



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 minimum 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 (\pm 11.0) | 3.6 (\pm 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 (\pm 15) | 72 (\pm 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 (\pm 25) | 130 (\pm 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 (\pm 2.9) | -2.6 (\pm 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 occurrences (all) | 2 / 80 (2.50%) 2 | | |
| Malaise subjects affected / exposed occurrences (all) | 2 / 80 (2.50%) 2 | | |
| Respiratory, thoracic and mediastinal disorders Productive cough subjects affected / exposed occurrences (all) | 4 / 80 (5.00%) 5 | | |
| Dyspnoea subjects affected / exposed occurrences (all) | 2 / 80 (2.50%) 2 | | |
| Pleural effusion subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 1 | | |
| Product issues Device failure subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 1 | | |
| Device occlusion subjects affected / exposed occurrences (all) | 2 / 80 (2.50%) 2 | | |
| Thrombosis in device subjects affected / exposed occurrences (all) | 7 / 80 (8.75%) 8 | | |
| Investigations Blood culture positive subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 1 | | |
| Blood potassium increased subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 2 | | |
| Endoscopy upper gastrointestinal tract subjects affected / exposed occurrences (all) | 1 / 80 (1.25%) 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 | | | |

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

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