



Clinical trial results:

Does Allopurinol regress Left Ventricular Hypertrophy in Patients with Treated Essential Hypertension?

Summary

EudraCT number	2014-002083-33
Trial protocol	GB
Global end of trial date	26 May 2017

Results information

Result version number	v1 (current)
This version publication date	20 December 2019
First version publication date	20 December 2019
Summary attachment (see zip file)	ALLAY Abstract (ALLAY Abstract for EudraCT.pdf)

Trial information

Trial identification

Sponsor protocol code	2012CV15
-----------------------	----------

Additional study identifiers

ISRCTN number	ISRCTN40476871
ClinicalTrials.gov id (NCT number)	NCT02237339
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Reference: 2012CV15

Notes:

Sponsors

Sponsor organisation name	University of Dundee
Sponsor organisation address	Ninewells Hospital, Dundee DD1 9SY, Dundee, United Kingdom, DD1 9SY
Public contact	McSwiggan, University of Dundee, 01382 383233, s.j.mcswiggan@dundee.ac.uk
Scientific contact	McSwiggan, University of Dundee, 01382 383233, s.j.mcswiggan@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	14 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 May 2017
Global end of trial reached?	Yes
Global end of trial date	26 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary research objective is to test if allopurinol can reduce thickening of the heart muscle in patients with treated high blood pressure.

Protection of trial subjects:

Safety bloods taken at every study visit

MRI safety check list completed to ensure safety/suitability for cardiac MRI

Urine pregnancy testing for female patients of child bearing potential

Recording/reporting of adverse events

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2014
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: 72
Worldwide total number of subjects	72
EEA total number of subjects	72

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)	22
From 65 to 84 years	48
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Recruitment 30/9/14 - 6/6/16. All recruited in Scotland.

Pre-assignment

Screening details:

200 were excluded

123 no echocardiographic LVH

53 uncontrolled hypertension

7 poor echo quality

7 contraindications to MRI

3 Gout

1 not hypertensive

1 change in BP medications <3 months

1 severe aortic stenosis

1 taking theophylline

1 active cancer treatment

1 atrial fibrillation

1 decided not to participate (issues with insurance)

Pre-assignment period milestones

Number of subjects started	72
Number of subjects completed	72

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

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Placebo Group
------------------	---------------

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Microcrystalline cellulose Ph Eur
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One capsule daily for one month (+/- one week) increased to one capsule twice daily for 11 months (+/- 2 weeks).

Arm title	Intervention Group
------------------	--------------------

Arm description: -

Arm type	Active comparator
----------	-------------------

Investigational medicinal product name	Allopurinol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

300mg daily for one month (+/- one week), then 300mg twice daily for 11 months (+/- 2 weeks).

Number of subjects in period 1	Placebo Group	Intervention Group
Started	36	36
Completed	30	32
Not completed	6	4
Adverse event non fatal/Consent withdrawn	6	4

Baseline characteristics

Reporting groups

Reporting group title	Placebo Group
Reporting group description: -	
Reporting group title	Intervention Group
Reporting group description: -	

Reporting group values	Placebo Group	Intervention Group	Total
Number of subjects	36	36	72
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)	12	10	22
From 65-84 years	23	25	48
85 years and over	1	1	2
Age continuous Units: years			
arithmetic mean	65.6	66.8	
standard deviation	± 10.4	± 9.4	-
Gender categorical Units: Subjects			
Female	16	16	32
Male	20	20	40
IHD Units: Subjects			
Yes	0	2	2
No	36	34	70
Dyslipidaemia Units: Subjects			
Yes	14	15	29
No	22	21	43
TIA/CVA Units: Subjects			
Yes	4	4	8
No	32	32	64
DM Units: Subjects			
Yes	3	1	4
No	33	35	68
PVD Units: Subjects			

Yes	1	0	1
No	35	36	71
Smoker			
Units: Subjects			
Yes	3	1	4
No	33	35	68
Ex-smoker			
Units: Subjects			
Yes	14	16	30
No	22	20	42
ACE-I			
Units: Subjects			
Yes	18	14	32
No	18	22	40
B-Blocker			
Units: Subjects			
Yes	8	13	21
No	28	23	51
Calcium Channel Blocker			
Units: Subjects			
Yes	26	22	48
No	10	14	24
a-blocker			
Units: Subjects			
Yes	7	9	16
No	29	27	56
Thiazide Diuretic			
Units: Subjects			
Yes	16	11	27
No	20	25	45
Loop Diuretic			
Units: Subjects			
Yes	4	2	6
No	32	34	66
Mineralocorticoid receptor antagonist			
Units: Subjects			
Yes	3	2	5
No	33	34	67
Angiotensin Receptor Blocker			
Units: Subjects			
Yes	12	17	29
No	24	19	43
Centrally Acting Anti-hypertensive			
Units: Subjects			
Yes	1	1	2
No	35	35	70
Renin Blocker			
Units: Subjects			
Yes	1	0	1
No	35	36	71

Body Mass Index Units: kg/m ² arithmetic mean standard deviation	30.9 ± 5.1	30.4 ± 5.3	-
Daytime Average Systolic BP Units: mmHg arithmetic mean standard deviation	125.6 ± 7.4	124.3 ± 8.8	-
Daytime Average Diastolic BP Units: mmHg arithmetic mean standard deviation	74.5 ± 7.2	72.9 ± 9.6	-
Haemoglobin Units: g/L arithmetic mean standard deviation	138.9 ± 12.2	139.75 ± 14.0	-
Creatinine Units: mmol/L arithmetic mean standard deviation	73.7 ± 10.8	67.5 ± 15.7	-
Glucose Units: mmol/L arithmetic mean standard deviation	5.39 ± 0.81	5.77 ± 0.95	-
Urate Units: mmol/L arithmetic mean standard deviation	374.3 ± 85.6	347.3 ± 108.3	-
Hs-CRP Units: mg/L arithmetic mean standard deviation	2.34 ± 3.40	2.14 ± 2.88	-
TBARs Units: uM arithmetic mean standard deviation	3.01 ± 1.01	2.81 ± 0.88	-
NTproBNP Units: pg/mL arithmetic mean standard deviation	657.59 ± 696.49	897.73 ± 1048.96	-
PICP Units: ng/L arithmetic mean standard deviation	1.74 ± 0.99	1.50 ± 0.70	-
Soluble ST2 Units: ng/mL arithmetic mean standard deviation	19.56 ± 7.76	19.76 ± 10.98	-
Echo LV Mass Units: gram(s) arithmetic mean standard deviation	245.0 ± 59.0	244.7 ± 57.2	-

Echo LV Mass Index Units: g/m2 arithmetic mean standard deviation	124.7 ± 20.4	123.3 ± 16.3	-
MRI LV Mass Units: gram(s) arithmetic mean standard deviation	130.56 ± 36.26	125.86 ± 38.86	-
MRI LV Mass Height 1.7 Units: g/m1.7 arithmetic mean standard deviation	53.9 ± 11.9	51.0 ± 11.8	-
MRI EDV Units: mL arithmetic mean standard deviation	142.16 ± 35.82	140.97 ± 31.77	-
MRI ESV Units: mL arithmetic mean standard deviation	36.94 ± 17.60	36.71 ± 13.29	-
MRI SV Units: ml arithmetic mean standard deviation	105.22 ± 22.08	104.26 ± 21.82	-
MRI Ejection Fraction Units: percent arithmetic mean standard deviation	75.0 ± 7.0	74.5 ± 5.6	-
FMD			
Flow Mediated Dilation			
Units: percent arithmetic mean standard deviation	5.4 ± 4.4	5.9 ± 3.7	-
AIx			
Augmentation Index			
Units: percent arithmetic mean standard deviation	20.4 ± 13.7	24.8 ± 14.2	-
PWV			
Pulse Wave Velocity			
Units: m/s arithmetic mean standard deviation	8.18 ± 1.05	8.49 ± 1.28	-

End points

End points reporting groups

Reporting group title	Placebo Group
Reporting group description: -	
Reporting group title	Intervention Group
Reporting group description: -	

Primary: To assess the effect of Allopurinol compared to placebo on change in MRI LV mass

End point title	To assess the effect of Allopurinol compared to placebo on change in MRI LV mass
End point description:	
End point type	Primary
End point timeframe:	
12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: g/m1.7				
arithmetic mean (standard deviation)	-1.60 (\pm 1.60)	-0.18 (\pm 2.39)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on on change in MRI LV mass

End point title	To assess the effect of Allopurinol compared to placebo on on change in MRI LV mass
End point description:	
End point type	Secondary

End point timeframe:
12 months

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: grams				
arithmetic mean (standard deviation)	-3.75 (\pm 3.89)	-0.37 (\pm 6.08)		

Statistical analyses

Statistical analysis title	Independant T Test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on on change in MRI LV end-diastolic volume.

End point title	To assess the effect of Allopurinol compared to placebo on on change in MRI LV end-diastolic volume.
End point description:	
End point type	Secondary
End point timeframe: 12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: ml				
arithmetic mean (standard deviation)	2.32 (\pm 18.26)	6.47 (\pm 16.35)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.349
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on on change in MRI LV end-systolic volume

End point title	To assess the effect of Allopurinol compared to placebo on on change in MRI LV end-systolic volume
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

12 months

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: ml				
arithmetic mean (standard deviation)	-1.02 (\pm 10.64)	1.59 (\pm 10.28)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.331
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on on change in MRI LV stroke volume

End point title	To assess the effect of Allopurinol compared to placebo on on change in MRI LV stroke volume
-----------------	--

End point description:

End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: ml				
arithmetic mean (standard deviation)	3.34 (\pm 10.90)	4.88 (\pm 10.84)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Intervention Group v Placebo Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.579
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in MRI LV ejection fraction

End point title	To assess the effect of Allopurinol compared to placebo on change in MRI LV ejection fraction
End point description:	
End point type	Secondary
End point timeframe:	
12 Months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: percent				
arithmetic mean (standard deviation)	1.03 (\pm 4.99)	0.25 (\pm 5.49)		

Statistical analyses

Statistical analysis title	Independent t test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.561
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in MRI LA End-diastolic volume

End point title	To assess the effect of Allopurinol compared to placebo on change in MRI LA End-diastolic volume
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	29		
Units: ml				
arithmetic mean (standard deviation)	3.81 (\pm 8.86)	2.57 (\pm 8.68)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Intervention Group v Placebo Group
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.605
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in MRI LA End-systolic volume

End point title	To assess the effect of Allopurinol compared to placebo on change in MRI LA End-systolic volume
End point description:	
End point type	Secondary

End point timeframe:
12 months

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	29		
Units: ml				
arithmetic mean (standard deviation)	2.88 (\pm 5.04)	2.32 (\pm 6.78)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.73
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in MRI LA stroke volume

End point title	To assess the effect of Allopurinol compared to placebo on change in MRI LA stroke volume
End point description:	
End point type	Secondary
End point timeframe: 12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	29		
Units: ml				
arithmetic mean (standard deviation)	0.93 (\pm 6.82)	0.26 (\pm 8.23)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.746
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in MRI LA ejection fraction

End point title	To assess the effect of Allopurinol compared to placebo on change in MRI LA ejection fraction
End point description:	
End point type	Secondary
End point timeframe: 12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: percent				
arithmetic mean (standard deviation)	-1.36 (± 4.93)	-1.07 (± 5.88)		

Statistical analyses

Statistical analysis title	Independant t test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.849
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in daytime systolic blood pressure

End point title	To assess the effect of Allopurinol compared to placebo on change in daytime systolic blood pressure
End point description:	
End point type	Secondary

End point timeframe:
12 months

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: mmHg				
arithmetic mean (standard deviation)	1.6 (\pm 7.3)	-0.9 (\pm 8.0)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Intervention Group v Placebo Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in daytime diastolic blood pressure

End point title	To assess the effect of Allopurinol compared to placebo on change in daytime diastolic blood pressure
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: mmHg				
arithmetic mean (standard deviation)	0.1 (\pm 5.4)	0.3 (\pm 5.7)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.846
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in Flow mediated dilation (FMD)

End point title	To assess the effect of Allopurinol compared to placebo on change in Flow mediated dilation (FMD)
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: percent				
arithmetic mean (standard deviation)	-0.23 (± 3.65)	0.14 (± 4.12)		

Statistical analyses

Statistical analysis title	Independent T Test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.718
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in Augmentation index (AIx)

End point title	To assess the effect of Allopurinol compared to placebo on change in Augmentation index (AIx)
End point description:	
End point type	Secondary

End point timeframe:
12 months

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	31		
Units: percent				
arithmetic mean (standard deviation)	-0.30 (\pm 13.46)	0.06 (\pm 12.41)		

Statistical analyses

Statistical analysis title	Independent T Test
Comparison groups	Intervention Group v Placebo Group
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.913
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in Pulse wave velocity (PWV)

End point title	To assess the effect of Allopurinol compared to placebo on change in Pulse wave velocity (PWV)
End point description:	
End point type	Secondary
End point timeframe: 12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: measure				
arithmetic mean (standard deviation)	-0.09 (\pm 1.12)	-0.25 (\pm 1.07)		

Statistical analyses

Statistical analysis title	Independent T Test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.581
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in Urate

End point title	To assess the effect of Allopurinol compared to placebo on change in Urate
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: umol/L				
arithmetic mean (standard deviation)	-1.33 (± 37.04)	-189.56 (± 91.95)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in High sensitivity C-Reactive Protein (HsCRP)

End point title	To assess the effect of Allopurinol compared to placebo on change in High sensitivity C-Reactive Protein (HsCRP)
End point description:	

End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	31		
Units: mg/L				
arithmetic mean (standard deviation)	-0.55 (± 2.10)	0.22 (± 1.71)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Intervention Group v Placebo Group
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.122
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in Thiobarbituric acid reactive substances (TBARs)

End point title	To assess the effect of Allopurinol compared to placebo on change in Thiobarbituric acid reactive substances (TBARs)
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	31		
Units: uM				
arithmetic mean (standard deviation)	-0.34 (± 0.83)	0.26 (± 0.85)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in N-terminalprohormone B-Type Natriuretic Peptide (NT-proBNP)

End point title	To assess the effect of Allopurinol compared to placebo on change in N-terminalprohormone B-Type Natriuretic Peptide (NT-proBNP)
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

12 months

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	31		
Units: pg/mL				
arithmetic mean (standard deviation)	109.08 (± 491.03)	-109.03 (± 612.84)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.131
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in Procollagen type I carboxy-terminal Propeptide (PICP)

End point title	To assess the effect of Allopurinol compared to placebo on change in Procollagen type I carboxy-terminal Propeptide (PICP)
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:
12 months

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	31		
Units: ng/L				
arithmetic mean (standard deviation)	-0.18 (± 0.60)	-0.05 (± 0.43)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.322
Method	t-test, 2-sided

Secondary: To assess the effect of Allopurinol compared to placebo on change in Soluble ST2 (sST2)

End point title	To assess the effect of Allopurinol compared to placebo on change in Soluble ST2 (sST2)
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:
12 months

End point values	Placebo Group	Intervention Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	31		
Units: ng/ml				
arithmetic mean (standard deviation)	-1.02 (± 3.39)	-0.61 (± 8.63)		

Statistical analyses

Statistical analysis title	Independent T test
Comparison groups	Placebo Group v Intervention Group
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.573
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAE), serious adverse reactions (SAR) and suspected unexpected serious adverse reaction (SUSAR) were reported to TASC pharmacovigilance section within twenty-four hours.

Adverse event reporting additional description:

Adverse events reporting was carried out in accordance with TASC SOP 11 (identifying, recording and reporting adverse events for clinical trials of IMP). At each study adverse events were assessed and recorded in the CRF or when alerted by subjects.

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	20
--------------------	----

Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Reporting group title	Allopurinol
-----------------------	-------------

Reporting group description: -

Serious adverse events	Placebo	Allopurinol	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Procedural intestinal perforation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			

subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Allopurinol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 36 (77.78%)	29 / 36 (80.56%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Orthostatic hypotension			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Cholecystectomy			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Skin lesion removal			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	4 / 36 (11.11%)	2 / 36 (5.56%)	
occurrences (all)	4	2	
Oedema peripheral			

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 36 (2.78%) 2	
Malaise subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Reproductive system and breast disorders Uterine polyp subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 36 (2.78%) 1	
Wheezing subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	
Pleurisy subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	0 / 36 (0.00%) 0	
Depression subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	2 / 36 (5.56%) 2	
Post traumatic stress disorder subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Investigations Weight increased subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Animal bite			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	2	
Atrial fibrillation			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	4 / 36 (11.11%)	4 / 36 (11.11%)	
occurrences (all)	4	4	
Headache			
subjects affected / exposed	1 / 36 (2.78%)	4 / 36 (11.11%)	
occurrences (all)	2	5	
Paraesthesia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Sciatica			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	

Syncope subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Pancytopenia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	
Eye disorders Diplopia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 36 (2.78%) 1	
Diarrhoea subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	5 / 36 (13.89%) 5	
Dyspepsia subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	5 / 36 (13.89%) 5	
Nausea subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	2 / 36 (5.56%) 4	
Rectal haemorrhage subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	

Toothache subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Vomiting subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Skin and subcutaneous tissue disorders Drug eruption subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 36 (2.78%) 1	
Pruritus subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	3 / 36 (8.33%) 3	
Rash subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 3	3 / 36 (8.33%) 4	
Blister subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Pain of skin subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 36 (2.78%) 1	
Nocturia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	
Urinary incontinence subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	
Chronic kidney disease subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 36 (2.78%) 1	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	4 / 36 (11.11%)	4 / 36 (11.11%)	
occurrences (all)	4	4	
Back pain			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	3	2	
Myalgia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	3	
Muscle spasms			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Urinary tract infection			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	
occurrences (all)	3	0	
Fungal infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Tooth infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 October 2014	AM01 1. Change in placebo from lactose to microcrystalline cellulose 2. Secondary Objective/Outcome measures changed 3. Typo's and other minor corrections/clarifications to protocol 4. Alterations to patient information sheet (PIS)
07 April 2015	AM02 1. Change in exclusion criteria 2. Addition of a recruitment source 3. Corrections/clarifications 4. Alterations in patient information sheet

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported