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Improving outcomes for patients with rheumatoid arthritis with intermediate disease - is intensive management more effective than standard care?

Submission date
16/01/2014

Recruitment status
No longer recruiting

Registration date
16/01/2014

Overall study status
Completed

Last Edited
26/09/2023

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
Rheumatoid arthritis is a major health problem that affects one adult in a hundred. Its NHS costs exceed £500 million yearly. The main problem in rheumatoid arthritis is swollen (inflamed) joints. If persistent these cause disability and reduce quality of life. It is accepted that patients with active early rheumatoid arthritis need intensive care. This type of care results in reduction in one third of patients. Such reductions minimise disability and maximise quality of life. However, two thirds of active patients fail to achieve this reduction. Their ongoing grumbling arthritis - neither active nor in remission - means most of them are likely to become very disabled in the fullness of time with current treatment approaches. This study focuses on these patients. It is designed to find out whether intensive care results in more reduction of disease in patients with intermediate disease activity. It will also see whether intensive management reduces disability, enhances quality of life and is acceptable to patients.

Who can participate?
The study will involve men and women aged over 18 years who have a diagnosis of Rheumatoid Arthritis.

What does the study involve?
Participants will be randomly chosen to receive intensive management or standard care. Patients receiving intensive management will have monthly sessions with a specialist nurse /health practitioner, drug treatment will be optimised and treatment support regarding pain management, exercise and adherence will be given. The other group will receive standard care. All participants will be in the trial for 12 months. Patients will be assessed initially and at six and 12 months through self-completed questionnaires and clinical evaluation.

What are the possible benefits and risks of participating?
There may not be any direct benefit to participants taking part in the study; however, their arthritis will be monitored very closely by the research team, and it is hoped that this research

will help improve the treatment and management of rheumatoid arthritis for all patients in the future. The risks involved in taking part in the study are small. Patients receiving intensive management are likely to receive more drug therapy. While it is possible that this will result in more side effects, there is little evidence that this will occur. This is because close monitoring and adjustment of treatment is more likely to limit the risk of side effects.

Where is the study run from?
The study will be recruiting through rheumatology departments across England. The study will be run from King's College London (UK).

When is the study starting and how long is it expected to run for?
Recruitment will begin around April 2014. Each participant is expected to be enrolled in the trial for a period of 12 months. The study is due to end in July 2017.

Who is funding the study?
The study is funded by a National Institute for Health Research (NIHR), UK.

Who is the main contact?
Dr Fowzia Ibrahim
fowzia.ibrahim@kcl.ac.uk

Study website
http://www.titrate.org.uk

Contact information

Type(s)
Scientific

Contact name
Dr Fowzia Ibrahim

ORCID ID
http://orcid.org/0000-0002-7069-8024

Contact details
Centre for Rheumatic Diseases
Department of Inflammation Biology
School of Immunology and Microbial Sciences
Faculty of Life Sciences & Medicine
King’s College London
Weston Education Centre
Room 3.55
10 Cutcombe Rd
London
United Kingdom
SE5 9RJ
02078485771
fowzia.ibrahim@kcl.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
15762

Study information

Scientific Title
A pragmatic randomised controlled open trial of the effect of intensive management (IM) compared with standard care (SC) on remission rates at 12 months in rheumatoid arthritis patients with intermediate disease activity

Acronym
TITRATE

Study objectives
TITRATE will formally test the hypothesis that patients with established RA who currently have intermediate disease activity (defined as DAS28-ESR 3.2-5.1 with at least 3 active joints) and are currently receiving at least one DMARD, are more likely to achieve remission at 12 months if they receive intensive management than if they continue to have standard care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West London Research Ethics Committee, 28/10/2013, ref: 13/LO/1308

Study design
Randomized controlled open interventional multicentre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not currently available in web format. Please use the contact details to request a patient information sheet.

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

Interventions
The study will compare standard care with intensive management over a period of 12 months. Intensive management will involve monthly sessions with a trained specialist nurse or health practitioner. A management algorithm will be used to optimise drug treatment and treatment support spanning pain management, exercise and adherence will be given. Drugs will be used within their licensed indications.

The control group will receive standard care according to local and national pathways, which normally involves six-monthly clinical reviews.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Disease remission at 12 months (final assessment) measured by the Disease Activity Score-28 (DAS28) criterion (DAS28-ESR<2.6)

Secondary outcome measures
1. Alternative assessments of remission: Remission measured by the DAS28-CRP and the Simplified Disease Activity Index (SDAI) (remission defined as SDAI≤3.3) at 12 months; remission assessed by all measures at six months.
2. Assessment of Individual Components of Remission: Tender joint counts (68 joints), swollen joint counts (66
joints), patient global assessments on 100mm visual analogue scales (VAS), physician global assessments on
100mm VAS, C-Reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) at baseline, 6 months and 12 months.
3. Disability: Health Assessment Questionnaire (HAQ) at baseline, 6 months and 12 months.
4. Joint Imaging (Predictor of future disability): Plain X-rays of the hands and feet read by a modified Larsen's score at baseline and 12 months.
5. Quality Of Life: EuroQOL 5 Dimensional score (EQ5D-5L) and patient-rated fatigue scale on 100mm VAS at baseline, six and 12 months.
6. Patient Acceptability: Modified version of the Measuring Actual Patient-led Expectations in Rheumatoid Arthritis (MAPLe-RA) questionnaire at baseline and 12 months, Medication Adherence Rating Scale (MARS) and adverse events at baseline, six and 12 months.
7. Economic Assessments: Modified Client Service Receipt Inventory (CSRI) at baseline, six and 12 months.

Overall study start date
01/04/2014

Completion date
14/07/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/06/2015:
1. Diagnosis of Rheumatoid Arthritis (by ACR, 2010 criteria)
2. Have received at least one DMARD for at least six months, and currently receiving at least one DMARD
3. Have intermediate disease activity, defined by:
3.1. DAS28-ESR 3.2-5.1.
3.2. At least three active joints (defined as swollen and/or tender) on 66/68 joint count, to include at least one swollen joint
4. Willing and able to follow an intensive management programme
5. Able and willing to give informed consent

Previous inclusion criteria:
1. Diagnosis of Rheumatoid Arthritis (by ACR, 2010 criteria); duration six months to 10 years
2. Have received at least one DMARD for at least six months, and currently receiving at least one DMARD
3. Have intermediate disease activity, defined by:
3.1. DAS28-ESR 3.2-5.1.
3.2. At least three swollen joints and three tender joints on 66/68 joint count
4. Willing and able to follow an intensive management programme
5. Able and willing to give informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
398

Total final enrolment
335

Key exclusion criteria
1. Major co-morbidities making intensive treatment inadvisable (e.g. heart failure)
2. Previously failed multiple DMARDs (more than or equal to 5 treatments) or having received biologics
3. Irreversible disability from extensive joint damage (for example, replacement of three or more major joints)

4. Women who are pregnant, breastfeeding or planning to conceive
5. Currently in early RA pathway
6. Current or recent (within the previous 12 weeks) participation in another interventional trial

Date of first enrolment
01/04/2014

Date of final enrolment
30/06/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
King's College London
London
United Kingdom
SE5 9RJ

Sponsor information

Organisation
King's College London

Sponsor details
Strand
London
England
United Kingdom
WC2R 2LS

Sponsor type
University/education

Website
http://www.kcl.ac.uk/index.aspx

ROR
https://ror.org/0220mzb33

Organisation
King's College Hospital NHS Foundation Trust

Sponsor details
Research & Development
161 Denmark Hill
London
England
United Kingdom
SE5 8EF

Sponsor type
Hospital/treatment centre

Website
https://www.kch.nhs.uk/

ROR
https://ror.org/01n0k5m85

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (NIHR) (UK) - Programme Grant for Applied Research, Ref: RP-PG-0610-10066

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
30/09/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as there is no consent to make this data available in the public domain. However, the researchers will be able to provide an appropriate request i.e. summary participant data after review by the TITRATE team.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2020	06/10/2020	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Secondary analysis	25/09/2023	26/09/2023	Yes	No