ISRCTN11081180 https://doi.org/10.1186/ISRCTN11081180

Does allopurinol reduce the size of the right side of the heart in patients who have chronic lung disease and high pressure in the blood vessels supplying the lungs?

Submission date
11/02/2015

Recruitment status
No longer recruiting

Registration date
17/02/2015

Overall study status
Completed

Last Edited
29/12/2020

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
People with lung disease are at an increased risk of heart complications. One of the biggest problems is that the muscle wall of the heart thickens. The medical term for this is right ventricular hypertrophy (RVH). RVH makes the heart work less well and patients with RVH are at a greater risk of heart complications than those without it. The pressure in the blood vessel between this heart chamber and the lungs can also increase. This is called pulmonary artery hypertension (PAH). This can leave patients more breathless as the blood is not picking up oxygen well from the lungs. It has previously been shown that a drug called allopurinol, which is usually used to treat gout, had the noteworthy side effect of being able to reduce thickening of the left side of the heart wall in patients who had kidney disease or diabetes. The aim now is to see if patients with lung disease and raised pressure in their right side of the heart may also benefit from treatment with allopurinol. If RVH can be reduced using allopurinol, this might be a new way to reduce cardiac risk in these patients and possibly improve their ability to exercise and reduce symptoms.

Who can participate?
Adult patients who have lung disease with raised PAH.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given allopurinol for a year. Those in group 2 are given a placebo for a year. All currently prescribed medication for each participants lung disease continue as normal throughout the study. All participants have a magnetic resonance imaging (MRI) scan of their heart before the study starts and after their treatment ends so that we can compare if there is a difference between normal treatment and addition of allopurinol.

What are the possible benefits and risks of participating?
Participants may find that taking part in this study improves their exercise tolerance and their

PAH symptoms. Adverse side effects may include a skin rash, nausea, vomiting, diarrhoea, dizziness, and an acute attack of gout.

Where is the study run from?
NHS Tayside - University of Dundee (UK)

When is the study starting and how long is it expected to run for?
February 2015 to July 2017

Who is funding the study?
British Heart Foundation (UK)

Who is the main contact?
Dr Patrick Liu Shiu Cheong
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2014-002305-38

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
2013CV11

Study information

Scientific Title
Does allopurinol reduce right ventricular mass in lung disease associated pulmonary hypertension?

Acronym
ALPHA

Study objectives
The aim of this study is to determine whether allopurinol reduces right ventricular mass in lung disease associated pulmonary hypertension

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Service, 11/08/2014, ref. 14/ES/1035

Study design
Randomised double-blinded placebo-controlled single-centre study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a patient information sheet: p.s.k.liushiucheong@dundee.ac.uk

Health condition(s) or problem(s) studied
Pulmonary hypertension and chronic obstructive pulmonary disease / interstitial lung disease

Interventions
1. Treatment arm: Allopurinol 100mg once daily for 2 weeks, then increased to 300mg once daily for 4 weeks and increased to 300mg twice daily for further 46 weeks.
2. Placebo arm: Microcrystalline cellulose one tablet daily for one month then twice daily for eleven months.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Allopurinol

Primary outcome measure
The change in right ventricular (RV) mass index with allopurinol versus placebo after 12 months of treatment. Cardiac Magnetic Resonance Imaging scan will be done at the baseline and at the end of the 12 month study period on a 3T Magnetom scanners (Siemens, Erlangen, Germany) using dedicated phase array cardiac and phosphorus spectroscopy coils. Analysis will be performed offline (Argus Software, Siemens) by a single blinded observer for the assessment of ventricular volumes. This single observer will analyse all the scans. The reproducibility of the RV mass assessment using MRI will be derived for this observer. The change RV mass index in participants treated with allopurinol will be compared with placebo.

Secondary outcome measures
1. Measure a change in RV end diastolic volume, RV ejection fraction, left ventricular (LV) mass, LV end systolic volume, LV end diastolic volume or LV ejection fraction and pulmonary compliance. Timescale: 12 months. Cardiac Magnetic Resonance Imaging scan will be done at the baseline and at the end of the 12 month study period on a 3T Magnetom scanners (Siemens, Erlangen, Germany) using dedicated phase array cardiac and phosphorus spectroscopy coils. Analysis will be performed offline (Argus Software, Siemens) by a single blinded observer for the assessment of ventricular volumes. This single observer will analyse all the scans.
2. Determine if there is a difference in pulmonary artery pressure, RVSP, or PAT with allopurinol compared with placebo. Timescale: 12 months. Cardiac Magnetic Resonance Imaging scan will be done at the baseline and at the end of the 12 month study period on a 3T Magnetom scanners (Siemens, Erlangen, Germany) using dedicated phase array cardiac and phosphorus spectroscopy coils. Analysis will be performed offline (Argus Software, Siemens) by a single blinded observer for the assessment of ventricular volumes. This single observer will analyse all the scans. Echocardiogram will be done at baseline and at the end of the 12 month study period.
3. Change in oxygen saturation as measured pre and post six minute walk test (6MWT) with allopurinol versus placebo. Timescale: 12 months. On each occasion that the 6MWT is carried out, it will be done twice with a break of at least 1 hour in between and on an even floor with vocal support from the investigator which is in full accord with American Thoracic Society guidelines. The distance achieved on the second walk will be taken as the main result as recommended for lung studies. Patients on long term oxygen therapy (LTOT) will undergo 6MWT off oxygen.
4. Change in exercise capacity as measured by 6MWT with allopurinol versus placebo. Timescale: 12 months. On each occasion that the 6MWT is carried out, it will be done twice with a break of at least 1 hour in between and on an even floor with vocal support from the investigator which is in full accord with American Thoracic Society guidelines. The distance achieved on the second walk will be taken as the main result as recommended for lung studies. Patients on long term oxygen therapy (LTOT) will undergo 6MWT off oxygen.
5. Change in quality of life (QOL) measures with allopurinol compared to placebo
Timescale: 12 months. QOL measures will be carried out at baseline and 12 month visits. St George's Respiratory Questionnaire (SGRQ) will be used as disease specific QOL measure in patients with COPD. King's Brief Interstitial Lung Disease (K-BILD) QOL questionnaire will be used as a measure of health status for patients with ILD. SF-36 questionnaire will be as a general QOL measure and BDI/TDI questionnaire will be used for assessment of functional impairment.
6. Change in inflammatory and other blood markers with allopurinol compared with placebo.

Timescale: 12 months. Research blood tests will be taken at baseline and at the final visit at month 12. They will include BNP, inflammatory markers and other markers of interest such as oxidative stress. Additional blood markers may be tested on the samples at a later date.

Overall study start date
01/02/2015

Completion date
16/06/2017

Eligibility

Key inclusion criteria
1. Aged 18 years or over
2. Previously diagnosed with COPD or ILD
3. Screening echocardiography based diagnosis of PH as indicated by RVSP >25 mmHg, and/or PAT <110 m/s2 and/or RVM >5.5 mm
4. Stable lung disease medication for at least 2 weeks prior to consent
5. Women of child bearing potential must agree to scheduled pregnancy testing prior to and during study treatment period and to use an appropriate method of contraception if sexually active

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
72

Total final enrolment
71

Key exclusion criteria
1. Documented allergy or intolerance to allopurinol
2. Objection to taking capsules made from animal-sourced gelatine
3. Left Ventricular Ejection Fraction <45% on echocardiography screening
4. Severe aortic stenosis on echocardiography (screening)
5. Already had gout or currently taking allopurinol
6. Severe hepatic disease
7. Renal disease; CKD class 3B or greater
8. Taking prohibited medication; azathioprine, 6 mercaptopurine, or theophylline
9. Malignancy (receiving active treatment) or other life threatening diseases

10. Pregnant or lactating
11. Women unwilling to agree to use an appropriate method of contraception during the study treatment period if sexually active
12. Any contraindication to MRI (claustrophobia, metal implants)
13. Patients who have participated in any other clinical trial of an investigational medicinal product within the previous 30 days will be excluded
14. Any other considered by a study physician to be inappropriate for inclusion

Date of first enrolment
01/03/2015

Date of final enrolment
31/07/2017

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
NHS Tayside - University of Dundee
Division of Cardiovascular & Diabetes Medicine
Ninewells Hospital & Medical School
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Sponsor information

Organisation
NHS Tayside - University of Dundee

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Sponsor type
Hospital/treatment centre

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

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Basic results		13/11/2018	13/11/2018	No	No
Basic results			21/04/2020	No	No
Results article	results	25/08/2020	29/12/2020	Yes	No
HRA research summary			26/07/2023	No	No