

Trial of stopping or continuing biologics ahead of orthopaedic surgery

Submission date 27/04/2023	Recruitment status Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 03/05/2023	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 11/10/2024	Condition category Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English Summary

Background and study aims

Rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis are common forms of inflammatory arthritis. They are caused by an overactive immune system and are treated with medicines that reduce pain and inflammation. In recent years, special immune-suppressing medicines, called biologics, have been developed, which are very effective in controlling the arthritis disease process and symptoms but can increase the risk of some infections. People with inflammatory arthritis often need orthopaedic surgery (e.g. joint replacement) to relieve pain and improve function due to the damage caused by arthritis. The potential for increased risk for surgical site infections is a particular concern for patients undergoing orthopaedic surgery as these can be associated with long-term pain and the need for further surgery. Currently, biologics are usually stopped before any planned operation to try and reduce the risk of infection and other complications such as slow wound healing. However, stopping biologics increases the risk of painful and debilitating flares and delays recovery from surgery. Flares are often treated with steroids, which can increase the infection risk and delay wound healing. There are no randomised trials to support the current guidance on stopping biologics before surgery.

Who can participate?

Patients over the age of 18 who have inflammatory arthritis, are taking biologic medications, and are due to have orthopaedic surgery.

What does the study involve?

Participants will either be asked to stop taking their biologic medication or continue taking it ahead of their surgery, this will be decided at random by a computer.

Both groups of participants will then be followed up for 1 year after their surgery to see whether there was a difference in their quality of life, arthritis disease activity, infections, hospital admissions, and the cost of these treatments.

What are the possible benefits and risks of participating?

The results of this study will help us find out how best to treat patients with inflammatory arthritis who need orthopaedic surgery in the future. As with any treatment, there are possible risks and benefits. The risk for these treatments includes the potential for a flare of arthritis and the potential for an infection after surgery. Participating in this study will not harm or

disadvantage participant's care and participants will be monitored regularly as part of usual NHS care.

Where is the study run from?
University of York (UK)

When is the study starting and how long is it expected to run for?
September 2022 to June 2026

Who is funding the study?
National Institute for Health and Social Care Research (NIHR) (UK)

Who is the main contact?
Samantha Brady, samantha.gascoyne@york.ac.uk

Study website

<https://www.york.ac.uk/healthsciences/research/trials/ytutrialsandstudies/trials/periscope/>

Contact information

Type(s)
Scientific

Contact name
Dr Samantha Brady

ORCID ID
<http://orcid.org/0000-0001-7763-2776>

Contact details
University of York
York Trials Unit
Department of Health Sciences
York
United Kingdom
YO10 5DD
+44 (0)1904 321926
samantha.gascoyne@york.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
321501

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

CPMS 55648, IRAS 321501

Study information

Scientific Title

PERI-operative biologic DMARD management: Stoppage or COntinuation during orthoPaEdic operations: The PERISCOPE trial

Acronym

PERISCOPE

Study hypothesis

What are the benefits and harms of continuation versus stoppage of biologics in patients with inflammatory arthritis undergoing orthopaedic surgery?

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 24/04/2023, West of Scotland REC 3, (West of Scotland Research Ethics Service, Ground Floor Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, UK; +44 (0)141 314 0212; WoSREC3@ggc.scot.nhs.uk), ref: 23/WS/0049

Study design

Multicentre superiority randomized controlled trial parallel-group and an internal pilot economic evaluation and nested qualitative study

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital, Internet/virtual, Medical and other records

Study type(s)

Treatment

Participant information sheet

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

Condition

Rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, forms of inflammatory arthritis

Interventions

Stoppage of biologic: Participants will stop their biologic ahead of surgery in line with the British Society of Rheumatology guidelines

Continuation of biologic: Participants will continue their biologic as normal ahead of surgery and throughout the peri-operative period

Trial design:

PERISCOPE is a multi-centre, 394-patient, superiority randomised controlled trial with parallel groups, with an internal pilot, economic evaluation and nested qualitative study.

Blinding: Blinding is not possible given the nature of the intervention.

Intervention arm:

Continuation of the named bDMARDs throughout the peri-operative period as prescribed prior to surgery. All other aspects of care will continue as per usual practice, including concomitant non-bDMARDs and post-surgical rehabilitation.

Usual care arm:

Stoppage of bDMARDs prior to surgery and recommencing treatment after wound healing and removal of sutures/clips, according to BSR recommendations. Given the pragmatic nature of the PERISCOPE trial, for any instances where a participant's surgery may be delayed (for medical or non-medical reasons), it will be at the clinician's discretion as to whether a participant needs to recommence bDMARDs whilst the surgery is rescheduled as per current clinical practice.

Data collection:

Following baseline assessments and randomisation, participants will be scheduled for their orthopaedic surgery and will complete follow-up assessments at 2, 4, 6, 9, 12, 26, and 52 weeks post-surgery. All outcome measures collected from patients are validated measures. The visits and the data collected are summarised below:

Screening: Confirmation of the participant's eligibility, including the type of inflammatory arthritis and biologic. This is collected by investigator CRF and review of patient medical history. This is a face-to-face visit in the clinic.

Baseline: Participant demographics, disease history, primary outcome data, secondary outcome data - note that outcomes relating to surgery (e.g. wound healing and surgical satisfaction), and adverse events are not collected at this time point. This is collected by a participant questionnaire, investigator CRF and review of patient medical history.

This is a face-to-face visit in the clinic.

2,6,12,52 Week Follow-ups: All Primary and secondary outcome measures. This is collected by a participant questionnaire, investigator CRF and review of patient medical history. These are face-to-face visits in the clinic that are research-specific visits, however, they may coincide with routine surgical follow-ups.

4,9 Week Follow-ups: The primary outcome measure is the only outcome collected at this timepoint and is collected by participant questionnaire. This is a remote visit (post/email)

26 Week follow-up: This is collected by a participant questionnaire. The primary and secondary outcomes are collected at this time point - note that as this data is collected remotely, outcomes collected by investigators (disease-specific measures, adverse events, disease activity (Physician), and wound healing are not collected at this time point.

This is a remote visit (post/email)

The disease-specific outcomes involve both patient questionnaires and clinician physical examinations and are completed at the baseline, 2-, 6-, 12-, and 52-week timepoints, these are collected as part of standard care.

Internal Pilot and recruitment rate:

An internal pilot phase in a small number of centres will run during the first 9 months of the main trial, which will assess the assumptions about recruitment and provide guidance on optimising the trial processes.

The recruitment projection is based on 20 centres recruiting 1-2 patients per month for 25 months. The total sample size is 394 participants.

Patient identification:

Patients will be screened for the study who are; aged 18 or over; who have a diagnosis of RA, PsA, AS (including the juvenile onset of all three), who are currently prescribed the following bDMARDs: TNF inhibitors (adalimumab /etanercept/ golimumab/certolizumab pegol/infliximab); CTLA4-Ig (abatacept); IL-6 inhibitors (tocilizumab/sarilumab); IL-12/23 inhibitors (ustekinumab); IL-17 inhibitors (secukinumab/ixekizumab); IL-23 p19 inhibitor (guselkumab/risankizumab); and are scheduled to undergo elective orthopaedic surgery.

Potentially eligible participants will be identified by screening the waiting lists for orthopaedic surgery across the participating sites. Many of these patients will be identified in the combined rheumatology-orthopaedic Multidisciplinary team clinics (MDT clinics). In addition, patients with inflammatory arthritis and on bDMARDs presenting to secondary care with an orthopaedic problem needing a surgical intervention will be screened for eligibility by the local team and approached to establish if they are potentially interested in participating in the study.

Only patients who are willing and able to give informed consent for participation in the study will be enrolled and they may request to leave the study at any time and without needing to provide the research team with a reason.

Pragmatic design: The trial is designed to be pragmatic and not to be a burden to patients; we intend to align follow-up assessments with regular hospital visits, which are common in patients who have undergone elective orthopaedic surgery. There will be three patient questionnaires at 4 (PROMIS-29 only), 9 (PROMIS-29 only), and 26 weeks, which do not align with hospital visits. These questionnaires will either be emailed to the participant, collected over the telephone with a researcher, or posted out for completion (a free post envelope will be included for return).

Qualitative study: The PERISCOPE trial will integrate a qualitative study in parallel to the internal pilot and full trial. This will focus on the patients' and clinicians' acceptability and experience of continuation/stoppage of bDMARDs in the perioperative period, and the impact post-operatively. Participation will be optional for patients (included on main study consent form).

Health care staff will be provided with a PIS and consent form. Interviews are likely to be a mixture of face-to-face, video (via Zoom) or telephone call. If interviews are conducted face to face this will be in a location convenient to the participant (i.e. their home, NHS premises).

Healthcare staff: Semi-structured interviews with approximately 10 orthopaedic surgeons and 10 rheumatologists. The interviews will last around 30 to 40 minutes.

Patients: Semi-structured interviews with 30 patients (25 trial participants and 5 patients who declined to participate in the trial). The purpose is to explore the acceptability and experience of continuing/stopping bDMARDs in the pre-operative period and how the potential trade-off between risks of infection versus disease flare is perceived by patients. The interview is likely to last between 30–60 minutes.

Declining site leads: A purposive sample of up to 10 of declining site leads will be invited to take part in brief, semi-structured telephone interviews lasting around 15-20 minutes. The interview questions will further explore the reasons why their site declined to take part in the trial.

PPI perspective: In preparation for the PERISCOPE trial a number of patient advisory group (PAG) meetings have been conducted in Leeds and Oxford. The patient engagement work has included 17 people with IA (RA, PsA, AS and JIA: all represented) who are taking bDMARDs and have had orthopaedic surgery. The study protocol presented here was co-produced with the PAG, including inclusion and exclusion criteria, study schedule and primary and secondary outcome measures, including outcome assessment tools, as well as ways to support diversity and inclusivity in PERISCOPE.

Intervention Type

Biological/Vaccine

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

bDMARDs and biosimilars of: TNF inhibitors (e.g. adalimumab /etanercept/ golimumab /certolizumab pegol/infliximab); CTLA4-Ig (e.g. abatacept); IL-6 inhibitors (e.g. tocilizumab /sarilumab); IL-12/23 inhibitors (e.g. ustekinumab); IL-17 inhibitors (e.g. secukinumab /ixekizumab); IL-23 p19 inhibitors (e.g. guselkumab/risankizumab)

Primary outcome measure

Self-reported physical, mental, and social health measured using the Patient Reported Outcomes: Measurement Information System (PROMIS-29) questionnaire over the first 12 weeks (2, 4, 6, 9, and 12 weeks) post-surgery

Secondary outcome measures

Current secondary outcome measures as of 16/02/2024:

1. Self-reported physical, mental, and social health measured using the Patient Reported Outcomes: Measurement Information System (PROMIS-29) questionnaire at 26 and 52 weeks post-surgery
 2. Level of disability measured using the PROMIS Health Assessment Questionnaire Disability Index (HAQ) at 2, 6, 12, 26, and 52 weeks post-surgery
 3. Health-related quality of life measured using EQ-5D-5L at 2, 6, 12, 26, and 52 weeks post-surgery
 4. Disease activity measured using a generic global numeric rating scale (NRS) at 2, 6, 12, 26, and 52 weeks post-surgery
 5. Medication use measured using patient medical records at 2, 6, 12, 26, and 52 weeks post-surgery
 6. Healthcare resource use measured using patient medical records at 2, 6, 12, 26, and 52 weeks post-surgery
 7. Disease activity measured using a generic global numeric rating scale as assessed by the treating physician at 2, 6, 12, and 52 weeks post-surgery
 8. Surgical site infection, defined by the 1992 CDC criteria, measured using patient medical records at 2,6,12,52 weeks post-surgery
 9. Delayed wound healing, defined as a surgical incision that has healed by primary intention without any evidence of gaping or dehiscence. Any wound that has not healed fully by primary intention by 2 weeks post-surgery, will be considered as "delayed wound healing" confirmed at 2, 6, 12, 52 weeks post surgery
 10. Disease-Specific outcomes are measured using the following methods at 2, 6, 12, and 52 weeks post surgery:
 - 10.1. Clinical Disease Activity Index for Rheumatoid Arthritis (CDAI)
 - 10.2. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
 - 10.3. Bath Ankylosing Spondylitis Functional Index (BASFI)
 - 10.4. Assessment of Spondyloarthritis International Society Health Index (ASAS-HI)
 - 10.5. 66/68 Joint count
 - 10.6. Leeds Enthesitis Index (LEI)
 - 10.7. Body surface area (BSA) for skin
 - 10.8. Dactylitis Severity Score (DSS)
 - 10.9. Numerical rating scale (NRS)
-

Previous secondary outcome measures:

1. Disease-specific outcomes measured using the PROMIS-29 questionnaire at 26 and 52 weeks post-surgery
2. Level of disability measured using the PROMIS Health Assessment Questionnaire Disability Index (HAQ) at 2, 6, 12, 26, and 52 weeks post-surgery
3. Health-related quality of life measured using EQ-5D-5L at 2, 6, 12, 26, and 52 weeks post-surgery
4. Disease activity measured using a generic global numeric rating scale (NRS) at 2, 6, 12, 26, and 52 weeks post-surgery
5. Medication use measured using patient medical records at 2, 6, 12, 26, and 52 weeks post-surgery
6. Healthcare resource use measured using patient medical records at 2, 6, 12, 26, and 52 weeks post-surgery
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 - 10.7. Body surface area (BSA) for skin
 - 10.8. Dactylitis Severity Score (DSS)
 - 10.9. Numerical rating scale (NRS)

Overall study start date

01/09/2022

Overall study end date

30/06/2026

Eligibility

Participant inclusion criteria

Current inclusion criteria as of 11/10/2024:

1. Adults aged 18 years and over with RA, PsA, or AS (including juvenile onset of all three)
2. Currently prescribed one of the following bDMARDs: TNF inhibitors (e.g. adalimumab /etanercept/ golimumab/certolizumab pegol/infliximab); CTLA4-Ig (e.g. abatacept); IL-6 inhibitors (e.g. tocilizumab/sarilumab); IL-12/23 inhibitors (e.g. ustekinumab); IL-17 inhibitors (e.g. secukinumab/ixekizumab); IL-23 p19 inhibitors (e.g. guselkumab/risankizumab).
3. Deemed by the clinical care team to be fit for surgery and have no contraindications to

continued bDMARD use

4. Scheduled to undergo elective orthopaedic surgery (Soft tissue, metalwork, or Joint replacement)

5. Able to consent and complete follow-up

Previous inclusion criteria:

1. Consenting adults aged 18 and over with RA, PsA, AS (including the juvenile onset of all three)

2. Currently prescribed the following bDMARDs: TNF inhibitors (adalimumab /etanercept/ golimumab/certolizumab pegol/infliximab); CTLA4-Ig (abatacept); IL-6 inhibitors (tocilizumab /sarilumab); IL-12/23 inhibitors (ustekinumab); IL-17 inhibitors (secukinumab/ixekizumab); IL-23 p19 inhibitor (guselkumab/risankizumab).

3. Scheduled to undergo elective orthopaedic surgery

4. Deemed by the clinical care team to be fit for surgery and have no contraindications to continued biologic use

5. Able to consent and complete follow-up

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 394; UK Sample Size: 394

Participant exclusion criteria

1. Currently prescribed JAK inhibitors

2. Currently being treated with rituximab

3. Current use of systemic steroids (< 3 months) other than those on a stable dose of < = 5mg per day

4. Previous history of native/prosthetic joint infection

5. Undergoing revision surgery

6. Patients who are pregnant

Recruitment start date

05/05/2023

Recruitment end date

30/04/2025

Locations

Countries of recruitment

England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre**St. James's University Hospital**

Beckett Street

Leeds

United Kingdom

LS9 7TF

Study participating centre**Northern General Hospital**

Herries Road

Sheffield

United Kingdom

S5 7AU

Study participating centre**Queens Medical Centre**

Derby Road

Nottingham

United Kingdom

NG7 2UH

Study participating centre**Leicester Royal Infirmary**

Infirmary Square

Leicester

United Kingdom

LE1 5WW

Study participating centre

John Radcliffe Hospital

Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre**James Cook University Hospital**

Marion Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre**Manchester University NHS Foundation Trust**

Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre**Frimley Health NHS Foundation Trust**

Portsmouth Road
Frimley
Camberley
United Kingdom
GU16 7UJ

Study participating centre**Belfast City Hospital**

51 Lisburn Rd
Belfast
United Kingdom
BT9 7AB

Study participating centre**Royal Albert Edward Infirmary**

Wigan Lane
Wigan

United Kingdom
WN1 2NN

Study participating centre

Dewi Sant Hospital

Albert Road
Pontypridd
United Kingdom
CF37 1LB

Study participating centre

Great Western Hospital

Marlborough Road
Swindon
United Kingdom
SN3 6BB

Study participating centre

Hywel Dda University Lhb

Corporate Offices, Ystwyth Building
Hafan Derwen
St Davids Park, Jobswell Road
Carmarthen
United Kingdom
SA31 3BB

Study participating centre

Yeovil District Hospital

Higher Kingston
Yeovil
United Kingdom
BA21 4AT

Study participating centre

Kings Mill Hospital

Mansfield Road
Sutton-In-Ashfield
United Kingdom
NG17 4JL

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
Southport and Ormskirk Hospital NHS Trust
Town Lane
Southport
United Kingdom
PR8 6PN

Study participating centre

Amersham Hospital

Whielden Street
Amersham
United Kingdom
HP7 0JD

Study participating centre**Royal Derby Hospital**

Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre**Lincoln County Hospital**

Greetwell Road
Lincoln
United Kingdom
LN2 5QY

Study participating centre**The Royal London Hospital**

80 Newark Street
London
United Kingdom
E1 2ES

Study participating centre**Westmorland General Hospital**

Burton Rd
Kendal
United Kingdom
LA9 7RG

Sponsor information

Organisation

University of Leeds

Sponsor details

The Secretariat
Woodhouse Lane
Leeds
England
United Kingdom
LS2 9JT
+44 (0)113 3437587
governance-ethics@leeds.ac.uk

Sponsor type

Hospital/treatment centre

Website

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

ROR

<https://ror.org/024mrx33>

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

Publication and dissemination plan

- 1. Results will be published in peer-reviewed journals.
- 2. The findings will also be presented at relevant speciality conferences.
- 3. Documentation relating to the study will be made available as the study progresses.

Intention to publish date

30/06/2027

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be available from catherine.hewitt@york.ac.uk upon reasonable request. The release of any data will be provided in an anonymised format and securely transferred to the requester. Data will only be released in accordance with participants' consent. External data requests will only be considered once the main results paper has been published and for as long as York Trials Unit retains the data. Data requests will be considered by the Trial Management Group who will notify the Sponsor.

To inform the decision on data release, the requester should provide a protocol of the planned work that includes what data are required, the planned analyses and where the data will be securely stored. Data will only be shared with projects that the group consider to be well-justified and valuable secondary research projects. An agreement stating the conditions of data release should be in place before any data are shared with the requester.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No
Protocol article		25/06/2024	25/06/2024	Yes	No