra.nhs.uk), ref: 24/SC/0277

Study design
Interventional double-blind randomized parallel group placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Screening, Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Rheumatoid arthritis

Interventions
Intervention Arm (Abatacept and Methotrexate):
Abatacept: 125 mg solution for injection, subcutaneous, weekly.
Methotrexate: Dose according to local guidelines.

Control Arm (Placebo and Methotrexate):
Placebo: Matching placebo injection, subcutaneous, weekly.
Methotrexate: Dose according to local guidelines.

Intervention Type
Drug

Pharmaceutical study type(s)
Others (The trial will investigate whether the presence of certain biomarkers can predict response to abatacept.)

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Orencia

Primary outcome measure
Clinical Disease Activity Index (CDAI) at baseline and 16 weeks

Secondary outcome measures

1. Percentage of patients with DAS28(ESR)<3.2 (LDA) at 16 weeks
2. Percentage of patients deemed responders using American College of Rheumatology 50 (ACR50) measure at 16 weeks
3. Percentage of patients with CDAI remission at 16 weeks
4. HAQ-DI at baseline and 16 weeks
5. SF-36 at baseline and 16 weeks

Overall study start date
01/08/2024

Completion date
01/09/2026

Eligibility

Key inclusion criteria
1. Adults (female and male) aged 18 years or over.
2. Willing and capable of giving informed consent.
3. 2010 ACR / EULAR classification criteria for a diagnosis of Rheumatoid Arthritis. *
4. Symptom duration of <12 months
5. At least one swollen joint, which is amenable to synovial biopsy (minimum grade 2 synovial thickening, as assessed at the biopsy visit).
6. Moderate and severe Disease Activity (DAS28>3.2)
7. No prior DMARD therapies (conventional, targeted or biologic DMARDs)
8. Patient is judged by the supervising clinician to be a suitable candidate based upon medical history, physical examination, vital signs, and routine laboratory tests.
9. Willing and able to comply with scheduled visits, laboratory tests, and other study procedures.
* The ACR/EULAR classification for a diagnosis of RA could have been at any time in the patient's disease history; the score does not need to be 6 or more at screening.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
200

Key exclusion criteria
1. Patients unable to tolerate synovial biopsy or in whom this is contraindicated including patients on anti-coagulants (e.g. warfarin). Patients on short-acting direct oral anticoagulant agents can be considered when anti-coagulant can be temporarily stopped, in line with local guidelines for procedures with a low risk of bleeding, taking into account the individual

thromboembolic risk. Oral anti-platelet agents are permitted.
2. Patients in whom there is no suitable joint for biopsy.
3. Hypersensitivity to the active substance or to any of the excipients of abatacept or methotrexate, or any other contraindications to the study medications, as per the current SmPC.
4. History of or current primary inflammatory joint disease or primary rheumatological autoimmune disease other than RA (if secondary to RA, then the patient is still eligible).
5. Prior exposure to any biologic/targeted DMARDs for RA
6. Treatment with any investigational agent ≤ 8 weeks prior to baseline or < 5 half-lives of the investigational drug (whichever is the longer)
7. Intra-articular or parenteral corticosteroids, or oral prednisolone more than 10mg/d or equivalent ≤ 4 weeks prior to screening visit.
8. Patients with a serious underlying medical disorder (e.g., end stage renal disease).
9. Active infection
10. Subject has a history or known presence of recurrent or chronic infection (eg, hepatitis B virus [HBV], hepatitis C virus [HCV], human immunodeficiency virus HIV]; recurrent urinary tract infections are allowed.
11. Subjects testing positive for acute or chronic hepatitis A, B, or C, unless they are indicative of prior hepatitis B vaccination or cured hepatitis A or B and accompanied by normal liver transaminase values.
12. Septic arthritis of a native joint within the last 12 months
13. Septic arthritis of a prosthetic joint within 12 months or indefinitely if the joint remains in situ
14. Latent TB infection unless they have completed adequate antibiotic prophylaxis
15. Receipt of live vaccine <3 months prior to first dose of study medication
16. Major surgery in 3 months prior to first dose of study medication
17. Presence of a transplanted organ (with the exception of a corneal transplant >3 months prior to screening).
18. Known recent substance abuse (drug or alcohol).
19. Patients currently recruited to other clinical trials or taking part in a CTIMP study in the previous 4 months.
20. Other severe acute or chronic medical or psychiatric condition, or laboratory abnormality that would impart, in the judgment of the investigator, excess risk associated with study participation or study drug administration, or which, in the judgment of the investigator, would make the patient inappropriate for entry into this study. This should include assessment of risk factors for known clinically important risks associated with a study drug.
21. Patients with severe hepatic impairment (Child Pugh C classification).
22. Patients that are primary or secondary immunodeficiency (history of or currently active).
23. Poor tolerability of venepuncture or lack of adequate venous access for required blood sampling during the study period.
24. Women who are pregnant or breast-feeding.
25. Women of child-bearing potential or males whose partners are women of child-bearing potential, unwilling to use an effective method of contraception (recommend double contraception) throughout the trial and beyond the end of trial treatment for the duration as defined in the relevant SmPC.
26. Individuals who are unable to give informed consent for any reason (vulnerable groups).

Date of first enrolment
23/06/2025

Date of final enrolment
01/09/2026

Locations

Countries of recruitment
Belgium

England

Italy

Netherlands

Portugal

Spain

United Kingdom

Study participating centre
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ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Government

Funder Name
The Innovative Medicines Initiative 2 Joint Undertaking IMI2 JU

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Conference presentation
Publication on website
Submission to regulatory authorities
Data that is shared will be anonymised and patients are asked to explicitly consent for their anonymous data to be shared with other researchers in the consent form.

Intention to publish date
01/09/2027

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date. Fully anonymised data may be uploaded, where appropriate, to a public location.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 4.0	27/11/2024	05/03/2025	No	Yes
Protocol file	version 2.0	18/09/2024	05/03/2025	No	No
Statistical Analysis Plan	version 1.0	04/03/2025	05/03/2025	No	No