

Allopurinol and cardiovascular outcomes in patients with ischaemic heart disease

Submission date 29/07/2013	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 16/08/2013	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 03/04/2024	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Allopurinol is a medication used to prevent gout. Allopurinol has several positive effects on heart and blood vessels, is inexpensive and is already widely used in patients. Ischaemic heart disease (heart attack) is the most common cause of death in people in the UK and treatment of patients with ischaemic heart disease costs the NHS billions of pounds each year. In this study, we want to improve the treatment of patients with ischaemic heart disease. We want to investigate whether adding allopurinol to these patients usual medications will reduce their risk of having a stroke, heart attack or of dying due to cardiovascular disease.

Who can participate?

Patients 60 years and over with ischaemic heart disease (IHD) can participate in the study

What does the study involve?

Patients will attend their local primary care centre (general practice) to take part in the study. Patients will be randomly allocated to receive 600mg daily allopurinol (300mg daily in those patients with mild to moderate renal impairment at screening) or no treatment in addition to their usual medications. They will then will be followed up for a period of around 4 years to count the number of heart attacks, strokes and cardiovascular deaths that occur. The numbers of these events that occur in different treatment groups will be compared to see if there is a benefit of adding allopurinol to their ongoing treatment. Most of the follow-up information will be collected electronically by accessing centrally held electronic records of hospital admissions and deaths, which will make the study easier for patients and more cost-efficient. We will also measure the quality of life and whether there is a cost benefit of using allopurinol in patients with ischaemic heart disease.

What are the possible benefits and risks of participating?

Although we are doing the study to find out whether allopurinol reduces the risk of heart attack, stroke and cardiovascular death in patients with ischaemic heart disease, there may be no direct benefit to a patient of taking part in this study. Some patients might experience side effects due to taking allopurinol, for example, rash, nausea or vomiting.

Where is the study run from?

Medicines Monitoring Unit (MEMO), University of Dundee/Ninewells Hospital (lead centre) and eight other hospitals in Northern England and Scotland (UK)

When is the study starting and how long is it expected to run for?

September 2013 to March 2022

Who is funding the study?

National Institute of Health Research (UK)

Who is the main contact?

Prof. Isla Mackenzie

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Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

2013-003559-39

Protocol serial number

HTA 11/36/41

Study information

Scientific Title

Allopurinol and cardiovascular outcomes in patients with ischaemic heart disease (ALL-HEART): a randomised controlled trial

Acronym

ALL-HEART

Study objectives

The hypothesis of the study is that adding allopurinol 600mg daily to usual therapy will improve cardiovascular outcomes in patients aged over 60 with ischaemic heart disease.

Ethics approval required

Old ethics approval format

Ethics approval(s)

East of Scotland Research Ethics Service, 16/09/2013, ref: 13/ES/0104

Study design

Multi-centre controlled prospective randomized open-label blinded endpoint (PROBE) trial

Primary study design

Interventional

Study type(s)

Prevention

Health condition(s) or problem(s) studied

Ischaemic heart disease (IHD)

Interventions

Interventions as of 04/04/2016:

Patients are randomised to two groups:

1. Receive standard care plus allopurinol (600 mg daily) (Allopurinol dose will be lower at 300mg daily in those patients with mild to moderate renal impairment at screening)
2. Standard care alone

They will be followed up for a period of around 4 years. Most of the follow up data will be collected electronically by accessing centrally held electronic records of hospital admissions and deaths

Original interventions:

Patients are randomised to two groups:

1. Receive standard care plus allopurinol (600 mg daily)
2. Standard care alone

They will be followed up for a period of around 4 years. Most of the follow up data will be collected electronically by accessing centrally held electronic records of hospital admissions and deaths

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Allopurinol

Primary outcome(s)

Composite (APTC) CV endpoint of non-fatal myocardial infarction (MI), non-fatal stroke and CV death is determined by record-linkage supported by information from medical records

Key secondary outcome(s)

1. Non-fatal MI
2. Non-fatal stroke
3. CV death
4. All-cause mortality
5. All CV hospitalisations
6. Hospitalisation for acute coronary syndrome (ACS)
7. Coronary revascularisation
8. Hospitalisation for ACS or revascularisation
9. Hospitalisation for heart failure
10. Quality of life and cost effectiveness of allopurinol

The secondary outcome measures 1-9 will primarily be determined by record-linkage supported by information from medical records. Quality of life is assessed by EQ-5D and Seattle Angina Questionnaires at 0, 1 and 5 years. The cost-effectiveness analysis is supported by information from service usage questionnaires at 1 and 5 years and additionally at 2, 3 and 4 years in a 25% sample of the study population.

Completion date

31/03/2022

Eligibility

Key inclusion criteria

1. Male or female patients aged 60 years and over
2. Ischaemic heart disease (IHD) defined as a diagnosis of angina or myocardial infarction (MI) at any time or other evidence of ischaemic heart disease (investigator opinion)

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Senior

Lower age limit

60 years

Sex

All

Total final enrolment

5937

Key exclusion criteria

1. History of gout
2. Known severe renal impairment (eGFR <30ml/min)
3. Moderate to severe heart failure (NYHA III-IV)
4. Significant hepatic disease (eg ALT >3 x upper limit of normal, cirrhosis, ascites) (investigator opinion)
5. Patients currently taking part in another interventional clinical trial of an investigational medicinal product or medical device (or taken part in one within the last 3 months)
6. Previous allergy to allopurinol
7. Previous serious adverse cutaneous (skin) reaction to any drug (eg Stevens Johnson syndrome, toxic epidermal necrolysis, hospitalisation due to skin reaction to drug) (investigator opinion)
8. Patients already taking urate lowering therapy (including allopurinol, febuxostat, sulfinpyrazone, benzbromarone, probenecid, rasburicase)
9. Patients taking azathioprine, mercaptopurine, ciclosporin or theophylline
10. Malignancy (except non-metastatic, non-melanoma skin cancers, cervical in-situ carcinoma, breast ductal carcinoma in situ, or stage 1 prostate carcinoma) within the last 5 years (investigator opinion)

Date of first enrolment

07/02/2014

Date of final enrolment

29/09/2017

Locations

Countries of recruitment

United Kingdom

England

Scotland

Study participating centre

Medicines Monitoring Unit (MEMO)

University of Dundee

Level 7 Ninewells Hospital

Dundee

United Kingdom

DD1 9SY

Study participating centre

Nottingham Digestive Diseases Centre

University Hospital

Derby Road

Nottingham

United Kingdom
NG7 2UH

Study participating centre
Aberdeen Royal Infirmary
Clinical Pharmacology Unit
Orange Zone Level 4
Foresterhill
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AB25 2ZN

Study participating centre
University Hospital Crosshouse
Department of Research & Development
NHS Ayrshire & Arran
58 Lister Street
Kilmarnock
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KA2 OBE

Study participating centre
Dumfries & Galloway Royal Infirmary
Research & Development Support Unit
Ground Floor
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United Kingdom
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Study participating centre
Royal Infirmary Edinburgh
Clinical Research Facility
Little France
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United Kingdom
EH16 4SA

Study participating centre
West Glasgow Ambulatory Care Hospital
Clinical Research & Development

Dalnair Street
Glasgow
United Kingdom
G3 8SW

Study participating centre
Raigmore Hospital
Research & Development Department
Centre for Health Science
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United Kingdom
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YO31 7EX

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Study participating centre
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IC1 Liverpool Science Park
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Study participating centre
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NG7 2UH

Sponsor information

Organisation
The University of Dundee (UK)

ROR
<https://ror.org/03h2bxq36>

Funder(s)

Funder type

Government

Funder Name

Health Technology Assessment Programme

Alternative Name(s)

NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to the limitations of participant consent. The data will be held in The University of Dundee, Dundee, UK.

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		08/10/2022	11/10/2022	Yes	No
Results article		01/03/2024	03/04/2024	Yes	No
Protocol article	protocol	08/09/2016		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes