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Allopurinol and cardiovascular outcomes in patients with ischaemic heart disease

Submission date 29/07/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 16/08/2013	**Overall study status** Completed	
Last Edited 03/04/2024	**Condition category** Circulatory System	

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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Study website
https://www.allheartstudy.org/

Contact information

Type(s)
Scientific

Contact name
Prof Isla Mackenzie

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Additional identifiers

EudraCT/CTIS number
2013-003559-39

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Prevention

Participant information sheet
Participant information sheet will be available on http://allheartstudy.org or can be requested using the contact details below (once all regulatory approvals have been obtained).

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 measure
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

Secondary outcome measures
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.

Overall study start date
01/09/2013

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 ofischaemic heart disease (investigator opinion)

Participant type(s)
Patient

Age group
Senior

Lower age limit
60 Years

Sex
Both

Target number of participants
5215

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
England

Scotland

United Kingdom

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
Aberdeen
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AB25 2ZN

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

Study participating centre
Dumfries & Galloway Royal Infirmary
Research & Development Support Unit
Ground Floor
Bankend Road
Dumfries
United Kingdom
DG1 4AP

Study participating centre
Royal Infirmary Edinburgh
Clinical Research Facility
Little France
Edinburgh
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 Deparment
Centre for Health Science
Inverness
United Kingdom
IV2 3JH

Study participating centre
NIHR Clinical Research Network: North East and North Cumbria
Regent Farm Road
Gosforth
Newcastle upon Tyne
United Kingdom
NE3 3HD

Study participating centre
Monklands Hospital
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United Kingdom
ML6 0JS

Study participating centre
University Hospital Hairmyres
East Kilbride
United Kingdom
G75 8RG

Study participating centre
NIHR Clinical Research Network: Kent Surrey and Sussex
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BN1 9PH

Study participating centre
NIHR Clinical Research Network Yorkshire & Humber
York NHS Foundation Trust Offices
York
United Kingdom
YO31 7EX

Study participating centre
NIHR Clinical Research Network South West Peninsula
Royal Devon & Exeter Hospital (Wonford)
Exeter
United Kingdom
EX2 5DW

Study participating centre
NIHR Clinical Research Network North West Coast
IC1 Liverpool Science Park
Liverpool
United Kingdom
L3 5TF

Study participating centre
NIHR Clinical Research Network West Midlands
c/o Nottingham Digestive Diseases Centre
University Hospital Derby Road
Nottingham
United Kingdom
NG7 2UH

Sponsor information

Organisation
The University of Dundee (UK)

Sponsor details
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Tayside medical Sciences Centre (TASC)
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DD1 9SY

Sponsor type
University/education

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The trial results will be reported in a peer-reviewed journal and at major scientific and clinical meetings. A non-technical summary of the results will also be produced to be sent to patients who participated in the trial, patient groups and cardiovascular charities, as well as communication of the results to the wider public via the media. Copies of the results will be sent to guideline groups for consideration and incorporation into revisions of guidelines.

Intention to publish date
31/08/2022

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?
Protocol article	protocol	08/09/2016		Yes	No
Results article		08/10/2022	11/10/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/03/2024	03/04/2024	Yes	No