

# Oral versus intramuscular glucocorticoids in rheumatoid arthritis

<b>Submission date</b> 26/11/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 04/02/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 01/09/2025	<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) causes joint pain and swelling affecting people's daily activities and quality of life. The National Institute for Health and Care Excellence advise treatment with drugs called anti-rheumatic medicines, but they can take up to 6 months to work. Whilst waiting for these medicines to take effect, patients are offered another type of drug, steroids, which act quickly to control symptoms. Unfortunately, steroids have long-term side effects such as diabetes, weight gain and skin changes, so should only be used for short periods of time. Steroids can be given as an injection into the muscle or as a daily tablet. Doctors currently do not know whether it matters which of these and what dose has the best balance between side effects and rapid symptom relief.

The LEADER trial aims to find the most effective and safest way of using steroids for patients with uncontrolled RA who are starting a new anti-rheumatic medicine.

### Who can participate?

To join this study, participants must be 18 or older and have rheumatoid arthritis that meets specific criteria. They should have active disease with at least three tender and three swollen joints. Participants must be planning to start, switch, or increase their medication for rheumatoid arthritis. They need to be open to being assigned to any treatment group in the study and must be able to give informed consent.

### What does the study involve?

The trial will compare 4 different doses/ways of taking steroids: 1) higher dose steroid tablets that reduce in dose over six weeks, 2) lower dose steroid tablets that reduce in dose over four weeks, 3) a one-off higher dose steroid injection or 4) a one-off lower dose steroid injection. Participants will be assessed regularly during the first 3 months and at 6 months to see how the treatment has affected their symptoms. The trial will compare how active the RA is, between tablets and injection and also dose levels, to find out which treatment is most effective. The trial will also look at what impact the different doses and ways of taking steroids have on fatigue, ability to do day-to-day activities and work, quality of life, the amount of pain killers used and value for money to the NHS. Side effects such as weight gain and mood changes will be assessed and an at-home finger-prick blood sample will test if the steroid has affected the ability to produce a key hormone that controls the body's stress response and blood pressure.

What are the possible benefits and risks of participating?

Benefits:

Not provided at time of registration

Risks:

The LEADER trial is comparing different routes of administration and regimes that are commonly used for standard care treatment. The IMPs (oral prednisolone tablets and intramuscular methylprednisolone) are being used in the LEADER trial within their licensed indications and have well established safety profiles. The prescribing and dispensing of all IMPs will follow usual practice at participating sites. Treatment is therefore comparable with standard medical care.

Burdens: One extra visit, Completion of weekly pain VAS, Longer standard of care visits, Completion of questionnaires

Completion of finger prick blood test at home.

Extra blood needed for the trial is being collected at the same time of routine blood when ever possible, so only 1 additional blood draw will be needed - at the week 2 visit which is an additional visit for the study only.

Where is the study run from?

University of Manchester (UK)

When is the study starting and how long is it expected to run for?

November 2024 to March 2027

Who is funding the study?

National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?

leader@ndorms.ox.ac.uk

## Contact information

**Type(s)**

Public, Scientific

**Contact name**

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**Type(s)**

Principal investigator

**Contact name**

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**Additional identifiers****Clinical Trials Information System (CTIS)**

Nil known

**Integrated Research Application System (IRAS)**

1010280

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

R130178, CPMS 57018

**Study information****Scientific Title**

The clinical and cost effectiveness of oral vErsus intrAmuscular glucocorticoiDs in rhEumatoid aRthritis

**Acronym**

LEADER

**Study objectives**

Primary objective:

To compare the mean DAS(CRP)-28 over 12 weeks in adult patients with active RA commencing IM or oral short-term bridging GC therapy who are initiating, escalating or switching DMARD therapy.

Secondary objectives:

1. To compare the effect of:

1.1. Two IM GC dose regimens on mean DAS(CRP)-28, American College of Rheumatology (ACR) response, and EULAR Modified Boolean remission over 24 weeks.

1.2. Two PO GC dose regimens on mean DAS(CRP)-28, ACR response, and EULAR Modified Boolean remission over 24 weeks.

1.3. Oral and IM GC on analgesic use.

1.4. Oral and IM GC on patient-reported outcomes.

1.5. Oral and IM GC on toxicity.

1.6. Oral and IM GC on cumulative GC dose.

2. To conduct an economic evaluation.

3. To assess GC bridging therapy acceptability.

4. To conduct a qualitative study of GC bridging therapy acceptability.

5. To conduct a qualitative study of patients who decide not to take part during the pilot phase to explore their views and perspectives of non-participation to identify barriers to recruitment.
6. To conduct a qualitative study of healthcare professionals to explore their experiences and views of delivering LEADER and recruitment and retention of trial participants.

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

approved 03/02/2025, Leicester Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048227 ; leicestercentral.rec@hra.nhs.uk), ref: 24/EM/0277

### **Study design**

Interventional assessor blinded randomized parallel group controlled trial

### **Primary study design**

Interventional

### **Study type(s)**

Safety, Efficacy

### **Health condition(s) or problem(s) studied**

Rheumatoid arthritis

### **Interventions**

Arm A (PO30) Oral glucocorticoid (prednisolone) tablets. Starting dose of 30 mg once daily tapered down after each week over 5 weeks to 5 mg once daily. Total treatment duration is 6 weeks.

Arm B (PO15) Oral glucocorticoid (prednisolone) tablets. Starting dose of 15mg once daily tapered down after each week over 3 weeks to 5mg once daily. Total treatment duration is 4 weeks.

Arm C (IM120) One-off 120mg intramuscular glucocorticoid injection (methylprednisolone). Treatment duration is 1 day.

Arm D (IM80) One-off 80mg intramuscular glucocorticoid injection (methylprednisolone). Treatment duration is 1 day.

Each participant will be followed up for 24 weeks from randomisation, with in-person appointments at Weeks 2, 4, 8, 12 and 24. The follow-up schedule is the same across all four trial arms.

The participant randomisation process will be completed online using a randomisation tool embedded within the trial database.

### **Intervention Type**

Drug

### **Phase**

## Phase III

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

Prednisolone, methylprednisolone

### Primary outcome(s)

DAS(CRP)-28 - disease activity at Baseline, Weeks 2, 4, 8, 12

### Key secondary outcome(s)

1. Disease activity is measured using EULAR Boolean remission and ACR20/50/70 at Baseline, Weeks 2, 4, 8, 12 and 24; and using DAS(CRP)-28 at Baseline, Weeks 2, 4, 8 and 12.
2. Patient-reported outcomes are measured using FACIT, VAS (pain), RA-QoL, WPAI, and HAQ-DI at Baseline, Weeks 2, 4, 8, 12, and 24; pain is measured weekly from Baseline to Week 24.
3. Analgesic use is measured by collecting patient's analgesic usage at Baseline, Weeks 2, 4, 8, 12, and 24.
4. Toxicity is measured using an early morning cortisol suppression at Week 12; collecting a GTI (glucocorticoid toxicity index) at Baseline, Weeks 12 and 24; collecting adverse events of special interest (AESIs) at Weeks 12 and 24; and by assessing for skin changes at injection site (IM arms only) at Weeks 2, 4, 8, 12 and 24.
5. Cumulative dose is measured by two methods: first, by collecting data from patient's medical notes on their GC dose prescribed, collected at Baseline, Weeks 2, 4, 8, 12, and 24; and secondly, by collecting data on patient's GC adherence to treatment allocation, collected from
  - (i) Oral Arm participants weekly from Baseline to Week 24 via participant-reported steroid diaries, and
  - (ii) from IM Arm participants at Baseline, Weeks 2, 4, 8, 12 and 24 via participant's medical notes.
6. Economic evaluation is measured using a healthcare resource utilisation questionnaire at Baseline, Weeks 2, 4, 8, 12, and 24; EQ-5D-5L at Baseline, Weeks 4, 12 and 24; and collecting Medication usage at Baseline, Weeks 2, 4, 8, 12 and 24.
7. Therapy acceptability to patients is measured using TFA at Weeks 12 and 24; BMQ-specific at Baseline, Weeks 12 and 24; and interviews and/or focus groups post-Week 24.
8. Barriers to recruitment are measured using 1:1 interviews with patients who decline participation during the first 9 months of recruitment.
9. Experience and views of healthcare professionals are measured using 1:1 interviews and/or focus groups from the start of recruitment to the end of the trial.

### Completion date

31/03/2027

## Eligibility

### Key inclusion criteria

1. Aged 18 years or over
2. Diagnosed with rheumatoid arthritis that either currently or historically fulfils 2010 ACR /EULAR RA classification criteria
3. Active disease defined as  $\geq 3$  tender and  $\geq 3$  swollen joints
4. Planning on initiating/switching to/escalating to a conventional synthetic (cs), biologic (b) or targeted synthetic (ts) DMARD
5. Willing and able to accept either trial arm allocation
6. Willing and able to give informed consent

### Participant type(s)

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

1. Oral, intramuscular or intra-articular glucocorticoid therapy within the past 3 months
2. Glucocorticoid therapy contraindicated (as determined by treating clinician)
3. Diagnosed within the last 6 months with fibromyalgia or chronic widespread pain
4. Known to be pregnant or female patient trying to conceive
5. Unstable or uncontrolled diabetes
6. Participating or planning to participate in another interventional clinical study/trial during the study period that in the opinion of the Investigator could affect LEADER outcomes
7. Any other severe concomitant disease that, in the opinion of the investigator, might interfere with trial procedures and/or assessments

**Date of first enrolment**

04/07/2025

**Date of final enrolment**

30/06/2026

## **Locations**

**Countries of recruitment**

United Kingdom

**Study participating centre**

**Pennine MSK Partnership Ltd**

Integrated Care Centre

New Radcliffe Street

Oldham

United Kingdom

OL1 1NL

**Study participating centre**

**Derriford Hospital**

Derriford Road

Derriford  
Plymouth  
United Kingdom  
PL6 8DH

**Study participating centre**

**Worthing Hospital**

Lyndhurst Road  
Worthing  
United Kingdom  
BN11 2DH

**Study participating centre**

**Eastbourne District General Hospital**

Kings Drive  
Eastbourne  
United Kingdom  
BN21 2UD

**Study participating centre**

**King's College Hospital**

Denmark Hill  
London  
United Kingdom  
SE5 9RS

**Study participating centre**

**Whiston Hospital**

Warrington Road  
Prescot  
United Kingdom  
L35 5DR

**Study participating centre**

**Rochdale Infirmary**

Whitehall Street  
Rochdale  
United Kingdom  
OL12 0NB

**Study participating centre**  
**Fairfield General Hospital**  
Rochdale Old Road  
Bury  
United Kingdom  
BL9 7TD

**Study participating centre**  
**Airedale NHS Foundation Trust**  
Airedale General Hospital  
Skipton Road  
Steeton  
Keighley  
United Kingdom  
BD20 6TD

**Study participating centre**  
**County Durham and Darlington NHS Foundation Trust**  
Darlington Memorial Hospital  
Hollyhurst Road  
Darlington  
United Kingdom  
DL3 6HX

## **Sponsor information**

**Organisation**  
University of Manchester

**ROR**  
<https://ror.org/027m9bs27>

## **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

## Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are/will be available upon request from the Chief Investigator and in accordance with the data sharing policies of OCTRU, the Sponsor and funder(s).

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes