Clinical trial results:
A controlled, randomized, multi-centre, double blind, phase II study to evaluate efficacy and safety of topical PeproStat in intraoperative surgical haemostasis

Summary

EudraCT number	2016-003661-26
Trial protocol	GB PL HR
Global end of trial date	23 August 2017

Results information

Result version number	v1 (current)
This version publication date	08 September 2018
First version publication date	08 September 2018
Summary attachment (see zip file)	CSR Synopsis (CLOTFAST 2_CSR Synopsis_Final v1.0__08032018 signed.pdf)

Trial information

Trial identification

Sponsor protocol code	HX-02-PEP

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03131336
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Haemostatix Limited
Sponsor organisation address	BioCity Nottingham, Nottingham, United Kingdom, NG1 1GF
Public contact	Information point, Haemostatix Limited, 0044 1159124512, info@ergomedplc.com
Scientific contact	Information point, Haemostatix Limited, 0044 1159124512, info@ergomedplc.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	10 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 July 2017
Global end of trial reached?	Yes
Global end of trial date	23 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy of PeproStat in intraoperative hemostasis in adult subjects who underwent liver/soft tissue surgery, vascular surgery or spine surgery.

Protection of trial subjects:

The study was conducted according to the protocol and in compliance with Good Clinical Practice (GCP), with the Declaration of Helsinki and with other applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2017
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	Bosnia and Herzegovina: 91
Country: Number of subjects enrolled	Serbia: 66
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Croatia: 14
Worldwide total number of subjects	214
EEA total number of subjects	57

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)	122
From 65 to 84 years	90

85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The recruitment started on 31 March 2017 and was completed on 14 July 2017. Subjects from Serbia, Croatia, Bosnia and Herzegovina, Poland, and UK were recruited into the study.

Pre-assignment

Screening details:

A total of 214 subjects were consented and screened, 203 subjects were randomised and 169 received treatment. 11 subjects were screen failures and 34 were extended screen failures (did not require a haemostat during their surgery).

Period 1

Period 1 title	Interventional study period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Gelatine sponge soaked in Peprostat

Arm description:

PeproStat 2.5 mg/mL (Investigational Product), soaked into absorbable haemostatic gelatin sponge (Spongostan).

Arm type	Experimental
Investigational medicinal product name	Peprostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for sealant
Routes of administration	Epilesional use

Dosage and administration details:

The dosage was 12.5 mg per vial.
The gelatine sponge was soaked with 1 vial; 5 mL 2.5 mg/mL PeproStat (12.5 mg nominal dose), moments before topical application to the target bleeding site during scheduled liver/soft tissue, vascular, or spine surgery. A maximum of 2 PeproStat soaked sponges could be used in each subject as appropriate for the size / number of bleeding sites.

Arm title	Gelatin sponge soaked in Saline

Arm description:

Saline 0.9% (control product), soaked into absorbable haemostatic gelatin sponge (Spongostan).

Arm type	Active comparator
Investigational medicinal product name	Saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Epilesional use

Dosage and administration details:

Each vial contained 5mL of 0.9% saline
The gelatine sponge was soaked with 1 vial; 5 mL of 0.9% saline, moments before topical application to the target bleeding site during scheduled liver/soft tissue, vascular, or spine surgery. A maximum of 2 saline soaked sponges could be used in each subject as appropriate for the size / number of bleeding sites.

Number of subjects in period 1[1]	Gelatine sponge soaked in Peprostat	Gelatin sponge soaked in Saline
Started	114	55
Completed	114	55

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: The number enrolled is all those who have signed the ICF. The number reported in the baseline period are the number treated.

Period 2

Period 2 title	Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Gelatine sponge soaked in Peprostat

Arm description:

PeproStat 2.5 mg/mL (Investigational Product), soaked into absorbable haemostatic gelatin sponge (Spongostan).

Arm type	Experimental
Investigational medicinal product name	Peprostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for sealant
Routes of administration	Epilesional use

Dosage and administration details:

The dosage was 12.5 mg per vial.
The gelatine sponge was soaked with 1 vial; 5 mL 2.5 mg/mL PeproStat (12.5 mg nominal dose), moments before topical application to the target bleeding site during scheduled liver/soft tissue, vascular, or spine surgery. A maximum of 2 PeproStat soaked sponges could be used in each subject as appropriate for the size / number of bleeding sites.

Arm title	Gelatin sponge soaked in Saline

Arm description:

Saline 0.9% (control product), soaked into absorbable haemostatic gelatin sponge (Spongostan).

Arm type	Active comparator
Investigational medicinal product name	Saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Epilesional use

Dosage and administration details:

Each vial contained 5mL of 0.9% saline
The gelatine sponge was soaked with 1 vial; 5 mL of 0.9% saline, moments before topical application to the target bleeding site during scheduled liver/soft tissue, vascular, or spine surgery. A maximum of 2 saline soaked sponges could be used in each subject as appropriate for the size / number of bleeding

sites.

Number of subjects in period 2	Gelatine sponge soaked in Peprostat	Gelatin sponge soaked in Saline
Started	114	55
Completed	112	53
Not completed	2	2
Adverse event, serious fatal	1	-
Lost to follow-up	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Gelatine sponge soaked in Peprostat
Reporting group description:	
PeproStat 2.5 mg/mL (Investigational Product), soaked into absorbable haemostatic gelatin sponge (Spongostan).	
Reporting group title	Gelatin sponge soaked in Saline
Reporting group description:	
Saline 0.9% (control product), soaked into absorbable haemostatic gelatin sponge (Spongostan).	

Reporting group values	Gelatine sponge soaked in Peprostat	Gelatin sponge soaked in Saline	Total
Number of subjects	114	55	169
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			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			
Units: years			
arithmetic mean	61.3	61.3	
standard deviation	± 11.55	± 12.52	-
Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female	58	31	89
Male	56	24	80

Subject analysis sets	
Subject analysis set title	FAS - Peprostat - open liver/soft tissue surgery
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing open liver/soft tissue surgery who received Peprostat	

Subject analysis set title	PP - Peprostat - open liver/soft tissue surgery
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation and who underwent open liver/soft tissue surgery and received Peprostat.

Subject analysis set title	FAS - Peprostat - vascular surgery
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing vascular surgery who received Peprostat

Subject analysis set title	FAS - Peprostat - spine surgery
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing spine surgery who received Peprostat

Subject analysis set title	PP - Preprostat - vascular surgery
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent vascular surgery and received Peprostat.

Subject analysis set title	PP - Peprostat - spine surgery
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent spine surgery and received Peprostat.

Subject analysis set title	FAS - Saline- open liver/soft tissue surgery
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing open liver/soft tissue surgery who received control treatment

Subject analysis set title	PP - Saline - open liver/soft tissue surgery
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent open liver/soft tissue surgery and received control treatment.

Subject analysis set title	FAS - Saline - vascular surgery
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing vascular surgery who received control treatment

Subject analysis set title	PP - Saline - vascular surgery
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent vascular surgery and received control treatment.

Subject analysis set title	FAS - Saline - spine surgery
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing spine surgery who received control treatment

Subject analysis set title	PP - Saline - spine surgery
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent spine surgery and received control treatment

Subject analysis set title	FAS - Peprostat - All surgeries
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing any of the surgeries who received Peprostat

Subject analysis set title	FAS - Saline - All surgeries
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing any of the surgeries who received control treatment

Subject analysis set title	PP - Peprostat - All surgeries
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who received Peprostat

Subject analysis set title	PP - Saline - All surgeries
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who received control treatment

Subject analysis set title	FAS - Peprostat all surgeries - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing all surgeries who received control Peprostat and who experienced mild bleeding during surgery

Subject analysis set title	FAS - Saline all surgeries - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing all surgeries who received control and experienced mild bleeding during surgery

Subject analysis set title	FAS - Peprostat vascular surgery- mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing vascular surgery who received Peprostat and experienced mild bleeding during surgery

Subject analysis set title	FAS - Peprostat open liver/soft tissue - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing open liver/soft tissue surgery who received Peprostat and experienced mild bleeding during surgery

Subject analysis set title	FAS - Peprostat spine surgery - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing spine surgery who received Peprostat and experienced mild bleeding during surgery

Subject analysis set title	FAS - Saline open liver/soft tissue - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing open liver / soft tissue surgery who received control treatment and experienced mild bleeding in surgery

Subject analysis set title	FAS - Saline spine surgery - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing spine surgery who received control treatment and experienced mild bleeding during surgery

Subject analysis set title	FAS - Saline vascular surgery - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing vascular surgery who received control treatment and experienced mild bleeding during surgery

Reporting group values	FAS - Peprostat - open liver/soft tissue surgery	PP - Peprostat - open liver/soft tissue surgery	FAS - Peprostat - vascular surgery
Number of subjects	39	37	36
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			
Units: years			
arithmetic mean	60.9	60.7	68.2
standard deviation	± 10.98	± 10.22	± 9.07
Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female	27	26	6
Male	12	11	30

Reporting group values	FAS - Peprostat - spine surgery	PP - Preprostat - vascular surgery	PP - Peprostat - spine surgery
Number of subjects	39	35	38
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years			

85 years and over			

Age continuous			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			
Units: years			
arithmetic mean	55.4	68.6	55.4
standard deviation	± 10.96	± 8.92	± 11.10
Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female	25	6	24
Male	14	29	14

Reporting group values	FAS - Saline- open liver/soft tissue surgery	PP - Saline - open liver/soft tissue surgery	FAS - Saline - vascular surgery
Number of subjects	19	17	18
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			
Units: years			
arithmetic mean	57.6	55.6	68.0
standard deviation	± 14.25	± 13.81	± 9.60
Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female	14	14	6
Male	5	3	12

Reporting group values	PP - Saline - vascular surgery	FAS - Saline - spine surgery	PP - Saline - spine surgery
Number of subjects	18	18	17
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			
Units: years			
arithmetic mean	68.0	58.4	57.8
standard deviation	± 9.6	± 10.89	± 10.88
Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female	6	11	10
Male	12	7	7

Reporting group values	FAS - Peprostat - All surgeries	FAS - Saline - All surgeries	PP - Peprostat - All surgeries
Number of subjects	114	55	110
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			

Units: years			
arithmetic mean	61.3	61.3	61.4
standard deviation	± 11.55	± 12.52	± 11.42

Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female	58	31	56
Male	56	24	54

Reporting group values	PP - Saline - All surgeries	FAS - Peprostat all surgeries - mild bleeding	FAS - Saline all surgeries - mild bleeding
Number of subjects	52	47	26
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			
Units: years			
arithmetic mean	60.6		
standard deviation	± 12.57	±	±
Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female	30		
Male	22		

Reporting group values	FAS - Peprostat vascular surgery-mild bleeding	FAS - Peprostat open liver/soft tissue - mild bleeding	FAS - Peprostat spine surgery - mild bleeding
Number of subjects	20	11	16
Age categorical			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			
Units: years arithmetic mean standard deviation	±	±	±
Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female Male			

Reporting group values	FAS - Saline open liver/soft tissue - mild bleeding	FAS - Saline spine surgery - mild bleeding	FAS - Saline vascular surgery - mild bleeding
Number of subjects	9	4	13
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Overall in the study the mean (SD) age was 61.3 (11.84) years. The mean (SD) ages were similar between PeproStat and Saline treatment groups within a surgery type, but mean (SD) age was lowest in subjects who underwent spine surgery (56.4 [10.93] years) and highest in subjects who underwent vascular surgery (68.1 [9.16] years).			
Units: years arithmetic mean standard deviation	±	±	±

Gender categorical			
Overall in the study, sex was almost split 1:1 between females (52.7%) and males (47.3%). However, sex stratified by surgery type revealed that approximately twice as many females underwent open liver/soft tissue surgery and spine surgery, while twice as many males underwent vascular surgery. The treatment groups within each surgery type followed the same patterns.			
Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Gelatine sponge soaked in Peprostat
Reporting group description:	
PeproStat 2.5 mg/mL (Investigational Product), soaked into absorbable haemostatic gelatin sponge (Spongostan).	
Reporting group title	Gelatin sponge soaked in Saline
Reporting group description:	
Saline 0.9% (control product), soaked into absorbable haemostatic gelatin sponge (Spongostan).	
Reporting group title	Gelatine sponge soaked in Peprostat
Reporting group description:	
PeproStat 2.5 mg/mL (Investigational Product), soaked into absorbable haemostatic gelatin sponge (Spongostan).	
Reporting group title	Gelatin sponge soaked in Saline
Reporting group description:	
Saline 0.9% (control product), soaked into absorbable haemostatic gelatin sponge (Spongostan).	
Subject analysis set title	FAS - Peprostat - open liver/soft tissue surgery
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing open liver/soft tissue surgery who received Peprostat	
Subject analysis set title	PP - Peprostat - open liver/soft tissue surgery
Subject analysis set type	Per protocol
Subject analysis set description:	
Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation and who underwent open liver/soft tissue surgery and received Peprostat.	
Subject analysis set title	FAS - Peprostat - vascular surgery
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing vascular surgery who received Peprostat	
Subject analysis set title	FAS - Peprostat - spine surgery
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing spine surgery who received Peprostat	
Subject analysis set title	PP - Preprostat - vascular surgery
Subject analysis set type	Per protocol
Subject analysis set description:	
Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent vascular surgery and received Peprostat.	
Subject analysis set title	PP - Peprostat - spine surgery
Subject analysis set type	Per protocol
Subject analysis set description:	
Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent spine surgery and received Peprostat.	
Subject analysis set title	FAS - Saline- open liver/soft tissue surgery
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing open liver/soft tissue surgery who received control treatment	
Subject analysis set title	PP - Saline - open liver/soft tissue surgery

Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent open liver/soft tissue surgery and received control treatment.

Subject analysis set title	FAS - Saline - vascular surgery
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing vascular surgery who received control treatment

Subject analysis set title	PP - Saline - vascular surgery
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent vascular surgery and received control treatment.

Subject analysis set title	FAS - Saline - spine surgery
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing spine surgery who received control treatment

Subject analysis set title	PP - Saline - spine surgery
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who underwent spine surgery and received control treatment

Subject analysis set title	FAS - Peprostat - All surgeries
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing any of the surgeries who received Peprostat

Subject analysis set title	FAS - Saline - All surgeries
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing any of the surgeries who received control treatment

Subject analysis set title	PP - Peprostat - All surgeries
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who received Peprostat

Subject analysis set title	PP - Saline - All surgeries
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol set is all patients that did not have protocol deviations that could have an effect on the efficacy and safety evaluation who received control treatment

Subject analysis set title	FAS - Peprostat all surgeries - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing all surgeries who received control Peprostat and who experienced mild bleeding during surgery

Subject analysis set title	FAS - Saline all surgeries - mild bleeding
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set represents the planned treatments for patients undergoing all surgeries who received control and experienced mild bleeding during surgery

Subject analysis set title	FAS - Peprostat vascular surgery- mild bleeding

Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing vascular surgery who received Peprostat and experienced mild bleeding during surgery	
Subject analysis set title	FAS - Peprostat open liver/soft tissue - mild bleeding
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing open liver/soft tissue surgery who received Peprostat and experienced mild bleeding during surgery	
Subject analysis set title	FAS - Peprostat spine surgery - mild bleeding
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing spine surgery who received Peprostat and experienced mild bleeding during surgery	
Subject analysis set title	FAS - Saline open liver/soft tissue - mild bleeding
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing open liver / soft tissue surgery who received control treatment and experienced mild bleeding in surgery	
Subject analysis set title	FAS - Saline spine surgery - mild bleeding
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing spine surgery who received control treatment and experienced mild bleeding during surgery	
Subject analysis set title	FAS - Saline vascular surgery - mild bleeding
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set represents the planned treatments for patients undergoing vascular surgery who received control treatment and experienced mild bleeding during surgery	

Primary: Time to haemostasis (TTH) at the primary target bleed site (TBS)

End point title	Time to haemostasis (TTH) at the primary target bleed site (TBS)
End point description:	
Observations were performed at 1, 2, 3, 5, 7 and 10 minutes following application of study treatment. If bleeding stopped during the 10-minute assessment period, time to haemostasis was recorded.	
End point type	Primary
End point timeframe:	
Within 10 minutes or to the end of the 10-minute assessment	

End point values	FAS - Peprostat - open liver/soft tissue surgery	PP - Peprostat - open liver/soft tissue surgery	FAS - Peprostat - vascular surgery	FAS - Peprostat - spine surgery
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	39	37	36	39
Units: minutes				
arithmetic mean (standard deviation)	5.5 (± 3.03)	5.4 (± 3.02)	3.6 (± 2.90)	3.7 (± 2.78)

End point values	PP - Preprostat - vascular surgery	PP - Peprostat - spine surgery	FAS - Saline- open liver/soft tissue surgery	PP - Saline - open liver/soft tissue surgery
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	38	19	17
Units: minutes				
arithmetic mean (standard deviation)	3.6 (± 2.93)	3.7 (± 2.82)	5.8 (± 3.22)	6.3 (± 3.08)

End point values	FAS - Saline - vascular surgery	PP - Saline - vascular surgery	FAS - Saline - spine surgery	PP - Saline - spine surgery
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	18	18	17
Units: minutes				
arithmetic mean (standard deviation)	5.4 (± 3.85)	5.4 (± 3.85)	5.7 (± 3.51)	5.6 (± 3.60)

End point values	FAS - Peprostat - All surgeries	FAS - Saline - All surgeries	PP - Peprostat - All surgeries	PP - Saline - All surgeries
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	114	55	110	52
Units: minutes				
arithmetic mean (standard deviation)	4.3 (± 3.01)	5.7 (± 3.47)	4.2 (± 3.01)	5.8 (± 3.48)

Statistical analyses

Statistical analysis title	Time to Haemostasis
Comparison groups	FAS - Peprostat - open liver/soft tissue surgery v FAS - Peprostat - vascular surgery v FAS - Peprostat - spine surgery v FAS - Saline- open liver/soft tissue surgery v FAS - Saline - vascular surgery v FAS - Saline - spine surgery
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: Median Time to Haemostasis

End point title	Median Time to Haemostasis

End point description:

End point type	Secondary

End point timeframe:

Median time to haemostasis in minutes from TxStart to the achievement of haemostasis or to the end of the 10-minute assessment period if haemostasis had not yet been achieved.

End point values	FAS - Peprostat - open liver/soft tissue surgery	PP - Peprostat - open liver/soft tissue surgery	FAS - Peprostat - vascular surgery	FAS - Peprostat - spine surgery
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	39	37	36	39
Units: minutes				
median (inter-quartile range (Q1-Q3))	5.00 (3.00 to 7.00)	5.00 (3.00 to 7.00)	2.50 (1.50 to 5.00)	3.00 (2.00 to 5.00)

End point values	PP - Preprostat - vascular surgery	PP - Peprostat - spine surgery	FAS - Saline- open liver/soft tissue surgery	PP - Saline - open liver/soft tissue surgery
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	38	19	17
Units: minutes				
median (inter-quartile range (Q1-Q3))	2.00 (1.00 to 5.00)	2.50 (2.00 to 5.00)	5.00 (3.00 to 10.00)	5.00 (5.00 to 10.00)

End point values	FAS - Saline - vascular surgery	PP - Saline - vascular surgery	FAS - Saline - spine surgery	PP - Saline - spine surgery
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	18	18	17
Units: minutes				
median (inter-quartile range (Q1-Q3))	5.00 (2.00 to 10.00)	5.00 (2.00 to 10.00)	5.00 (3.00 to 10.00)	5.00 (3.00 to 10.00)

End point values	FAS - Peprostat - All surgeries	FAS - Saline - All surgeries	PP - Peprostat - All surgeries	PP - Saline - All surgeries
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	114	55	110	52
Units: minutes				
median (inter-quartile range (Q1-Q3))	3.00 (2.00 to 6.00)	5.00 (3.00 to 10.00)	3.00 (2.00 to 6.00)	5.00 (3.00 to 10.00)

Statistical analyses

No statistical analyses for this end point

Post-hoc: Post hoc analysis for subjects with mild bleeding

End point title	Post hoc analysis for subjects with mild bleeding

End point description:

Overall, 56.8% of subjects presented moderate bleeding and 43.2% of subjects presented mild bleeding in the FAS. For both open liver/soft tissue surgery and spine surgery most subjects presented moderate bleeding, whilst for vascular surgery the majority of subjects presented mild bleeding.
Therefore, a Post-Hoc analysis was conducted to analyse and compare bleeding time in subjects who presented mild and moderate bleeding in the same manner as conducted in comparable trials.

End point type	Post-hoc

End point timeframe:

Within 10 minutes or to the end of the 10-minute assessment

End point values	FAS - Peprostat all surgeries - mild bleeding	FAS - Saline all surgeries - mild bleeding	FAS - Peprostat vascular surgery- mild bleeding	FAS - Peprostat open liver/soft tissue - mild bleeding
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	47	26	20	11
Units: minutes				
arithmetic mean (standard deviation)	3.2 (± 2.10)	5.9 (± 3.57)	3.3 (± 2.40)	3.2 (± 1.54)

End point values	FAS - Peprostat spine surgery - mild bleeding	FAS - Saline open liver/soft tissue - mild bleeding	FAS - Saline spine surgery - mild bleeding	FAS - Saline vascular surgery - mild bleeding
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	9	4	13
Units: minutes				
arithmetic mean (standard deviation)	3.1 (± 2.16)	5.8 (± 3.67)	7.0 (± 3.56)	5.6 (± 3.73)

Statistical analyses

Statistical analysis title	time to haemostasis in patients with mild bleeding
Comparison groups	FAS - Peprostat vascular surgery- mild bleeding v FAS - Peprostat open liver/soft tissue - mild bleeding v FAS - Peprostat spine surgery - mild bleeding v FAS - Saline open liver/soft tissue - mild bleeding v FAS - Saline spine surgery -

	mild bleeding v FAS - Saline vascular surgery - mild bleeding
Number of subjects included in analysis	73
Analysis specification	Post-hoc
Analysis type	superiority
P-value	≤ 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from patient informed consent to last visit (follow-up) at Day 30.

Adverse event reporting additional description:

Adverse events reported spontaneously by the subject, in response to an open-ended question, or revealed by observation by the Investigator.
AEs of Special Interest: transfusion requirement, re-bleed at the TBSs during surgery and re-operation due to re-bleed at the TBS.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	safety population - Peprostat - all surgeries

Reporting group description:

This group is the patients who underwent surgery (all types) and received treatment with Peprostat. One subject, who underwent scheduled spine surgery, was randomised to receive PeproStat, but actually received Saline. This is why there are 113 subjects in the safety group but 114 in the FAS (planned treatments).

Reporting group title	safety population - saline - all surgeries

Reporting group description:

This group is the patients who underwent surgery (all types) and received treatment with the control (saline). One subject, who underwent scheduled spine surgery, was randomised to receive PeproStat, but actually received Saline. This is why there are 56 subjects in the safety group but 55 in the FAS (planned treatments).

Reporting group title	safety population - Peprostat - open liver/soft tissue surgery

Reporting group description:

This group is the patients who underwent over liver / soft tissue surgery and received treatment with Peprostat

Reporting group title	safety population - saline - open liver/soft tissue surgery

Reporting group description:

This group is the patients who underwent open liver / soft tissue surgery and received treatment with control (saline)

Reporting group title	safety population - Peprostat - vascular surgery

Reporting group description:

This group is the patients who underwent vascular surgery and received treatment with Peprostat

Reporting group title	safety population - saline - vascular surgery

Reporting group description:

This group is the patients who underwent vascular surgery and received treatment with control (saline)

Reporting group title	safety population - Peprostat - spine surgery

Reporting group description:

This group is the patients who underwent spine surgery and received treatment with Peprostat

Reporting group title	safety population - saline - spine surgery

Reporting group description:

This group is the patients who underwent spine surgery and received treatment with control (saline)

Serious adverse events	safety population - Peprostat - all surgeries	safety population - saline - all surgeries	safety population - Peprostat - open liver/soft tissue surgery
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 113 (7.96%)	3 / 56 (5.36%)	2 / 39 (5.13%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	1	0	1
Injury, poisoning and procedural complications			
Nerve injury			
subjects affected / exposed	0 / 113 (0.00%)	1 / 56 (1.79%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 113 (0.00%)	1 / 56 (1.79%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Lymphorrhoea			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 113 (0.00%)	1 / 56 (1.79%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Vascular stent thrombosis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Perihepatic abscess			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 113 (0.88%)	1 / 56 (1.79%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	safety population - saline - open liver/soft tissue surgery	safety population - Peprostat - vascular surgery	safety population - saline - vascular surgery
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 19 (5.26%)	6 / 36 (16.67%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Injury, poisoning and procedural complications			
Nerve injury			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Lymphorrhoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Vascular stent thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Pulmonary embolism			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Perihepatic abscess			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 19 (5.26%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	safety population - Peprostat - spine surgery	safety population - saline - spine surgery	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 38 (2.63%)	1 / 19 (5.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Nerve injury			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			

subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Lymphorrhoea			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 38 (2.63%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 38 (0.00%)	1 / 19 (5.26%)	
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			
Vascular stent thrombosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Perihepatic abscess			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	safety population - Peprostat - all surgeries	safety population - saline - all surgeries	safety population - Peprostat - open liver/soft tissue surgery
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 113 (35.40%)	17 / 56 (30.36%)	7 / 39 (17.95%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 113 (0.00%)	2 / 56 (3.57%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Hypertension			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Hypotension			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Infusion site extravasation			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Impaired healing			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Confusional state			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood count abnormal			
subjects affected / exposed	6 / 113 (5.31%)	1 / 56 (1.79%)	2 / 39 (5.13%)
occurrences (all)	6	1	2
Haematocrit decreased			
subjects affected / exposed	0 / 113 (0.00%)	2 / 56 (3.57%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Blood albumin decreased			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Blood sodium decreased			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 113 (0.88%)	1 / 56 (1.79%)	0 / 39 (0.00%)
occurrences (all)	1	1	0
Protein total decreased			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Red blood cell count decreased			

subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	5 / 113 (4.42%)	2 / 56 (3.57%)	0 / 39 (0.00%)
occurrences (all)	5	2	0
wound dehiscence			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	2 / 113 (1.77%)	2 / 56 (3.57%)	0 / 39 (0.00%)
occurrences (all)	2	2	0
Monoparesis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 113 (9.73%)	3 / 56 (5.36%)	1 / 39 (2.56%)
occurrences (all)	13	3	1

Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	4 / 113 (3.54%)	1 / 56 (1.79%)	1 / 39 (2.56%)
occurrences (all)	4	1	1
Abdominal pain			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Colitis ulcerative			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
diarrhoea			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
pain in extremity			
subjects affected / exposed	3 / 113 (2.65%)	1 / 56 (1.79%)	0 / 39 (0.00%)
occurrences (all)	3	1	0
Back pain			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 113 (0.00%)	2 / 56 (3.57%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Folliculitis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			

Diabetes mellitus			
subjects affected / exposed	3 / 113 (2.65%)	0 / 56 (0.00%)	0 / 39 (0.00%)
occurrences (all)	3	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 113 (0.88%)	0 / 56 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1

Non-serious adverse events	safety population - saline - open liver/soft tissue surgery	safety population - Peprostat - vascular surgery	safety population - saline - vascular surgery
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 19 (10.53%)	17 / 36 (47.22%)	8 / 18 (44.44%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Hypertension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Infusion site extravasation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Confusional state			

subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood count abnormal			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Haematocrit decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood albumin decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Blood sodium decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	1 / 18 (5.56%)
occurrences (all)	0	1	2
Protein total decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Red blood cell count decreased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	3 / 36 (8.33%)	1 / 18 (5.56%)
occurrences (all)	1	3	1
wound dehiscence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Bradycardia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Monoparesis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	5 / 36 (13.89%)	1 / 18 (5.56%)
occurrences (all)	0	5	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Colitis ulcerative			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0

diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 36 (2.78%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 19 (0.00%)	3 / 36 (8.33%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Hypomagnesaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 36 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	safety population - Peprostat - spine surgery	safety population - saline - spine surgery	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 38 (42.11%)	7 / 19 (36.84%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Hypertension			

subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	1 / 38 (2.63%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Infusion site extravasation			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Impaired healing			
subjects affected / exposed	1 / 38 (2.63%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Confusional state			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Investigations			
Blood count abnormal			
subjects affected / exposed	3 / 38 (7.89%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Haematocrit decreased			
subjects affected / exposed	0 / 38 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Blood albumin decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Blood sodium decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Haemoglobin decreased			

subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Protein total decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Red blood cell count decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	2 / 38 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
wound dehiscence			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	2 / 38 (5.26%)	2 / 19 (10.53%)	
occurrences (all)	2	2	
Monoparesis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Dizziness			

subjects affected / exposed	1 / 38 (2.63%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 38 (13.16%)	2 / 19 (10.53%)	
occurrences (all)	7	2	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 38 (7.89%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Abdominal pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Colitis ulcerative			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
diarrhoea			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
pain in extremity			
subjects affected / exposed	2 / 38 (5.26%)	1 / 19 (5.26%)	
occurrences (all)	2	1	
Back pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Folliculitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	

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