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A single-site study to understand the best route of delivery for a new cell-based treatment created from patient's own white blood cells for rheumatoid arthritis

Submission date
18/05/2023

Recruitment status
No longer recruiting

Registration date
27/09/2023

Overall study status
Ongoing

Last Edited
31/10/2025

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
Rheumatoid arthritis (RA) is a long-term autoimmune condition, caused by the immune system attacking healthy body tissue. We have previously trialled a new therapy for RA called tolerogenic dendritic cells (tolDC) which is manufactured from the patient's own white blood cells. The AuToDeCRA trial showed that tolDCs could be made from the white blood cell samples of patients with RA and that the treatment was safe to give to patients with active arthritis. In that trial, tolDCs were injected directly into affected knee joints but we do not know if this is the best way to introduce the therapy. The AuToDeCRA-2 trial will compare a range of different administration routes and doses to see if how we administer the treatment impacts how well the treatment works at reducing the symptoms of RA. It will also look to identify any changes in the body’s immune system triggered by the treatment.

Who can participate?
Adult patients with RA

What does the study involve?
We aim to treat 20 patients, 16 with tolDC in addition to standard care and 4 with standard care alone. Three different routes of administration will be tested, directly into the lymph nodes, into the skin of the upper thigh and into a knee joint. Lymph nodes are small glands in the body where cells from the immune system congregate. Because we think that tolDC need to get to the lymph nodes to work, we are also testing whether a lower dose would be sufficient when injecting directly into a lymph node.

Participants will be randomised to one of the five groups, attending 7-8 visits over a period of up to 25 weeks. Those randomised to receive tolDC will undergo a procedure called leukapheresis to collect the white blood cells from which the treatment will be manufactured. During the trial

blood and lymph node samples will be collected to identify changes in the immune system triggered by the treatment. Participants will also be assessed for signs of safety, efficacy and acceptability.

What are the possible benefits and risks of participating?
We cannot promise that this trial will benefit participants directly, although there is a possibility that the treatment may help improve their RA. The information gathered from this trial may also help improve the treatment of future patients.

This is a Phase II trial of a novel new therapy for RA. While no tolDC trial has yet demonstrated robust clinical efficacy, tolDC appears to be a safe and well-tolerated intervention. However, there is a risk of adverse events in response to the treatment. The major safety concern for tolDC therapy is that, following administration, the tolDC could acquire an altered, proinflammatory phenotype and trigger a worsening of the disease. Participants will be closely monitored immediately post-injection and throughout the duration of the trial. Should a participant develop a worsening of their RA symptoms, a 'flare visit' will be arranged. Clinical and immunological assessment will occur and the participant will be managed accordingly if a disease flare is confirmed. Participants will be provided with a 24-hour contact number in case of questions or concerns between study visits.

The leukapheresis procedure to collect the necessary white blood cells is a routine clinical procedure with a recognised risk profile and low potential for unexpected adverse reactions. Risks associated with the procedure include citrate toxicity resulting in a pins and needles sensation, pain and bruising from needle insertion and a small risk of anaemia. The procedure will be conducted by specialist staff, experienced in identifying and treating any symptoms. Similarly, the lymph node aspirate procedure may result in slight discomfort and bruising. The procedure, which is routinely performed within the NHS, will be conducted under ultrasound visualisation by an experienced radiologist. Study visits have been minimised as much as possible to reduce patient burden.

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

When is the study starting and how long is it expected to run for?
May 2023 to June 2026

Who is funding the study?
Versus Arthritis (UK)

Who is the main contact?
Dr Ema-Louise Long, nuth.ad2@nhs.net

Contact information

Type(s)
Public, Scientific

Contact name
Dr Ema-Louise Long

Contact details

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Type(s)
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Additional identifiers

Clinical Trials Information System (CTIS)
2023-000020-11

Integrated Research Application System (IRAS)
1006392

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
08669, CPMS 56373, IRAS 1006392

Study information

Scientific Title
A single-centre, experimental medicine study investigating the route of delivery and potential efficacy of autologous tolerogenic dendritic cell (tolDC) therapy for rheumatoid arthritis

Acronym
AuToDeCRA-2

Study objectives
Primary objective:
To seek signals of immune modulation when TolDCcitpep are administered to patients with RA

Secondary objectives:
1. To seek signs of potential efficacy when TolDCcitpep are administered to patients with RA.
2. To provide further evidence of TolDCcitpep safety in patients with RA.
3. To provide further evidence of patient acceptability of TolDCcitpep therapy for RA.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 25/09/2023, London – West London & GTAC Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8098; westlondon.rec@hra.nhs.uk), ref: 23/LO/0494

Study design
Randomized controlled open-label parallel-group study

Primary study design
Interventional

Study type(s)
Efficacy, Safety, Treatment

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

Interventions
Participants will be randomly allocated by a computer (Sealed Envelope) to one of five groups. One group will receive the current usual treatment for RA, and the other four groups will receive a single dose of TolDCcitpep in addition to the current usual treatment. Of the four treatment groups, one will receive a dose of 10^7 TolDCcitpep via intra-dermal injection to the upper thigh, one will receive a dose of 10^7 TolDCcitpep via intra-articular injection to the knee, one will receive a dose of 10^5 TolDCcitpep via intra-nodal injection into an inguinal lymph node and one will receive a dose of 10^7 TolDCcitpep via intra-nodal injection into an inguinal lymph node. TolDCcitpep is manufactured from the participant's white blood cells, and collected via leukapheresis one week before treatment. All participants will be closely monitored over 12 weeks.

Intervention Type
Biological/Vaccine

Phase
Phase II

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

Primary outcome(s)
Signs of immunomodulation will be measured from fresh blood, cryopreserved PBMC samples and lymph node aspirate samples. As there is currently no agreed biomarker for tolerance induction, we will use a range of modalities to identify levels of cell types and cell markers.

Blood samples will be collected at baseline, 1, 3, and 6 weeks. Lymph node aspirate will be collected at baseline and 1 week.

Key secondary outcome(s))
1. Efficacy is measured using changes in American College of Rheumatology (ACR) criteria of a 20% improvement in the core set measures for a patient to reach improvement (ACR20), ACR50, ACR70 and Disease Activity Score (DAS-28) scores from baseline to weeks 1, 3, 6, and 12
2. Safety is measured using the reporting of adverse events and serious adverse events at baseline, 1, 3, 6, and 12 weeks
3. Patient acceptability is measured using a 1-5 Likert scale questionnaire at 12 weeks

Completion date
30/06/2026

Eligibility

Key inclusion criteria
1. Adults aged 18 years old or over
2. Rheumatoid Arthritis fulfilling 1987 ARA criteria or 2010 ACR/EULAR Classification Criteria
3. ACPA positive (>3x upper limit of normal)
4. Able and willing to give informed consent and comply with the study protocol
5. Disease duration at least 4 months and less than ten years
6. ACR Functional Class I-III
7. DAS 28 <5.1
8. If receiving disease-modifying anti-rheumatic drugs (DMARD) these can be at any dose or combination of methotrexate, sulphasalazine, azathioprine, hydroxychloroquine, abatacept, rituximab (last dose >6 months ago), TNF-alpha inhibitors and IL6 receptor antagonists but must have been stable for 4 weeks.
9. Stable dose of non-steroidal anti-inflammatory drugs (NSAID) for at least 4 weeks prior to screening (only applicable for patients taking NSAID as part of their standard care)
10. Possess at least one copy of a shared epitope HLA DRB1 allele (0101; 0102; 0105; 0401; 0404; 0405; 0408; 0409; 0410; 0413; 0416; 0419; 0421; 1001; 1402; 1406; 1409; 1413; 1417; 1419; 1420; 1421)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment

Key exclusion criteria
1. Use of other investigational medicinal products within 30 days prior to study entry (defined as date of consent into study)
2. Any Rheumatoid Arthritis treatment or dose changes within 4 weeks of study entry.
3. Current treatment with Janus kinase inhibitors or leflunomide. Previous treatment is permitted provided at least 12 weeks have elapsed since discontinuation of the therapy and study entry
4. Receiving glucocorticoids by any route within 4 weeks of study entry, apart from topical, intra-nasal or inhaled
5. Serious or unstable co-morbidity that prohibits participation in the study at the discretion of the investigator, eg. Significant COPD, significant cardiac failure, active malignancy
6. Active infection at study entry (except fungal nail infection)
7. Infection requiring hospitalisation, or IV antibiotics, within 4 weeks prior to study entry
8. Immunisation with live, attenuated vaccines planned within 14 days of baseline visit (administration of TolDCcitpep) and with non-live vaccines planned within 7 days of baseline visit
9. History of hepatitis B or C, HIV, or HTLV-1/2 infection(s)
10. Recent history of CMV infection (positive for CMV IgM antibodies) or syphilis infection (positive PCR test)
11. Major surgery within 8 weeks prior to study entry or planned within 12 weeks of baseline visit.
12. Pregnancy, or women planning to become pregnant within the study period, or women who are breast feeding
13. Females of child bearing potential engaging in heterosexual relationships unwilling to use adequate contraception for duration of study
14. Patients taking anticoagulants that cannot be interrupted and are, in the judgement of the investigator, likely to interfere with study procedures
15. Known hypersensitivity to local anaesthetic
16. Poor venous access or medical condition precluding leukapheresis e.g. unstable cardiac arrythmia (atrial fibrillation permitted)
17. Hb<10g/dL; neutrophils< 1.00 x10^9/L; platelets <100x10^9/L

Date of first enrolment
08/01/2024

Date of final enrolment
31/03/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Victoria Infirmary
Clinical Research Facility

Newcastle upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Charity

Funder Name
Versus Arthritis

Alternative Name(s)
Arthritis UK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Until the publication of the trial results, access to the full dataset will be limited to the Trial Management Group and to the authors of the publication. At the end of the study, a de-identified dataset including metadata will be prepared and made available on a publicly accessible database. Requests for data sharing with bona fide study teams outside of Newcastle University or Newcastle upon Tyne Hospitals will be considered by a Data Access Committee, with representation from the Sponsor and CI, and will be subject to the presentation of a clear plan of what the data will be used for, how the data will be analysed, how the results will be

disseminated, and who the authors will be. Data transfer will be subject to the completion of a Data Sharing Agreement between Newcastle University and the end users. Data will not be withheld from bona fide research requesting access unless the criteria for sharing are not met.

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		07/08/2025	08/08/2025	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes