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Validation of advanced treatment for rheumatoid arthritis (tolDC)

Submission date
12/11/2020

Recruitment status
No longer recruiting

Registration date
13/04/2021

Overall study status
Completed

Last Edited
18/07/2023

Condition category
Musculoskeletal Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Rheumatoid arthritis is a long-term condition that causes pain, swelling and stiffness in the joints. This research study is about obtaining white blood cells using a routine procedure, leukapheresis (a laboratory procedure in which white blood cells are separated from a sample of blood), in order to produce a new treatment for rheumatoid arthritis (RA) known as tolerogenic dendritic cells (tolDC). Therapy with tolDC has great potential for the treatment of conditions caused by problems with the immune system, such as RA.
We are now preparing to carry out a clinical trial to test the best administration route of tolDC and look any effects the treatment has on the immune system in RA patients. Before carrying the clinical trial we need to adapt the way tolDCs are made so that they can be followed in the body. We need to demonstrate that the manufacturing process for the altered tolDC therapy is tested (validated) and ensure that it is at clinical grade standard before use in patients.
It is not feasible to obtain the quantity of white blood cells needed to make clinical-grade tolDC from routine blood donations, therefore, six participants with RA will be recruited to donate white blood cells by leukapheresis as part of this study. This study concerns the validation of the manufacturing process only.
The study aim is to collect white blood cells from rheumatoid arthritis patients to use for GMP validation of the manufacturing process of tolerogenic dendritic cells (tolDC).

Who can participate?
Patients aged 18 years or older, with ACPA positive rheumatoid arthritis and who are able to provide informed consent are able to participate.

What does the study involve?
This research study involves obtaining white blood cells using a routine procedure called leukapheresis. White blood cells will be collected once and will be used to produce a new treatment for Rheumatoid Arthritis (RA); tolerogenic dendritic cells (tolDC). Participants will under a screening process before the procedure which involved taking blood samples.

What are the benefits and risks of participating?
Participants will not receive any treatment as part of the study. There is no direct benefit to the participant though the study findings will be used to inform the manufacture of a new

treatment for patients with RA.
Leukapheresis is carried out routinely in the haematology ward and you will be looked after by experienced members of staff. As with all medical procedures there are risks associated with leukapheresis but routine procedures are in place to minimise these risks.

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

When is the study starting and how long is it expected to run for?
December 2018 to June 2022.

Who is funding the study?
Versus Arthritis (UK)

Who is the main contact?
Prof. John Isaacs (scientific), john.isaacs@newcastle.ac.uk
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
276044

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 276044

Study information

Scientific Title
Collection of white blood cells [using leukapheresis] from rheumatoid arthritis patients for the validation of an advanced treatment for rheumatoid arthritis (tolDC)

Study objectives
The purpose of this study is to collect samples of leukocytes from Rheumatoid Arthritis (RA) patients which can be used to validate the production and quality of an advanced therapy medicinal product (tolDC).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/07/2020, Yorkshire & The Humber - Sheffield Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 104 8237; sheffield.rec@hra.nhs.uk), ref: 20/YH/0203

Study design
Single-centre non-controlled validation study

Primary study design
Observational

Study type(s)
Other

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

Interventions
Leukocytes will be collected from Anti-citrullinated protein antibody (ACPA) positive Rheumatoid Arthritis (RA) patients and used for the GMP process and product validation of an advanced therapy medicinal product, called tolDC.

Leukocyte samples, used to manufacture tolDC, will be collected from participants by leukapheresis.

Participants will be asked to undergo a number of screening assessments including ECG and blood tests to confirm that they have no contraindications to leukapheresis. Participants meeting all the ineligibility criteria will undergo a single cycle of leukapheresis to obtain the leukocyte sample.

The acquired leukocyte samples will be transferred to the Newcastle Cellular Therapies Facility, a sterile GMP (Good Manufacturing Practice) facility, where the tolDC manufacture and validation work will be carried out.

Intervention Type
Other

Primary outcome(s)
The number of patients who successfully complete the leukaphereis procedure, where success is determined by the collection of a leukocyte sample of 100mls at a single time point

Key secondary outcome(s))
Properties of the final product measured at a single time point:
1. Cell number measured using Flow cytometry
2. Viability measured using Flow Cytometry/Trypan Blue Exclusion Assay (TBC)
3. Yield (number compared to cells at the start of the process) measured using Flow Cytometry
4. Purity (number of TolDC cells compared to non-TolDC cells) measured using Flow Cytometry
5. Potency (ability of cells to function as intended) measured using Functional assay measuring IFNy in co-culture

Completion date
30/06/2022

Eligibility

Key inclusion criteria
1. ACPA positive RA based on local NHS laboratory cut-off. If ACPA titre is <3 times laboratory upper limit of normal, patients must also be RF positive based on local NHS laboratory cut-off
2. Age 18 years or over
3. Ability to provide written informed consent
4. Receiving methotrexate, either as monotherapy or in combination with additional conventional synthetic disease modifying drug(s) (csDMARDs) at a stable dose for at least 4 weeks prior to screening
5. At least 6 months since diagnosis of RA
6. ACR Functional Class I-III
7. Active disease – DAS 28 >3.2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Use of investigational medicinal products within 30 days prior to screening date
2. Receiving biologic DMARD or targeted synthetic DMARD (tsDMARD)
3. Receiving glucocorticoids by any route accept topical/inhaled within 4 weeks of screening (nasal spray permitted)
4. Receiving non-steroidal anti-inflammatory drugs (NSAID) at an unstable dose. Patients may be receiving NSAID prior to screening, provided the dose has been stable for at least 4 weeks prior to screening.
5. Serious or unstable co-morbidity deemed unsuitable by PI, eg. COPD, cardiac failure
6. Any known medical condition or contra-indication to leukapheresis, e.g. positive serology screen for hepatitis B or C, HIV infections
7. History of hepatitis B or C, syphilis, HIV, CMV or HTLV-1/2 infections
8. History of recurrent or chronic infection
9. Pregnancy, or women planning to become pregnant within the study period, or women who are breast feeding
10. Known hypersensitivity to local or systemic corticosteroid therapy or local anaesthetic
11. Poor venous access or medical condition precluding leukapheresis
12. Infection requiring hospitalization or IV antibiotics within 6 weeks of leukapheresis procedure
13. Immunization with live vaccine within 6 weeks of leukapheresis procedure
14. Anaemia defined as Hb<10g/dL; neutrophils< 2.00 x109/L; platelets <150x109/L
15. Known active infection at screening visit or at screening (except fungal nail infection)

Date of first enrolment
05/04/2021

Date of final enrolment
04/05/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Victoria Infirmary
Clinical Research Facility
Level 6
Leazes Wing

Newcastle Upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Freeman Hospital
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

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

The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			18/07/2023	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet version 3.0	11/11/2025	11/11/2025	No	Yes
Protocol file		27/06/2022	23/08/2022	No	No