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Identifying the best combinations of drugs for treating inflammatory diseases

Submission date
18/10/2024

Recruitment status
No longer recruiting

Registration date
15/01/2025

Overall study status
Ongoing

Last Edited
11/09/2025

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
The goal of treatment in rheumatoid and psoriatic arthritis is disease remission, i.e. removing inflammation completely, which is important in protecting joints from damage caused by inflammation. One group of biological medicines called tumour necrosis factor inhibitors is commonly used to treat rheumatoid arthritis and psoriatic arthritis. In many patients, inflammation is reduced but not removed completely. Based on blood samples from patients with rheumatoid and psoriatic arthritis who have been treated with tumour necrosis factor, researchers have found evidence that another group of biological medicine, interleukin-6 inhibitors, may remove the remaining inflammation in those individuals who did not achieve remission. The goal of this study is to test whether this is true.

Who can participate?
Patients aged 18 years and over with rheumatoid or psoriatic arthritis who are receiving any one of the following inhibitors: etanercept, adalimumab, golimumab, certolizumab or infliximab, but still have active inflammation in their joints.

What does the study involve?
Tocilizumab, an interleukin-6 inhibitor which is an approved treatment for rheumatoid arthritis will be added to their current treatment. The initial dose will be half the normal dose. If patients tolerate treatment without any side effects, after 8 weeks the dose will be escalated to full dose. Treatment will last 24 weeks. The outcome of the study is the percentage of patients who will achieve disease remission. The secondary goal is to determine the tolerability of adding tocilizumab to tumour necrosis factor inhibitors.

What are the possible benefits and risks of participating?
It is hoped that administering tocilizumab in combination with another treatment can reduce the rate of progression of joint damage and improve physical function. If successful, this study could potentially help patients get access to treatment that is otherwise not provided. However, you may not benefit from participating in this study. Your condition may remain the same, improve or worsen. Your participation will not limit the access to the standard treatments, in case of benefit or progression after the treatments dispensed in this study.
By participating in this research, you will be helping scientists and clinicians better understand

arthritis which may improve future treatment options. The information from this study will also hopefully help future patients.
Study treatment may be responsible for some side effects. All of them are not identified, even though the study drug tocilizumab has been used extensively for several years. Most of them are variable from one patient to another. They can be mild, moderate, or sometimes severe. Some may go away as soon as you stop taking the study treatment. If you experience any side effects, your doctor will give you medicines to help reduce the side effects where possible.
It is important that you inform your doctor of any medication, dietary supplement, or herbal supplements that you are taking or intend to take during the study as interactions may exist between the drugs.
The safety of study treatment will be assessed at each visit by your doctor. Additional treatments may be prescribed to control side effects. If they are significant, your doctor may change the treatment doses or stop study treatment for a given time or permanently. Likewise, it is important that, apart from these regular visits, you contact your doctor immediately in the event of uncomfortable toxicity.

Where is the study run from?
Cardiff University (UK)

When is the study starting and how long is it expected to run for?
October 2024 to June 2026

Who is funding the study?
Horizon 2020

Who is the main contact?
Ian Thomas, DOCTIS@cardiff.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Ernest Choy

Contact details
Division of Infection & Immunity
School of Medicine
Tenovus Building
Heath Park
Cardiff
United Kingdom
CF14 4XN
+44 (0)2920 687350
choyeh@cardiff.ac.uk

Type(s)
Public

Contact name

Mr Ian Thomas

Contact details
Centre for Trials Research
College of Biomedical & Life Sciences
Cardiff University
6th Floor Neuadd Meirionnydd
Heath Park
Cardiff
United Kingdom
CF14 4YS
+44 (0)2922 510531
doctis@cardiff.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2024-518011-19

Integrated Research Application System (IRAS)
1010423

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
SPON 2002-24

Study information

Scientific Title
Decision on optimal combinatorial therapies in imids using systems approaches

Acronym
DocTIS

Study objectives
The objective of this clinical Trial is to provide proof-of-principle validation of the efficacy of combining TNF and IL-6 inhibitors to achieve higher remission than current therapies in RA and PsA. Remission will be defined as Clinical Disease Activity Index (CDAI) 2.8 or < 2.8 in RA, or DAPSA <4 in PsA.

A secondary objective is to provide preliminary safety and tolerability data on the selected combination therapy and improvement in disease activity as measured by validated outcome measures. Safety will include number of Serious Adverse Events and Adverse Events (AEs), including any infection requiring hospitalisation. Disease specific activity scores and percentage improvement in disease activity as reported by patients, using validated questionnaires.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/11/2024, Wales Research Ethics Committee 1 Cardiff (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2920 785738; Wales.REC1@wales.nhs.uk), ref: 24/WA/0336

Study design
Interventional phase II study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Rheumatoid arthritis (RA) and psoriatic arthritis (PsA)

Interventions
The DocTIS trial is a single-arm, adaptive basket trial design. In this study, the researchers will recruit patients with rheumatoid or psoriatic arthritis who are receiving any one of the following inhibitors, etanercept, adalimumab, golimumab, certolizumab or infliximab but still have active inflammation in their joints. Tocilizumab, an interleukin-6 inhibitor which is an approved treatment for rheumatoid arthritis will be added to their current treatment. Initially dosing will be 162 mg SC every fortnight for 8 weeks. If the patient tolerates treatment without adverse events the dose will be increased to 162 mg SC weekly. Treatment will last 24 weeks.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
The proportion of patients who achieve disease remission at week 24. A total of 36 patients are required to assess the primary endpoint, with an expectation of up to 10% drop-out, resulting in a total patient population of 40.

Key secondary outcome(s))
1. Safety will include the number of serious adverse events (SAEs), adverse events (AEs), adverse events of special interest (AESIs) and withdrawals due to SAEs, AEs or AESIs. Severe infection requiring hospitalisation will be included as AESI.
2. Disease-specific activity scores and percentage improvement in disease activity measured using:
2.1. RA: American College of Rheumatology (ACR) and European Alliance of Associations for Rheumatology (EULAR) response criteria, change in Clinical Disease Activity Index (CDAI) and Disease Activity Score with Erythrocyte Sedimentation Rate (DASESR) scores, physical disability by modified Health Assessment Questionnaire (mHAQ)

2.2. PsA: Disease Activity in Psoriatic Arthritis (DAPSA), American College of Rheumatology (ACR) response, Psoriatic Arthritis Response Criteria (PsARC) response, physical disability by modified Health Assessment Questionnaire (mHAQ)

Safety will be measured and evaluated throughout the trial and reported cumulatively in both diseases separately.

Completion date
01/06/2026

Eligibility

Key inclusion criteria
1. Adult patients (≥18 years old)
2. Patient must fulfil either European Alliance of Associations for Rheumatology (EULAR) /Albumin: Creatinine Ratio (ACR) classification criteria for the diagnosis of Rheumatoid Arthritis (RA), or Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) criteria for Psoriatic Arthritis (PsA)
3. Current treatment with any approved Tumour Necrosis Factor inhibitors (TNFis)
4. Active arthritis as defined by:
4.1. DAS28 score >3.2 for Rheumatoid Arthritis (RA)
4.2. Disease Activity in Psoriatic Arthritis (DAPSA) >14 for Psoriatic Arthritis PsA
5. Signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current key exclusion criteria as of 11/09/2025:
1. Contraindications to any of the biologic treatment e.g. active infection
2. Previous treatment with any IL-6is (tocilizumab or sarilumab)
3. Women who are pregnant or breast-feeding
4. Women of child-bearing potential, or males whose partners are women of childbearing potential, unwilling to use effective contraception during the study and for at least 3 months after stopping study treatment
5. History of or current primary inflammatory joint disease or primary autoimmune disease other than RA
6. Intra articular or parenteral corticosteroids ≤ 4 weeks prior Visit 2

7. Oral prednisolone more than 10mg per day or equivalent ≤ 4 weeks prior to Visit 2
8. Active infection
9. Septic arthritis within a native joint within the last 12 months
10. Sepsis of a prosthetic joint within 12 months or indefinitely if the joint remains in situ
11. Known HIV or hepatitis B/C infection (satisfactory hepatitis B screening test must have been done previously)
12. Malignancy (other than basal cell carcinoma) within the last 10 years
13. New York Heart Association (NYHA) grade 3 or 4 congestive cardiac failure
14. Demyelinating disease
15. Any other contra-indication to the study medications as detailed in their summaries of product characteristics (SmPC), including low IgG levels at clinician's discretion
16. Receipt of live vaccine <4 weeks prior to first infusion
17. Major surgery in 3 months prior to first infusion
18. Presence of a transplanted organ (with the exception of a corneal transplant >3 months prior to screening)
19. Known recent substance abuse (drug or alcohol)
20. Poor tolerability of venepuncture or lack of adequate venous access for required blood sampling during the study period
21. Patients currently recruited to other clinical trial(s) involving an Investigational Medicinal Product ([IMP)], except any observational follow-up periods not involving an IMP)
22. Other severe acute or chronic medical or psychiatric condition, or laboratory abnormality that would impart, in the judgment of the investigator, excess risk associated with study participation or study drug administration, or which, in the judgment of the investigator, would make the patient inappropriate for entry into this study

Previous key exclusion criteria:
1. Contraindications to any of the biologic treatment e.g. active infection
2. Previous treatment with any IL-6is (tocilizumab or sarilumab)
3. Women who are pregnant or breast-feeding
4. Women of child-bearing potential, or males whose partners are women of childbearing potential, unwilling to use effective contraception during the study and for at least 3 months after stopping study treatment
5. History of or current primary inflammatory joint disease or primary autoimmune disease other than RA
6. Intra articular or parenteral corticosteroids ≤ 4 weeks prior Visit 2
7. Oral prednisolone more than 10mg per day or equivalent ≤ 4 weeks prior to Visit 2
8. Active infection
9. Septic arthritis within a native joint within the last 12 months
10. Sepsis of a prosthetic joint within 12 months or indefinitely if the joint remains in situ
11. Known HIV or hepatitis B/C infection (hepatitis B screening test must be performed at or in the preceding 3 months of screening visit)
12. Malignancy (other than basal cell carcinoma) within the last 10 years
13. New York Heart Association (NYHA) grade 3 or 4 congestive cardiac failure
14. Demyelinating disease
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sampling during the study period
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22. Other severe acute or chronic medical or psychiatric condition, or laboratory abnormality that would impart, in the judgment of the investigator, excess risk associated with study participation or study drug administration, or which, in the judgment of the investigator, would make the patient inappropriate for entry into this study

Date of first enrolment
15/04/2025

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
United Kingdom

Study participating centre
Not provided at time of registration
United Kingdom
-

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Government

Funder Name
Horizon 2020

Alternative Name(s)

EU Framework Programme for Research and Innovation, Horizon 2020 - Research and Innovation Framework Programme, European Union Framework Programme for Research and Innovation

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study may be made available upon request from Ian Thomas, thomasif@cardiff.ac.uk subject to a review process by the Sponsor, which includes a review of the robustness of the proposed use of the data and any ethical and legal considerations of the transfer process and subsequent storage of the data. Pseudonymised data only may be provided, after all primary publications have been completed.

IPD sharing plan summary
Available on request

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