Clinical trial results:
A Phase III Randomized, Controlled, Superiority Study Evaluating the Fibrin Pad Versus Standard of Care Treatment in Controlling Severe Soft Tissue Bleeding During Abdominal, Retroperitoneal, Pelvic, and Thoracic Surgery

Summary

EudraCT number	2008-004835-39
Trial protocol	GB DE
Global end of trial date	06 April 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	400-08-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00977925
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ethicon Inc., a Johnson & Johnson Co.
Sponsor organisation address	Route 22 West , Somerville, United States,
Public contact	Jonathan Batiller, Ethicon Inc., a Johnson & Johnson Co., 001 9082182492, JBatill2@its.jnj.com
Scientific contact	Jonathan Batiller, Ethicon Inc., a Johnson & Johnson Co., 001 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	06 April 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 March 2011
Global end of trial reached?	Yes
Global end of trial date	06 April 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and haemostatic effectiveness of the Fibrin Pad (FP) versus standard of care treatment (SoC) in controlling severe soft tissue bleeding during abdominal, pelvic, retroperitoneal, and (non-cardiac) thoracic surgery.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator:

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

Actual start date of recruitment	31 August 2009
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	United Kingdom: 21
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	New Zealand: 29
Country: Number of subjects enrolled	Australia: 21
Worldwide total number of subjects	91
EEA total number of subjects	41

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)	44
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first subject was recruited on the 31 August 2009 and the last subject was 3 March 2011

Pre-assignment

Screening details:

Prospective 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.

Period 1

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

Blinding implementation details:

N/A

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 intended for topical use. After placement of the treatment article, manual compression was to be applied continuously and was maintained until 4 minutes post randomization. The surgeon may have used a surgical sponge (laparotomy pad or surgical gauze) to assist in providing adequate pressure to stem all bleeding over the entire treated surface area at the TBS. A maximum of 4 units (each unit is 4 x 4 inches) of FP may have been applied (left in place at the bleeding site) per subject assigned to be treated with FP.

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	FIBRIN PAD	Standard of care
Started	59	32
Completed	53	23
Not completed	6	9
Adverse event, serious fatal	3	2
Consent withdrawn by subject	2	4
Lost to follow-up	1	3

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	59	32	91
Age categorical Units: Subjects			
18 - <50 Years	9	4	13
50 - <65 Years	20	11	31
65 - <75 Years	19	9	28
>=75 Years	11	8	19
Gender categorical Units: Subjects			
Female	19	15	34
Male	40	17	57

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: Proportion of subjects achieving hemostatic success at the TBS at 4 minutes after randomization with no rebleeding requiring treatment at the TBS at any time prior to wound closure

End point title	Proportion of subjects achieving hemostatic success at the TBS at 4 minutes after randomization with no rebleeding requiring treatment at the TBS at any time prior to wound closure
End point description:	
End point type	Primary
End point timeframe:	
4 minutes after randomization	

End point values	FIBRIN PAD	Standard of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	32		
Units: Achievement of hemostasis	50	10		

Statistical analyses

Statistical analysis title	Primary efficacy endpoint
Comparison groups	FIBRIN PAD v Standard of care
Number of subjects included in analysis	91
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:

End point type	Secondary

End point timeframe:

10 minutes after randomization

End point values	FIBRIN PAD	Standard of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	32		
Units: Hemostatic success	58	22		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis
Comparison groups	FIBRIN PAD v Standard of care
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Logistics model
Parameter estimate	Log odds ratio
Point estimate	2.384
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.949
upper limit	3.819

Secondary: Absolute time to hemostasis

End point title	Absolute time to hemostasis

End point description:

Absolute time to hemostasis is 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 hemostasis

End point values	FIBRIN PAD	Standard of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	32		
Units: Minutes				
arithmetic mean (confidence interval 95%)	6.1 (2.5 to 9.6)	17.8 (6.1 to 29.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects requiring retreatment at the TBS prior to wound closure

End point title	Proportion of subjects requiring retreatment at the TBS prior to wound closure

End point description:

End point type	Secondary

End point timeframe:

Between 4 minutes and wound closure

End point values	FIBRIN PAD	Standard of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	32		
Units: Number requiring retreatment	3	17		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis
Comparison groups	FIBRIN PAD v Standard of care
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logistic model
Parameter estimate	Log odds ratio
Point estimate	-2.462
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.661
upper limit	-1.262

Secondary: Incidence of treatment failure

End point title	Incidence of treatment failure
End point description:	
Treatment failure is defined as hemostasis was not achieved within 4 minutes or if bleeding requiring retreatment prior to wound closure.	
End point type	Secondary
End point timeframe:	
Prior to wound closure	

End point values	FIBRIN PAD	Standard of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	32		
Units: Number of treatment failures	9	22		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis
Comparison groups	FIBRIN PAD v Standard of care
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logistic model
Parameter estimate	Log odds ratio
Point estimate	-2.354
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.503
upper limit	-1.205

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	10.1

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	15 / 59 (25.42%)	10 / 32 (31.25%)	
number of deaths (all causes)	4	3	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic leak	Additional description: 1		
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Post procedural bile leak			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary anastomotic leak			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			

subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised intraabdominal fluid collection			
subjects affected / exposed	0 / 59 (0.00%)	2 / 32 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatorenal syndrome			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Aspiration			

subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 59 (3.39%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 59 (1.69%)	2 / 32 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (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	0 / 59 (0.00%)	3 / 32 (9.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Bacterial sepsis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 59 (1.69%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 59 (1.69%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdiaphragmatic abscess			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 59 (1.69%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	2 / 59 (3.39%)	2 / 32 (6.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 2	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	58 / 59 (98.31%)	32 / 32 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 59 (6.78%)	1 / 32 (3.13%)	
occurrences (all)	6	2	
Hypotension			
subjects affected / exposed	23 / 59 (38.98%)	16 / 32 (50.00%)	
occurrences (all)	26	19	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 59 (6.78%)	0 / 32 (0.00%)	
occurrences (all)	4	0	
Hypothermia			
subjects affected / exposed	5 / 59 (8.47%)	2 / 32 (6.25%)	
occurrences (all)	5	2	
Oedema peripheral			
subjects affected / exposed	3 / 59 (5.08%)	5 / 32 (15.63%)	
occurrences (all)	3	6	
Pain			
subjects affected / exposed	18 / 59 (30.51%)	14 / 32 (43.75%)	
occurrences (all)	20	15	
Pyrexia			
subjects affected / exposed	11 / 59 (18.64%)	13 / 32 (40.63%)	
occurrences (all)	16	15	
Respiratory, thoracic and mediastinal disorders			

Atelectasis			
subjects affected / exposed	7 / 59 (11.86%)	2 / 32 (6.25%)	
occurrences (all)	7	2	
Cough			
subjects affected / exposed	5 / 59 (8.47%)	3 / 32 (9.38%)	
occurrences (all)	5	3	
Dyspnoea			
subjects affected / exposed	3 / 59 (5.08%)	1 / 32 (3.13%)	
occurrences (all)	3	1	
Hiccups			
subjects affected / exposed	2 / 59 (3.39%)	3 / 32 (9.38%)	
occurrences (all)	2	3	
Hypoxia			
subjects affected / exposed	3 / 59 (5.08%)	1 / 32 (3.13%)	
occurrences (all)	3	1	
Pleural effusion			
subjects affected / exposed	9 / 59 (15.25%)	7 / 32 (21.88%)	
occurrences (all)	10	10	
Pneumothorax			
subjects affected / exposed	4 / 59 (6.78%)	2 / 32 (6.25%)	
occurrences (all)	4	2	
Respiratory failure			
subjects affected / exposed	1 / 59 (1.69%)	3 / 32 (9.38%)	
occurrences (all)	1	3	
Tachypnoea			
subjects affected / exposed	1 / 59 (1.69%)	3 / 32 (9.38%)	
occurrences (all)	1	4	
Psychiatric disorders			
Agitation			
subjects affected / exposed	3 / 59 (5.08%)	2 / 32 (6.25%)	
occurrences (all)	3	2	
Insomnia			
subjects affected / exposed	5 / 59 (8.47%)	4 / 32 (12.50%)	
occurrences (all)	5	4	
Investigations			

Blood fibrinogen increased			
subjects affected / exposed	2 / 59 (3.39%)	2 / 32 (6.25%)	
occurrences (all)	3	3	
Blood magnesium decreased			
subjects affected / exposed	5 / 59 (8.47%)	1 / 32 (3.13%)	
occurrences (all)	5	1	
Blood phosphorus decreased			
subjects affected / exposed	0 / 59 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Haemoglobin decreased			
subjects affected / exposed	5 / 59 (8.47%)	0 / 32 (0.00%)	
occurrences (all)	5	0	
Lymphocyte count decreased			
subjects affected / exposed	3 / 59 (5.08%)	2 / 32 (6.25%)	
occurrences (all)	4	2	
Platelet count increased			
subjects affected / exposed	2 / 59 (3.39%)	2 / 32 (6.25%)	
occurrences (all)	2	2	
Renal function test			
subjects affected / exposed	0 / 59 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Anaesthetic complication			
subjects affected / exposed	0 / 59 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Procedural hypotension			
subjects affected / exposed	1 / 59 (1.69%)	2 / 32 (6.25%)	
occurrences (all)	1	2	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	5 / 59 (8.47%)	3 / 32 (9.38%)	
occurrences (all)	5	3	
Bradycardia			
subjects affected / exposed	7 / 59 (11.86%)	5 / 32 (15.63%)	
occurrences (all)	7	6	
Cardiac disorder			

subjects affected / exposed	2 / 59 (3.39%)	2 / 32 (6.25%)	
occurrences (all)	2	2	
Tachycardia			
subjects affected / exposed	5 / 59 (8.47%)	3 / 32 (9.38%)	
occurrences (all)	8	5	
Nervous system disorders			
Lethargy			
subjects affected / exposed	1 / 59 (1.69%)	2 / 32 (6.25%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 59 (18.64%)	7 / 32 (21.88%)	
occurrences (all)	12	12	
Coagulopathy			
subjects affected / exposed	0 / 59 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	4	
Leukocytosis			
subjects affected / exposed	1 / 59 (1.69%)	2 / 32 (6.25%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	4 / 59 (6.78%)	1 / 32 (3.13%)	
occurrences (all)	4	1	
Abdominal pain			
subjects affected / exposed	6 / 59 (10.17%)	3 / 32 (9.38%)	
occurrences (all)	8	3	
Constipation			
subjects affected / exposed	26 / 59 (44.07%)	11 / 32 (34.38%)	
occurrences (all)	26	12	
Diarrhoea			
subjects affected / exposed	9 / 59 (15.25%)	6 / 32 (18.75%)	
occurrences (all)	11	7	
Localised intraabdominal fluid collection			
subjects affected / exposed	1 / 59 (1.69%)	2 / 32 (6.25%)	
occurrences (all)	1	2	
Nausea			

subjects affected / exposed	35 / 59 (59.32%)	14 / 32 (43.75%)	
occurrences (all)	39	16	
Vomiting			
subjects affected / exposed	16 / 59 (27.12%)	9 / 32 (28.13%)	
occurrences (all)	17	12	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	3 / 59 (5.08%)	1 / 32 (3.13%)	
occurrences (all)	3	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 59 (5.08%)	0 / 32 (0.00%)	
occurrences (all)	3	0	
Oliguria			
subjects affected / exposed	7 / 59 (11.86%)	5 / 32 (15.63%)	
occurrences (all)	7	7	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	4 / 59 (6.78%)	0 / 32 (0.00%)	
occurrences (all)	5	0	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	4 / 59 (6.78%)	5 / 32 (15.63%)	
occurrences (all)	5	5	
Oral candidiasis			
subjects affected / exposed	4 / 59 (6.78%)	2 / 32 (6.25%)	
occurrences (all)	4	2	
Pneumonia			
subjects affected / exposed	1 / 59 (1.69%)	4 / 32 (12.50%)	
occurrences (all)	2	5	
Sepsis			
subjects affected / exposed	3 / 59 (5.08%)	4 / 32 (12.50%)	
occurrences (all)	3	4	
Urinary tract infection			
subjects affected / exposed	5 / 59 (8.47%)	2 / 32 (6.25%)	
occurrences (all)	5	2	

Wound infection			
subjects affected / exposed	4 / 59 (6.78%)	2 / 32 (6.25%)	
occurrences (all)	5	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 59 (6.78%)	0 / 32 (0.00%)	
occurrences (all)	4	0	
Dehydration			
subjects affected / exposed	3 / 59 (5.08%)	2 / 32 (6.25%)	
occurrences (all)	3	2	
Hypoalbuminaemia			
subjects affected / exposed	1 / 59 (1.69%)	2 / 32 (6.25%)	
occurrences (all)	1	2	
Hypokalaemia			
subjects affected / exposed	10 / 59 (16.95%)	6 / 32 (18.75%)	
occurrences (all)	11	6	
Hyponatraemia			
subjects affected / exposed	4 / 59 (6.78%)	1 / 32 (3.13%)	
occurrences (all)	4	1	
Hypophosphataemia			
subjects affected / exposed	1 / 59 (1.69%)	2 / 32 (6.25%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 February 2010	Amendment 2 - Clarification around: Interim analysis TBS definition exclusion of sealants for SoC subjects. venue of study centers SAE definition In addition there was an increase in number of sites and an addition of a 60-day follow up visit

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Please note that there are 2 subjects (Pt 15019 and 20007) who died after completion of their participation in the study. These deaths are included in the adverse events provided.

Notes: