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

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
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

Study type(s)
Treatment

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(s)
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)

Key secondary outcome(s))
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])

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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
United Kingdom

Scotland

Study participating centre
Vascular and Inflammatory Diseases Research Unit
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
University of Dundee (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

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes