



## Clinical trial results:

### A RANDOMIZED, CONTROLLED, MULTICENTER PHASE 2 STUDY TO EVALUATE THE EFFICACY AND SAFETY OF FIBRIN SEALANT VH S/D 500 S-APR (TISSEEL) FOR HEMOSTASIS IN SUBJECTS UNDERGOING HEPATIC RESECTION

#### Summary

EudraCT number	2010-018480-42
Trial protocol	DE
Global end of trial date	26 July 2011

#### Results information

Result version number	v1 (current)
This version publication date	08 November 2017
First version publication date	08 November 2017

#### Trial information

##### Trial identification

Sponsor protocol code	550904
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01244425
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Baxter Healthcare Corporation
Sponsor organisation address	1 Baxter Parkway, Deerfield, United States, 60015
Public contact	Clinical Trials Disclosure Group, Baxter Healthcare Corporation, joe_archer@Baxter.com
Scientific contact	Clinical Trials Disclosure Group, Baxter Healthcare Corporation, joe_archer@Baxter.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	26 July 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 July 2011
Global end of trial reached?	Yes
Global end of trial date	26 July 2011
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of FS VH S/D 500 s-apr for hemostasis in subjects undergoing partial hepatic resection, as compared to a control arm treated by manual compression with a surgical gauze swab.

Protection of trial subjects:

If no hemostasis occurred within 10 minutes of treatment, the surgeon was free to use other additional hemostatic measures (ie, rescue therapy) as he/she felt appropriate. In the same way, the surgeon was, at any time in the procedure, free to abort study participation if convinced that medical circumstances made it necessary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2010
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	Germany: 95
Worldwide total number of subjects	95
EEA total number of subjects	95

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)	95
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Subjects were to undergo planned, elective resection of at least 1 anatomical segment of the liver for any reason by laparotomy.

### Pre-assignment

Screening details:

Subjects were evaluated for eligibility at screening within 21 days prior to surgery, and enrolled as soon as informed consent was obtained after meeting all inclusion and exclusion criteria. A total of 95 subjects were enrolled, 25 subjects were not randomized (23 were screen failures, 2 discontinued).

### Pre-assignment period milestones

Number of subjects started	95
Number of subjects completed	70

### Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failures: 23
Reason: Number of subjects	Operated by non-investigator: 1
Reason: Number of subjects	Prolonged operation and IP could not be used: 1

### Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	FS VH S/D 500 s-apr
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Arm description:

Fibrin Sealant, Vapor Heated, Solvent/Detergent treated with 500 IU/mL thrombin and synthetic aprotinin (FS VH S/D 500 s-apr), sprayed onto the oozing resection surface of the liver, not to exceed 20mL per participant. Hemostasis will be assessed at 4, 6, 8 and 10 minutes after application of the study treatment.

Arm type	Experimental
Investigational medicinal product name	Fibrin Sealant (FS) VH S/D 500 s-apr
Investigational medicinal product code	
Other name	Tisseel
Pharmaceutical forms	Sealant
Routes of administration	Topical use

Dosage and administration details:

Single application, sprayed onto the oozing resection surface of the liver, not to exceed 20mL.

<b>Arm title</b>	Manual Compression
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Arm description:

A dry surgical gauze swab will be used to apply by hand an even light pressure onto the oozing resection surface of the liver. Hemostasis will be assessed at 4, 6, 8 and 10 minutes after application of the study treatment.

Arm type	No intervention
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No investigational medicinal product assigned in this arm

<b>Number of subjects in period 1</b> <sup>[1]</sup>	FS VH S/D 500 s-apr	Manual Compression
Started	35	35
Completed	32	32
Not completed	3	3
Adverse event, serious fatal	1	1
Consent withdrawn by subject	2	2

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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: Baseline period represents subjects randomized into study, and included in both the Full Analysis Set (FAS) and Safety populations. Worldwide number reflects total number enrolled including those not randomized and those who did not receive treatment.

## Baseline characteristics

### Reporting groups

Reporting group title	FS VH S/D 500 s-apr
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Reporting group description:

Fibrin Sealant, Vapor Heated, Solvent/Detergent treated with 500 IU/mL thrombin and synthetic aprotinin (FS VH S/D 500 s-apr), sprayed onto the oozing resection surface of the liver, not to exceed 20mL per participant. Hemostasis will be assessed at 4, 6, 8 and 10 minutes after application of the study treatment.

Reporting group title	Manual Compression
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Reporting group description:

A dry surgical gauze swab will be used to apply by hand an even light pressure onto the oozing resection surface of the liver. Hemostasis will be assessed at 4, 6, 8 and 10 minutes after application of the study treatment.

Reporting group values	FS VH S/D 500 s-apr	Manual Compression	Total
Number of subjects	35	35	70
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	54.7	59.8	
standard deviation	± 14.5	± 12.8	-
Gender categorical Units: Subjects			
Female	15	16	31
Male	20	19	39

## End points

### End points reporting groups

Reporting group title	FS VH S/D 500 s-apr
Reporting group description: Fibrin Sealant, Vapor Heated, Solvent/Detergent treated with 500 IU/mL thrombin and synthetic aprotinin (FS VH S/D 500 s-apr), sprayed onto the oozing resection surface of the liver, not to exceed 20mL per participant. Hemostasis will be assessed at 4, 6, 8 and 10 minutes after application of the study treatment.	
Reporting group title	Manual Compression
Reporting group description: A dry surgical gauze swab will be used to apply by hand an even light pressure onto the oozing resection surface of the liver. Hemostasis will be assessed at 4, 6, 8 and 10 minutes after application of the study treatment.	

### Primary: Percentage of participants with intraoperative hemostasis at 4 minutes after application of the randomized treatment

End point title	Percentage of participants with intraoperative hemostasis at 4 minutes after application of the randomized treatment
End point description: Hemostasis defined as no visible bleeding on the liver resection surface (liver surgical site) after treatment application. Hemostasis had to be maintained until surgical closure. Time recording started with treatment application, ie, with the start of spraying Fibrin Sealant, Vapor Heated, Solvent/Detergent treated with 500 IU/mL thrombin and synthetic aprotinin (FS VH S/D 500 s-apr) or with the application of manual compression.  The following were regarded as treatment failures: - No hemostasis achieved at 4 minutes post treatment application (for the FS VH S/D 500 s-apr arm, the "time to hemostasis" was used; a time window of +5 seconds was acceptable for showing a success) - Additional hemostatic treatment (ie, hemostatics in addition to the randomized treatment) was required - Reapplication of FS VH S/D 500 s-apr after 4 minutes - Intraoperative rebleeding after the first 4 minutes of the observation period	
End point type	Primary
End point timeframe: 4 minutes post start of treatment application	

End point values	FS VH S/D 500 s-apr	Manual Compression		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: percentage of participants				
number (confidence interval 95%)	82.9 (68.3 to 92.8)	37.1 (22.5 to 53.6)		

### Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	FS VH S/D 500 s-apr v Manual Compression

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	likelihood-ratio chi square test

### Secondary: Percentage of participants with intraoperative hemostasis at 6 minutes after application of the randomized treatment

End point title	Percentage of participants with intraoperative hemostasis at 6 minutes after application of the randomized treatment
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End point description:

Hemostasis defined as no visible bleeding on the liver resection surface (liver surgical site) after treatment application. Hemostasis had to be maintained until surgical closure. Time recording started with treatment application, ie, with the start of spraying Fibrin Sealant, Vapor Heated, Solvent/Detergent treated with 500 IU/mL thrombin and synthetic aprotinin (FS VH S/D 500 s-apr) or with the application of manual compression.

End point type	Secondary
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End point timeframe:

6 minutes after start of treatment application

End point values	FS VH S/D 500 s-apr	Manual Compression		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: percentage of participants				
number (confidence interval 95%)	91.4 (79.3 to 97.8)	57.1 (40.7 to 72.6)		

### Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis
Comparison groups	FS VH S/D 500 s-apr v Manual Compression
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	likelihood ratio chi-square test

### Secondary: Percentage of participants with intraoperative hemostasis at 8 minutes after application of the randomized treatment

End point title	Percentage of participants with intraoperative hemostasis at 8 minutes after application of the randomized treatment
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End point description:

Hemostasis defined as no visible bleeding on the liver resection surface (liver surgical site) after

treatment application. Hemostasis had to be maintained until surgical closure. Time recording started with treatment application, ie, with the start of spraying Fibrin Sealant, Vapor Heated, Solvent/Detergent treated with 500 IU/mL thrombin and synthetic aprotinin (FS VH S/D 500 s-apr) or with the application of manual compression.

End point type	Secondary
End point timeframe:	8 minutes after start of treatment application

End point values	FS VH S/D 500 s-apr	Manual Compression		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: percentage of participants				
number (confidence interval 95%)	91.4 (79.3 to 97.8)	71.4 (55.3 to 84.5)		

### Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	FS VH S/D 500 s-apr v Manual Compression
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028
Method	likelihood ratio chi-square test

### Secondary: Percentage of participants with intraoperative hemostasis at 10 minutes after application of the randomized treatment

End point title	Percentage of participants with intraoperative hemostasis at 10 minutes after application of the randomized treatment
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End point description:

Hemostasis defined as no visible bleeding on the liver resection surface (liver surgical site) after treatment application. Hemostasis had to be maintained until surgical closure. Time recording started with treatment application, ie, with the start of spraying Fibrin Sealant, Vapor Heated, Solvent/Detergent treated with 500 IU/mL thrombin and synthetic aprotinin (FS VH S/D 500 s-apr) or with the application of manual compression.

End point type	Secondary
End point timeframe:	10 minutes after start of treatment application

<b>End point values</b>	FS VH S/D 500 s-apr	Manual Compression		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: percentage of participants				
number (confidence interval 95%)	94.3 (83.4 to 99.0)	74.3 (58.4 to 86.7)		

### Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis
Comparison groups	FS VH S/D 500 s-apr v Manual Compression
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	likelihood ratio chi-square test

### Secondary: Percentage of participants with intraoperative rebleeding after occurrence of hemostasis

End point title	Percentage of participants with intraoperative rebleeding after occurrence of hemostasis
End point description:	Intraoperative rebleeding from the treated liver resection surface after occurrence of hemostasis.
End point type	Secondary
End point timeframe:	Intraoperative day 0

<b>End point values</b>	FS VH S/D 500 s-apr	Manual Compression		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: percentage of participants				
number (confidence interval 95%)	2.9 (0.2 to 12.0)	8.6 (2.2 to 20.7)		

### Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis
Comparison groups	FS VH S/D 500 s-apr v Manual Compression

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.293
Method	likelihood ratio chi-square test

### Secondary: Percentage of participants with postoperative rebleeding

End point title	Percentage of participants with postoperative rebleeding
End point description:	Rebleeding until discharged from the surgical ward, defined as any rebleeding from the treated liver resection surface requiring surgical reexploration
End point type	Secondary
End point timeframe:	Day 0 Postoperative until discharged from surgical ward (within 48 hours after end of surgery or longer)

End point values	FS VH S/D 500 s-apr	Manual Compression		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Percentage of participants				
number (confidence interval 95%)	2.9 (0.1 to 14.9)	0.0 (0.0 to 10.0)		

### Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	FS VH S/D 500 s-apr v Manual Compression
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.237
Method	likelihood ratio chi-square test

### Secondary: Percentage of participants with transfusion requirements until discharged from surgical ward

End point title	Percentage of participants with transfusion requirements until discharged from surgical ward
End point description:	Transfusions administered included whole blood, packed red blood cells, fresh frozen plasma, and thrombocyte concentrate.
End point type	Secondary
End point timeframe:	Day ) Intra- and Postoperative until discharged from surgical ward (within 48 hours after end of surgery

or longer)

<b>End point values</b>	FS VH S/D 500 s-apr	Manual Compression		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: percentage of participants				
number (confidence interval 95%)	40.0 (24.9 to 56.5)	42.9 (27.4 to 59.3)		

### Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis
Comparison groups	FS VH S/D 500 s-apr v Manual Compression
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.808
Method	likelihood ratio chi-square test

### Secondary: Median total volume of postoperative drainage fluid within 48 hours after surgery

End point title	Median total volume of postoperative drainage fluid within 48 hours after surgery
End point description:	
End point type	Secondary
End point timeframe:	Within 48 hours after surgery

<b>End point values</b>	FS VH S/D 500 s-apr	Manual Compression		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: mL				
median (full range (min-max))	415.0 (70 to 10800)	410.0 (0 to 3690)		

### Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Screening (within 21 days prior to surgery) through end of study (20-40 days after surgery)

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	unspecific
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### Reporting groups

Reporting group title	FS VH S/D 500 s-apr
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Reporting group description: -

Reporting group title	Manual Compression
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Reporting group description: -

<b>Serious adverse events</b>	FS VH S/D 500 s-apr	Manual Compression	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 35 (25.71%)	11 / 35 (31.43%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic haematoma			
subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (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	4 / 35 (11.43%)	3 / 35 (8.57%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Post procedural haemorrhage subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small-for-size liver syndrome subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders Disseminated intravascular coagulation subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions Multi-organ failure subjects affected / exposed	1 / 35 (2.86%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders Ascites subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			

subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hepatobiliary disorders</b>			
Portal vein thrombosis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Respiratory, thoracic and mediastinal disorders</b>			
Aspiration			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
Liver abscess			
subjects affected / exposed	1 / 35 (2.86%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			
subjects affected / exposed	0 / 35 (0.00%)	3 / 35 (8.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Subdiaphragmatic abscess			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (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 %

<b>Non-serious adverse events</b>	FS VH S/D 500 s-apr	Manual Compression	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 35 (62.86%)	23 / 35 (65.71%)	
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Chemical peritonitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Operative Haemorrhage			
subjects affected / exposed	1 / 35 (2.86%)	3 / 35 (8.57%)	
occurrences (all)	1	3	
Pneumothorax traumatic			
subjects affected / exposed	2 / 35 (5.71%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Post procedural haematoma			
subjects affected / exposed	4 / 35 (11.43%)	2 / 35 (5.71%)	
occurrences (all)	4	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 35 (5.71%)	2 / 35 (5.71%)	
occurrences (all)	3	2	
Hypotension			

subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	1 / 35 (2.86%) 1	
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	1 / 35 (2.86%)	3 / 35 (8.57%)	
occurrences (all)	1	3	
Oedema peripheral			
subjects affected / exposed	1 / 35 (2.86%)	3 / 35 (8.57%)	
occurrences (all)	1	3	
Pyrexia			
subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 35 (2.86%)	4 / 35 (11.43%)	
occurrences (all)	1	4	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	7 / 35 (20.00%)	9 / 35 (25.71%)	
occurrences (all)	9	14	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Infection			
subjects affected / exposed	2 / 35 (5.71%)	4 / 35 (11.43%)	
occurrences (all)	2	4	
Urinary tract infection			
subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	5 / 35 (14.29%)	2 / 35 (5.71%)	
occurrences (all)	5	2	
Hypokalaemia			

subjects affected / exposed	1 / 35 (2.86%)	5 / 35 (14.29%)	
occurrences (all)	1	5	

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported