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/m2 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 (± 1.60)	-0.18 (± 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 (± 3.89)	-0.37 (± 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 (± 18.26)	6.47 (± 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 (± 10.64)	1.59 (± 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 (± 10.90)	4.88 (± 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 (± 4.99)	0.25 (± 5.49)		

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	= 0.561
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 (± 8.86)	2.57 (± 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 (± 5.04)	2.32 (± 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 (± 6.82)	0.26 (± 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 (± 7.3)	-0.9 (± 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 (± 5.4)	0.3 (± 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 (± 13.46)	0.06 (± 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 (± 1.12)	-0.25 (± 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	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	2	
Malaise			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Peripheral swelling			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Wheezing			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Pleurisy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Depression			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Post traumatic stress disorder			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Investigations			
Weight increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	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	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Pancytopenia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	4 / 36 (11.11%)	5 / 36 (13.89%)	
occurrences (all)	4	5	
Dyspepsia			
subjects affected / exposed	4 / 36 (11.11%)	5 / 36 (13.89%)	
occurrences (all)	4	5	
Nausea			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	4	
Rectal haemorrhage			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	

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