



Clinical trial results:

A Phase III Randomized, Controlled, Superiority Study Evaluating the Fibrin Pad Versus Standard of Care Treatment in Controlling Parenchymal Bleeding During Elective Hepatic Surgery

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2010-019427-58 |
| Trial protocol | DE GB NL |
| Global end of trial date | 17 October 2011 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 05 August 2016 |
| First version publication date | 05 August 2016 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 400-10-001 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01166243 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Ethicon Inc.,a Johnston & Johnson co. |
| Sponsor organisation address | Route 22 West , Somerville, United States, |
| Public contact | Jonathan Batiller, Ethicon Inc., a Johnston & Johnson co., +1 9082182492, jbatill2@its.jnj.com |
| Scientific contact | Jonathan Batiller, Ethicon Inc., a Johnston & Johnson co., +1 9082182492, jbatill2@its.jnj.com |

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 | 25 October 2011 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 17 October 2011 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 October 2011 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and hemostatic effectiveness of Fibrin Pad(FP) versus Standard of Care (SOC)treatment in controlling parenchymal bleeding during hepatic surgery.

Protection of trial subjects:

The protocol and consent form were provided to the appropriate Ethics Committee for approval.

Background therapy:

Not applicable

Evidence for comparator:

The control group was to be treated with the surgeon's Standard of Care (SoC) methods. Standard of Care is a composite of techniques/methods typically used by the surgeon to control parenchymal bleeding after conventional methods (e.g. suture, ligature, cautery) are ineffective or impractical. For this study, SoC was to be initiated with continuous firm manual compression with or without gauze or sponge and with or without a topical absorbable hemostat (TAH).

| | |
|---|--------------|
| Actual start date of recruitment | 14 June 2010 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | United Kingdom: 27 |
| Country: Number of subjects enrolled | Germany: 25 |
| Country: Number of subjects enrolled | Australia: 34 |
| Country: Number of subjects enrolled | New Zealand: 16 |
| Worldwide total number of subjects | 104 |
| EEA total number of subjects | 54 |

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 | 0 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 50 |
| From 65 to 84 years | 54 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The first subject was recruited on the 14 June 2010 and the last subject was 25 August 2011

Pre-assignment

Screening details:

Subjects were screened within 21 days prior to surgery. Prior to any study related procedures, subjects were fully informed of all aspects of the study and asked to sign a consent form. A 'run-in' phase in which the first eligible subject for each investigator without prior clinical experience with the FP was not randomized and were treated with FP

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | FIBRIN PAD |

Arm description:

FP is a sterile bio-absorbable combination product consisting of two constituent parts— a flexible matrix and a coating of two biological components. The matrix consists of polyglactin 910 (PG910) filaments needle punched into a backing fabric of Oxidized Regenerated Cellulose (ORC). The biological components are Human Thrombin and Human Fibrinogen.

| | |
|--|----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fibrin Pad |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sealant matrix |
| Routes of administration | Topical use |

Dosage and administration details:

FP is a sterile bio-absorbable combination product consisting of two constituent parts— a flexible matrix and a coating of two biological components. The matrix consists of polyglactin 910 (PG910) filaments needle punched into a backing fabric of Oxidized Regenerated Cellulose (ORC). The biological components are Human Thrombin and Human Fibrinogen. FP was supplied in units of 10.2 x 10.2 cm (4 x 4 inches). The TBS required to be adequately covered with a single unit of FP, with an overlap 1-2 cm beyond the margins of the wound. If required, FP could be cut to fit the size of the bleeding site. If breakthrough bleeding occurred at the TBS during the 4-minute treatment period, the surgeon was permitted to retreat with FP. If bleeding was due to insufficient coverage of the TBS, the additional units were to be applied so that they overlapped the previously applied product. If bleeding was due to incomplete adherence to the tissue, the previous unit was removed and replaced with a new unit

| | |
|------------------|------------------|
| Arm title | Standard of care |
|------------------|------------------|

Arm description:

Standard of care

| | |
|---|------------------|
| Arm type | Standard of care |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1^[1] | FIBRIN PAD | Standard of care |
|---|------------|------------------|
| Started | 40 | 44 |
| Completed | 39 | 42 |
| Not completed | 1 | 2 |
| Consent withdrawn by subject | - | 1 |
| Lost to follow-up | 1 | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: There were 20 subjects included in the run-in phase so these patients were included in the safety analysis set not in the ITT.

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | FIBRIN PAD |
|-----------------------|------------|

Reporting group description:

FP is a sterile bio-absorbable combination product consisting of two constituent parts— a flexible matrix and a coating of two biological components. The matrix consists of polyglactin 910 (PG910) filaments needle punched into a backing fabric of Oxidized Regenerated Cellulose (ORC). The biological components are Human Thrombin and Human Fibrinogen.

| | |
|-----------------------|------------------|
| Reporting group title | Standard of care |
|-----------------------|------------------|

Reporting group description:

Standard of care

| Reporting group values | FIBRIN PAD | Standard of care | Total |
|------------------------|------------|------------------|-------|
| Number of subjects | 40 | 44 | 84 |
| Age categorical | | | |
| Units: Subjects | | | |
| 18-<50 years | 6 | 7 | 13 |
| 50-<65 years | 12 | 14 | 26 |
| 65-<75 years | 13 | 13 | 26 |
| >=75 years | 9 | 10 | 19 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 16 | 20 | 36 |
| Male | 24 | 24 | 48 |

End points

End points reporting groups

| | |
|---|------------------|
| Reporting group title | FIBRIN PAD |
| Reporting group description: FP is a sterile bio-absorbable combination product consisting of two constituent parts— a flexible matrix and a coating of two biological components. The matrix consists of polyglactin 910 (PG910) filaments needle punched into a backing fabric of Oxidized Regenerated Cellulose (ORC). The biological components are Human Thrombin and Human Fibrinogen. | |
| Reporting group title | Standard of care |
| Reporting group description: Standard of care | |

Primary: hemostasis at 4-minutes at TBS and with no re-bleeding requiring treatment prior to wound closure

| | |
|---|---|
| End point title | hemostasis at 4-minutes at TBS and with no re-bleeding requiring treatment prior to wound closure |
| End point description: Proportion of subjects achieving hemostasis at the TBS at 4-minutes following randomization and with no re-bleeding requiring treatment at the TBS anytime prior to initiation of wound closure (latest point in time where FP is visible to confirm hemostasis). Hemostasis is defined as no detectable bleeding at the TBS. | |
| End point type | Primary |
| End point timeframe: haemostasis at 4 minutes | |

| End point values | FIBRIN PAD | Standard of care | | |
|---------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 44 | | |
| Units: haemostasis at 4 minutes | | | | |
| Hemostasis achieved at 4 min | 33 | 13 | | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Primary efficacy endpoint |
| Statistical analysis description: The proportion of subjects achieving hemostatic success at 4 minutes after randomization with no re-bleeding requiring treatment prior to initiation of wound closure. Hemostasis is defined as no detectable bleeding at the TBS. The triangular test for a binary response variable was utilized (PEST 4.4 software) with a two-sided alpha 0.05 and power 0.90. Subjects were randomized with a 1:1 allocation ratio, FP to SoC. The assumed success rate in the control arm was 50%, and FP was 75%. | |
| Comparison groups | FIBRIN PAD v Standard of care |

| | |
|---|---------------|
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Chi-squared |

Secondary: Proportion of subjects achieving hemostatic success at 10 minutes following randomization

| | |
|-----------------|---|
| End point title | Proportion of subjects achieving hemostatic success at 10 minutes following randomization |
|-----------------|---|

End point description:

Proportion of subjects achieving hemostatic success at 10 minutes following randomization (defined as achievement of hemostasis at 10 minutes and no further bleeding requiring re-treatment prior to wound closure)

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

End point timeframe:

10 minutes following randomization

| End point values | FIBRIN PAD | Standard of care | | |
|----------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 44 | | |
| Units: Achievement of hemostasis | 38 | 30 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute time to hemostasis

| | |
|-----------------|-----------------------------|
| End point title | Absolute time to hemostasis |
|-----------------|-----------------------------|

End point description:

Absolute time to hemostasis (defined as the absolute time to achieve hemostasis at or after 4 minutes from randomization)

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

End point timeframe:

Absolute time to achieve hemostasis at or after 4 minutes from randomization

| End point values | FIBRIN PAD | Standard of care | | |
|----------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 44 | | |
| Units: minutes | | | | |
| median (confidence interval 95%) | 4 (4 to 4) | 9.7 (4 to 10) | | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Secondary endpoint analysis |
| Comparison groups | FIBRIN PAD v Standard of care |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | < 0.0001 |
| Method | Wilcoxon Rank -Sum Test |

Notes:

[1] - Secondary endpoint analysis therefore no formal hypothesis testing

Secondary: Proportion of subjects who, after the initial hemostatic success at 4 minutes, have breakthrough bleeding requiring treatment

| | |
|-----------------|---|
| End point title | Proportion of subjects who, after the initial hemostatic success at 4 minutes, have breakthrough bleeding requiring treatment |
|-----------------|---|

End point description:

The proportion of subjects who, after the initial hemostatic success at 4 minutes, have breakthrough bleeding requiring treatment

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

End point timeframe:

Proportion of subjects who, after the initial hemostatic success at 4 minutes, have breakthrough bleeding requiring treatment

| End point values | FIBRIN PAD | Standard of care | | |
|--|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 44 | | |
| Units: Breakthrough bleeding requiring treatment | 1 | 1 | | |

Statistical analyses

| | |
|-----------------------------------|-------------------------------|
| Statistical analysis title | secondary endpoint analysis |
| Comparison groups | Standard of care v FIBRIN PAD |

| | |
|---|----------------|
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | logistic model |
| Parameter estimate | Log odds ratio |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.994 |
| upper limit | 2.994 |

Secondary: The proportion of subjects who, after the initial establishment of hemostasis (after 4 minutes), had breakthrough bleeding requiring treatment

| | |
|-----------------|--|
| End point title | The proportion of subjects who, after the initial establishment of hemostasis (after 4 minutes), had breakthrough bleeding requiring treatment |
|-----------------|--|

End point description:

The proportion of subjects who, after the initial establishment of hemostasis (after 4 minutes), had breakthrough bleeding requiring treatment

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

End point timeframe:

The proportion of subjects who, after the initial establishment of hemostasis (after 4 minutes), had breakthrough bleeding requiring treatment

| End point values | FIBRIN PAD | Standard of care | | |
|--|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 44 | | |
| Units: breakthrough bleeding requiring treatment | 4 | 27 | | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Secondary endpoint analysis |
| Comparison groups | FIBRIN PAD v Standard of care |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | logistic model |
| Parameter estimate | Log odds ratio |
| Point estimate | -1.82 |

| Confidence interval | |
|---------------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.947 |
| upper limit | -0.692 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE's were collected from the start of randomization, during the procedure, throughout hospital admission, and until completion of the 60 day follow up visit.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 11.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | FIBRIN PAD |
|-----------------------|------------|

Reporting group description:

FP is a sterile bio-absorbable combination product consisting of two constituent parts— a flexible matrix and a coating of two biological components. The matrix consists of polyglactin 910 (PG910) filaments needle punched into a backing fabric of Oxidized Regenerated Cellulose (ORC). The biological components are Human Thrombin and Human Fibrinogen.

| | |
|-----------------------|------------------|
| Reporting group title | Standard of care |
|-----------------------|------------------|

Reporting group description:

Standard of care

| Serious adverse events | FIBRIN PAD | Standard of care | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 59 (27.12%) | 10 / 45 (22.22%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Post procedural bile leak | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 2 / 45 (4.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal haematoma | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound dehiscence | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Vena cava thrombosis | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intra-abdominal haemorrhage | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised intraabdominal fluid collection | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 3 / 45 (6.67%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Hepatobiliary disorders | | | |
| Biloma | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 45 (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: 5 %

| Non-serious adverse events | FIBRIN PAD | Standard of care | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 56 / 59 (94.92%) | 43 / 45 (95.56%) | |
| Vascular disorders | | | |

| | | | |
|---|------------------------|------------------------|--|
| Hypertension subjects affected / exposed occurrences (all) | 6 / 59 (10.17%) 10 | 10 / 45 (22.22%) 11 | |
| Hypotension subjects affected / exposed occurrences (all) | 21 / 59 (35.59%) 25 | 17 / 45 (37.78%) 22 | |
| General disorders and administration site conditions | | | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 4 / 59 (6.78%) 4 | 9 / 45 (20.00%) 10 | |
| Pain subjects affected / exposed occurrences (all) | 15 / 59 (25.42%) 23 | 18 / 45 (40.00%) 24 | |
| Pyrexia subjects affected / exposed occurrences (all) | 15 / 59 (25.42%) 18 | 12 / 45 (26.67%) 19 | |
| Immune system disorders | | | |
| Hypersensitivity subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 1 / 45 (2.22%) 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 4 / 59 (6.78%) 4 | 2 / 45 (4.44%) 2 | |
| Hypoxia subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 1 / 45 (2.22%) 1 | |
| Pleural effusion subjects affected / exposed occurrences (all) | 7 / 59 (11.86%) 7 | 8 / 45 (17.78%) 8 | |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 8 / 59 (13.56%) 9 | 3 / 45 (6.67%) 3 | |
| Confusional state | | | |

| | | | |
|--|------------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 5 / 45 (11.11%) 6 | |
| Delirium subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 3 / 45 (6.67%) 3 | |
| Hallucination subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 4 | 5 / 45 (11.11%) 5 | |
| Insomnia subjects affected / exposed occurrences (all) | 9 / 59 (15.25%) 10 | 7 / 45 (15.56%) 8 | |
| Investigations | | | |
| Liver function test abnormal subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 0 / 45 (0.00%) 0 | |
| Prothrombin time prolonged subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 1 / 45 (2.22%) 1 | |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 4 / 45 (8.89%) 5 | |
| Post procedural bile leak subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 4 / 45 (8.89%) 4 | |
| Procedural pain subjects affected / exposed occurrences (all) | 12 / 59 (20.34%) 18 | 7 / 45 (15.56%) 9 | |
| Wound dehiscence subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 3 / 45 (6.67%) 3 | |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 3 / 45 (6.67%) 3 | |
| Sinus tachycardia | | | |

| | | | |
|---|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 2 / 45 (4.44%) 3 | |
| Tachycardia subjects affected / exposed occurrences (all) | 6 / 59 (10.17%) 9 | 5 / 45 (11.11%) 6 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 9 / 59 (15.25%) 10 | 7 / 45 (15.56%) 9 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 14 / 59 (23.73%) 14 | 11 / 45 (24.44%) 11 | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 4 / 45 (8.89%) 4 | |
| Constipation subjects affected / exposed occurrences (all) | 22 / 59 (37.29%) 24 | 20 / 45 (44.44%) 23 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 5 | 2 / 45 (4.44%) 2 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 0 / 45 (0.00%) 0 | |
| Flatulence subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 3 / 45 (6.67%) 3 | |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 1 / 45 (2.22%) 1 | |
| Localised intraabdominal fluid collection subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 6 / 45 (13.33%) 6 | |
| Nausea | | | |

| | | | |
|---|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 31 / 59 (52.54%) 42 | 28 / 45 (62.22%) 34 | |
| Vomiting subjects affected / exposed occurrences (all) | 20 / 59 (33.90%) 24 | 14 / 45 (31.11%) 20 | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 4 / 59 (6.78%) 4 | 3 / 45 (6.67%) 3 | |
| Renal and urinary disorders Incontinence subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 5 / 45 (11.11%) 6 | |
| Urinary retention subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 3 / 45 (6.67%) 3 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 8 / 59 (13.56%) 8 | 7 / 45 (15.56%) 8 | |
| Back pain subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 3 / 45 (6.67%) 3 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | 3 / 45 (6.67%) 4 | |
| Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | 3 / 45 (6.67%) 3 | |
| Pneumonia subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 2 / 45 (4.44%) 2 | |
| Metabolism and nutrition disorders Hyperglycaemia | | | |

| | | |
|---|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | 5 / 45 (11.11%) 5 |
| Hypoglycaemia subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 0 / 45 (0.00%) 0 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 14 / 59 (23.73%) 15 | 11 / 45 (24.44%) 13 |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 9 / 59 (15.25%) 10 | 3 / 45 (6.67%) 4 |
| Hyponatraemia subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 3 / 45 (6.67%) 3 |
| Hypophosphataemia subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | 4 / 45 (8.89%) 4 |

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