Clinical trial results:
A Phase I/II, randomized, prospective, controlled, multi-center, open-label, two arm study evaluating the safety and preliminary efficacy of sFilm-FS in controlling liver bleeding during elective surgery.

Summary

EudraCT number	2018-000434-34
Trial protocol	SI AT
Global end of trial date	18 May 2023

Results information

Result version number	v1 (current)
This version publication date	24 January 2025
First version publication date	24 January 2025

Trial information

Trial identification

Sponsor protocol code	HEM-01-17

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04660721
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sealantium Medical Ltd.
Sponsor organisation address	Ha'Amal 11 St., Rosh Ha'Ayin, Israel,
Public contact	Prof. Orgad Laub, Sealantium Medical Ltd., +972 0544434387, orgad@sealantium-med.com
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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	18 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the safety of sFilm-FS versus an active-comparator (TACHOSIL®) when used as adjunct to conventional hemostatic techniques during elective hepatic surgery. Safety will be assessed from randomization of patients until the last follow-up visit and will include evaluation of treatment emergent adverse events.
The secondary endpoints of the study are related to product hemostatic efficacy. For this purpose, hemostasis and treatment failure are defined. Hemostasis is defined as an absence/cessation of bleeding at the target bleeding site (TBS) according to the surgeon’s judgement, so that the surgical closure of the field could be started.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator:

TACHOSIL® is a fibrin sealant patch composed of an equine collagen patch coated with Human Fibrinogen and Human Thrombin. The product is ready for use and for the study it will be supplied in patch size of 4.8 x 4.8 cm (1.9 x 1.9 inch).

Actual start date of recruitment	12 May 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	Slovenia: 6
Country: Number of subjects enrolled	Austria: 17
Worldwide total number of subjects	33
EEA total number of subjects	23

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)	20
From 65 to 84 years	12
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients undergoing elective, open abdominal surgery in which liver bleeding is expected, with presence of an appropriate target bleeding site (TBS) identified intra-operatively by the Investigator. 33 completed patients have been enrolled in this study.

Pre-assignment

Screening details:

1. Patients (males or females) aged ≥ 18 years old
2. Patients requiring elective surgery in which liver bleeding will be encountered
3. Hemoglobin ≥ 8.0 g/dL within 24 hours prior to surgical procedure
4. Patients providing their informed consent prior to participation
5. Patients able to attend the visit and procedures foreseen in protocol

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental
Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Intraabdominal use , Soft tissue use , Use in body cavities , Epilesional use

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator

Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Intraabdominal use , Soft tissue use , Use in body cavities , Epilesional use

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 1	Group A	Group B
Started	17	16
Completed	17	16

Period 2

Period 2 title	Visit 2 (Baseline)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental
Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Intraabdominal use , Soft tissue use , Use in body cavities , Epilesional use

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator
Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 2	Group A	Group B
Started	17	16
Completed	8	8
Not completed	9	8
V2 skipped if V1 was performed one day before V3	9	-
V2 skipped if V1 was performed one day before V3	-	8

Period 3

Period 3 title	Visit 3 (Surgery)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental

Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator
Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 3	Group A	Group B
Started	8	8
Completed	17	16

Joined	9	8
As per protocol, V2 (Baseline) skipped in case V1	9	8

Period 4

Period 4 title	Visit 4 (Post-Surgery)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental
Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator
Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 4	Group A	Group B
Started	17	16
Completed	17	16

Period 5

Period 5 title	Visit 5 (Hospital Discharge)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental
Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator
Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 5	Group A	Group B
Started	17	16
Completed	16	16
Not completed	1	0
Adverse event, non-fatal	1	-

Period 6

Period 6 title	Visit 6 (Follow-up Day 30)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental
Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator
Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 6	Group A	Group B
Started	16	16
Completed	15	14
Not completed	1	2
Adverse event, serious fatal	-	1
Consent withdrawn by subject	-	1
Protocol deviation	1	-

Period 7

Period 7 title	Visit 7 (Follow-up Day 60)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental
Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator
Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 7	Group A	Group B
Started	15	14
Completed	11	7
Not completed	5	7
V7 and V8 were introduced with Protocol V5.0	5	7
Joined	1	0
One patient didn't attend V6 but continued study	1	-

Period 8

Period 8 title	Visit 8 (Follow-up Day 120)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental

Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator
Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 8	Group A	Group B
Started	11	7
Completed	11	8

Joined	0	1
V7 and V8 were introduced with Protocol V5.0	-	1

Period 9

Period 9 title	Visit 9 (Follow-up Day 180)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Group A

Arm description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Arm type	Experimental
Investigational medicinal product name	sFilm-FS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

sFilm-FS is a sterile bio-compatible bio-absorbable patch which consists of a polymeric film composed of a tri-block polymer (device component) containing Polyethylene Glycol (PEG) Poly-Caprolactone (PCL) and Poly-Lactide Acid (PLA), embedded with lyophilized powders of Human Fibrinogen, Human Thrombin (biological components) and calcium chloride. sFilm-FS is supplied ready to use in the patch size of 5 x 5 cm (~ 2 x 2 inch).

Arm title	Group B

Arm description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Arm type	Active comparator
Investigational medicinal product name	TACHOSIL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Epilesional use, Intraabdominal use , Soft tissue use , Use in body cavities

Dosage and administration details:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Number of subjects in period 9	Group A	Group B
Started	11	8
Completed	16	14

Joined	5	6
V9 was performed on all patients still in study	5	6

Baseline characteristics

Reporting groups	
Reporting group title	Group A
Reporting group description:	
sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.	
Reporting group title	Group B
Reporting group description:	
TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.	

Reporting group values	Group A	Group B	Total
Number of subjects	17	16	33
Age categorical			
Patients (males or females) aged ≥ 18 years old			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	10	10	20
From 65-84 years	7	5	12
85 years and over	0	1	1
Age continuous			
Patients (males or females) aged ≥ 18 years old			
Units: years			
arithmetic mean	63.5	57.8	
standard deviation	± 10.46	± 19.28	-
Gender categorical			
Patients (males or females) aged ≥ 18 years old			
Units: Subjects			
Female	8	7	15
Male	9	9	18

End points

End points reporting groups

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be

assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Subject analysis set title	Vital Signs: Systolic Blood Pressure
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Measurement of vital signs (Systolic Blood Pressure - mmHg)

Subject analysis set title	Vital Signs: Diastolic Blood Pressure
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Measurement of vital signs (Diastolic Blood Pressure - mmHg)

Subject analysis set title	Vital Signs: Heart Rate
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Measurement of vital signs (Heart Rate - beats/min)

Subject analysis set title	Vital Signs: Respiratory Rate
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Measurement of vital signs (Respiratory Rate - breaths/min)

Subject analysis set title	Vital Signs: Body Temperature
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Measurement of vital signs (Body Temperature - °C)

Subject analysis set title	Urine - pH
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Measurement of urine pH

Subject analysis set title	Urine - Specific Gravity
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Measurement of Urine Specific Gravity (g/L)

Subject analysis set title	Urine - Glucose
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Detection of Glucose in Urine.

Subject analysis set title	Urine - Proteins
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Detection of Proteins in Urine.

Subject analysis set title	Urine - Blood
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Detection of Blood in Urine.

Subject analysis set title	Urine - Ketones
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Detection of Ketones in Urine.

Subject analysis set title	Physical Abnormalities

Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Detection of Physical Abnormalities.	
Subject analysis set title	Blood/coagulation Parameters - MCHC
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Mean Cell Hemoglobin Concentration - g/L)	
Subject analysis set title	Blood/coagulation Parameters - MCH
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Mean Cell Hemoglobin - pg)	
Subject analysis set title	Blood/coagulation Parameters - MCV
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Mean Corpuscular Volume - fL)	
Subject analysis set title	Blood/coagulation Parameters - Red Blood Cell
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Red Blood Cell - 10^12/L)	
Subject analysis set title	Blood/coagulation Parameters - White Blood Cell
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (White Blood Cell - 10^9/L)	
Subject analysis set title	Blood/coagulation Parameters - Platelet
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Platelet - 10^9/L)	
Subject analysis set title	Blood/coagulation Parameters - Fibrinogen
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Fibrinogen - g/L)	
Subject analysis set title	Blood/coagulation Parameters - D-Dimer
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (D-Dimer - microg/mL)	
Subject analysis set title	Blood/coagulation Parameters - ESR
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Erythrocyte Sedimentation Rate - mm/hr)	
Subject analysis set title	Blood/coagulation Parameters - CRP
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (C-Reactive Protein - mg/dL)	
Subject analysis set title	Blood/coagulation Parameters - BUN
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Blood Urea Nitrogen - mmol/L)	
Subject analysis set title	Blood/coagulation Parameters - Creatinine

Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Creatinine - micromol/L)	
Subject analysis set title	Blood/coagulation Parameters - Uric Acid
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Uric Acid - micromol/L)	
Subject analysis set title	Blood/coagulation Parameters - Total Bilirubin
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Total Bilirubin - micromol/L)	
Subject analysis set title	Blood/coagulation Parameters - LDH
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Lactate Dehydrogenase - microkat/L)	
Subject analysis set title	Blood/coagulation Parameters - SGOT/AST
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Serum Glutamic Oxaloacetic Transaminase/Aspartate Aminotransferase - microkat/L)	
Subject analysis set title	Blood/coagulation Parameters - SGPT/ALT
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Serum Glutamic Pyruvic Transaminase/Alanine Aminotransferase - microkat/L)	
Subject analysis set title	Blood/coagulation Parameters - Gamma-GT
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Gamma-GT - microkat/L)	
Subject analysis set title	Blood/coagulation Parameters - Sodium
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Sodium - mmol/L)	
Subject analysis set title	Blood/coagulation Parameters - Calcium
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Calcium - mmol/L)	
Subject analysis set title	Blood/coagulation Parameters - Phosphorous
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Phosphorous - mmol/L)	
Subject analysis set title	Blood/coagulation Parameters - Glucose
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Glucose - mmol/L)	
Subject analysis set title	Blood/coagulation Parameters - Albumin
Subject analysis set type	Per protocol
Subject analysis set description:	
Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Albumin - g/L)	
Subject analysis set title	Blood/coagulation Parameters - Total Protein
Subject analysis set type	Per protocol

Subject analysis set description:

Eligibility Criteria evaluation. Measurement of blood/coagulation parameters (Total Protein - g/L)

Primary: Safety - Vital Signs (Diastolic Blood Pressure)

End point title	Safety - Vital Signs (Diastolic Blood Pressure)[1]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by measuring Diastolic Blood Pressure (mmHg)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: mmHg				
arithmetic mean (standard deviation)	81.0 (± 10.59)	76.0 (± 7.27)	75.4 (± 8.33)	81.7 (± 13.61)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	13	14	12
Units: mmHg				
arithmetic mean (standard deviation)	61.6 (± 14.60)	62.3 (± 10.87)	74.2 (± 12.23)	75.6 (± 11.52)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	15	14
Units: mmHg				
arithmetic mean (standard deviation)	74.9 (± 9.50)	79.9 (± 11.58)	79.7 (± 7.90)	81.6 (± 8.45)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	11	8
Units: mmHg				
arithmetic mean (standard deviation)	80.8 (± 9.96)	81.4 (± 6.88)	81.0 (± 11.86)	82.7 (± 7.57)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: mmHg				
arithmetic mean (standard deviation)	79.4 (± 9.58)	82.3 (± 11.56)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Vital Signs (Respiratory Rate)

End point title	Safety - Vital Signs (Respiratory Rate)[2]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by measuring Respiratory Rate (breaths/min)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: breaths/min				
arithmetic mean (standard deviation)	14.5 (± 3.14)	13.5 (± 1.83)	14.5 (± 2.27)	15.4 (± 2.56)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: breaths/min				
arithmetic mean (standard deviation)	15.8 (± 7.59)	15.0 (± 3.13)	15.0 (± 2.88)	16.8 (± 3.76)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	15	14

Units: breaths/min				
arithmetic mean (standard deviation)	15.4 (± 3.12)	22.4 (± 27.55)	13.7 (± 2.32)	12.9 (± 1.00)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	11	8
Units: breaths/min				
arithmetic mean (standard deviation)	13.1 (± 1.81)	14.3 (± 1.80)	14.6 (± 2.29)	13.4 (± 1.41)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: breaths/min				
arithmetic mean (standard deviation)	13.6 (± 2.36)	14.1 (± 1.44)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Vital Signs (Heart Rate)

End point title	Safety - Vital Signs (Heart Rate)[3]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by measuring Heart Rate (beats/min)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: beats/min				
arithmetic mean (standard deviation)	72.2 (± 13.44)	74.6 (± 11.94)	74.5 (± 12.39)	79.0 (± 16.98)

End point values	Group A	Group B	Group A	Group B

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	13	14	12
Units: beats/min				
arithmetic mean (standard deviation)	69.0 (± 19.94)	79.2 (± 13.93)	77.1 (± 11.17)	80.9 (± 18.18)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	15	14
Units: beats/min				
arithmetic mean (standard deviation)	79.1 (± 11.56)	84.2 (± 14.87)	77.3 (± 16.62)	78.1 (± 17.17)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	11	8
Units: beats/min				
arithmetic mean (standard deviation)	74.2 (± 14.26)	83.1 (± 8.45)	73.7 (± 10.11)	74.4 (± 7.61)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: beats/min				
arithmetic mean (standard deviation)	73.7 (± 16.23)	73.7 (± 13.78)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Vital Signs (Body Temperature)

End point title	Safety - Vital Signs (Body Temperature)[4]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by measuring Body Temperature (°C)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: °C				
arithmetic mean (standard deviation)	36.5 (± 0.39)	36.7 (± 0.33)	36.6 (± 0.44)	36.4 (± 0.40)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	13	14	12
Units: °C				
arithmetic mean (standard deviation)	36.4 (± 0.77)	36.3 (± 0.61)	36.6 (± 0.44)	36.8 (± 0.51)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	15	14
Units: °C				
arithmetic mean (standard deviation)	36.7 (± 0.39)	36.7 (± 0.52)	36.4 (± 0.53)	36.4 (± 0.43)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	11	8
Units: °C				
arithmetic mean (standard deviation)	36.5 (± 0.34)	36.8 (± 0.17)	36.3 (± 0.59)	36.8 (± 0.20)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: °C				
arithmetic mean (standard deviation)	36.5 (± 0.39)	36.3 (± 0.30)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Physical Examination

End point title	Safety - Physical Examination[5]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by physical examination: the detection of the number of patients with clinical abnormalities in different body areas (abdomen, eyes, skin, cardiovascular)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	16	16
Units: number of abnormalities	6	7	3	5

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	11	7
Units: number of abnormalities	6	5	4	5

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	8	16	14
Units: number of abnormalities	6	5	6	4

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Urine Analysis (pH)

End point title	Safety - Urine Analysis (pH)[6]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by urine analysis (pH)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been

calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	8	8
Units: not applicable				
arithmetic mean (standard deviation)	5.5 (± 0.60)	5.9 (± 0.84)	5.7 (± 0.59)	5.9 (± 0.88)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	11	10
Units: not applicable				
arithmetic mean (standard deviation)	5.4 (± 0.68)	5.9 (± 0.88)	6.2 (± 1.01)	6.7 (± 1.09)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	13
Units: not applicable				
arithmetic mean (standard deviation)	6.3 (± 1.01)	5.8 (± 0.81)	5.7 (± 0.78)	6.0 (± 0.90)

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Vital Signs (Systolic Blood Pressure)

End point title	Safety - Vital Signs (Systolic Blood Pressure)[7]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by measuring Systolic Blood Pressure (mmHg)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: mmHg				
arithmetic mean (standard deviation)	137.1 (± 12.63)	129.8 (± 16.75)	138.9 (± 11.89)	133.0 (± 11.10)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	13	14	13
Units: mmHg				
arithmetic mean (standard deviation)	118.9 (± 20.50)	111.4 (± 14.75)	129.1 (± 16.97)	131.4 (± 21.22)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	15	14
Units: mmHg				
arithmetic mean (standard deviation)	133.1 (± 20.14)	130.7 (± 21.08)	131.6 (± 13.53)	123.6 (± 17.35)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	11	8
Units: mmHg				
arithmetic mean (standard deviation)	133.5 (± 12.52)	130.0 (± 15.46)	130.6 (± 17.12)	133.4 (± 10.34)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: mmHg				
arithmetic mean (standard deviation)	127.0 (± 19.49)	134.5 (± 19.07)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Urine Analysis (Specific Gravity)

End point title	Safety - Urine Analysis (Specific Gravity)[8]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by urine analysis (Specific Gravity)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	12	8	8
Units: g/L				
arithmetic mean (standard deviation)	1021.6 (± 9.52)	1018.8 (± 7.25)	1017.2 (± 4.65)	1019.2 (± 8.61)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	11	10
Units: g/L				
arithmetic mean (standard deviation)	1027.2 (± 11.07)	1022.4 (± 7.59)	1018.2 (± 8.94)	1024.9 (± 21.39)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	12	8
Units: g/L				
arithmetic mean (standard deviation)	1019.9 (± 7.62)	1019.7 (± 8.96)	1017.4 (± 6.02)	1020.1 (± 7.61)

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Urine Analysis (Glucose)

End point title	Safety - Urine Analysis (Glucose)[9]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by urine analysis (Presence of Glucose - Positive, Strong Positive and Traces)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	8	8
Units: Presence				
Positive	0	1	0	0
Strong Positive	1	0	0	0
Traces	5	3	1	0

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	11	10
Units: Presence				
Positive	0	0	1	0
Strong Positive	1	0	0	0
Traces	4	4	6	4

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	13
Units: Presence				
Positive	0	0	0	0
Strong Positive	1	0	1	1
Traces	4	4	1	2

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Urine Analysis (Proteins)

End point title	Safety - Urine Analysis (Proteins)[10]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by urine analysis (Presence of Proteins - Positive, Strong Positive and Traces)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	16	8	8
Units: presence				
Positive	2	0	0	0
Strong Positive	0	0	0	0
Traces	2	3	1	2

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	11	9
Units: presence				
Positive	1	0	0	0
Strong Positive	2	0	0	0
Traces	5	6	1	3

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	15	13
Units: presence				
Positive	0	1	0	0
Strong Positive	0	0	0	0
Traces	4	3	0	2

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Urine Analysis (Ketones)

End point title	Safety - Urine Analysis (Ketones)[11]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by urine analysis (Presence of Ketones - Positive, Strong Positive and Traces)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	8	8
Units: presence				
Positive	0	1	0	0
Strong Positive	0	0	0	1
Traces	2	1	0	1

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	11	10
Units: presence				
Positive	0	0	0	0
Strong Positive	1	1	0	0
Traces	5	2	4	3

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	13
Units: presence				
Positive	1	0	0	0
Strong Positive	0	0	0	0
Traces	2	1	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Hb)

End point title	Safety - Blood/Coagulation Parameters (Hb)[12]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Hemoglobin - g/L)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: g/L				
arithmetic mean (standard deviation)	136.1 (± 20.54)	135.6 (± 14.00)	138.0 (± 15.13)	135.0 (± 15.60)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: g/L				
arithmetic mean (standard deviation)	118.8 (± 10.64)	121.9 (± 12.74)	104.5 (± 17.14)	108.4 (± 15.96)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: g/L				
arithmetic mean (standard deviation)	106.8 (± 16.19)	111.7 (± 19.80)	117.3 (± 17.02)	122.1 (± 15.45)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: g/L				
arithmetic mean (standard deviation)	118.8 (± 14.03)	119.3 (± 14.66)	126.8 (± 12.66)	128.9 (± 18.64)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: g/L				
arithmetic mean (standard deviation)	129.7 (±	136.3 (±		

11.66)	18.77)

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (MCH)

End point title	Safety - Blood/Coagulation Parameters (MCH)[13]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Mean Cell Hemoglobin - pg)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: pg				
arithmetic mean (standard deviation)	29.8 (± 3.00)	29.5 (± 2.27)	31.3 (± 2.01)	28.2 (± 2.22)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: pg				
arithmetic mean (standard deviation)	30.4 (± 1.95)	29.3 (± 2.17)	30.1 (± 2.11)	29.6 (± 2.05)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: pg				
arithmetic mean (standard deviation)	30.1 (± 1.81)	29.3 (± 2.45)	28.7 (± 2.26)	29.1 (± 2.89)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: pg				
arithmetic mean (standard deviation)	28.7 (± 2.38)	27.5 (± 3.00)	28.8 (± 3.26)	27.1 (± 3.10)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	14		
Units: pg				
arithmetic mean (standard deviation)	29.4 (± 2.53)	29.6 (± 3.27)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (MCHC)

End point title	Safety - Blood/Coagulation Parameters (MCHC)[14]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Mean Cell Hemoglobin Concentration - g/L)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: g/L				
arithmetic mean (standard deviation)	337.3 (± 15.40)	337.5 (± 11.83)	335.5 (± 8.14)	337.5 (± 8.40)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: g/L				
arithmetic mean (standard deviation)	338.3 (± 12.16)	337.7 (± 12.56)	336.6 (± 10.82)	333.8 (± 11.41)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: g/L				
arithmetic mean (standard deviation)	335.9 (± 10.53)	333.6 (± 12.87)	322.6 (± 12.02)	332.1 (± 12.48)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: g/L				
arithmetic mean (standard deviation)	324.9 (± 11.02)	326.7 (± 16.71)	329.8 (± 11.91)	326.6 (± 8.88)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: g/L				
arithmetic mean (standard deviation)	329.9 (± 10.77)	334.9 (± 15.16)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (MCV)

End point title	Safety - Blood/Coagulation Parameters (MCV)[15]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Mean Corpuscular Volume - fL)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at east 6 months)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: f/L				
arithmetic mean (standard deviation)	88.5 (± 6.83)	87.8 (± 7.34)	93.1 (± 4.70)	84.3 (± 8.21)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: f/L				
arithmetic mean (standard deviation)	90.4 (± 5.84)	86.8 (± 6.91)	89.5 (± 5.62)	88.9 (± 6.35)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: f/L				
arithmetic mean (standard deviation)	89.9 (± 4.51)	87.6 (± 7.31)	88.9 (± 5.43)	87.9 (± 8.29)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: f/L				
arithmetic mean (standard deviation)	88.5 (± 6.51)	84.3 (± 8.79)	86.9 (± 7.83)	82.9 (± 8.30)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: f/L				
arithmetic mean (standard deviation)	88.2 (± 6.96)	88.8 (± 9.02)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Red Blood Cell)

End point title	Safety - Blood/Coagulation Parameters (Red Blood Cell)[16]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Red Blood Cell - 10^12/L)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: 10^12/L				
arithmetic mean (standard deviation)	4.6 (± 0.57)	4.6 (± 0.53)	4.4 (± 0.40)	4.8 (± 0.57)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: 10^12/L				
arithmetic mean (standard deviation)	3.9 (± 0.41)	4.2 (± 0.57)	3.5 (± 0.58)	3.7 (± 0.63)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: 10^12/L				
arithmetic mean (standard deviation)	3.6 (± 0.61)	3.8 (± 0.66)	4.1 (± 0.58)	4.2 (± 0.52)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: 10^12/L				
arithmetic mean (standard deviation)	4.1 (± 0.43)	4.4 (± 0.52)	4.4 (± 0.34)	4.8 (± 0.63)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: 10^12/L				

arithmetic mean (standard deviation)	4.5 (± 0.31)	4.6 (± 0.71)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (White Blood Cell)

End point title	Safety - Blood/Coagulation Parameters (White Blood Cell)[17]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (White Blood Cell - 10^9/L)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: 10^9/L				
arithmetic mean (standard deviation)	7.2 (± 2.47)	8.0 (± 2.58)	8.1 (± 2.00)	9.2 (± 3.21)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: 10^9/L				
arithmetic mean (standard deviation)	11.9 (± 3.81)	10.9 (± 6.43)	9.5 (± 4.61)	12.1 (± 6.26)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: 10^9/L				
arithmetic mean (standard deviation)	8.2 (± 2.93)	9.6 (± 5.23)	6.8 (± 2.33)	8.1 (± 2.01)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: 10^9/L				
arithmetic mean (standard deviation)	6.2 (± 3.20)	7.4 (± 2.47)	6.3 (± 2.56)	8.0 (± 2.24)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: 10^9/L				
arithmetic mean (standard deviation)	8.4 (± 4.42)	7.8 (± 1.53)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Platelet)

End point title	Safety - Blood/Coagulation Parameters (Platelet)[18]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Platelet - 10^9/L)

End point type	Primary

End point timeframe:

From Visit 1 to Visit 9 (at least 6 months)

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: 10^9/L				
arithmetic mean (standard deviation)	241.6 (± 104.69)	278.7 (± 90.90)	241.6 (± 82.68)	308.2 (± 125.23)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: 10^9/L				
arithmetic mean (standard deviation)	227.4 (± 100.21)	275.0 (± 122.16)	238.4 (± 104.66)	312.6 (± 173.32)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: 10^9/L				
arithmetic mean (standard deviation)	308.4 (± 153.07)	403.5 (± 272.79)	260.9 (± 111.99)	330.1 (± 189.33)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: 10^9/L				
arithmetic mean (standard deviation)	216.8 (± 114.38)	397.3 (± 204.51)	203.8 (± 115.82)	342.9 (± 169.86)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: 10^9/L				
arithmetic mean (standard deviation)	250.2 (± 98.07)	276.4 (± 141.69)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Fibrinogen)

End point title	Safety - Blood/Coagulation Parameters (Fibrinogen)[19]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Fibrinogen - g/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: g/L				
arithmetic mean (standard deviation)	4.1 (± 1.16)	4.3 (± 1.88)	3.8 (± 0.87)	4.3 (± 0.82)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: g/L				
arithmetic mean (standard deviation)	3.0 (± 0.81)	3.5 (± 0.63)	4.9 (± 1.21)	5.8 (± 2.48)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	13	15	13
Units: g/L				
arithmetic mean (standard deviation)	5.2 (± 1.10)	5.8 (± 2.46)	4.7 (± 1.68)	4.4 (± 1.88)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: g/L				
arithmetic mean (standard deviation)	3.7 (± 0.75)	4.6 (± 2.05)	3.6 (± 0.95)	3.6 (± 0.71)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: g/L				
arithmetic mean (standard deviation)	3.8 (± 0.96)	3.2 (± 0.47)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (D-Dimer)

End point title	Safety - Blood/Coagulation Parameters (D-Dimer)[20]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (D-Dimer - microg/mL)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	15	8	8
Units: microg/mL				
arithmetic mean (standard deviation)	1.1 (± 0.81)	0.9 (± 0.90)	0.8 (± 0.46)	1.3 (± 1.51)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: microg/mL				
arithmetic mean (standard deviation)	3.8 (± 3.58)	2.8 (± 2.57)	5.0 (± 3.32)	3.3 (± 1.76)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	12	15	13
Units: microg/mL				
arithmetic mean (standard deviation)	4.8 (± 4.54)	4.9 (± 3.69)	2.3 (± 1.78)	2.2 (± 3.09)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: microg/mL				
arithmetic mean (standard deviation)	1.1 (± 0.68)	1.3 (± 1.33)	1.2 (± 1.05)	0.6 (± 0.30)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: microg/mL				

arithmetic mean (standard deviation)	1.4 (± 2.03)	4.0 (± 11.25)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (ESR)

End point title	Safety - Blood/Coagulation Parameters (ESR)[21]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Erythrocyte Sedimentation Rate - mm/hr)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	12	8	8
Units: mm/hr				
arithmetic mean (standard deviation)	18.3 (± 11.60)	23.7 (± 18.44)	20.6 (± 14.29)	21.9 (± 6.85)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	12	10
Units: mm/hr				
arithmetic mean (standard deviation)	17.6 (± 12.87)	18.9 (± 13.30)	48.5 (± 25.46)	53.7 (± 37.18)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	13	10
Units: mm/hr				
arithmetic mean (standard deviation)	55.7 (± 31.99)	61.9 (± 41.07)	39.8 (± 28.87)	55.1 (± 51.17)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	11	8
Units: mm/hr				
arithmetic mean (standard deviation)	16.5 (± 10.56)	46.9 (± 37.53)	18.0 (± 14.13)	28.1 (± 18.64)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: mm/hr				
arithmetic mean (standard deviation)	17.7 (± 13.24)	18.0 (± 9.86)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (CRP)

End point title	Safety - Blood/Coagulation Parameters (CRP)[22]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (C-Reactive Protein - mg/dL)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	16	7	8
Units: mg/dL				
arithmetic mean (standard deviation)	1.1 (± 1.11)	1.3 (± 2.30)	1.2 (± 1.46)	0.9 (± 0.66)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: mg/dL				
arithmetic mean (standard deviation)	0.7 (± 0.90)	0.7 (± 0.48)	8.2 (± 8.91)	11.4 (± 10.02)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: mg/dL				
arithmetic mean (standard deviation)	5.6 (± 5.35)	5.5 (± 6.64)	2.6 (± 4.97)	1.6 (± 2.02)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	11	8
Units: mg/dL				
arithmetic mean (standard deviation)	0.8 (± 1.31)	1.0 (± 1.17)	0.5 (± 0.47)	0.4 (± 0.14)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: mg/dL				
arithmetic mean (standard deviation)	0.6 (± 0.86)	0.5 (± 0.35)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (BUN)

End point title	Safety - Blood/Coagulation Parameters (BUN)[23]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Blood Urea Nitrogen - mmol/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: mmol/L				
arithmetic mean (standard deviation)	5.3 (± 1.58)	5.2 (± 1.28)	5.8 (± 1.09)	4.6 (± 2.03)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: mmol/L				
arithmetic mean (standard deviation)	5.1 (± 1.34)	4.7 (± 1.98)	5.2 (± 3.98)	4.9 (± 2.49)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: mmol/L				
arithmetic mean (standard deviation)	4.7 (± 2.14)	4.3 (± 1.73)	5.1 (± 2.08)	4.6 (± 1.65)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: mmol/L				
arithmetic mean (standard deviation)	5.7 (± 1.53)	4.1 (± 1.38)	5.5 (± 1.32)	4.7 (± 1.55)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: mmol/L				
arithmetic mean (standard deviation)	4.2 (± 1.42)	4.2 (± 2.31)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Creatinine)

End point title	Safety - Blood/Coagulation Parameters (Creatinine)[24]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Creatinine - micromol/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: micromol/L				
arithmetic mean (standard deviation)	73.6 (± 18.12)	61.7 (± 11.56)	82.1 (± 21.02)	68.9 (± 10.62)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: micromol/L				
arithmetic mean (standard deviation)	71.9 (± 18.48)	66.5 (± 19.42)	67.6 (± 34.13)	58.7 (± 19.73)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: micromol/L				
arithmetic mean (standard deviation)	66.7 (± 19.76)	59.8 (± 14.82)	69.0 (± 16.50)	60.0 (± 7.58)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: micromol/L				
arithmetic mean (standard deviation)	71.7 (± 16.01)	62.7 (± 13.46)	73.4 (± 21.88)	65.9 (± 15.73)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: micromol/L				

arithmetic mean (standard deviation)	72.4 (± 17.81)	61.6 (± 9.91)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Uric Acid)

End point title	Safety - Blood/Coagulation Parameters (Uric Acid)[25]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Uric Acid - micromol/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	7	8
Units: micromol/L				
arithmetic mean (standard deviation)	434.0 (± 324.04)	376.1 (± 306.72)	320.4 (± 84.22)	346.5 (± 102.24)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: micromol/L				
arithmetic mean (standard deviation)	534.2 (± 585.91)	401.1 (± 296.09)	505.9 (± 550.82)	304.8 (± 153.16)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	15	14
Units: micromol/L				
arithmetic mean (standard deviation)	426.7 (± 423.50)	343.7 (± 210.83)	358.1 (± 307.01)	431.3 (± 435.82)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	11	8
Units: micromol/L				
arithmetic mean (standard deviation)	317.9 (± 87.80)	340.0 (± 59.81)	321.4 (± 90.98)	338.1 (± 124.09)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: micromol/L				
arithmetic mean (standard deviation)	401.6 (± 345.94)	312.4 (± 111.15)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Total Bilirubin)

End point title	Safety - Blood/Coagulation Parameters (Total Bilirubin)[26]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Total Bilirubin - micromol/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: micromol/L				
arithmetic mean (standard deviation)	10.9 (± 6.71)	12.0 (± 6.93)	10.8 (± 7.62)	11.6 (± 4.63)

End point values	Group A	Group B	Group A	Group B

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: micromol/L				
arithmetic mean (standard deviation)	18.5 (± 15.69)	11.6 (± 6.25)	16.9 (± 19.88)	13.1 (± 12.01)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: micromol/L				
arithmetic mean (standard deviation)	9.8 (± 6.61)	8.0 (± 4.57)	9.4 (± 5.11)	7.1 (± 2.51)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	9	8
Units: micromol/L				
arithmetic mean (standard deviation)	8.7 (± 5.89)	6.7 (± 2.15)	10.1 (± 5.55)	7.9 (± 5.51)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: micromol/L				
arithmetic mean (standard deviation)	11.0 (± 7.60)	11.3 (± 6.10)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (LDH)

End point title	Safety - Blood/Coagulation Parameters (LDH)[27]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Lactate Dehydrogenase - microkat/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	15	8	8
Units: microkat/L				
arithmetic mean (standard deviation)	3.7 (± 0.68)	3.9 (± 2.28)	3.6 (± 0.50)	3.4 (± 0.75)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	12	13	12
Units: microkat/L				
arithmetic mean (standard deviation)	8.1 (± 6.18)	5.5 (± 2.72)	4.8 (± 2.30)	4.6 (± 1.29)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: microkat/L				
arithmetic mean (standard deviation)	4.0 (± 0.92)	4.5 (± 1.19)	3.5 (± 0.64)	3.6 (± 0.90)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: microkat/L				
arithmetic mean (standard deviation)	3.6 (± 0.44)	3.7 (± 1.01)	3.3 (± 1.63)	3.0 (± 1.60)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: microkat/L				
arithmetic mean (standard deviation)	2.9 (± 0.83)	3.1 (± 1.08)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (SGOT/AST)

End point title	Safety - Blood/Coagulation Parameters (SGOT/AST)[28]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Serum Glutamic Oxaloacetic Transaminase/Aspartate Aminotransferase - microkat/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	15	8	8
Units: microkat/L				
arithmetic mean (standard deviation)	0.6 (± 0.29)	0.4 (± 0.23)	0.5 (± 0.21)	0.4 (± 0.11)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: microkat/L				
arithmetic mean (standard deviation)	4.2 (± 4.42)	1.8 (± 1.58)	2.3 (± 3.42)	1.2 (± 1.07)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: microkat/L				
arithmetic mean (standard deviation)	0.7 (± 0.34)	0.9 (± 0.62)	0.5 (± 0.22)	0.4 (± 0.14)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	9	8
Units: microkat/L				
arithmetic mean (standard deviation)	0.5 (± 0.30)	0.5 (± 0.16)	0.5 (± 0.31)	0.4 (± 0.24)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		

Units: microkat/L				
arithmetic mean (standard deviation)	0.5 (± 0.21)	0.5 (± 0.21)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (SGPT/ALT)

End point title	Safety - Blood/Coagulation Parameters (SGPT/ALT)[29]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Serum Glutamic Pyruvic Transaminase/Alanine Aminotransferase - microkat/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	15	8	8
Units: microkat/L				
arithmetic mean (standard deviation)	0.6 (± 0.47)	0.4 (± 0.23)	0.4 (± 0.22)	0.5 (± 0.17)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: microkat/L				
arithmetic mean (standard deviation)	3.2 (± 3.53)	1.4 (± 1.34)	2.9 (± 3.86)	1.4 (± 1.53)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: microkat/L				
arithmetic mean (standard deviation)	0.8 (± 0.58)	1.4 (± 1.28)	0.7 (± 1.09)	0.4 (± 0.23)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: microkat/L				
arithmetic mean (standard deviation)	0.5 (± 0.41)	0.4 (± 0.23)	0.5 (± 0.31)	0.4 (± 0.14)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: microkat/L				
arithmetic mean (standard deviation)	0.5 (± 0.30)	0.4 (± 0.20)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Gamma-GT)

End point title	Safety - Blood/Coagulation Parameters (Gamma-GT)[30]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Gamma-GT - microkat/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	15	8	8
Units: microkat/L				
arithmetic mean (standard deviation)	2.9 (± 7.82)	1.1 (± 1.10)	0.6 (± 0.33)	0.8 (± 1.20)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: microkat/L				
arithmetic mean (standard deviation)	2.8 (± 7.85)	0.7 (± 0.89)	4.7 (± 7.43)	1.1 (± 0.91)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: microkat/L				
arithmetic mean (standard deviation)	3.0 (± 6.16)	1.7 (± 1.23)	3.8 (± 7.12)	1.3 (± 0.96)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	11	8
Units: microkat/L				
arithmetic mean (standard deviation)	0.8 (± 0.82)	0.8 (± 0.91)	0.8 (± 0.95)	0.8 (± 0.85)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: microkat/L				
arithmetic mean (standard deviation)	1.2 (± 1.18)	0.9 (± 1.01)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Na)

End point title	Safety - Blood/Coagulation Parameters (Na)[31]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Sodium - mmol/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: mmol/L				
arithmetic mean (standard deviation)	141.1 (± 2.26)	139.9 (± 1.89)	140.0 (± 3.59)	139.0 (± 3.89)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	12	13	12
Units: mmol/L				
arithmetic mean (standard deviation)	140.9 (± 2.72)	139.8 (± 2.63)	139.1 (± 3.19)	139.7 (± 2.85)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: mmol/L				
arithmetic mean (standard deviation)	139.4 (± 3.38)	140.6 (± 3.07)	140.9 (± 2.00)	139.1 (± 2.41)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: mmol/L				
arithmetic mean (standard deviation)	141.5 (± 2.54)	139.9 (± 2.41)	140.8 (± 2.10)	140.5 (± 2.78)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: mmol/L				
arithmetic mean (standard deviation)	140.3 (± 1.62)	140.6 (± 2.79)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Ca)

End point title	Safety - Blood/Coagulation Parameters (Ca)[32]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Calcium - mmol/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: mmol/L				
arithmetic mean (standard deviation)	2.4 (± 0.10)	2.3 (± 0.16)	2.4 (± 0.11)	2.3 (± 0.12)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: mmol/L				
arithmetic mean (standard deviation)	2.1 (± 0.11)	2.1 (± 0.11)	2.1 (± 0.14)	2.1 (± 0.12)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	14
Units: mmol/L				
arithmetic mean (standard deviation)	2.2 (± 0.16)	2.2 (± 0.13)	2.5 (± 0.45)	3.0 (± 1.93)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: mmol/L				
arithmetic mean (standard deviation)	2.4 (± 0.11)	2.4 (± 0.05)	2.4 (± 0.16)	2.4 (± 0.10)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: mmol/L				

arithmetic mean (standard deviation)	2.4 (± 0.16)	2.4 (± 0.09)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (P)

End point title	Safety - Blood/Coagulation Parameters (P)[33]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Phosphorous - mmol/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	15	7	8
Units: mmol/L				
arithmetic mean (standard deviation)	1.0 (± 0.12)	1.1 (± 0.21)	1.2 (± 0.08)	1.1 (± 0.16)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: mmol/L				
arithmetic mean (standard deviation)	1.2 (± 0.20)	1.1 (± 0.33)	0.90 (± 0.32)	0.89 (± 0.24)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	15	14
Units: mmol/L				
arithmetic mean (standard deviation)	1.0 (± 0.19)	1.0 (± 0.30)	1.1 (± 0.11)	1.1 (± 0.19)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: mmol/L				
arithmetic mean (standard deviation)	1.1 (± 0.28)	1.1 (± 0.17)	1.0 (± 0.24)	1.1 (± 0.15)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: mmol/L				
arithmetic mean (standard deviation)	1.2 (± 0.20)	8.7 (± 28.57)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Glucose)

End point title	Safety - Blood/Coagulation Parameters (Glucose)[34]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Glucose - mmol/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: mmol/L				
arithmetic mean (standard deviation)	6.5 (± 2.51)	5.6 (± 1.27)	6.7 (± 3.15)	6.4 (± 3.78)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: mmol/L				
arithmetic mean (standard deviation)	8.1 (± 2.50)	7.6 (± 2.65)	6.1 (± 1.91)	6.5 (± 2.23)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	14	14
Units: mmol/L				
arithmetic mean (standard deviation)	6.4 (± 1.62)	6.0 (± 1.50)	6.2 (± 1.52)	5.9 (± 1.91)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: mmol/L				
arithmetic mean (standard deviation)	5.9 (± 1.59)	6.9 (± 3.83)	5.2 (± 1.73)	7.1 (± 5.50)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: mmol/L				
arithmetic mean (standard deviation)	6.0 (± 1.83)	5.7 (± 3.37)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Albumin)

End point title	Safety - Blood/Coagulation Parameters (Albumin)[35]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Albumin - g/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: g/L				
arithmetic mean (standard deviation)	42.4 (± 4.16)	42.5 (± 5.67)	42.6 (± 3.89)	44.0 (± 4.99)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: g/L				
arithmetic mean (standard deviation)	32.8 (± 4.77)	34.5 (± 4.95)	28.6 (± 4.71)	30.7 (± 5.08)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	12
Units: g/L				
arithmetic mean (standard deviation)	32.4 (± 5.25)	34.0 (± 6.81)	40.0 (± 3.35)	41.1 (± 4.85)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: g/L				
arithmetic mean (standard deviation)	41.7 (± 2.95)	41.9 (± 3.93)	42.9 (± 4.38)	44.6 (± 5.01)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: g/L				
arithmetic mean (standard deviation)	43.2 (± 4.71)	43.8 (± 4.92)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (Total Proteins)

End point title	Safety - Blood/Coagulation Parameters (Total Proteins)[36]

End point description:

Safety has been assessed from randomization of patients until the last follow-up visit by blood/coagulation parameters profiles analysis (Total Proteins - g/L)

End point type	Primary

End point timeframe:

From visit 1 to visit 9 (at least 6 months)

Notes:

[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	8	8
Units: g/L				
arithmetic mean (standard deviation)	73.2 (± 5.93)	73.0 (± 9.29)	71.1 (± 5.41)	74.9 (± 8.89)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	12	14	12
Units: g/L				
arithmetic mean (standard deviation)	56.6 (± 8.07)	62.0 (± 8.83)	54.9 (± 8.68)	60.5 (± 10.16)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	15	12
Units: g/L				
arithmetic mean (standard deviation)	63.2 (± 9.92)	64.5 (± 9.60)	75.0 (± 6.53)	76.1 (± 9.44)

End point values	Group A	Group B	Group A	Group B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	7	10	8
Units: g/L				
arithmetic mean (standard deviation)	72.4 (± 4.99)	79.3 (± 8.28)	75.1 (± 6.15)	77.7 (± 8.10)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: g/L				

arithmetic mean (standard deviation)	74.8 (± 6.21)	75.3 (± 5.42)		

Statistical analyses

No statistical analyses for this end point

Primary: Safety - Blood/Coagulation Parameters (anti-Fb antibodies)

End point title	Safety - Blood/Coagulation Parameters (anti-Fb antibodies)[37]

End point description:

End point type	Primary

End point timeframe:

End of Trial

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Considering the exploratory nature of the study (Phase I/II) no a priori hypotheses testing were formulated; only descriptive statistics and 95% Confidence Limits between treatment have been calculated where appropriate.

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: participants	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point title	Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point description:

Proportion of patients achieving hemostasis at TBS (absence of bleeding) at 2 (for sFilm-FS product only), 3, 5, 7 or 10 minutes following first product application, without the occurrence of re-bleeding, starting from 10 minutes after product application and until the completion of surgical closure

End point type	Secondary

End point timeframe:

Day of Surgery

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: participants				
2 minutes after application (only for sFilm-FS)	11	0		
3 minutes after application	12	12		
5 minutes after application	12	12		
7 minutes after application	12	12		
10 minutes after application	14	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point title	Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point description:

Incidence of re-treatment (one or more additional patch of sFilm-FS or TACHOSIL®) at the TBS at the different time points (2 for sFilm-FS, 3, 5, 7, 10 minutes from first product application)

End point type	Secondary

End point timeframe:

Day of surgery

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: participants				
2 minutes after application (only for sFilm-FS)	0	0		
3 minutes after application	0	0		
5 minutes after application	0	0		
7 minutes after application	0	0		
10 minutes after application	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point title	Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point description:

Percentage of total patients (patients that achieved hemostasis with a single patch application and patients that required additional patches) that have achieved hemostasis 10 minutes after first product application and therefore did not need to convert to standard of care treatment at the end of these 10 minutes

End point type	Secondary

End point timeframe:

Day of surgery

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: participants	14	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point title	Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point description:

Incidence of treatment failure, based on pre-defined treatment failure criteria (in case the bleeding at TBS (or re-bleeding) is still observed after 10 minutes following first application of study product; if hemostasis at TBS is achieved, but the Investigator decides that an additional treatment is required to ensure the durability of hemostasis; if there is a breakthrough bleeding requiring treatment other than the study product, at any time)

End point type	Secondary

End point timeframe:

Day of surgery

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: participants	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point title	Evaluation the Hemostatic Efficacy of sFilm-FS in Controlling Parenchymal Bleeding During Surgery

End point description:

Incidence of transfusion requirements in the 6 months follow-up period

End point type	Secondary

End point timeframe:

From surgery, up to 6 months

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: participants	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Visit 1 to Visit 9 (at least 6 months)

Adverse event reporting additional description:

All patients experienced at least one adverse event during the study, none of them related to the study intervention.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Group A

Reporting group description:

sFilm-FS will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. The sFilm-FS should cover adequately the entire TBS. Following application of sFilm-FS, the Investigator will immediately apply manual compression continuously for at least 2 minutes. A surgical sponge may be used to assist in providing adequate pressure. Hemostasis will be assessed after carefully releasing the compression at the site. sFilm-FS should not be removed once bleeding has stopped. A maximum of 4 units of sFilm-FS may be used per patient.

Reporting group title	Group B

Reporting group description:

TACHOSIL® will be applied at the target bleeding site immediately after conventional methods of control have been exhausted. TACHOSIL® should be applied as per the approved prescribing information, with manual compression for at least 3 minutes. A maximum of 4 units of TACHOSIL® may be used per patient.

Serious adverse events	Group A	Group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 17 (35.29%)	2 / 16 (12.50%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to liver			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Disease progression			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal wall haematoma			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatorenal failure			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Muscle atrophy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Group A	Group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)	16 / 16 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adrenal gland cancer			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cholangiocarcinoma			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Gallbladder cancer			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Haemangioma of spleen			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Metastases to liver			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	

Metastases to lung			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Neuroendocrine carcinoma metastatic			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 17 (17.65%)	2 / 16 (12.50%)	
occurrences (all)	3	2	
Hypotension			
subjects affected / exposed	2 / 17 (11.76%)	2 / 16 (12.50%)	
occurrences (all)	3	5	
Inferior vena cava dilatation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Blood volume expansion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Colonic lavage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Dermabrasion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Haematoma evacuation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Prophylaxis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	

Chest pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Death			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Disease progression			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Generalised oedema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Impaired healing			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Inflammatory pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 17 (5.88%)	2 / 16 (12.50%)	
occurrences (all)	1	5	
Pain			
subjects affected / exposed	3 / 17 (17.65%)	5 / 16 (31.25%)	
occurrences (all)	4	11	
Pyrexia			
subjects affected / exposed	2 / 17 (11.76%)	3 / 16 (18.75%)	
occurrences (all)	2	3	
Reproductive system and breast disorders			
Genital haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Penile haematoma			

subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Penile pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Atelectasis			
subjects affected / exposed	0 / 17 (0.00%)	3 / 16 (18.75%)	
occurrences (all)	0	3	
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Hiccups			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Hypoxia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Lung infiltration			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	3 / 16 (18.75%)	
occurrences (all)	2	3	
Pleural effusion			
subjects affected / exposed	1 / 17 (5.88%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Pulmonary embolism			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Pulmonary hypertension			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Confusional state			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Insomnia			
subjects affected / exposed	2 / 17 (11.76%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Restlessness			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Sleep disorder			
subjects affected / exposed	3 / 17 (17.65%)	2 / 16 (12.50%)	
occurrences (all)	3	3	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Blood albumin increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			

subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Haemoglobin decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
White blood cell count increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Confusional state			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Drain site complication			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hepatic seroma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Lumbar vertebral bile leak			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Post procedural bile leak			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Procedural hypotension			

subjects affected / exposed	3 / 17 (17.65%)	0 / 16 (0.00%)	
occurrences (all)	3	0	
Procedural pain			
subjects affected / exposed	11 / 17 (64.71%)	9 / 16 (56.25%)	
occurrences (all)	13	11	
Seroma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	3	
Wound complication			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			
Factor II deficiency			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	2 / 17 (11.76%)	1 / 16 (6.25%)	
occurrences (all)	3	2	
Atrial tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cor pulmonale			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Cardiomegaly			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Mitral valve incompetence			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Pericardial cyst			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Right ventricular enlargement			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Right ventricular failure			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Sinus bradycardia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Systolic dysfunction			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	3 / 16 (18.75%)	
occurrences (all)	2	4	
Tricuspid valve incompetence			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Ventricular hypokinesia			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Hypoaesthesia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Lethargy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Polyneuropathy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Radiculopathy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 17 (11.76%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Blood loss anaemia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Coagulopathy			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Leukocytosis			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Splenic infarction			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Thrombocytosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	3	
Abdominal pain			
subjects affected / exposed	2 / 17 (11.76%)	1 / 16 (6.25%)	
occurrences (all)	3	1	
Abdominal pain upper			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Abdominal wall haematoma			
subjects affected / exposed	2 / 17 (11.76%)	2 / 16 (12.50%)	
occurrences (all)	2	2	
Abnormal faeces			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	3 / 17 (17.65%)	1 / 16 (6.25%)	
occurrences (all)	3	1	
Diarrhoea			

subjects affected / exposed	2 / 17 (11.76%)	2 / 16 (12.50%)	
occurrences (all)	2	5	
Duodenal ulcer			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Duodenitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gastric ileus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Haematemesis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Ileus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Inflammatory bowel disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Intestinal obstruction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Intra-abdominal haematoma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Lower gastrointestinal haemorrhage			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	12 / 17 (70.59%)	5 / 16 (31.25%)	
occurrences (all)	14	5	
Vomiting			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hepatic failure			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hepatic steatosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hepatorenal failure			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Hypertransaminasaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Excessive granulation tissue			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Lipodystrophy acquired			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Pruritus allergic			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 17 (11.76%)	3 / 16 (18.75%)	
occurrences (all)	2	3	
Oliguria			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Renal infarct			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Flank pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Muscle atrophy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Pain in extremity			

subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Bacterial infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Candida infection			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Clostridium difficile infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Infection susceptibility increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Oral candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Post procedural infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Staphylococcal infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	2 / 17 (11.76%)	3 / 16 (18.75%)	
occurrences (all)	3	5	

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Dehydration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Diabetes mellitus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Folate deficiency			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Hypercholesterolaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	1 / 17 (5.88%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Hyperkalaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	
Hypoalbuminaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hypocalcaemia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Hypokalaemia			
subjects affected / exposed	8 / 17 (47.06%)	5 / 16 (31.25%)	
occurrences (all)	12	5	
Hyponatraemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Hypophagia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hypophosphataemia			
subjects affected / exposed	3 / 17 (17.65%)	3 / 16 (18.75%)	
occurrences (all)	4	3	
Magnesium deficiency			
subjects affected / exposed	5 / 17 (29.41%)	1 / 16 (6.25%)	
occurrences (all)	5	1	
Malnutrition			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2019	FDA Immediate Response requests: Various updates/ clarifications/ alignments with regulatory requirements, including extended subject monitoring, immunogenicity testing and addition of secondary endpoints.
19 May 2021	Changes of Sponsor: • Various updates/ clarifications • Increase of sample size • Inclusion of U.S. site
05 July 2021	Removal of TEG testing and related exclusion criteria.
08 July 2021	Changes of Sponsor/ FDA requests: • Removal of TEG testing and related exclusion criteria • Various updates/ clarifications/ alignments with regulatory requirements, including additional stopping criteria, addition of follow up visits and addition of MRI assessment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported