ISRCTN70603700 https://doi.org/10.1186/ISRCTN70603700

Severe psoriatic arthritis – early intervention to control disease

Submission date
15/04/2019

Recruitment status
No longer recruiting

Registration date
26/04/2019

Overall study status
Completed

Last Edited
28/02/2025

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Psoriatic arthritis (PsA) is a type of inflammatory arthritis that can cause pain and joint damage if left untreated. We have already shown that a 'Treat to Target' approach where treatment is increased until a target was achieved for the patients for improved arthritis, psoriasis, quality of life, pain and function. However, there are no studies looking at which drugs work best in this 'Treat to Target' approach. The usual strategy is 'step-up' approach for all patients, whether they have mild or severe disease. This means at first one standard arthritis drug is used, then two standard drugs together and finally newer stronger biologic drugs for patients not responding to the other drugs. Previous studies in patients with severe disease suggested they may do better if they are treated with stronger drugs earlier. So the aim of this study is to see if patients with moderate to severe PsA do better if they start treatment with two drugs together at the beginning of their treatment or if they start on a biologic drug from the beginning.

Who can participate?
Patients recently diagnosed with moderate to severe PsA who have not previously taken any disease-modifying drugs (DMARDs) for arthritis.

What does the study involve?
Participants are randomly allocated to one of three treatment groups receiving: (1) the standard 'step-up' of arthritis drugs – receiving the standard drugs before the stronger biologics; (2) two standard arthritis drugs together; (3) stronger biologic therapy at the start. They have 12 weekly appointments up to 48 weeks which include clinical assessments of their PsA, blood tests and completion of questionnaires.

What are the possible benefits and risks of participating?
The drugs to be used are all current standard treatments for PsA, each with known safety profiles and side effects. The difference for participants is the timing of treatment and therefore the risk of side effects of the treatments received. The potential benefit is an improvement in symptoms and quality of life at an earlier timepoint but this is exploratory as yet.

Where is the study run from?
1. Oxford University Hospitals NHS Foundation Trust

2. Royal United Hospitals Bath NHS Foundation Trust
3. Cambridge University Hospitals NHS Foundation Trust

When is the study starting and how long is it expected to run for?
March 2017 to February 2025

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Laura Coates
laura.coates@ndorms.ox.ac.uk

Study website
https://www.ndorms.ox.ac.uk/octru/trials-portfolio/trials-open-to-recruitment/monitor

Contact information

Type(s)
Scientific

Contact name
Dr Laura Coates

Contact details
Botnar Research Centre
Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences
University of Oxford
Windmill Road
Oxford
United Kingdom
OX3 7LD
+44 (0)1865 737905
laura.coates@ndorms.ox.ac.uk

Additional identifiers

EudraCT/CTIS number
2017-004542-24

IRAS number

ClinicalTrials.gov number
NCT03739853

Secondary identifying numbers
37702

Study information

Scientific Title
Clinical effectiveness of standard step up care (methotrexate) compared to early combination DMARD therapy with standard step up care compared to early use of TNF inhibitors with standard step up care for the treatment of moderate to Severe Psoriatic arthritis: a 3-arm parallel group randomised controlled trial.

Acronym
SPEED

Study objectives
To compare the initial effectiveness of early combination DMARD therapy (arm 2) and early use of TNF inhibitors (arm 3) with standard step up care (received in the TWiCs cohort; arm 1).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 01/05/2018, South Central- Oxford B Research Ethic Committee (Whitefriars, Level 3, Block B, Lewin's Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)2071048058; nrescommittee.southcentral-oxfordb@nhs.net), ref: 18/SC/0107

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Psoriatic arthritis

Interventions
This is a randomised open-label clinical trial assessing three treatment regimens for PsA:
1. Standard care
2. Early combination DMARD therapy
3. Early biologics (TNF inhibitor) therapy

The trial forms part of a “Trials within Cohorts” or TWiCs design where participants in the cohort may be offered interventional studies subject to meeting the relevant inclusion/exclusion

criteria. Consent is requested in the cohort study for data from any control arm to be used without further approach.

A maximum of 315 newly diagnosed patients will be recruited (105 per arm) over a 3 year period. Each participant will be followed for 48 weeks within this trial, all arms will then revert to standard care within the cohort. Participants will attend for study visits at baseline and weeks 12, 24, 36 and 48 in their normal healthcare clinic. At each visit they will be assessed clinically for disease activity, including blood tests, and will be asked to complete patient-reported outcomes questionnaires. Adverse event information will be sought at each visit and recorded, assessed and reported as required by the protocol.

Data will be entered into an electronic CRF and appropriate validation checks carried out. Data will be analysed in accord with a statistical analysis plan starting with the null hypothesis that there is no difference in the proportion of participants achieving a PASDAS good response at week 24 between any of the three treatment arms. If this is significant at the 5% level further analyses will compare each intervention against the control arm.

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
Response according to PASDAS. This will be reported as the proportion achieving a PASDAS good response (reduction from baseline of ≥1.6 and final score of ≤3.2) in each of the three treatment groups (standard step up therapy in the cohort, early combination DMARD or early TNF inhibitor therapy) at week 24.

Secondary outcome measures
1. Time to achievement of minimal disease activity (MDA), assessed every 12 weeks
2. The proportion of patients achieving a PASDAS good response at week 48; proportion achieving PASDAS moderate response at week 24 and 48
3. Change in PsA impact of disease (PSAID) score from baseline to follow up
4. Proportion achieving PSAID patient acceptable symptom state (≤4) at follow up
5. Change in work productivity (absenteeism, presenteeism and productivity loss) as measured by WPAI at follow up.
6. Cost per QALY in each treatment arm to calculate ICER
7. Clinical assessment, patient questionnaires and blood tests all performed at weeks 0, 24 and 48
8. Healthcare resource use data and health-related quality of life throughout the study

Overall study start date
01/03/2017

Completion date
28/02/2025

Eligibility

Key inclusion criteria

1. Participant is willing and able to give informed consent for participation in the trial.
2. Male or Female, aged 18 years or above.
3. Participants consented to the PsA inception cohort (MONITOR-PsA REC Ref 17/SC/0556) and to be approached for alternate interventional therapies.
4. Poor prognostic factors at baseline. Either:
4.1 Polyarticular disease with > = 5 active joints at baseline assessment OR
4.2 Oligoarticular disease with < 5 active joints at baseline but with one or more of the following poor prognostic factors: raised C reactive protein, radiographic damage, health assessment questionnaire> 1
5. Female participants of child bearing potential and male participants whose partner is of child bearing potential must be willing to ensure that they or their partner use effective contraception during the trial and for 3 months thereafter (or 2 years if received leflunomide unless treated with washout therapy) as in standard practice.
6. Participant has clinically acceptable laboratory results within 28 days of baseline:
6.1 Haemoglobin count > 8.5 g/dL
6.2 White blood count (WBC) > 3.5 x 109/L
6.3 Absolute neutrophil count (ANC) > 1.5 x 109/L
6.4 Platelet count > 100 x 109/L
6.5 AST or ALT and alkaline phosphatase levels < 3 x upper limit of normal
7. In the Investigator's opinion, is able and willing to comply with all trial requirements.
8. Willing to allow his or her GP and consultant, if appropriate, to be notified of participation in the trial.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 206; UK Sample Size: 206

Total final enrolment
206

Key exclusion criteria
1. Previous treatment for articular disease with disease modifying drugs (DMARDs) including, but not limited to, methotrexate, sulfasalazine, leflunomide and ciclosporin
2. Female patient who is pregnant, breast-feeding or planning pregnancy during the course of the trial.
3. Significant renal or hepatic impairment.
4. Patients who test positive for Hepatitis B, C or HIV.
5. Contraindication to any of the investigative drugs.
6. Currently abuse drugs or alcohol
7. Scheduled elective surgery or other procedures requiring general anaesthesia during the trial.

8. Life expectancy of less than 6 months.
9. Any other significant disease or disorder which, in the opinion of the Investigator, may either put patients at risk because of participation in the trial, or may influence the result of the trial, or their ability to participate in the trial.
10. Participation in another research trial involving an investigational product in the past 12 weeks.
11. Additional exclusion criteria apply to patients randomised to arm 3 and receiving adalimumab therapy:
11.1 Active tuberculosis (TB), chronic viral infections, recent serious bacterial infections, those receiving live vaccinations within 3 months of the anticipated first dose of study medication, or those with chronic illnesses that would, in the opinion of the investigator, put the participant at risk.
11.2 Latent TB unless they have received appropriate anti-tuberculous treatment as per local guidelines
11.3 History of cancer in the last 5 years, other than non-melanoma skin cell cancers cured by local resection or carcinoma in situ.

Date of first enrolment
31/05/2019

Date of final enrolment
31/01/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Royal United Hospitals Bath NHS Foundation Trust
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
University Hospital
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Haywood Hospital
Burslem
Stoke-on-trent
United Kingdom
ST6 7AG

Study participating centre
Torbay and South Devon NHS Foundation Trust
Torbay Hospital
Newton Road
Torquay
United Kingdom
TQ2 7AA

Study participating centre

Christchurch Hospital
Fairmile Road
Christchurch
United Kingdom
BH23 2JX

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

Study participating centre
The Royal Wolverhampton NHS Trust
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Wirral University Teaching Hospital NHS Foundation Trust
Arrowe Park Hospital
Arrowe Park Road
Upton
Wirral
United Kingdom
CH49 5PE

Study participating centre
Royal National Orthopaedic Hospital NHS Trust
Brockley Hill
Stanmore
United Kingdom
HA7 4LP

Study participating centre

East Suffolk and North Essex NHS Foundation Trust
Colchester Dist General Hospital
Turner Road
Colchester
United Kingdom
CO4 5JL

Sponsor information

Organisation
University of Oxford

Sponsor details
Joint Research Office
Headington
Oxford
England
United Kingdom
OX3 7LE
+44 (0)1865289886
ctrg@admin.ox.ac.uk

Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR Academy; Grant Codes: CS-2016-16-016

Results and Publications

Publication and dissemination plan
1. The researchers intend to publish the methodology of this study in a protocol paper.
2. Peer reviewed scientific journals
3. Conference presentation

4. Publication on website
5. The researchers will also be working with their PPI contributors in case there are any further dissemination routes that should be pursued

Intention to publish date
28/02/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon reasonable request from laura.coates@ndorms.ox.ac.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol article		30/05/2024	28/02/2025	Yes	No