Clinical trial results:
Does ALlopurinol regress lefT ventricular hypertrophy in End stage REnal Disease: The ALTERED study

Summary

EudraCT number	2013-001436-22
Trial protocol	GB
Global end of trial date	30 June 2016

Results information

Result version number	v1 (current)
This version publication date	18 October 2020
First version publication date	18 October 2020

Trial information

Trial identification

Sponsor protocol code	2012CV07

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01951404
WHO universal trial number (UTN)	-
Other trial identifiers	British Heart Foundation (Funder) Reference: 29743

Notes:

Sponsors

Sponsor organisation name	University of Dundee
Sponsor organisation address	Ninewells Hospital, Dundee DD1 9SY, Dundee, United Kingdom, DD1 9SY
Public contact	Professor Jacob George, University of Dundee, 01382 383656, j.George@dundee.ac.uk
Scientific contact	Professor Jacob George, University of Dundee, 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	30 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2016
Global end of trial reached?	Yes
Global end of trial date	30 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is split into two phases.
Phase 1: is a dose finding study.
The objective here is to find the minumum dose of allopurinol that will give an average 41% reduction in blood urate levels

Phase 2 is the Main Trial.
The primary objective here will be to see if Allopurinol can reverse harmful thickening of the heart muscle wall in patients undergoing dialysis.

Protection of trial subjects:

This study was conducted in accordance with the protocol, International Conference on Harmonisation (ICH) E6 Good Clinical Practice (GCP), the Declaration of Helsinki and all other applicable regulatory requirements.

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. Access to collated participant data will be restricted to those clinicians treating the participants.
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	05 August 2013
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: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	80
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

96 subjects were screened, 80 subjects who fulfilled the eligibility criteria were recruited into the study.

Pre-assignment

Screening details:

Between January 2014 and June 2015, 96 haemodialysis patients consented to participate in the main ALTERED study. This represented 26% of all approached subjects. Of those who consented, 16 participants were not eligible for randomisation following formal screening, 80 participants were therefore randomised.

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	Investigator, Monitor, Data analyst, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Allopurinol

Arm description: -

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:

100mg, 200mg, 250mg, 300mg or 350mg

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:

Participants will be given blinded medication. At the randomisation visit they will be dosed with either allopurinol 100mg or matched placebo.
They will then be asked to take one tablet after each dialysis session for two weeks (+/-one dialysis session).
Thereafter the medication will be increased weekly as tolerated (+/- 2 days) to the dose decided in the phase 1 dose escalation study – ie one week at 200mg, one week at 250mg, one week at 300mg and up to 350mg, or placebo as determined by pilot data.
Compliance will be checked and documented using tablet counts at each visit. If non compliant, they will be encouraged to become compliant. If they persist as non compliant (<70% compliance), they will stay in the study, but not on study medication, in order to do an "intention to treat" analysis.

Number of subjects in period 1	Allopurinol	Placebo
Started	40	40
Completed	28	25
Not completed	12	15
Consent withdrawn by subject	1	4
unknown	1	-
Frailty	1	1
New MRI contraindication	1	-
Death	2	5
Transplanted	6	5

Baseline characteristics

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

Reporting group values	Allopurinol	Placebo	Total
Number of subjects	40	40	80
Age categorical Units: Subjects			
Adults (18-64 years)	27	29	56
From 65-84 years	13	11	24
Age continuous Units: years			
arithmetic mean	57.8	58.0	
standard deviation	± 11.6	± 13.0	-
Gender categorical Units: Subjects			
Female	20	20	40
Male	20	20	40

End points

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

Primary: change in LVMI	
End point title	change in LVMI
End point description:	
End point type	Primary
End point timeframe:	
12 Months	

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: g/m2				
log mean (standard deviation)	1.6 (± 11.0)	3.6 (± 10.4)		

Statistical analyses

Statistical analysis title	LVMI over 12
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.489
Method	ANOVA

Secondary: change in LVM	
End point title	change in LVM
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: g/m2				
log mean (standard deviation)	2.38 (± 18.82)	6.58 (± 19.01)		

Statistical analyses

Statistical analysis title	change in LVM
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.422
Method	ANOVA

Secondary: Change in LVEF

End point title	Change in LVEF

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: percent				
log mean (standard deviation)	-1.3 (± 5.6)	-1.0 (± 7.2)		

Statistical analyses

Statistical analysis title	Change in LVEF
Comparison groups	Allopurinol v Placebo

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.858
Method	ANOVA

Secondary: Blood Pressure Pre-dialysis Systolic

End point title	Blood Pressure Pre-dialysis Systolic

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: mmHg				
log mean (standard deviation)	144 (± 28)	141 (± 22)		

Statistical analyses

Statistical analysis title	Blood Pressure
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.626
Method	ANOVA

Secondary: BP - Pre-dialysis Diastolic

End point title	BP - Pre-dialysis Diastolic

End point description:

End point type	Secondary

End point timeframe:

12 Months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: mmHg				
log mean (standard deviation)	70 (± 15)	72 (± 13)		

Statistical analyses

Statistical analysis title	BP -Pre-dialysis Diastolic
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.547
Method	ANOVA

Secondary: BP -Post-dialysis Systolic

End point title	BP -Post-dialysis Systolic

End point description:

End point type	Secondary

End point timeframe:

12 Months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: mmHg				
log mean (standard deviation)	131 (± 25)	130 (± 19)		

Statistical analyses

Statistical analysis title	Post-dialysis Systolic
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.772
Method	ANOVA

Secondary: BP -Post-dialysis Diastolic

End point title	BP -Post-dialysis Diastolic

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: mmHg				
log mean (standard deviation)	66 (± 12)	66 (± 16)		

Statistical analyses

Statistical analysis title	Post-dialysis Diastolic
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.973
Method	ANOVA

Secondary: Mean 24-hour

End point title	Mean 24-hour

End point description:

End point type	Secondary

End point timeframe:

24 hour

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: mmHg				
median (inter-quartile range (Q1-Q3))	134 (122 to 148)	146 (136 to 147)		

Statistical analyses

Statistical analysis title	Systolic BP
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.73
Method	ANOVA

Secondary: Mean 24-hour Diastolic BP

End point title	Mean 24-hour Diastolic BP

End point description:

End point type	Secondary

End point timeframe:

24 hour

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: mmHg				
median (inter-quartile range (Q1-Q3))	70 (59 to 91)	80 (61 to 95)		

Statistical analyses

Statistical analysis title	Diastolic BP
Comparison groups	Allopurinol v Placebo

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.413
Method	ANOVA

Secondary: Flow Mediated Dilation (FMD)Change in endothelial dependent flow mediated dilation

End point title	Flow Mediated Dilation (FMD)Change in endothelial dependent flow mediated dilation

End point description:

Change in endothelial dependent flow mediated dilation

End point type	Secondary

End point timeframe:

9 months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: percent				
log mean (standard deviation)	0.0 (± 2.9)	-2.6 (± 4.0)		

Statistical analyses

Statistical analysis title	Change in endothelial dependent flow mediated dila
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.124
Method	ANOVA

Secondary: Flow Mediated Dilation (FMD)Change in endothelial dependent flow mediated dilation

End point title	Flow Mediated Dilation (FMD)Change in endothelial dependent flow mediated dilation

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: percent				
median (inter-quartile range (Q1-Q3))	-0.4 (-2.1 to -0.0)	1.4 (-3.4 to 5.2)		

Statistical analyses

Statistical analysis title	Change in endothelial dependent flow mediated dila
Statistical analysis description: Change in endothelial dependent flow mediated dilation	
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.546
Method	ANOVA

Secondary: Flow Mediated Dilation (FMD)Change in endothelial independent nitrate mediated dilation

End point title	Flow Mediated Dilation (FMD)Change in endothelial independent nitrate mediated dilation
End point description:	
End point type	Secondary
End point timeframe: 9 months	

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: percent				
log mean (standard deviation)	-1.5 (± 6.0)	-4.9 (± 4.3)		

Statistical analyses

Statistical analysis title	Flow Mediated Dilation (FMD)
Statistical analysis description: Change in endothelial independent nitrate mediated dilation at 9 months	
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.193
Method	ANOVA

Secondary: Flow Mediated Dilation (FMD)Change in endothelial independent nitrate mediated dilation

End point title	Flow Mediated Dilation (FMD)Change in endothelial independent nitrate mediated dilation
End point description:	
End point type	Secondary
End point timeframe: 12 months	

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: percent				
log mean (standard deviation)	-2.3 (± 5.2)	-0.4 (± 4.9)		

Statistical analyses

Statistical analysis title	Flow Mediated Dilation (FMD)
Statistical analysis description: Change in endothelial independent nitrate mediated dilation at 12 months	
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.54
Method	ANOVA

Secondary: Pulse Wave Analysis (PWA)Change in PWV at 9 months

End point title	Pulse Wave Analysis (PWA)Change in PWV at 9 months

End point description:

End point type	Secondary

End point timeframe:
9 months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: m/s				
log mean (standard deviation)	0.9 (± 2.7)	0.5 (± 1.8)		

Statistical analyses

Statistical analysis title	Change in PWV at 9 months
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.719
Method	ANOVA

Secondary: Pulse Wave Analysis (PWA)Change in PWV at 12 months

End point title	Pulse Wave Analysis (PWA)Change in PWV at 12 months

End point description:

End point type	Secondary

End point timeframe:
12 Months

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: m/s				
log mean (standard deviation)	1.1 (± 1.7)	0.7 (± 2.0)		

Statistical analyses

Statistical analysis title	Pulse Wave Analysis (PWA)
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.718
Method	ANOVA

Secondary: Change in radial Aix at 12 months

End point title	Change in radial Aix at 12 months
End point description:	
End point type	Secondary
End point timeframe: 12 month	

End point values	Allopurinol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: percent				
log mean (standard deviation)	-1.4 (± 8.8)	3.6 (± 9.9)		

Statistical analyses

Statistical analysis title	Change in radial Aix at 12 months
Comparison groups	Allopurinol v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.255
Method	ANOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events reported from August 2013 to June 2016

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

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	16 / 80 (20.00%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Arteriovenous fistula site haematoma			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Colectomy			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Colectomy total			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal resection			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Intestinal ischaemia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			

subjects affected / exposed	2 / 80 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Endocarditis bacterial			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Randomised Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 80 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Intermittent claudication			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Peripheral vascular disorder			

subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Surgical and medical procedures			
Arteriovenous fistula operation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Arteriovenous graft			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Catheterisation venous			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Enterostomy			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Haemodialysis			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Nephrectomy			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Parathyroidectomy			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Tooth extraction			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Vascular catheterisation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Vascular cauterisation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Vascular stent insertion			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		

General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Catheter site erythema			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Catheter site inflammation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Catheter site pain			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Catheter site related reaction			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Chest discomfort			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	4 / 80 (5.00%)		
occurrences (all)	9		
Chills			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Complication associated with device			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Feeling cold			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Influenza like illness			

subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	4 / 80 (5.00%)		
occurrences (all)	5		
Dyspnoea			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Pleural effusion			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Product issues			
Device failure			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Device occlusion			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Thrombosis in device			
subjects affected / exposed	7 / 80 (8.75%)		
occurrences (all)	8		
Investigations			
Blood culture positive			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Blood potassium increased			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	2		
Endoscopy upper gastrointestinal tract			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Injury, poisoning and procedural			

complications				
Arteriovenous fistula aneurysm				
subjects affected / exposed	3 / 80 (3.75%)			
occurrences (all)	3			
Arteriovenous fistula maturation failure				
subjects affected / exposed	3 / 80 (3.75%)			
occurrences (all)	3			
Arteriovenous fistula site complication				
subjects affected / exposed	3 / 80 (3.75%)			
occurrences (all)	3			
Arteriovenous fistula site haemorrhage				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
sunburn				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Joint injury				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
fall				
subjects affected / exposed	4 / 80 (5.00%)			
occurrences (all)	7			
Limb injury				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Post procedural complication				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Procedural headache				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Procedural vomiting				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Vascular graft complication				

subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Vascular graft thrombosis			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Fistulogram			
subjects affected / exposed	3 / 80 (3.75%)		
occurrences (all)	3		
Gram stain negative			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Imaging procedure			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Liver function test abnormal			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Troponin increased			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Aortic valve thickening			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Atrial fibrillation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Bradyarrhythmia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Supraventricular tachycardia			
subjects affected / exposed	3 / 80 (3.75%)		
occurrences (all)	5		

Intracardiac thrombus				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Myocardial infarction				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Non STEMI				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Palpitations				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Pericardial effusion				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Pericarditis				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Tachyarrhythmia				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Aortic valve incompetence				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Nervous system disorders				
Dizziness				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Headache				
subjects affected / exposed	4 / 80 (5.00%)			
occurrences (all)	4			
Hypoaesthesia				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Hypoglycaemic unconsciousness				

subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Restless legs syndrome			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	4 / 80 (5.00%)		
occurrences (all)	5		
Diverticular perforation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Haematemesis			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Intestinal ischaemia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		

Mouth ulceration subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 1		
Nausea subjects affected / exposed occurrences (all)	3 / 80 (3.75%) 3		
Rectal haemorrhage subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 1		
Toothache subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 1		
Vomiting subjects affected / exposed occurrences (all)	6 / 80 (7.50%) 7		
Hepatobiliary disorders			
Acute hepatic failure subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 1		
Biliary dilatation subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 1		
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	4 / 80 (5.00%) 4		
Rash subjects affected / exposed occurrences (all)	3 / 80 (3.75%) 3		
skin ulcer subjects affected / exposed occurrences (all)	1 / 80 (1.25%) 1		
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	2 / 80 (2.50%) 2		

Costochondritis			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	3 / 80 (3.75%)		
occurrences (all)	3		
Infections and infestations			
Arteriovenous fistula site infection			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	2		
Arthritis infective			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Beta haemolytic streptococcal infection			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	6 / 80 (7.50%)		
occurrences (all)	9		
Viral diarrhoea			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	2		
Viral pericarditis			

subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Wound infection				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Wound infection staphylococcal				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Catheter site infection				
subjects affected / exposed	4 / 80 (5.00%)			
occurrences (all)	7			
Cellulitis				
subjects affected / exposed	4 / 80 (5.00%)			
occurrences (all)	5			
Device related infection				
subjects affected / exposed	5 / 80 (6.25%)			
occurrences (all)	5			
Device related sepsis				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Empyema				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	5			
Endocarditis bacterial				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	2 / 80 (2.50%)			
occurrences (all)	2			
graft infections				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Hepatic cyst infection				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Herpes zoster				

subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Infected fistula				
subjects affected / exposed	2 / 80 (2.50%)			
occurrences (all)	2			
Infected skin ulcer				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Infection				
subjects affected / exposed	2 / 80 (2.50%)			
occurrences (all)	2			
Influenza				
subjects affected / exposed	2 / 80 (2.50%)			
occurrences (all)	2			
Lower respiratory tract infection				
subjects affected / exposed	9 / 80 (11.25%)			
occurrences (all)	9			
Nail bed infection				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	4 / 80 (5.00%)			
occurrences (all)	4			
Osteomyelitis				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Peritonsillar abscess				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	1 / 80 (1.25%)			
occurrences (all)	1			
pulmonary sep				

subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Sepsis			
subjects affected / exposed	4 / 80 (5.00%)		
occurrences (all)	4		
Staphylococcal infection			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	5 / 80 (6.25%)		
occurrences (all)	9		
Gout			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported