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Can we predict which patients with psoriatic arthritis will respond to treatment using precision medicine?

Submission date
03/03/2021

Recruitment status
No longer recruiting

Registration date
23/03/2021

Overall study status
Ongoing

Last Edited
06/12/2024

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 arthritis that affects some people with the skin condition psoriasis. It typically causes affected joints to become swollen, stiff and painful.
PsA is an inflammatory arthritis that develops in around 15% of people with psoriasis, causing swollen and painful joints. For patients who do not respond to standard arthritis drugs, two classes of biologic drugs are available (TNF or IL-17 blockers). A similar proportion of patients respond to both with around 50% achieving a good response. However, we do not know how to predict which patient will respond best to each drug.
Our aim is to test whether we can predict if people with psoriatic arthritis (PsA) will respond to certain biologic drugs using blood tests. We will test if high levels of a type of T cells (activated Th17 cells) or other laboratory tests predict response. We will use statistical tests to estimate how effective these approaches would be for each individual. If successful, this approach could ensure that patients receive their best option first, ensuring their disease is controlled and quality of life improved, while avoiding unnecessary drug use. This is likely to save money for the NHS.

Who can participate?
Patients aged 18 years or older, with PsA about to start their first biologic treatment will be invited to join the study.

What does the study involve?
Participants will have a blood sample taken to measure their activated Th17 cells. The patients will be allocated to receive either TNF or IL-17 blocking biologics. We will measure how well they respond after 6 months of treatment and test whether the initial blood test result could have predicted their response.

What are the possible benefits and risks of participating?
Participants are not expected to benefit directly from participating in the study however they should see an improvement in their PsA symptoms from the treatment they receive. Study visits have been aligned with routine NHS visits to minimise burden and inconvenience but will take

longer and participants will be asked to complete extra questionnaires. Participants will need to have additional blood samples taken which may result in bruising but research samples will be taken at the same time as routine NHS blood tests wherever possible.
Participants at 3 sites (Oxford, Glasgow, & St Guys & St Thomas's) will be asked to attend a short additional visit to enable the collection of an additional blood sample. Travel costs will be reimbursed for this additional visit to minimise any financial burden.
There are no additional risks from the treatment as the study uses the same treatments that would be prescribed routinely for these patients.

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

When is the study starting and how long is it expected to run for?
February 2021 to September 2026

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

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

Contact information

Type(s)
Scientific

Contact name
Dr Laura Coates

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
287528

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 48066, IRAS 287528

Study information

Scientific Title
Optimising Psoriatic Arthritis Therapy with Immunological Methods to Increase Standard Evaluation

Acronym
OPTIMISE

Study objectives
A precision choice of bDMARDs in PsA based on lymphocyte cell surface markers guiding selection of either TNF inhibitor or IL17A inhibitor will give superior results to patients having a choice of bDMARD based on clinical characteristics alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/02/2021, North West - Preston REC (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8206; Preston.rec@hra.nhs.uk), ref: 21/NW/0016

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

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
Arthritis that affects some people with the skin condition psoriasis

Interventions
All patients will be treated with a biologic drug (TNF inhibitors (adalimumab) or IL-17A inhibitors (secukinumab) in keeping with routine clinical practice. At present both TNF inhibitors and IL-17 inhibitors are licensed and NICE approved as first line biologics in PsA. Patients will be

randomised in a 1:1 ratio to receive either TNF or IL-17A inhibitors, stratified by baseline immunophenotype, for 24 weeks.

The TNF inhibitor to be used is adalimumab (any brand) and it is to be given at the usual licensed dose, as per the SmPC:
-The licenced dose of adalimumab for psoriatic arthritis is always 40 mg by subcutaneous injection every 2 weeks, with no loading doses.

The IL-17A inhibitor to be used is secukinumab, brand name Cosentyx, and is to be given at the usual licensed dose as per the SmPC:
-The licensed dose of secukinumab for psoriatic arthritis varies based on the level of baseline skin psoriasis. For patients with concomitant moderate to severe plaque psoriasis, the recommended dose is 300mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4 followed by a monthly maintenance dose. For other patients the recommended dose is 150mg by subcutaneous injection at the same timepoints. This study will follow routine practice and the current label by using the appropriate dose of secukinumab based on the baseline psoriasis disease activity with the cut off for moderate to severe psoriasis as 10% body surface area. Dose escalation as per the licence is permitted.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Adalimumab, secukinumab

Primary outcome measure
Clinical response as measured by the minimal disease activity (MDA) criteria at baseline and week 24

Secondary outcome measures
1. Clinical disease pattern at baseline measured by the minimal disease activity (MDA) criteria
2. Immunophenotype data at baseline measuring activated Th17 and intracellular levels of IL-17
3. Activated Th17 proportion and intracellular levels of IL-17 at baseline and week 24
4. Clinical response as measured by the minimal disease activity (MDA) criteria at week 12/16 and week 24
5. Cell-specific transcriptomic data and whole blood transcriptomes from samples collected at baseline and week 24

Overall study start date
01/02/2021

Completion date
30/09/2026

Eligibility

Key inclusion criteria

Current inclusion criteria as of 15/08/2022:
1. Participant is willing and able to give informed consent for participation in the study
2. Male or female, age 18 years or over
3. Diagnosis of PsA confirmed by the CASPAR criteria
4. Is planned to have biologic therapy for psoriatic arthritis using NICE/SMC criteria (failure of ≥2 csDMARDs and ≥3 tender and ≥3 swollen joints)

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Previous inclusion criteria:
1. Participant is willing and able to give informed consent for participation in the study
2. Male or female, age 18 years or over
3. Diagnosis of PsA confirmed by the CASPAR criteria
4. Is planned to have biologic therapy for psoriatic arthritis using NICE/SMC criteria (failure of >=2 csDMARDs and >=3 tender/swollen joints)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 424; UK Sample Size: 424

Key exclusion criteria
1. Contraindications to either TNF inhibitor or secukinumab:
1.1. History of previous demyelinating disease including multiple sclerosis
1.2. Heart failure (NYHA class 3 or 4)
1.3. Serious infections: active tuberculosis (TB), chronic viral infections (including hepatitis B, C and HIV), recent serious bacterial infections
1.4. Latent TB unless they have received appropriate anti-tuberculous treatment as per local guidelines
1.5. Active symptomatic inflammatory bowel disease
1.6. History of cancer in the last 5 years, other than non-melanoma skin cell cancers cured by local resection or carcinoma in situ
1.7. Hypersensitivity to active ingredient or excipients
2. Current or previous treatment with biologic DMARDs or targeted synthetic DMARDs
3. Use of investigational therapies within 1 month or 5 half-lives (whichever is longer) of baseline
4. Women who are pregnant, lactating or planning pregnancy during the following 12 months

Date of first enrolment
01/01/2022

Date of final enrolment

31/12/2024

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

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

Study participating centre
St Thomas's Hospital
249 Westminster Bridge Road
London
United Kingdom
SE1 7EH

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

Study participating centre
St Georges Hospital
Midlands Partnership NHS Foundation Trust
Corporation Street
Stafford
United Kingdom
ST16 3SR

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

Study participating centre
Cardiff and Vale University Health Board
UHB Headquarters
Woodlands House
2nd Floor
Maes y Coed Rd
Heath Park
Cardiff
United Kingdom
CF14 4HH

Study participating centre
Royal Berkshire Hospital
Royal Berkshire NHS Foundation Trust
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
Royal United Hospital
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
St George's Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Sponsor information

Organisation
University of Oxford

Sponsor details
Joint Research Office, 1st Floor, Boundary Brook House,
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Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR129023

Funder Name
National Institute for Health Research (NIHR) (UK)

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
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/09/2026

Individual participant data (IPD) sharing plan
The participant-level data set and statistical code will be available upon reasonable request from Laura Coates (laura.coates@ndorms.ox.ac.uk) and the Oxford Clinical Trials Research Unit (OCTRU; octrutrialshub@ndorms.ox.ac.uk) once the study findings have been published in full and for as long as this data is useful. Consent has been provided consent to share with the funder and other researchers based at hospitals, universities, non-profit institutions or commercial laboratories worldwide; however, some specific data items may not be shared in order to maintain participant anonymity.

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		28/03/2023	29/09/2023	Yes	No
Protocol file	version 8.0	07/11/2023	08/11/2023	No	No