

# Biopsy-based prospective research study in patients with rheumatoid arthritis

<b>Submission date</b> 25/04/2024	<b>Recruitment status</b> Recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 26/04/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 24/06/2025	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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)  
emrclinicaltrials@qmul.ac.uk

## Contact information

### Type(s)

Scientific

### Contact name

Dr Liliane Fossati-Jimack

### Contact details

EMR Clinical Trials team  
2nd Floor  
John Vane Science Centre  
London  
United Kingdom  
EC1M 6BQ  
+44 (0)20 7882 7275  
emrclinicaltrials@qmul.ac.uk

### Type(s)

Principal Investigator

### Contact name

Prof Costantino Pitzalis

### Contact details

2nd Floor  
John Vane Science Centre  
London  
United Kingdom  
EC1M 6BQ

+44 (0)20 7882 8191  
c.pitzalis@qmul.ac.uk

### **Type(s)**

Public

### **Contact name**

Dr Alessia Baseggio Conrado

### **Contact details**

EMR Clinical Trials team  
2nd Floor  
John Vane Science Centre  
London  
United Kingdom  
EC1M 6BQ  
+44 (0)20 7882 8191  
emrclinicaltrials@qmul.ac.uk

## **Additional identifiers**

### **EudraCT/CTIS number**

Nil known

### **IRAS number**

330277

### **ClinicalTrials.gov number**

Nil known

### **Secondary identifying numbers**

159798, IRAS 330277, 10055567, CPMS 58515

## **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

**Study design**

Exploratory observational biopsy-based prospective research study

**Primary study design**

Observational

**Secondary study design**

Prospective

**Study setting(s)**

Hospital

**Study type(s)**

Quality of life, Treatment

**Participant information sheet**

Not available in web format, please use the contact details to request a participant information sheet

**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 measure**

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

**Secondary outcome measures**

1. The percentage of patients with ultrasound-defined remission (ST/PD $\leq$ 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

**Overall study start date**

29/06/2023

**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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

45-60

**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  $\leq 4$  weeks prior to the biopsy/baseline visit.
5. Oral prednisolone more than 10 mg/d or equivalent  $\leq 4$  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**

Austria

England

Italy

Netherlands

Norway

Sweden

United Kingdom

**Study participating centre**

**Mile End Hospital Cdc**

Mile End Hospital  
275 Bancroft Road  
London  
United Kingdom  
E1 4DG

**Study participating centre**

**Medical University of Vienna**

Spitalgasse 23  
Vienna  
Austria  
1090

**Study participating centre**

**Istituto Clinico Humanitas Mirasole S.p.A.**

Via A. Manzoni 56  
Milan  
Italy  
20089

**Study participating centre**

**Academisch Ziekenhuis Leiden**

Albinusdreef 2  
Leiden  
Netherlands  
2333

**Study participating centre**

**Karolinska Institute**

Solnavagen 1

Stockholm  
Sweden  
17177

**Study participating centre**  
**Diakonhjemmet Hospital**  
Diakonveien 12  
Oslo  
Norway  
0370

## **Sponsor information**

### **Organisation**

Queen Mary University of London

### **Sponsor details**

c/o Dr Mays Jawad  
Dept W, Research Services  
69-89 Mile End Road  
London  
England  
United Kingdom  
E1 4UJ  
+44 (0)20 7882 7275/6574  
research.governance@qmul.ac.uk

### **Sponsor type**

University/education

### **Website**

<http://www.qmul.ac.uk/>

### **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**

**Publication and dissemination plan**

1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on a website
4. Submission to regulatory authorities
5. 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**

30/06/2028

**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