Clinical trial results:
A Prospective Study to Evaluate the Effect of Allopurinol on Muscle Energetics in Older People with Impaired Physical Function.

Summary

EudraCT number	2014-004122-18
Trial protocol	GB
Global end of trial date	06 July 2017

Results information

Result version number	v1 (current)
This version publication date	22 December 2019
First version publication date	22 December 2019
Summary attachment (see zip file)	Abstract (ALFIE - Abstract.docx)

Trial information

Trial identification

Sponsor protocol code	2012GR12

Additional study identifiers

ISRCTN number	ISRCTN03331094
ClinicalTrials.gov id (NCT number)	NCT01550107
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Reference: 2012GR12

Notes:

Sponsors

Sponsor organisation name	University of Dundee
Sponsor organisation address	Ninewells Hospital & Medical School George Pirie Way , Dundee, United Kingdom, DD1 9SY
Public contact	Professor Jacob George, University of Dundee Tayside Medical Sciences Centre , 01382 383656, j.George@dundee.ac.uk
Scientific contact	Professor Jacob George, University of Dundee Tayside Medical Sciences Centre , 01382 383656, j.George@dundee.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2017
Global end of trial reached?	Yes
Global end of trial date	06 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective will be to see if Allopurinol can improve tiredness in the legs after exercise. To measure this we will be assessing the rate of metabolism (how quickly or efficiently the leg muscle uses up energy) before, during and after exercising leg muscles and using an MRI machine to measure this.

Protection of trial subjects:

The CI and study staff involved with this study will comply with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. The CI and study staff will also adhere, if appropriate, to the current version of the NHS Scotland Code of Practice on Protecting Patient Confidentiality. Access to collated participant data will be restricted to the CI and appropriate study staff.
Computers used to collate the data will have limited access measures via user names and passwords. Published results will not contain any personal data that could allow identification of individual participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 February 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 124
Worldwide total number of subjects	124
EEA total number of subjects	124

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	96
85 years and over	28

Subject disposition

Recruitment

Recruitment details:

142 subjects were screened, 124 subjects who fulfilled the eligibility criteria were recruited into the study.

Pre-assignment

Screening details:

142 subjects were screened using four separate sources, outpatient clinics across NHS Tayside, Research Database, Tayside Medicine for the elderly service and the Scottish Primary Care Research Network.

Pre-assignment period milestones

Number of subjects started	124
Number of subjects completed	124

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Double blind medication (allopurinol or placebo) will be manufactured, prepared, packaged and labelled by Tayside Pharmaceuticals. Medication will come labelled as "Participant ID No. 001", "Participant ID No. 002", etc.

Arms

Are arms mutually exclusive?	Yes
Arm title	Allopurinol Arm

Arm description:

Received Allopurinol

Arm type	Active comparator
Investigational medicinal product name	Allopurinol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300mg, start dose for 4 weeks once daily then increased to 300mg twice daily, if tolerated, for a further 16 weeks

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300mg, start dose for 4 weeks once daily then increased to 300mg twice daily, if tolerated, for a further

16 weeks

Number of subjects in period 1	Allopurinol Arm	Placebo
Started	62	62
Completed	58	58
Not completed	4	4
Consent withdrawn by subject	1	3
Physician decision	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Allopurinol Arm
Reporting group description: Received Allopurinol	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Allopurinol Arm	Placebo	Total
Number of subjects	62	62	124
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	62	62	124
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	29	30	59
Male	33	32	65

End points

End points reporting groups	
Reporting group title	Allopurinol Arm
Reporting group description: Received Allopurinol	
Reporting group title	Placebo
Reporting group description: -	

Primary: Normalised ViPCr	
End point title	Normalised ViPCr
End point description:	
End point type	Primary
End point timeframe: 20 weeks	

End point values	Allopurinol Arm	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	62		
Units: Percentage				
number (confidence interval 95%)	0.60 (0.33 to 0.94)	0.59 (0.43 to 0.82)		

Statistical analyses

Statistical analysis title	Statistical Analysis Plan
Comparison groups	Allopurinol Arm v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.05
Method	The primary analysis population will be

Notes:
[1] - Modified intention to treat

Primary: UN-normalised ViPCr	
End point title	UN-normalised ViPCr
End point description:	
End point type	Primary

End point timeframe:
20 weeks

End point values	Allopurinol Arm	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	62		
Units: percentage				
number (confidence interval 95%)	28227 (16818 to 51171)	29005 (17810 to 42279)		

Statistical analyses

Statistical analysis title	Statistical Analysis plan
Comparison groups	Allopurinol Arm v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	The primary analysis population will be

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire duration of study	
Adverse event reporting additional description:	
Recorded all AEs and SAEs	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Randomised Patients

Reporting group description: -

Serious adverse events	Randomised Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 124 (0.81%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Nervous system disorders			
Guillain-Barre syndrome			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Randomised Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 124 (28.23%)		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 124 (7.26%)		
occurrences (all)	9		
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed occurrences (all)	10 / 124 (8.06%) 11		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 8 / 124 (6.45%) 11 8 / 124 (6.45%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2016	Orbital X-ray as part of standard care safety screening

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported