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Study of patients with early rheumatoid arthritis: The TACERA (Towards a Cure for Early Rheumatoid Arthritis) Study

Submission date
25/09/2012

Recruitment status
No longer recruiting

Registration date
05/10/2012

Overall study status
Completed

Last Edited
07/08/2020

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Patients newly diagnosed with Rheumatoid Arthritis (autoimmune disease that causes inflammation in your joints) are treated conventionally according to National Institute for Health and Clinical Excellence (NICE) guidelines. There is no cure for Rheumatoid arthritis (RA), instead, the goal is to achieve low disease activity and ultimately disease remission. It is not currently possible to predict which drug (or drugs) will produce a favourable response in a particular patient and it is currently difficult to identify patients in clinical remission. This study aims to define predictors of clinical response and define what true remission is in patients with early RA. The plan is to use this information to develop an 'immunological toolkit' to help predict which patients will respond well to particular treatments so that patients can be treated with individualised drug combinations that are most likely to induce and sustain remission.

Who can participate?
The study will recruit 410 participants over the age of 18 within 4 weeks of diagnosis with Rheumatoid Arthritis. They will not have received disease-modifying antirheumatic drugs (DMARDs) or corticosteroid treatment for the current episode of inflammatory arthritis. In addition all subjects will be positive for Rheumatoid Factor and Anti-citrullinated protein antibody (ACPA).

What does the study involve?
Patients will receive standard treatment following national guidelines throughout the study period. The study duration will be 18 months. Patients will be assessed at months 0, 3, 6, 9, 12, 15 and 18 using standard validated questionnaires and blood tests as set out in current guidelines. Biological sampling (blood and urine) will be carried out at each assessment for the purpose of developing an 'immunological toolkit'. X-rays will be taken at 0, 12 and 18 months.

What are the possible benefits and risks of participating?
Although not of direct benefit to participants in the study, it is hoped that the information we get from this study will help improve the treatment of people with rheumatoid arthritis in the future.

As this is an observational study there are no additional risks relating to taking medication involved beyond those which you would experience in routine care. However, there is a modest risk of side effects including pain, bruising, light headedness, and, on rare occasions, infection that could arise as a consequence of having blood taken. To minimise this risk, blood will be taken by a clinical professional trained and experienced in taking blood from patients. In all we will need to take seven lots of blood samples from you, in total about 1.5 - 3 egg cups of blood on each occasion, during this study.

Where is the study run from?
The study is being managed by King's College London. Between 26 and 40 recruitment sites will be set up across England and Scotland.

When is the study starting and how long is it expected to run for?
It is anticipated that recruitment will start Sept/Oct 2012 with the study ending after four years.

Who is funding the study?
The study is funded as part of a programme grant from the Medical Research Council (MRC).

Who is the main contact?
Professor Andrew Cope
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Study Co-ordinator
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Contact information

Type(s)
Scientific

Contact name
Prof Andrew Cope

Contact details
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School of Medicine
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Great Maze Pond
London
United Kingdom
SE1 1UL

Additional identifiers

Protocol serial number
97747

Study information

Scientific Title
The TACERA Study: a longitudinal observational study of patients with early rheumatoid arthritis

Acronym
TACERA

Study objectives
Our working hypothesis is that a suite of immunological assays (hereafter termed 'the immunological toolkit') can be used to accurately predict clinical responses to therapy at a molecular and cellular level. We also propose that immune-based assays can be adapted to define an immune signature associated with a state of sustained clinical remission in patients with early RA. This study protocol seeks to recruit a large cohort of patients with early RA. Biological samples will be acquired from study subjects and used to develop the immunological toolkit, through the identification of baseline biomarker signatures (prior to starting therapy), and by documenting the changes in the immune system in response to therapeutic intervention.

Several principles underpin this study:
1. RA is associated with detectable perturbations of the immune system at very early stages of disease.
2. Clinical remission is associated with a biological state that has similarities to a healthy immune system.
3. The healthy immune system is associated with a distinct immunological fingerprint defined by serum, cellular and/or molecular signatures in peripheral blood.
4. Restoration of this state of immune health may be induced with therapies that target these perturbations.

More details can be found at http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=12364

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Central Research Ethics Committee, 02/05/2012, ref: 12/LO/0469
Acknowledgment of compliance with conditions received 07/06/2012

Primary study design
Observational

Study design
Longitudinal observational 18-month multicentre study

Study type(s)
Treatment

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

Interventions
The study is observational, meaning that we are just looking at how arthritis responds to standard therapy in patients, rather than testing the effects of new treatments. Patients who have been diagnosed with early RA, within 6 months of symptom onset, will receive treatment

according to NICE guidelines. Patients will participate in the study for 18 months, attending assessments every 3 months. During these visits a detailed assessment of disease activity (including standard blood monitoring for DMARDs and TNF-inhibitors) will take place along with completion of a number of questionnaires and the provision of additional blood and urine samples for immunoanalysis.

At each study assessment the following will take place:

Patients will complete the following with the research nurse:
1. Disease Activity Score (DAS28 & extended swollen and tender joint counts 66/68, patient global assessment)
2. HAQ (Health assessment questionnaire measuring disability)
3. Lifestyle Factors Questionnaire

The following questionnaires will be completed at Baseline, 6, 12 and 18 months only:
1. SF36 (Quality of life questionnaire)
2. EQ5D (Health outcome questionnaire)
3. FACIT-F questionnaire (Functional assessment of Chronic Illness Therapy)
4. IPQ-R-RA (Illness Perception Questionnaire)
5. MAPLe-RA (Measuring Actual Patient-Led expectations)

The following will be reviewed:
1. Concomitant Diseases and medication
2. Current Medication
3. Adverse events

The following samples will be taken:
1. Blood samples for routine safety monitoring and ESR and CRP values
2. Blood and urine samples for the immunoanalysis.

X-rays of hands and feet will be taken at Baseline, 12 and 18 months.

HRUS (High Resolution Ultrasonography) will be undertaken at baseline, 6 and 12 months (an 18 month scan will be optional). This ultasound based imaging is optional and will be offered to patients at those recruiting centres that provide this service as part of routine clinical care.

Patients may also be telephoned by their Research Nurse in between study visits to check how well their disease is being controlled by their medication.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Current primary outcome measures as of 10/06/2015:
Disease remission at 6 months will be the primary outcome and this will be measured using either the long established DAS28 criterion (DAS28 score <2.6) or the Simplified Disease Activity Index (SDAI) ≤ 3.3, or the new ACR/EULAR 2010 remission criteria:
1. Swollen joint count ≤1
2. Tender joint count ≤ 1

3. CRP ≤ 1 (mg/dl)
4. Patient global ≤ 1 (on a 1 to 10 scale)

Previous primary outcome measures:
Disease remission at 6 months will be the primary outcome and this will be measured using both the long established DAS28 criterion (DAS28 score <2.6) and the new ACR/EULAR remission criteria:
1. Swollen joint count ≤1
2. Tender joint count ≤ 1
3. CRP ≤ 1 (mg/dl)
4. Patient global ≤ 1 (on a 1 to 10 scale)
5. Simplified Disease Activity Index (SDAI) ≤ 3.3

Key secondary outcome(s)
1. Extended (66/68) Joint Count DAS28
2. Simple Disease Activity Score (SDAI)
3. Clinical Disease Activity Score (CDAI)
4. Health Assessment Questionnaire (HAQ) scores
5. EQ5D scores
6. SF-36
7. Radiographic progression of hands and feet X-rays scored by Larsens or van der Heijde Sharpe Modified Scores
8. Disease remission (as defined in primary outcome measure) at 12 and 18 months
9. Immune signatures derived from the analysis of biological samples

Completion date
21/01/2016

Eligibility

Key inclusion criteria
1. Patients should fulfill either 1987 ACR or 2010 ACR/EULAR classification criteria for diagnosis of early RA
2. Positive for serum rheumatoid factor and anti-citrullinated protein autoantibodies (ACPA)
3. Within 6 months of symptom onset
4. Supervising rheumatologist considers that starting therapy with Disease-modifying antirheumatic drugs (DMARDs) is appropriate
5. At least 18 years of age
6. Able and willing to give informed consent to provide clinical data and blood samples at defined time points for the duration of the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit

18 Years

Sex
All

Total final enrolment
267

Key exclusion criteria
1. Previous treatment with DMARDs or biologics
2. Corticosteroid treatment for the current episode of inflammatory arthritis within the last 6 months (patients with a previous episode of inflammatory arthritis treated with corticosteroids more than 6 months before screening will be permitted providing this episode was not ongoing)
3. Use of intramuscular steroid injections between the first clinic attendance (when the diagnosis of RA is made) and study entry
4. Significant co-morbidities (e.g. severe congestive heart failure, renal, hepatic, malignant disease), as judged by the supervising physician
5. Pregnant or wishing to conceive
6. Participating in trials of investigational medicinal products or devices, or other interventions (e.g. exercise) which may have an impact on the patients treatment, immune status or disease activity

Date of first enrolment
05/02/2013

Date of final enrolment
10/07/2015

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Birmingham City Hospital
Dudley Road
Birmingham
United Kingdom
B18 7QH

Study participating centre
Cannock Chase Hospital
Brunswick Road

Cannock
United Kingdom
WS11 5XY

Study participating centre
Chapel Allerton
Chapeltown Road
Leeds
United Kingdom
LS7 4SA

Study participating centre
University Hospital of North Durham
Durham North Road
Durham
United Kingdom
DH1 5TW

Study participating centre
Darlington Memorial Hospital
Hollyhurst Rd
Darlington
United Kingdom
DL3 6HX

Study participating centre
Croydon University Hospital
530 London Road
Croydon
United Kingdom
CR7 7YE

Study participating centre
Doncaster Royal Infirmary
Armthorpe Rd
Doncaster
United Kingdom
DN2 5LT

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

Study participating centre
The Great Western Hospital
Marlborough Road
Swindon
United Kingdom
SN3 6BB

Study participating centre
Gartnaval General Hospital
1053 Great Western Road
United Kingdom
G12 0YN

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
Guy's Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Homerton University Hospital
Homerton Row
London
United Kingdom
E9 6SR

Study participating centre
The James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

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

Study participating centre
University Hospital Lewisham
High Street
Lewisham
London
United Kingdom
SE13 6LH

Study participating centre
Manchester Royal Infirmary
Oxford Rd
Manchester
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M13 9WL

Study participating centre
Mile-End Hospital
Bancroft Road
London
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E1 4DG

Study participating centre
Nuffield Orthopedic Hospital
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Oxford
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OX3 7LD

Study participating centre
Northwick Park Hospital
Watford Road
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United Kingdom
HA1 3UJ

Study participating centre
Poole Hospital
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BH15 2JB

Study participating centre
University Elizabeth Hospital
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B15 2TH

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NE9 6SX

Study participating centre
Queen’s Hospital Burton
Belvedere Rd
Burton-on-Trent
United Kingdom
DE13 0RB

Study participating centre
Queen’s Medical Centre
Derby Rd
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Royal Surrey County Hospital
Egerton Road
Guildford
United Kingdom
GU2 7XX

Study participating centre
Russells Hall Hospital
Pensnett Road
Dudley
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DY1 2HQ

Study participating centre
Queen Elizabeth Hospital, Woolwich
Stadium Rd
London
United Kingdom
SE18 4QH

Study participating centre
University College London Hospital
235 Euston Rd
Fitzrovia

London
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NW1 2BU

Study participating centre
Wishaw General Hospital
50 Netherton St
Wishaw
United Kingdom
ML2 0DP

Sponsor information

Organisation
King's College London (UK)

Organisation
Guy's & St Thomas' Foundation NHS Trust

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council [MRC] (UK) ref: 97747

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
National Institute for Health Research

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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Preprint results	results	12/03/2020	07/08/2020	No	No