ISRCTN57761809 https://doi.org/10.1186/ISRCTN57761809

Effect of anti-tumour necrosis factor alpha (TNFα) therapy on blood vessel health in patients with rheumatoid arthritis

Submission date	Recruitment status	[ ] Prospectively registered
07/04/2008	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
09/05/2008	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
02/02/2015	Musculoskeletal Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
ETADA90 v1

Study information

Scientific Title
Effect of anti-tumour necrosis factor alpha (TNFα) therapy on endothelial function and other surrogate markers of cardiovascular disease in patients with rheumatoid arthritis

Study objectives
Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder characterized by a symmetrical erosive polyarthritis with inflammatory multisystemic involvement. Most patients exhibit a chronic fluctuating course of disease that, if left untreated, results in progressive joint destruction, deformity, and disability. The patient with RA has their life span shortened by 15-20%, with 34-40% of excess deaths being due to cardiovascular disease.

Study aim:
To assess the effect of the TNFa blocking drug etanercept and adalimumab on endothelial dysfunction and other surrogate markers of cardiovascular diseases in patients with RA. We hypothesised that the biologic drugs have the potential to improve endothelial dysfunction and other surrogate markers of cardiovascular disease (CVD) in patients with RA. We believe that if etanercept and adalimumab can improve endothelial dysfunction in RA patients they may be able to reduce the cardiovascular morbidity and mortality seen in this group of patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Tayside Committee on Medical Research Ethics. Date of approval: 05/09/2005 (ref: 05/S1401 /112)

Study design
Observational open-label single-centre study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Not 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
This is an observational study. The drugs are prescribed by the rheumatology team, and this study assesses the impact of those drugs on blood vessel health.

90 RA patients (30 due to be started on methotrexate, 30 due to be started on etanercept and 30 due to be started on adalimumab) will be recruited from rheumatology clinics throughout Tayside. Treatment allocation (etanercept, adalimumab or methotrexate) will be decided by the rheumatologists in the clinic.

The drugs are normally prescribed as:
Etanercept: Subcutaneous injections 25 mg twice a week or 50 mg once a week
Adalimumab: Subcutaneous injections 40 mg every other week
Methotrexate: Orally once a week. Doses range from 7.5 mg a week to 25 mg a week

Surrogate markers of cardiovascular disease will be measured at baseline (before commencement of methotrexate/ etanercept/ adalimumab), 2 months and at 4 months.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Endothelial function measured by the following at baseline, 2 and 4 months:
1. Laser Doppler flowmetry after iontophoretic delivery of acetylcholine and sodium nitroprusside (microvascular)
2. Brachial artery flow mediated dilatation (macrovascular)

Secondary outcome measures
The following were assessed at baseline, 2 and 4 months:
1. Endothelial function measured by blood testing of vascular function and damage (E selectin, thrombomodulin)
2. Arterial stiffness measured by ultrasound echo tracking and applanation tonometry
3. Oxidative stress (Isoprostane levels)
4. RA disease activity (28-item Disease Activity Score [DAS28], Health Assessment Questionnaire [HAQ], 36-item Short Form health survey [SF-36])

Overall study start date
10/02/2006

Completion date
25/04/2008

Eligibility

Key inclusion criteria

1. Both males and females, 18 years old or over
2. Fulfil the 1987 American College of Rheumatology (ACR) classification criteria for rheumatoid arthritis
3. No exposure to anti-TNFa drugs in the last 3 months
4. Fulfil the National Institute for Clinical Excellence guidelines on the use of anti-TNFa drugs in rheumatoid arthritis* and be:
4.1. About to start etanercept or adalimumab (treatment group)
4.2. About to start methotrexate (control group)

* The patients in the control group must have had adequate therapeutic trial of at least one previous Disease Modifying Anti-Rheumatic Drug (DMARD) rather than two

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
90

Key exclusion criteria
1. Previous cardiovascular or cerebrovascular event in the last 3 years
2. Undergoing treatment for a cardiovascular risk factor except:
2.1. Patients with hypertension on stable medication for the last 3 months
2.2. Patients with hypercholesterolaemia on stable medication for the last 3 months

Date of first enrolment
10/02/2006

Date of final enrolment
25/04/2008

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Vascular and Inflammatory Diseases Research Unit
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Sponsor type
University/education

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ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Industry

Funder Name
Wyeth

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2010		Yes	No