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# Effect of folic acid supplementation and allopurinol on blood vessel health in patients with rheumatoid arthritis

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| **Submission date**<br>07/04/2008 | **Recruitment status**<br>Stopped | [ ] Prospectively registered<br>[ ] Protocol<br>[ ] Statistical analysis plan<br>[ ] Results<br>[ ] Individual participant data<br>[ ] Record updated in last year |
| **Registration date**<br>09/05/2008 | **Overall study status**<br>Stopped | |
| **Last Edited**<br>21/06/2017 | **Condition category**<br>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
MTXa54 v1 04/04/05

# Study information

### Scientific Title
Effect of folic acid supplementation and allopurinol on endothelial function in patients with rheumatoid arthritis treated with methotrexate

### 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 up to 40% of excess deaths being due to cardiovascular disease.

Study aim:
To evaluate whether endothelial function and other surrogate markers of cardiovascular disease can be improved by the addition of extra folic Acid (above the dose conventionally given) and allopurinol (which attenuates oxidative stress) in patients with RA taking methotrexate.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Tayside Committee on Medical Research Ethics, 26/05/2005, ref: 05/S1401/55

### Study design
Single-centre randomised double-blind placebo-controlled trial

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### 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

The participants will be randomised to the following:

Control group: 5 mg of folic acid (oral) once a week as per methotrexate protocol
"Active" group: 5 mg of folic acid (oral) 7 days a week (extra folic acid)

At 4 months, both groups will be randomised again to receive either allopurinol (oral) 300 mg a day or placebo in addition to their folate/control medication for 8 weeks.

### Intervention Type
Drug

### Phase
Not Applicable

### Drug/device/biological/vaccine name(s)
Folic acid, allopurinol and methotrexate

### Primary outcome measure
Endothelial function measured by the following at baseline, 4 and 6 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, 4 and 6 months:
1. Endothelial function measured by blood testing of vascular function and damage (E selectin, thrombomodulin)
2. Arterial stiffness measured by applanation tonometry
3. Oxidative stress (Isoprostane levels)
4. Serum homocysteine, folic acid and uric acid levels
5. RA disease activity (28-item Disease Activity Score [DAS28], Health Assessment Questionnaire [HAQ], the 36-item short form health survey [SF-36])

### Overall study start date
21/08/2006

### Completion date
14/03/2008

### Reason abandoned (if study stopped)
Lack of funding/sponsorship

## 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 RA
3. On methotrexate for at least 6 months

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
80

### Key exclusion criteria
1. Previous cardiovascular or cerebrovascular events 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 hypercholesterolemia on stable medication for the last 3 months
3. Contraindications to allopurinol (moderate to severe renal impairment, liver impairment, concomitant treatment with azathioprine, known allergy to allopurinol)

### Date of first enrolment
21/08/2006

### Date of final enrolment
14/03/2008

## Locations

### Countries of recruitment
Scotland

United Kingdom

### Study participating centre
**Vascular and Inflammatory Diseases Research Unit**
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## Sponsor information

### Organisation

University of Dundee (UK)

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### Sponsor type
University/education

### Website
http://www.dundee.ac.uk

### ROR
https://ror.org/03h2bxq36

## Funder(s)

### Funder type
Charity

### Funder Name
Tenovus Scotland (ref: T05/31) (UK)

### Funder Name
Anonymous Trust, University of Dundee (UK)

## 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