

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

<b>Submission date</b> 25/09/2012	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 05/10/2012	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 07/08/2020	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> 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

[andrew.cope@kcl.ac.uk](mailto:andrew.cope@kcl.ac.uk)

Study Co-ordinator

[kch-tr.tacera@nhs.net](mailto:kch-tr.tacera@nhs.net)

## Contact information

### Type(s)

Scientific

### Contact name

Prof Andrew Cope

### Contact details

King's College London

Academic Department of Rheumatology

School of Medicine

New Hunt's House

Guys Hospital Campus

Great Maze Pond

London

United Kingdom

SE1 1UL

## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

## Secondary identifying numbers

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

## Study design

Longitudinal observational 18-month multicentre study

## Primary study design

Observational

## Secondary study design

Longitudinal study

## Study setting(s)

Hospital

## **Study type(s)**

Treatment

## **Participant information sheet**

Not currently available in web format, please use the contact details below to request a patient information sheet

## **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 ultrasound 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 measure**

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)  $\leq 3.3$ , or the new ACR/EULAR 2010 remission criteria:

1. Swollen joint count  $\leq 1$
2. Tender joint count  $\leq 1$
3. CRP  $\leq 1$  (mg/dl)
4. Patient global  $\leq 1$  (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  $\leq 1$
2. Tender joint count  $\leq 1$
3. CRP  $\leq 1$  (mg/dl)
4. Patient global  $\leq 1$  (on a 1 to 10 scale)
5. Simplified Disease Activity Index (SDAI)  $\leq 3.3$

## **Secondary outcome measures**

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

## **Overall study start date**

30/09/2012

## **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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

274 (final recruitment figure 275)

**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**

England

Scotland

United Kingdom

**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**  
**Gartnavel 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  
United Kingdom  
M13 9WL

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

**Study participating centre**  
**Nuffield Orthopedic Hospital**  
Windmill Rd  
Oxford  
United Kingdom  
OX3 7LD

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

**Study participating centre**  
**Poole Hospital**  
Longfleet Road  
Poole  
United Kingdom  
BH15 2JB

**Study participating centre**  
**University Elizabeth Hospital**  
Queen Elizabeth Medical Centre

Birmingham  
United Kingdom  
B15 2TH

**Study participating centre**  
**Queen Elizabeth Hospital Gateshead**  
Queen Elizabeth Avenue  
Gateshead  
United Kingdom  
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  
United Kingdom  
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  
United Kingdom  
NW1 2BU

**Study participating centre****Wishaw General Hospital**

50 Netherton St  
Wishaw  
United Kingdom  
ML2 0DP

**Sponsor information****Organisation**

King's College London (UK)

**Sponsor details**

c/o Mr Keith Brennan  
Hodgkin Building  
Guy's Campus  
London

England  
United Kingdom  
SE1 4UL

**Sponsor type**

University/education

**Website**

<http://www.kcl.ac.uk/>

**Organisation**

Guy's & St Thomas' Foundation NHS Trust

**Sponsor details**

c/o Karen Ignatian  
R&D Department  
16th Floor  
Tower Wing  
Great Maze Pond  
London  
England  
United Kingdom  
SE1 9RT

**Sponsor type**

Hospital/treatment centre

**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, 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

**Publication and dissemination plan**

To be confirmed at a later date

**Intention to publish date****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?
<a href="#">Preprint results</a>	results	12/03/2020	07/08/2020	No	No