ISRCTN13161614 https://doi.org/10.1186/ISRCTN13161614

Imaging with a novel radioactive tracer called 99mTc-Maraciclatide to detect inflammation in the joint in individuals with arthritis

Submission date
11/06/2024

Recruitment status
Recruiting

Registration date
29/07/2024

Overall study status
Ongoing

Last Edited
29/07/2024

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) and Psoriatic Arthritis (PsA) are autoimmune diseases that cause inflammation in joints. Over time, if the inflammation is not treated, it can cause permanent joint damage, disability and impaired quality of life. It is now known that in RA and PsA, starting treatment earlier in the course of the disease can improve long-term outcomes. Imaging techniques such as ultrasound (US) and magnetic resonance imaging (MRI) can help identify joint inflammation in individuals with RA and PsA, to understand the best treatment to use. Both techniques tend to focus on specific joints rather than assessing inflammation in the whole body. In addition, MRI is expensive, not always readily accessible, and is incompatible with pacemakers and other metallic implants. Therefore, other imaging techniques able to detect joint inflammation at the whole body level are required. The purpose of this study is to understand whether a whole-body imaging technique called gamma scintigraphy, using a very small amount of radioactive material (a radiotracer called Technetium-99m Maraciclatide), can help detect inflammation in and around the joint in individuals with RA and PsA, and to compare the results to established imaging techniques. A UK company, called Serac Healthcare Ltd is in the late stages of developing 99mTc-maraciclatide which has been designed to be attracted to cells within inflamed joints. When the tracer is added to a very small dose of radiation (an amount similar to a standard chest CT scan) it is expected to help imaging specialists and other doctors to see inflamed joints. So far, the radiotracer (99mTc-maraciclatide) has been given to 25 healthy volunteers and over 130 patients. There have been no harmful side effects. It was also shown that the scan could make it easier for doctors to see inflamed joints.

Who can participate?
Individuals with RA and PsA

What does the study involve?
This study involves a clinical assessment, and imaging of the joints via MRI, US and gamma scintigraphy with a radioactive tracer called 99mTc-Maraciclatide. This study also includes an optional joint biopsy.

What are the possible benefits and risks of participating?
It cannot guaranteed that participants will gain personal benefit from this study. However, the results obtained from this study may help to develop new imaging techniques to improve the detection of joint inflammation in individuals with RA and PsA, which could be used in routine clinical care. The procedures in this study use ionising radiation to form images of the body. Ionising radiation may cause cancer many years or decades after exposure, but taking part in this study will only increase the risk of developing cancer by about 0.03%. As part of the MRI scan, participants may receive an injection of contrast. This is a routine procedure and is usually problem-free. Occasionally there may be some local irritation at the site of the injection. There is a very small risk of a serious allergic reaction to the contrast injection (1 in 100,000 to 1 in 10,000), in which case further injections would be given to treat the allergic reaction. The risks of having blood taken from a vein include pain, bruising or infection at the site where the blood was taken, and fainting. Blood samples will be taken from an experienced research nurse or trained phlebotomist in the clinic.

Where is the study run from?
Leeds Teaching Hospitals Trust

When is the study starting and how long is it expected to run for?
August 2023 to March 2026

Who is funding the study?
SERAC Healthcare Ltd

Who is the main contact?
Tim Hardy, T.Hardy@leeds.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
319320

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 58998, IRAS 319320

Study information

Scientific Title
Molecular imaging using 99mTc-maraciclatide for detection of joint inflammation in inflammatory arthritis

Acronym
IMAGE-IA

Study objectives
It is hypothesised that whole-body imaging using 99mTc-Maraciclatide will:
1. Detect joint and extra-capsular inflammation in individuals with rheumatoid and psoriatic arthritis; and,
2. Demonstrate good sensitivity and specificity compared to MRI and US measures of joint and extra-capsular inflammation

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 08/05/2024, West Midlands - South Birmingham Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8345; southbirmingham.rec@hra.nhs.uk), ref: 24/WM/0068

Study design
Observational cross-sectional study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Whole-body imaging using 99mTc-Maraciclatide for rheumatoid and psoriatic arthritis

Interventions
STUDY DESIGN: Cross-sectional Observational Imaging Study. This study includes a maximum of four research visits. All visits will occur at Leeds Teaching Hospitals Trust, Chapel Allerton Hospital or St James University Hospital. At separate visits post-screening and in a randomised visit order, all participants will undergo:
1) Whole body multi-joint contrast-enhanced MRI scan and Ultrasound scan
2) Whole-body multi-joint gamma scintigraphy imaging using 99mTc-Maraciclatide In addition, there is the option to take synovial biopsy samples from participants, which may occur during an additional visit. There will be a maximum of 14 days between MRI and 99mTc-Maraciclatide imaging visits.

RECRUITMENT: In this study, individuals with Rheumatoid Arthritis and Psoriatic Arthritis will be recruited from routine clinics at Chapel Allerton Hospital. The IMAGE-IA research team members are embedded in NHS clinics and therefore form part of the direct care team. Other potential participants would be referred to the research team (by LTHT colleagues in NHS clinics) for initial review/approach.

Screening: After the participant has had a chance to review the information sheet, and to discuss any queries with a study investigator, they will be asked to complete and sign a consent form, and will be allocated a unique study ID code.

The research team will then perform the following routine checks to ensure that it is appropriate and safe for the participant to take part, some of which may be additional to regular care:
• Blood tests (Liver Function Test [LFT], Urea and Electrolytes [U&E], Erythrocyte Sedimentation Rate [ESR], C-Reactive Protein [CRP], high-sensitivity CRP[hsCRP], Rheumatoid Factor [RF], anti-CCP Ab)
• Pregnancy test (for females of childbearing potential, i.e. where the individual has had a menstrual period in the last 24 months and has not had a hysterectomy or surgical sterilisation)
• Height and body mass
• Medical history
• Physical exam
• Vital signs
• Review of medications

• Questionnaires
• Joint assessment
• Physician assessment of disease activity (VAS)
• X-ray Skull (only to be performed if there is a need to confirm/exclude)

In patients with PsA, the following assessments will also be performed:
• Enthesitis Index (a measure of inflammation where the tendons or ligaments attach to the bone)
• Dactylitis Count (a measure of swelling in the fingers and toes)
• HLA-B27 (a genetic marker of disease activity/classification). This will be accessed from routine clinical care where available.

The screening period will last up to 2 weeks, at which point the study doctor will be able to confirm eligibility. This 2-week period provides time for receipt and review of all screening tests as there may be a delay in the processing of laboratory tests. It is expected that only a single screening visit will be required. The order of the next two visits (MRI and US Imaging vs. Nuclear Medicine Imaging) will be randomised, once eligibility has been confirmed.

Screening data from ineligible participants will be recorded at the source, entered into the study database, and may be used for analysis.

RANDOMISATION: The order of the imaging visits will be randomised between participants. Participants in each study group (RA and PsA) will be randomised 1:1 to undergo MRI and PDUS Imaging at Visit 2 or 99mTc-Maraciclatide Imaging at Visit 2. The remaining Imaging Visit will be allocated to Visit 3 for each participant. Randomisation will be performed using the permuted blocks method using commercially available software (https://www.sealedenvelope.com). The block sizes will be concealed from the investigators. The purpose of visit randomisation is to control against any visit order effect influencing the results of the imaging assessments.

MRI and US Imaging
Participants will have an MRI scan which will last approximately 2 hours. Participants will complete a safety questionnaire to ensure that they have no history of surgery involving metallic surgical clips or have metal particles in their bodies. In a small proportion of individuals where this is not clear, an x-ray of the relevant body part to exclude the presence of any metallic objects will be performed before MRI. The participant will lie down inside the MRI scanner in different positions for joint imaging. The MRI scanner will take images of the shoulders, wrists, hands, knees, ankles and feet. A single injection in the participant's arm will be performed partway through the scan. The injection is done to see any changes in the joints more clearly and is commonly called ‘a contrast agent’. The contrast agent in this study is called ‘Gadolinium’, which is routinely used in NHS care to provide clearer MRI images.

An ultrasound (US) examination of the joints will also be performed during this visit. This will last approximately 45 minutes.

Nuclear Medicine Imaging (Maraciclatide Scan): This imaging visit will take place at St James University Hospital, within the Nuclear Medicine Department. First, participants will have a small injection into a vein in their arm. This injection will contain a very small amount of radioactive material called a radiotracer (Maraciclatide). The participant will wait for up to approximately 2 hours after the injection to allow time for the radiotracer to circulate through the body. Participants will be able to leave and return to the Nuclear Medicine Department during this time.

Next, participants will lie down on a table between two specialist cameras, which will image their whole body. This procedure will last for ~20 minutes. After the whole-body scan, we will take focused scans of the hands and feet specifically.

In total, the scans of the hands and feet will last for ~10 minutes. In total this visit will last for up to 3 hours.

OPTIONAL: Joint Biopsy (synovial tissue) Participants will be offered the option of having a biopsy of one of their symptomatic (inflamed) joints. This is not mandatory for participation in the study. The biopsy will take place at a separate visit, or during the MRI and US Imaging visit. The biopsy will take place in a clinic room at Chapel Allerton Hospital. An appropriately trained MSK radiographer will perform the biopsy.

A small amount of tissue from the lining of an inflamed joint will be taken using a special instrument and guided by an ultrasound scan. Some joint fluid may also be collected. The joint chosen is usually the knee but can be another joint depending on which joints are actively inflamed. This procedure will take approximately 30 minutes and uses a small narrow instrument (less than the width of a pencil). The joint will be injected with local anaesthetic to minimise any pain. The instruments needed to take the biopsy are passed through the anaesthetised skin. All these instruments are removed at the end of the procedure. The joint will need to be rested for at least one day following the procedure.

IMAGING ABNORMALITIES: Any clinical abnormalities identified during any of the imaging assessments will be reported to the patient's clinical care team. This process will follow standard NHS care procedures.

SERIOUS ADVERSE EVENTS (SAEs): SAEs will be recorded from participant arrival at each respective imaging visit to 24 hours after the respective imaging assessment. The Investigator must instruct the participant to report all SAEs during these periods. Participants will be asked to report any suspected SAEs to an investigator via telephone. If a suspected SAE occurs, participants will be invited to return to the clinic for a clinical evaluation. All SAEs will be reported to the Sponsor [governance-ethics@leeds.ac.uk] using the ‘non-CTIMP Safety Report Form’, available from the HRA website. Any SAE that is considered as both likely to be related to the protocol treatment and unexpected, as determined by the Chief Investigator, will be deemed a related and unexpected SAE (RUSAE). All RUSAEs will be reported to the study Sponsor [governance-ethics@leeds.ac.uk] using the ‘non-CTIMP Safety Report Form’, available from the HRA website. All RUSAEs will be reported to the Sponsor within 1 working day of awareness. The CI will then inform the Research Ethics Committee (REC) that gave a favourable opinion for the study of RUSAEs within the required expedited reporting timescales. RUSAEs must be reported to the REC within 15 calendar days of the CI (or their research team) being informed of the event.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Individual site (enthesis/tendon/joint) inflammation (synovitis) measured by 99mTc-Maraciclatide present Y/N (0 absent, 1 present) at one time point

Key secondary outcome(s))

The following secondary outcome measures are assessed at one time point:
1. Individual joint inflammation RAMRIS synovitis score measured using contrast-enhanced MRI (0-3) (MCPs and wrist joints only)
2. Individual site (enthesis/tendon/joint) inflammation (synovitis) measured using contrast-enhanced MRI (0-2)
3. Total entheseal inflammation count measured using contrast-enhanced MRI (0-10)
4. Total tendon inflammation count measured using contrast-enhanced MRI (0-10)
5. Small joint inflammation (synovitis) count measured using contrast-enhanced MRI (0-32)
6. Total joint inflammation (synovitis) count measured using contrast-enhanced MRI (0-38)
7. Individual site (enthesis/tendon/joint) inflammation (synovitis) score measured using PDUS (0-3)
8. Individual site (enthesis/tendon/joint) inflammation (synovitis) measured using PDUS present Y/N (0=0 absent, >0=1 present)
9. Total entheseal inflammation count measured using PDUS (0-10)
10. Total tendon inflammation count measured using PDUS (0-26)
11. Small joint inflammation (synovitis) count measured using PDUS (0-32)
12. Total joint inflammation (synovitis) count measured using PDUS (0-38)
13. Total extra-joint inflammation count measured using 99mTc-Maraciclatide uptake in sites co-located with entheses (0-10)
14. Total extra-joint inflammation count measured using 99mTc-Maraciclatide uptake in sites co-located with tendons (0-20)
15. Small joint inflammation (synovitis) count measured using 99mTc-Maraciclatide uptake (0-32)
16. Total joint inflammation (synovitis) count measured using 99mTc-Maraciclatide uptake (0-38)
17. (Optional) Individual joint inflammation (synovitis) score measured using histopathology (0-9)
18. (Optional) Individual joint inflammation (synovitis) measured using histopathology present Y/N (0-1 negative; 2-9 positive)
19. Health status measured using the Health Assessment Questionnaire Disability Index (HAQ-DI) (0-3) and participant completed general health VAS (0-100)
20. Physician assessment of disease activity measured using VAS (0-100)
21. Participant assessment of disease activity measured using VAS (0-100)
22. Participant assessment of fatigue measured using VAS (0-100)
23. Number of tender joints measured using Tender Joint Count (TJC) 28/68
24. Number of swollen joints measures by Swollen Joint Count (SJC) 28/66
25. Number of joints with enthesitis in participants with PsA measured using Leeds Enthesitis Index (0-6)
26. Number of joints with dactylitis in participants with PsA measure by Total Dactylitis Count (0-20)
27. Disease activity score measured using DAS28 (0-10) in participants with RA and DAPSA (0-164) in participants with PsA

Completion date
23/03/2026

Eligibility

Key inclusion criteria
1. Age > = 18 years old
2. The participant is able and willing to comply with all study procedures as described in the protocol
3. Is capable of understanding and signing an informed consent form

4. Prior diagnosis of Rheumatoid Arthritis (RA) as determined by the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Classification Criteria; or prior diagnosis of PsA according to the CASPAR criteria
5. Low, moderate or high disease activity as determined by DAS28 score (RA) or DAPSA score (PsA). Individuals in remission, as determined by DAS28 or DAPSA, will not be included.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. The participant size or body mass is not compatible with imaging as determined by the investigator
2. The participant has a known allergy to or has had an adverse reaction to any components or excipients of Maraciclatide (99mTc) Injection
3. The participant is pregnant or currently breastfeeding, and are unwilling to stop breastfeeding for a minimum of 12 hours after the Maraciclatide (99mTc) Imaging visit
4. The participant has any severe, acute, or chronic medical conditions and/or psychiatric conditions and/or laboratory abnormalities that would impart, in the judgment of the investigator, excess risk associated with any of the study procedures that would deem the participant inappropriate for study participation
5. Participant with severe renal disease (eGFR < 45 ml/min/1.73m2) or acutely deteriorating renal function, who would be at risk of nephrogenic systemic fibrosis
6. The participant has hepatic insufficiency as demonstrated by alanine aminotransferase (ALT) or aspartate aminotransferase (AST) of > 3 times the upper limit of normal
7. The participant has a known allergy or previous anaphylactic reaction to a gadolinium-based contrast agent
8. The participant has: a pacemaker, surgical clips within the head*, certain inner ear implants, or neuro-electrical stimulators or metal fragments within the eye or head
9. The participant has any other known contraindication, in the opinion of the investigator, to contrast-enhanced MRI imaging
10. The participant that has one of the following joints unavailable for imaging (e.g. due to injury, joint-replacement, or missing joints): shoulder, wrist, MCP, PIP, knee, ankle, MTP
11. The participant has received any radiopharmaceutical within 7 days or 10 half-lives before screening
12. The participant has received intramuscular or intravenous steroids < = 4 weeks before screening
13. The participant has received intra-articular corticosteroid injections < = 4 weeks before

screening
14. The participant has a known inability to manage pain effectively with alternative forms of analgesia to NSAIDs (e.g. Paracetamol, Codeine)

*X-ray may be requested if there is a need to confirm/exclude the presence of surgical clips or metal fragments in the eye/head.

Date of first enrolment
15/07/2024

Date of final enrolment
23/02/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St. James's University Hospital
Beckett Street
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Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Serac Healthcare Ltd

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

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	Participant information sheet	11/11/2025	11/11/2025	No	Yes