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Biopsy-based prospective research study in patients with rheumatoid arthritis

Submission date
25/04/2024

Recruitment status
Recruiting

Registration date
26/04/2024

Overall study status
Ongoing

Last Edited
24/06/2025

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Rheumatoid arthritis (RA) is a chronic inflammatory disease, characterised by persistent synovitis (joint inflammation), systemic inflammation (inflammation throughout the whole body), and autoantibodies (antibodies that react with the body's own proteins, particularly rheumatoid factor and citrullinated peptide, thought to play critical roles in initiating inflammatory responses in RA). In industrialised 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, the vast majority of 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, the treatment of RA patients according to their biomarkers would provide better care (avert delays in starting a more effective drug), prevent unnecessary exposure to potentially toxic drugs and additionally be cost-saving.
The aim of this study is to create a biomedical resource for the deep immunophenotyping (a technique to study the proteins expressed by cells) of synovial biopsies (joint tissue samples), including at the single-cell level, in order to validate the response signatures from previous biopsy-driven studies (R4RA, STRAP), as well as provide samples to develop models to assess drug response.

Who can participate?
Patients aged 18 years and over with RA

What does the study involve?
Rheumatology patients will undergo a biopsy of their joint and then will receive either an anti-TNF, IL6i or JAKi according to their routine care. Patients will attend 4-weekly visits for up to 16 weeks, followed by a 30-day safety follow-up visit.

What are the possible benefits and risks of participating?
Participating patients may experience an improvement in the symptoms of their arthritis or may not benefit directly from this study. However, the study will generate essential information, which could be of benefit to others in the future.
An ultrasound-guided synovial biopsy is a quick, safe and well-tolerated procedure; patients who

consent to the study and therefore synovial biopsy will have a longer appointment in hospital and may experience discomfort from the local anaesthetic and biopsy procedure. However, published data on this procedure confirms that it is well tolerated and safe, and patients are agreeable to multiple biopsies.
The risks of venepuncture may include fainting, pain and/or bruising at the site of the needle puncture. Every possible effort will be taken to minimise the potential of these risks occurring.

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?
June 2023 to June 2027

Who is funding the study?
UK Research and Innovation (UKRI), ref: 10055567

Who is the main contact?
Centre for Experimental Medicine & Rheumatology (EMR) Clinical Trials team, Queen Mary University of London (UK)
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Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
330277

Central Portfolio Management System (CPMS)
58515

Protocol serial number
159798, , 10055567

Study information

Scientific Title
The SQUEEZE exposure study (Bio-Test study)

Acronym
SQUEEZE Bio-Test Study

Study objectives
The main objective of this clinical study is to create a biomedical resource for the deep immunophenotyping of synovial biopsies, including at single-cell level, in order to validate the response signatures from previous biopsy-driven studies (R4RA, STRAP), as well as provide ex vivo samples to develop in vitro models to assess drug response.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 25/10/2023, South Birmingham REC (2 Redman Place, Stratford, Health Research Authority, London, E20 1JQ, United Kingdom; +44 (0)207 104 8345; southbirmingham.rec@hra.nhs.uk), ref: 23WM0209

Primary study design
Observational

Study design
Exploratory observational biopsy-based prospective research study

Study type(s)
Quality of life, Treatment

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

Interventions
Patients will be recruited who are starting a new drug treatment within one of the following drug classes as part of routine care: TNF-inhibitor, IL6R-inhibitor, or JAK-inhibitor. Following a minimally invasive, ultrasound-guided synovial biopsy, patients will start their routine treatment and will be followed up every 4 weeks until their final 16-week study visit, where a repeat option biopsy may be performed.

Intervention Type
Other

Primary outcome(s)
Rheumatoid arthritis disease activity measured in the Clinical Disease Activity Index at 16 weeks from baseline at week 0 in each medication group (Tumor Necrosis Factor, Interleukin 6, & Janus kinase inhibitors) and within the whole population

Key secondary outcome(s)
1. The percentage of patients with ultrasound-defined remission (ST/PD<=1) vs patients with active synovitis at ultrasound (ST/PD>1) at 16 weeks
2. The percentage of patients with Disease Activity Score-28 for Rheumatoid Arthritis with ESR (DAS28-ESR) below 3.2 at 16 weeks
3. The percentage of patients with a Clinical Disease Activity Index between 2.8 and 10 (Low Disease Activity) at 16 weeks
4. The percentage of patients with a Clinical Disease Activity Index below 2.8 (in remission) at 16 weeks
5. Disability, pain, medication effects, costs of care, and mortality measured using the Health Assessment Questionnaire (HAQ-DI) at 16 weeks from baseline at week 0
6. Health status of particular populations measured using the Short Form Health Survey (SF-36) at 16 weeks from baseline at week 0

Completion date
30/06/2027

Eligibility

Key inclusion criteria

Current inclusion criteria as of 24/06/2025:
1. Adults (aged 18 years and over) with a diagnosis of rheumatoid arthritis (2010 ACR/EULAR criteria)
2. Failure of TNF inhibitor, either as monotherapy or in combination with csDMARDs, switching to a different TNFi, an IL6Ri or a JAKi
3. Eligible to start a TNFi, IL6Ri, or JAKi, according to local pathways/guidelines
4. Patients on any other additional csDMARDs at the time of starting their biologic should be on a stable dose in the 4 weeks prior to the baseline visit
5. At least one swollen joint amenable to synovial biopsy (minimum grade 2 synovial thickening, as assessed at the biopsy visit)
6. Minimum three swollen joints (including the joint selected for biopsy) and a minimum DAS28 (ESR) score of 3.2 at screening
7. Patient is judged by the supervising clinician to be a suitable candidate based upon medical history, physical examination, vital signs, and routine laboratory tests
8. Willing and capable of giving informed consent, which must be obtained prior to any study-specific screening procedures
9. Willing and able to comply with scheduled visits, laboratory tests, and other study procedures

Previous inclusion criteria:
1. Adults (aged 18 years and over) with a diagnosis of rheumatoid arthritis (2010 ACR/EULAR criteria)
2. Primary failure of first-line TNF inhibitor, either as monotherapy or in combination with csDMARDs, switching to a different TNFi, an IL6Ri or a JAKi
3. Eligible to start a TNFi, IL6Ri, or JAKi, according to local pathways/guidelines
4. Patients must be receiving methotrexate therapy and be on a stable dose for a minimum of 4 weeks prior to entry into the trial
5. Patients on any other additional csDMARDs at the time of starting their biologic should be on a stable dose in the 4 weeks prior to the baseline visit
6. At least one swollen joint amenable to synovial biopsy (minimum grade 2 synovial thickening, as assessed at the biopsy visit)
7. Minimum three swollen joints (including the joint selected for biopsy) and a minimum DAS28 (ESR) score of 3.2 at screening
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 capable of giving informed consent, which must be obtained prior to any study-specific screening procedures
10. Willing and able to comply with scheduled visits, laboratory tests, and other study procedures

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex
All

Key exclusion criteria
1. Patients unable to tolerate synovial biopsy or in whom this is contraindicated including patients on anti-coagulants (e.g. warfarin), or in whom this is contraindicated at physician's discretion (e.g. patients with bleeding disorders, or patients with liver disease). Patients on short-acting direct oral anticoagulant agents can be considered when the 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 antiplatelet agents are permitted.
2. Patients in whom there is no suitable joint for biopsy
3. Patients who are stopping their previously prescribed TNF inhibitor due to toxicity/side effects, rather than failure to respond.
4. Intra-articular or parenteral corticosteroids ≤4 weeks prior to the biopsy/baseline visit.
5. Oral prednisolone more than 10 mg/d or equivalent ≤4 weeks prior to the biopsy/baseline visit. If patients are taking oral corticosteroids during this period, they must be on a stable dose (i.e. they must not start or change the dose during this period).
6. Patients with a serious underlying medical disorder (e.g. end-stage renal disease)
7. Poor tolerability of venepuncture or lack of adequate venous access for required blood sampling during the study period
8. Active infection or any other contraindications to start TNFi, IL6Ri, or JAKi, as per local /international guidelines and SmPc (including specific risk assessment for CV events, venous thromboembolism (VTE), cancer, and infections for JAKi)
9. Individuals who are unable to give informed consent for any reason (vulnerable groups)

Date of first enrolment
16/04/2024

Date of final enrolment
30/06/2027

Locations

Countries of recruitment
United Kingdom

England

Austria

Italy

Netherlands

Norway

Sweden

Study participating centre

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Sponsor information

Organisation
Queen Mary University of London

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Government

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made 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