Clinical trial results:
A pragmatic pilot randomised phase II controlled trial of Prothrombin Complex Concentrates (PCC) versus Fresh Frozen Plasma (FFP) in adult patients who are Undergoing Heart Surgery (PROPHESY)

Summary

EudraCT number	2018-003041-41
Trial protocol	GB
Global end of trial date	29 January 2020

Results information

Result version number	v1 (current)
This version publication date	11 November 2020
First version publication date	11 November 2020

Trial information

Trial identification

Sponsor protocol code	012507

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03715348
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Queen Mary University of London
Sponsor organisation address	5 Walden Street, London, United Kingdom, E1 2EF
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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	29 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 January 2020
Global end of trial reached?	Yes
Global end of trial date	29 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the recruitment rate – defined as the proportion of participants who consent to the randomised study out of all eligible patients,
and the proportion who are randomised and receive intervention out of consenting participants .

Protection of trial subjects:

Patients who were not randomised to study intervention were treated as per standard care. Patients who were randomised to receive study intervention were treated as per standard care following one dose of the intervention they were randomised to. Patients were free to withdraw from the study at any time without giving reasons and without prejudicing his/her further treatment. Safety events were regularly reviewed by an independent Data Monitoring Committee, who advised the investigators if there were any safety concerns.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 134
Worldwide total number of subjects	134
EEA total number of subjects	134

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)	53
From 65 to 84 years	77

85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Recruitment began on 28/02/2019 and ended on 28/10/2019.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	134
Number of subjects completed	134

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Fresh Frozen Plasma (FFP)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Fresh Frozen Plasma (FFP)
Investigational medicinal product code	
Other name	FFP
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

A 15mL/Kg dose of FFP was used which was rounded up to the following:
- 3 units if <=60kg
- 4 units if 61 to 90 kg
- 5 units if >90 kg

FFP must be administered by intravenous infusion after thawing, using an infusion set, over 5-20 min per unit. There is no maximum allowed dose for FFP. If bleeding continues, after administration of the first dose of FFP, patient will continue to receive standard care, and this may require further FFP transfusion.
FFP will be stored at ≤-25°C for up to 36 months. Prior to use, FFP requires thawing at 37°C (between 33°C-37°C is acceptable) for 20 minutes in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. Once thawed, FFP must not be refrozen and should be transfused as soon as possible. Transfusion of FFP should be completed within 4 hours of issue out of a controlled temperature environment. Administration of FFP should be by ABO-blood group compatibility.

Arm title	Prothrombin Complex Concentrate (PCC)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Prothrombin Complex Concentrate (PCC)
Investigational medicinal product code	
Other name	PCC, Octaplex
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Octaplex is presented as a powder and comes in two different package sizes: 500 IU and 1000 IU. The

following dose schedule was used:
<=60 kg 500 IU (1 vial)
61 – 90 kg 1000 IU (2 vials)
>90 kg 1,500 IU (3 vials)
Octaplex will be administered intravenously at a slow speed: Initially 1 mL per minute, not faster than 2-3 mL per minute will be administered. If bleeding continues after administration of the first dose of PCC, patient will continue to receive standard care,
and this does not include PCC. Therefore, no further PCC will be administered to patient.

Octaplex should be stored below 25°C for up to 3 years, and in its original package in order to protect from light.After reconstitution the solution must be used immediately. Please refer to SmPC for instructions for reconstitution and infusion.

Arm title	Not randomised
Arm description:	
Patient did not bleed during or within 24 hours of surgery and was not randomised to receive either FFP or PCC	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Fresh Frozen Plasma (FFP)	Prothrombin Complex Concentrate (PCC)	Not randomised
Started	25	25	84
Completed	25	25	84

Baseline characteristics

Reporting groups	
Reporting group title	Fresh Frozen Plasma (FFP)
Reporting group description: -	
Reporting group title	Prothrombin Complex Concentrate (PCC)
Reporting group description: -	
Reporting group title	Not randomised
Reporting group description:	
Patient did not bleed during or within 24 hours of surgery and was not randomised to receive either FFP or PCC	

Reporting group values	Fresh Frozen Plasma (FFP)	Prothrombin Complex Concentrate (PCC)	Not randomised
Number of subjects	25	25	84
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	66	69	67.5
inter-quartile range (Q1-Q3)	57 to 74	63 to 73	57 to 75.5
Gender categorical Units: Subjects			
Female	9	9	31
Male	16	16	53
Race Units: Subjects			
White	20	21	66
Asian	1	1	6
African	1	0	4
Mixed	0	0	1
Unknown/Not reported	3	3	7
Diabetes mellitus Units: Subjects			
Non-diabetic	19	19	66
Diabetic	6	6	13
Unknown	0	0	5
Hypertension Units: Subjects			

non-Hypertensive	12	6	29
Hypertensive	13	19	50
Unknown	0	0	5
Angina			
History of angina			
Units: Subjects			
No	19	19	67
Yes	6	6	12
Unknown	0	0	5
Previous PCI Units: Subjects			
No	23	22	77
Yes	2	3	2
Unknown	0	0	5
Previous cardiac Surgery Units: Subjects			
No	24	23	75
Yes	1	2	4
Unknown	0	0	5
Type of surgery Units: Subjects			
Elective surgery	20	19	71
Non-elective Surgery	5	6	8
Unknown	0	0	5
Procedure Units: Subjects			
Valve only	7	5	34
Major aortic only	0	2	3
CABG + valve	5	6	17
complex/combined procedures	13	12	25
Unknown	0	0	5
Antiplatelet use Units: Subjects			
No	18	18	78
Yes	7	7	1
Unknown	0	0	5
Anticoagulant use Units: Subjects			
No	18	16	72
Yes	7	9	7
Unknown	0	0	5
Weight Units: kg			
arithmetic mean	80.5	76.1	78
standard deviation	± 16.2	± 19.7	± 17.3
Height Units: cm			
arithmetic mean	168.1	167.3	169.3
standard deviation	± 10.7	± 9.5	± 10.2
BMI Units: kg/m2			

arithmetic mean	28.5	27.0	27.1
standard deviation	± 5.3	± 5.8	± 5.8
EuroSCORE			
Units: unit			
median	2.94	3.73	2.19
inter-quartile range (Q1-Q3)	1.83 to 4.86	2.25 to 5.86	1.26 to 3.94
EQ5D index score			
Units: unit			
median	0.9	0.9	0.86
inter-quartile range (Q1-Q3)	0.75 to 0.96	0.78 to 1	0.7 to 0.94
Hemoglobin			
laboratory test at screening			
Units: g/L			
median	135	130	133
inter-quartile range (Q1-Q3)	121 to 145	124 to 141	130 to 135
Platelet count			
laboratory test at screening			
Units: Thousand/uL			
median	227	239	227
inter-quartile range (Q1-Q3)	184 to 271	194 to 259	184 to 271
PT			
Prothrombin time at screening			
Units: seconds			
median	11	11	11
inter-quartile range (Q1-Q3)	11 to 12	11 to 12	10.8 to 11.8
APTT			
Activated partial thromboplastin time at screening			
Units: seconds			
median	25	27	26
inter-quartile range (Q1-Q3)	23 to 27	25 to 29	24 to 28

Reporting group values	Total		
Number of subjects	134		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
median			
inter-quartile range (Q1-Q3)	-		

Gender categorical Units: Subjects			
Female	49		
Male	85		
Race Units: Subjects			
White	107		
Asian	8		
African	5		
Mixed	1		
Unknown/Not reported	13		
Diabetes mellitus Units: Subjects			
Non-diabetic	104		
Diabetic	25		
Unknown	5		
Hypertension Units: Subjects			
non-Hypertensive	47		
Hypertensive	82		
Unknown	5		
Angina			
History of angina			
Units: Subjects			
No	105		
Yes	24		
Unknown	5		
Previous PCI Units: Subjects			
No	122		
Yes	7		
Unknown	5		
Previous cardiac Surgery Units: Subjects			
No	122		
Yes	7		
Unknown	5		
Type of surgery Units: Subjects			
Elective surgery	110		
Non-elective Surgery	19		
Unknown	5		
Procedure Units: Subjects			
Valve only	46		
Major aortic only	5		
CABG + valve	28		
complex/combined procedures	50		
Unknown	5		
Antiplatelet use Units: Subjects			

No	114		
Yes	15		
Unknown	5		
Anticoagulant use Units: Subjects			
No	106		
Yes	23		
Unknown	5		
Weight Units: kg arithmetic mean standard deviation	- -		
Height Units: cm arithmetic mean standard deviation	- -		
BMI Units: kg/m2 arithmetic mean standard deviation	- -		
EuroSCORE Units: unit median inter-quartile range (Q1-Q3)	- -		
EQ5D index score Units: unit median inter-quartile range (Q1-Q3)	- -		
Hemoglobin			
laboratory test at screening			
Units: g/L median inter-quartile range (Q1-Q3)	- -		
Platelet count			
laboratory test at screening			
Units: Thousand/uL median inter-quartile range (Q1-Q3)	- -		
PT			
Prothrombin time at screening			
Units: seconds median inter-quartile range (Q1-Q3)	- -		
APTT			
Activated partial thromboplastin time at screening			
Units: seconds median inter-quartile range (Q1-Q3)	- -		

Subject analysis sets	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
includes only those patients who completed the treatment originally allocated	
Subject analysis set title	Intention-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
includes all patients as originally allocated after randomisation	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Includes all patients who received FFP or PCC, in order to obtain data on event rates in both groups to help estimate the sample size for the large trial	
Subject analysis set title	Eligible patients
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients who met the eligibility criteria for the trial. The number in the analysis set is 180 with 134 of these consenting.	
Subject analysis set title	Consenting patients
Subject analysis set type	Full analysis
Subject analysis set description:	
All eligible patients who consent	
Subject analysis set title	Non-consenting patients
Subject analysis set type	Full analysis
Subject analysis set description:	
Proportion of eligible patients who do not consent to enter trial	
Subject analysis set title	FFP per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
Freash Frozen Plasma (FFP) per protocol analysis set	
Subject analysis set title	PCC per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
PCC per protocol analysis set	

Reporting group values	Per protocol	Intention-to-treat	Safety population
Number of subjects	42	50	55
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous Units: years			
median	68	68	68
inter-quartile range (Q1-Q3)	57 to 73	60 to 74	56 to 74
Gender categorical Units: Subjects			
Female	16	18	19
Male	26	32	36
Race Units: Subjects			
White	34	41	45
Asian	2	2	2
African	1	1	1
Mixed	0	0	0
Unknown/Not reported	5	6	7
Diabetes mellitus Units: Subjects			
Non-diabetic	33	38	44
Diabetic	9	12	11
Unknown	0	0	0
Hypertension Units: Subjects			
non-Hypertensive	16	18	19
Hypertensive	26	32	36
Unknown	0	0	0
Angina			
History of angina			
Units: Subjects			
No	32	38	42
Yes	10	12	13
Unknown	0	0	0
Previous PCI Units: Subjects			
No	38	45	50
Yes	4	5	5
Unknown	0	0	0
Previous cardiac Surgery Units: Subjects			
No	39	47	51
Yes	3	3	4
Unknown	0	0	0
Type of surgery Units: Subjects			
Elective surgery	31	39	43
Non-elective Surgery	11	11	12
Unknown	0	0	0
Procedure Units: Subjects			
Valve only	9	12	12
Major aortic only	2	2	3
CABG + valve	10	11	11

complex/combined procedures	21	25	29
Unknown	0	0	0
Antiplatelet use Units: Subjects			
No	30	36	42
Yes	12	14	13
Unknown	0	0	0
Anticoagulant use Units: Subjects			
No	38	34	38
Yes	14	16	17
Unknown	0	0	0
Weight Units: kg			
arithmetic mean	78.0	78.3	77.3
standard deviation	± 17.7	± 18.0	± 17.6
Height Units: cm			
arithmetic mean	167.6	167.7	168.5
standard deviation	± 10.0	± 10.1	± 10.3
BMI Units: kg/m2			
arithmetic mean	27.7	27.8	27.1
standard deviation	± 5.3	± 5.6	± 5.4
EuroSCORE Units: unit			
median	3.51	3.42	3.47
inter-quartile range (Q1-Q3)	1.94 to 5.46	1.83 to 5.46	1.83 to 5.86
EQ5D index score Units: unit			
median	0.87	0.90	0.87
inter-quartile range (Q1-Q3)	0.75 to 0.95	0.76 to 1	0.75 to 0.95
Hemoglobin			
laboratory test at screening			
Units: g/L			
median	133	133	132
inter-quartile range (Q1-Q3)	123 to 142	123 to 145	122 to 142.5
Platelet count			
laboratory test at screening			
Units: Thousand/uL			
median	241	238	227
inter-quartile range (Q1-Q3)	194 to 283	187 to 271	175.5 to 264.5
PT			
Prothrombin time at screening			
Units: seconds			
median	11.25	11.35	11.2
inter-quartile range (Q1-Q3)	10.8 to 11.9	10.8 to 12	10.8 to 11.9
APTT			
Activated partial thromboplastin time at screening			
Units: seconds			
median	26	26	26

inter-quartile range (Q1-Q3)	24 to 28	24 to 28	24 to 28

Reporting group values	Eligible patients	Consenting patients	Non-consenting patients
Number of subjects	134	134	46
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
median		68	
inter-quartile range (Q1-Q3)		57 to 74	
Gender categorical Units: Subjects			
Female		49	
Male		85	
Race Units: Subjects			
White	107	107	
Asian	85	85	
African	5	5	
Mixed	1	1	
Unknown/Not reported	59	13	46
Diabetes mellitus Units: Subjects			
Non-diabetic	104	104	
Diabetic	25	25	
Unknown	51	5	46
Hypertension Units: Subjects			
non-Hypertensive	47	47	
Hypertensive	82	82	
Unknown	51	5	46
Angina			
History of angina			
Units: Subjects			
No	105	105	
Yes	24	24	
Unknown	51	5	46
Previous PCI			

Units: Subjects			
No	122	122	
Yes	7	7	
Unknown	51	5	46
Previous cardiac Surgery Units: Subjects			
No	122	122	
Yes	7	7	
Unknown	51	5	46
Type of surgery Units: Subjects			
Elective surgery	110	110	
Non-elective Surgery	19	19	
Unknown	51	5	46
Procedure Units: Subjects			
Valve only	46	46	
Major aortic only	5	5	
CABG + valve	28	28	
complex/combined procedures	50	50	
Unknown	51	5	46
Antiplatelet use Units: Subjects			
No	114	114	
Yes	15	15	
Unknown	51	5	46
Anticoagulant use Units: Subjects			
No	106	106	
Yes	23	23	
Unknown	51	5	46
Weight Units: kg			
arithmetic mean		78.1	
standard deviation	±	± 17.5	±
Height Units: cm			
arithmetic mean		168.7	
standard deviation	±	± 10.1	±
BMI Units: kg/m2			
arithmetic mean		27.4	
standard deviation	±	± 5.4	±
EuroSCORE Units: unit			
median		2.50	
inter-quartile range (Q1-Q3)		1.54 to 4.40	
EQ5D index score Units: unit			
median		0.87	
inter-quartile range (Q1-Q3)		0.70 to 0.95	

Hemoglobin			
laboratory test at screening			
Units: g/L			
median		133	
inter-quartile range (Q1-Q3)		123 to 144	
Platelet count			
laboratory test at screening			
Units: Thousand/uL			
median		229	
inter-quartile range (Q1-Q3)		185 to 271	
PT			
Prothrombin time at screening			
Units: seconds			
median		11.1	
inter-quartile range (Q1-Q3)		10.8 to 11.9	
APTT			
Activated partial thromboplastin time at screening			
Units: seconds			
median		26	
inter-quartile range (Q1-Q3)		24 to 28	

Reporting group values	FFP per protocol	PCC per protocol	
Number of subjects	21	21	
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
median	63	69	
inter-quartile range (Q1-Q3)	54 to 73	63 to 73	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	13	13	
Race			
Units: Subjects			
White	16	18	
Asian	1	1	
African	1	0	
Mixed	0	0	
Unknown/Not reported	3	2	
Diabetes mellitus			

Units: Subjects			
Non-diabetic	17	16	
Diabetic	4	5	
Unknown	0	0	
Hypertension Units: Subjects			
non-Hypertensive	10	6	
Hypertensive	11	15	
Unknown	0	0	
Angina			
History of angina			
Units: Subjects			
No	16	16	
Yes	5	5	
Unknown	0	0	
Previous PCI Units: Subjects			
No	19	19	
Yes	2	2	
Unknown	0	0	
Previous cardiac Surgery Units: Subjects			
No	20	19	
Yes	1	2	
Unknown	0	0	
Type of surgery Units: Subjects			
Elective surgery	16	15	
Non-elective Surgery	5	6	
Unknown	0	0	
Procedure Units: Subjects			
Valve only	4	5	
Major aortic only	0	2	
CABG + valve	5	5	
complex/combined procedures	12	9	
Unknown	0	0	
Antiplatelet use Units: Subjects			
No	15	15	
Yes	6	6	
Unknown	0	0	
Anticoagulant use Units: Subjects			
No	15	13	
Yes	6	8	
Unknown	0	0	
Weight Units: kg			
arithmetic mean	79.8	76.2	
standard deviation	± 16.8	± 18.7	

Height			
Units: cm			
arithmetic mean	168.6	166.6	
standard deviation	± 11.0	± 9.1	
BMI			
Units: kg/m2			
arithmetic mean	28.0	27.3	
standard deviation	± 5.3	± 5.4	
EuroSCORE			
Units: unit			
median	3.3	3.73	
inter-quartile range (Q1-Q3)	1.94 to 5.46	2.25 to 5.28	
EQ5D index score			
Units: unit			
median	0.90	0.87	
inter-quartile range (Q1-Q3)	0.72 to 0.98	0.78 to 0.94	
Hemoglobin			
laboratory test at screening			
Units: g/L			
median	135	130	
inter-quartile range (Q1-Q3)	123 to 145	124 to 140	
Platelet count			
laboratory test at screening			
Units: Thousand/uL			
median	261	240.5	
inter-quartile range (Q1-Q3)	172 to 300	201 to 258.5	
PT			
Prothrombin time at screening			
Units: seconds			
median	10.8	11.4	
inter-quartile range (Q1-Q3)	10.7 to 12.4	10.9 to 11.9	
APTT			
Activated partial thromboplastin time at screening			
Units: seconds			
median	25	26	
inter-quartile range (Q1-Q3)	23 to 27	25 to 28	

End points

End points reporting groups

Reporting group title	Fresh Frozen Plasma (FFP)
Reporting group description: -	
Reporting group title	Prothrombin Complex Concentrate (PCC)
Reporting group description: -	
Reporting group title	Not randomised
Reporting group description:	
Patient did not bleed during or within 24 hours of surgery and was not randomised to receive either FFP or PCC	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
includes only those patients who completed the treatment originally allocated	
Subject analysis set title	Intention-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
includes all patients as originally allocated after randomisation	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Includes all patients who received FFP or PCC, in order to obtain data on event rates in both groups to help estimate the sample size for the large trial	
Subject analysis set title	Eligible patients
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients who met the eligibility criteria for the trial. The number in the analysis set is 180 with 134 of these consenting.	
Subject analysis set title	Consenting patients
Subject analysis set type	Full analysis
Subject analysis set description:	
All eligible patients who consent	
Subject analysis set title	Non-consenting patients
Subject analysis set type	Full analysis
Subject analysis set description:	
Proportion of eligible patients who do not consent to enter trial	
Subject analysis set title	FFP per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
Freash Frozen Plasma (FFP) per protocol analysis set	
Subject analysis set title	PCC per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
PCC per protocol analysis set	

Primary: Proportion of eligible participants who consent

End point title	Proportion of eligible participants who consent[1]
End point description:	
End point type	Primary

End point timeframe:

8 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: This is a single point estimate not a comparison between groups. The software does not allow entry of the confidence interval when there is only one group. The proportion (95% CI) for this endpoint is 0.744 (0.674, 0.806)

End point values	Eligible patients			
Subject group type	Subject analysis set			
Number of subjects analysed	180			
Units: subjects				
Non-consenting	46			
Consenting	134			

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of participants who are randomised and receive intervention within 24 hours of surgery, out of all consenting participants

End point title	Proportion of participants who are randomised and receive intervention within 24 hours of surgery, out of all consenting participants[2]

End point description:

End point type	Primary

End point timeframe:

within 24 hours following surgery

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: This is a single point estimate not a comparison between groups. The software does not allow entry of the confidence interval when there is only one group. The proportion (95% CI) for this endpoint is 0.351 (0.270, 0.438)

End point values	Consenting patients			
Subject group type	Subject analysis set			
Number of subjects analysed	134			
Units: subjects				
Not randomised and receiving intervention	87			
Randomised and receiving intervention	47			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to administration of study drug (PCC) or control (FFP) to patient

End point title	Time to administration of study drug (PCC) or control (FFP) to patient

End point description:

Defined as time in minutes from telephoning laboratory to first administration to patient

End point type	Secondary

End point timeframe:

within 24 hours following surgery

End point values	Fresh Frozen Plasma (FFP)	Prothrombin Complex Concentrate (PCC)	Not randomised	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22[3]	25	0[4]	
Units: minutes				
median (inter-quartile range (Q1-Q3))	72 (40 to 114)	63 (36 to 108)	(to)	

Notes:

[3] - 3 patients in the FFP group did not receive intervention

[4] - These patients consented but did not bleed and so did not enter the randomised part of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients for whom clinical outcome data were collected up to 90 days, or death, whichever occur first

End point title	Proportion of patients for whom clinical outcome data were collected up to 90 days, or death, whichever occur first

End point description:

End point type	Secondary

End point timeframe:

90 days following surgery

End point values	Intention-to-treat			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: subjects				
Lost to follow-up	4			
90 day Follow-up	46			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients who bleed and are randomised within 24 hours of surgery

End point title	Proportion of patients who bleed and are randomised within 24 hours of surgery

End point description:

End point type	Secondary

End point timeframe:

within 24 hours following surgery

End point values	Consenting patients			
Subject group type	Subject analysis set			
Number of subjects analysed	134			
Units: subjects				
Not randomised	84			
Randomised	50			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of consenting patients who are not randomised within 24 hours of surgery

End point title	Proportion of consenting patients who are not randomised within 24 hours of surgery

End point description:

End point type	Secondary

End point timeframe:

within 24 hours following surgery

End point values	Consenting patients			
Subject group type	Subject analysis set			
Number of subjects analysed	134			
Units: subjects				
Not randomised	84			
Randomised	50			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of consenting participants who bleed and receive a protocol intervention within 24 hours of surgery (whether or not they are randomised)

End point title	Proportion of consenting participants who bleed and receive a protocol intervention within 24 hours of surgery (whether or not they are randomised)

End point description:

End point type	Secondary

End point timeframe:

within 24 hours following surgery

End point values	Safety population			
Subject group type	Subject analysis set			
Number of subjects analysed	134			
Units: subjects				
No intervention	79			
Received study intervention	55			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients for whom timing of administration, and completion of intervention(s) were documented

End point title	Proportion of patients for whom timing of administration, and completion of intervention(s) were documented

End point description:

End point type	Secondary

End point timeframe:

within 24 hours following surgery

End point values	Intention-to-treat			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: subjects				
Data incomplete	3			
Data complete	47			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients where there was protocol adherence

End point title	Proportion of patients where there was protocol adherence

End point description:

End point type	Secondary

End point timeframe:

90 days

End point values	Intention-to-treat			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: subjects				
Protocol deviation	8			
Protocol adherance	42			

Statistical analyses

No statistical analyses for this end point

Secondary: Reasons for non-participation of eligible patients

End point title	Reasons for non-participation of eligible patients

End point description:

End point type	Secondary

End point timeframe:

Recruitment period

End point values	Eligible patients			
Subject group type	Subject analysis set			
Number of subjects analysed	180			
Units: 1.1				
Patient declined	37			
Language barrieer	6			
Partial sightedness	1			
Procedure did not meet eligibility criteria	1			
Clinician decision	1			
Patient enrolled	134			

Statistical analyses

No statistical analyses for this end point

Secondary: Reasons for intervention non-compliance

End point title	Reasons for intervention non-compliance

End point description:

End point type	Secondary

End point timeframe:

within 24 hours following surgery

End point values	Per protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: subjects				
Stopped bleeding before intervention	3			
Already received FFP	1			
Received treatment to which they were randomised	46			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients who do not consent to intervention, but agree to consenting of their de- identified data for up to 24 hours after surgery

End point title	Proportion of patients who do not consent to intervention, but agree to consenting of their de- identified data for up to 24 hours after surgery

End point description:

End point type	Secondary

End point timeframe:
Recruitment period

End point values	Non-consenting patients			
Subject group type	Subject analysis set			
Number of subjects analysed	46			
Units: subjects				
Not available	46			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PT from baseline to 1 hour

End point title	Change in PT from baseline to 1 hour

End point description:
Change in clotting factors from baseline to 1 hour

End point type	Secondary

End point timeframe:
1 hour

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	16		
Units: seconds				
median (inter-quartile range (Q1-Q3))	-4 (-6.1 to -2.1)	-2.6 (-4.85 to -1.3)		

Statistical analyses

Statistical analysis title	Change in PT from baseline to 1 hour

Statistical analysis description:
Difference in change between groups and 95% CIs.

Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Median difference (net)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.94
upper limit	3.94

Secondary: Change in PT from baseline to 24 hours

End point title	Change in PT from baseline to 24 hours
End point description:	
Difference between groups in change from baseline to 24 hours	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: seconds				
median (inter-quartile range (Q1-Q3))	-4.45 (-6.6 to -2.75)	-3.9 (-6.1 to -1.9)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority[5]
Parameter estimate	Median difference (net)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	4.5

Notes:

[5] - Descriptive

Secondary: Change in APTT from baseline to 1 hour	
End point title	Change in APTT from baseline to 1 hour
End point description: Change in clotting factors at 1 hour	
End point type	Secondary
End point timeframe: 1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	15		
Units: seconds				
median (inter-quartile range (Q1-Q3))	-12.9 (-40.7 to -6.4)	-4.2 (-16.8 to 0.1)		

Statistical analyses

Statistical analysis title	Change in APPT from baseline to 1 hour
Statistical analysis description: Median change(95% CI)	
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Median difference (net)
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	30.6
Notes: [6] - Descriptive	

Secondary: Change in APTT from baseline to 24 hours	
End point title	Change in APTT from baseline to 24 hours
End point description: Change in clotting factors at 24 hours	
End point type	Secondary
End point timeframe: 24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	13		
Units: seconds				
median (inter-quartile range (Q1-Q3))	-30.55 (-49.4 to -7.1)	-7.9 (-23.9 to -6.1)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	Median difference (net)
Point estimate	28.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.19
upper limit	57.39

Notes:

[7] - Descriptive

Secondary: Change in fibrinogen at 1 hour

End point title	Change in fibrinogen at 1 hour
End point description: Change in clotting factors at 1 hour	
End point type	Secondary
End point timeframe: 1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: g/L				
median (inter-quartile range (Q1-Q3))	0.34 (0.2 to 0.6)	0.01 (-0.1 to 0.26)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	Median difference (net)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	-0.07

Notes:

[8] - Descriptive

Secondary: Change in fibrinogen at 24 hours

End point title	Change in fibrinogen at 24 hours

End point description:

End point type	Secondary

End point timeframe:

24 hours

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: g/L				
median (inter-quartile range (Q1-Q3))	1.85 (1.19 to 2.57)	1.7 (1.06 to 2.08)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	Median difference (net)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.04
upper limit	0.8

Notes:

[9] - Deacriptive

Secondary: Change in D-Dimer at 1 hour

End point title	Change in D-Dimer at 1 hour

End point description:

End point type	Secondary

End point timeframe:

1 hour

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: mg/L FEU				
median (inter-quartile range (Q1-Q3))	-0.13 (-0.93 to 0.05)	-0.04 (-0.18 to 0.27)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	PCC per protocol v FFP per protocol
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Median difference (net)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	0.49

Notes:

[10] - Descriptive

Secondary: Change in D-Dimer at 24 hours

End point title	Change in D-Dimer at 24 hours

End point description:

End point type	Secondary

End point timeframe:

24 hours

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: mg/L FEU				
median (inter-quartile range (Q1-Q3))	-0.08 (-0.68 to -0.01)	-0.04 (-0.36 to 0.05)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Median difference (net)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.6

Notes:

[11] - Descriptive

Secondary: Change in Factor II at 1 hour

End point title	Change in Factor II at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	11.4 (4.5 to 16.3)	22.4 (20.3 to 27.3)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[12]
Parameter estimate	Median difference (net)
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.86
upper limit	19.14

Notes:

[12] - Descriptive

Secondary: Change in Factor II at 24 hours

End point title	Change in Factor II at 24 hours

End point description:

End point type	Secondary

End point timeframe:

24 hours

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	21.1 (3.55 to 28.8)	21.45 (11.2 to 31.9)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[13]
Parameter estimate	Median difference (net)
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.82
upper limit	13.82

Notes:

[13] - Descriptive

Secondary: Change in Factor V at 1 hour	
End point title	Change in Factor V at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	26.2 (12.8 to 40.3)	0.3 (-2 to 6.6)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[14]
Parameter estimate	Median difference (net)
Point estimate	-25.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.4
upper limit	-13.4

Notes:
[14] - Descriptive

Secondary: Change in factor V at 24 hours	
End point title	Change in factor V at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	59.3 (28.2 to 82.25)	33.45 (15.3 to 55.9)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[15]
Parameter estimate	Median difference (net)
Point estimate	-19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.6
upper limit	13.6

Notes:
[15] - Descriptive

Secondary: Change in factor VII at 1 hour

End point title	Change in factor VII at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	16.7 (8 to 28.2)	16.4 (12.5 to 23.8)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[16]
Parameter estimate	Median difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.49
upper limit	9.89

Notes:
[16] - Descriptive

Secondary: Change in Factor VII at 24 hours

End point title	Change in Factor VII at 24 hours

End point description:

End point type	Secondary

End point timeframe:
24 hours

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	-4.55 (-10.7 to 17.5)	8.2 (-14.1 to 13.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	11.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.65
upper limit	31.85

Secondary: Change in Factor VIII at 1 hour	
End point title	Change in Factor VIII at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	8.4 (-14.3 to 40.8)	1 (-7.3 to 31.7)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.09
upper limit	22.29

Secondary: Change in Factor VIII at 24 hours	
End point title	Change in Factor VIII at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	106.1 (79.65 to 121.05)	87.45 (57.1 to 127.4)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-60.8
upper limit	39.4

Secondary: Change in Factor IX at 1 hour

End point title	Change in Factor IX at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	7.2 (-8.6 to 24.9)	14.9 (3.4 to 21)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.73
upper limit	26.13

Secondary: Change in Factor IX at 24 hours	
End point title	Change in Factor IX at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	28.35 (6.5 to 40.2)	27.1 (4 to 40.4)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	PCC per protocol v FFP per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.02
upper limit	23.42

Secondary: Change in Factor X at 1 hour	
End point title	Change in Factor X at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	11.6 (4.8 to 18.1)	20.9 (17.2 to 26.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	17.89

Secondary: Change in Factor X at 24 hours	
End point title	Change in Factor X at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	22.25 (6.3 to 27)	22.45 (9.3 to 29.8)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.5
upper limit	13.7

Secondary: Change in Factor XI at 1 hour	
End point title	Change in Factor XI at 1 hour
End point description:	
End point type	Secondary
End point timeframe: 1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	8.4 (3.1 to 27.1)	0 (-3.9 to 6.8)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.9
upper limit	4.1

Secondary: Change in Factor XI at 24 hours	
End point title	Change in Factor XI at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	20.75 (9.4 to 38.3)	5.65 (0 to 21.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-16.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.84
upper limit	3.04

Secondary: Change in Factor XII at 1 hour	
End point title	Change in Factor XII at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: U/dL				
median (inter-quartile range (Q1-Q3))	10.5 (1.5 to 17.4)	-2.2 (-7.2 to 3.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-12.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.46
upper limit	-0.94

Secondary: Change in Factor XII at 24 hours	
End point title	Change in Factor XII at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: U/dL				
median (inter-quartile range (Q1-Q3))	21.5 (-0.5 to 32.7)	10.75 (0.3 to 24.2)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.34
upper limit	8.14

Secondary: Change in Factor XIII at 1 hour

End point title	Change in Factor XIII at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	10.5 (2.7 to 19.1)	-1.8 (-5.5 to 3.2)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.26
upper limit	-2.34

Secondary: Change in Factor XIII at 24 hours	
End point title	Change in Factor XIII at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	7.05 (4.1 to 14.3)	0.9 (-16.3 to 12.3)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	PCC per protocol v FFP per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.02
upper limit	5.82

Secondary: Change in VWF antigen at 1 hour	
End point title	Change in VWF antigen at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	16		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	1.7 (-14.9 to 28.6)	20.35 (-5.75 to 39)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	18.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.96
upper limit	49.76

Secondary: Change in VWF antigen at 24 hours	
End point title	Change in VWF antigen at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	69.65 (5.45 to 119.25)	83.95 (53.9 to 124.4)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	16.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.51
upper limit	74.71

Secondary: Change in VWF activity at 1 hour

End point title	Change in VWF activity at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	16		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	20.1 (-0.9 to 42.7)	17.35 (-0.5 to 88.6)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.59
upper limit	52.59

Secondary: Change in VWF activity at 24 hours	
End point title	Change in VWF activity at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	87.65 (29.55 to 129.7)	101.6 (82.2 to 124.2)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	9.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.45
upper limit	69.85

Secondary: Change in AT activity at 1 hour	
End point title	Change in AT activity at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	16		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	9.9 (4.5 to 12.9)	0.5 (-2 to 3.7)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.96
upper limit	-4.04

Secondary: Change in AT activity at 24 hours	
End point title	Change in AT activity at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	22.25 (8.1 to 29.4)	14.75 (4.7 to 18.1)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.34
upper limit	3.34

Secondary: Change in PC activity at 1 hour

End point title	Change in PC activity at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	11.2 (5.8 to 21)	19.9 (9.1 to 29)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	18.12

Secondary: Change in PC activity at 24 hours	
End point title	Change in PC activity at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	21.25 (14.05 to 36.65)	18.85 (-0.2 to 33.8)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.55
upper limit	14.35

Secondary: Change in TAT at 1 hour	
End point title	Change in TAT at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	16		
Units: µg/L				
median (inter-quartile range (Q1-Q3))	0 (0 to 0.3)	0 (0 to 0.2)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.79
upper limit	3.79

Secondary: Change in TAT at 24 hours	
End point title	Change in TAT at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	13		
Units: µg/L				
median (inter-quartile range (Q1-Q3))	-5 (-12.4 to 0)	-2.4 (-12.1 to 0)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.85
upper limit	12.05

Secondary: Change in HMWK at 1 hour

End point title	Change in HMWK at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	15		
Units: U/dL				
median (inter-quartile range (Q1-Q3))	-3.15 (-4.1 to 02)	10.9 (-2.6 to 23.3)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.29
upper limit	24.29

Secondary: Change in HMWK at 24 hours	
End point title	Change in HMWK at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	12		
Units: U/dL				
median (inter-quartile range (Q1-Q3))	6.3 (-7.9 to 21.4)	14.6 (-9.75 to 24.45)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.3
upper limit	34.1

Secondary: Change in PRK at 1 hour	
End point title	Change in PRK at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	15		
Units: U/dL				
median (inter-quartile range (Q1-Q3))	10.3 (-2.85 to 18.1)	-4 (-12 to 14.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-17.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.7
upper limit	0.9

Secondary: Change in PRK at 24 hours	
End point title	Change in PRK at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	12		
Units: U/dL				
median (inter-quartile range (Q1-Q3))	5.55 (-6.4 to 25.7)	-2.8 (-34.75 to 13.3)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.12
upper limit	19.52

Secondary: Change in C1-inhibitor at 1 hour

End point title	Change in C1-inhibitor at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	16		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	7.2 (-6.4 to 13.1)	2.3 (-7.55 to 7.1)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.62
upper limit	4.82

Secondary: Change in C1-inhibitor at 24 hours	
End point title	Change in C1-inhibitor at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	34.15 (8.1 to 45.95)	24.2 (10.9 to 40.2)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.15
upper limit	19.95

Secondary: change in a2-antiplasmin at 1 hour	
End point title	change in a2-antiplasmin at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	8.4 (4.2 to 16.7)	-1 (-2.9 to 7.2)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.15
upper limit	-1.65

Secondary: change in a2-antiplasmin at 24 hours	
End point title	change in a2-antiplasmin at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	34.85 (16.5 to 43.25)	23.95 (6.3 to 36)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.82
upper limit	13.42

Secondary: Change in plasminogen at 1 hour

End point title	Change in plasminogen at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	17		
Units: U/dL				
median (inter-quartile range (Q1-Q3))	6.7 (1.3 to 11.7)	-1 (-4.2 to 1)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.31
upper limit	-2.09

Secondary: Change in plasminogen at 24 hours

End point title	Change in plasminogen at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: U/dL				
median (inter-quartile range (Q1-Q3))	16.35 (8.25 to 22.85)	2.6 (-3.8 to 10.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.05
upper limit	-2.15

Secondary: Change in tPA:Ag activity at 1 hour	
End point title	Change in tPA:Ag activity at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	16		
Units: µg/L				
median (inter-quartile range (Q1-Q3))	-0.3 (-1.7 to 1.1)	0 (-1.35 to 1.1)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.7

Secondary: Change in tPA:Ag at 24 hours	
End point title	Change in tPA:Ag at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	13		
Units: µg/L				
median (inter-quartile range (Q1-Q3))	0.2 (-1.4 to 3.95)	-1.5 (-3.4 to 0)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.36
upper limit	1.76

Secondary: Change in Prothrombin F.1+2 at 1 hour

End point title	Change in Prothrombin F.1+2 at 1 hour
End point description:	
End point type	Secondary
End point timeframe: 1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	16		
Units: pM				
median (inter-quartile range (Q1-Q3))	13 (0 to 219.5)	0 (-233.5 to 137)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	PCC per protocol v FFP per protocol

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-244.38
upper limit	192.38

Secondary: Change in Prothrombin F.1+2 at 24 hours

End point title	Change in Prothrombin F.1+2 at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	13		
Units: pM				
median (inter-quartile range (Q1-Q3))	-524.5 (-920 to -317)	-651 (-934 to -398)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-153
Confidence interval	
level	95 %
sides	2-sided
lower limit	-542.95
upper limit	236.95

Secondary: Change in PAP at 1 hour	
End point title	Change in PAP at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	16		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	104 (-34 to 336)	-54 (-139 to 38.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-157
Confidence interval	
level	95 %
sides	2-sided
lower limit	-386.64
upper limit	72.64

Secondary: change in PAP at 24 hours	
End point title	change in PAP at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	13		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	179 (-73 to 391)	-49 (-220 to 320)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-228
Confidence interval	
level	95 %
sides	2-sided
lower limit	-593.96
upper limit	137.96

Secondary: Change in TAFI at 1 hour

End point title	Change in TAFI at 1 hour
End point description:	
End point type	Secondary
End point timeframe: 1hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	16		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))	9 (3 to 16)	4 (-1 to 7)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	1

Secondary: Change in TAFI at 24 hours	
End point title	Change in TAFI at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	13		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))	13 (7.5 to 21.5)	8 (-2 to 11)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	PCC per protocol v FFP per protocol
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.96
upper limit	5.96

Secondary: Change in thrombomodulin at 1 hour	
End point title	Change in thrombomodulin at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	16		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	100 (30 to 524)	183.5 (67 to 406.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	146
Confidence interval	
level	95 %
sides	2-sided
lower limit	-131.72
upper limit	423.72

Secondary: Change in thrombomodulin at 24 hours	
End point title	Change in thrombomodulin at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	13		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	38 (-67 to 251)	70 (3 to 169)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-162.33
upper limit	226.33

Secondary: Change in Tissue Factor at 1 hour

End point title	Change in Tissue Factor at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	16		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	0.8 (-0.7 to 8.4)	0.05 (-2.05 to 1.35)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.79
upper limit	4.19

Secondary: Change in Tissue Factor at 24 hours

End point title	Change in Tissue Factor at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	13		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	1 (-0.5 to 2.2)	0 (-2.1 to 0.4)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.21
upper limit	1.21

Secondary: Change in sEPCR at 1 hour	
End point title	Change in sEPCR at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	16		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))	0 (0 to 749)	0 (-1319 to 713.5)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1129.98
upper limit	1129.98

Secondary: Change in sEPCR at 24 hours	
End point title	Change in sEPCR at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	13		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))	0 (-1167 to 0)	-362 (-2189 to 167)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	362
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2202.82
upper limit	1478.82

Secondary: Change in TG-ETP at 1 hour	
End point title	Change in TG-ETP at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	17		
Units: nM Thrombin				
median (inter-quartile range (Q1-Q3))	350 (-237 to 667)	159 (-352 to 714)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	191
Confidence interval	
level	95 %
sides	2-sided
lower limit	-765.84
upper limit	383.84

Secondary: Change in TG-ETP at 24 hours

End point title	Change in TG-ETP at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: nM Thrombin				
median (inter-quartile range (Q1-Q3))	581.5 (112 to 961)	686 (116 to 1407)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-763.25
upper limit	817.25

Secondary: Change in TG- Peak thrombin at 1 hour	
End point title	Change in TG- Peak thrombin at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	17		
Units: nM Thrombin				
median (inter-quartile range (Q1-Q3))	88 (-48 to 118)	6 (-57 to 64)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-194.68
upper limit	30.68

Secondary: Change in TG- Peak thrombin at 24 hours	
End point title	Change in TG- Peak thrombin at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: nM Thrombin				
median (inter-quartile range (Q1-Q3))	82.5 (-29 to 166)	53 (-7 to 223)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-141.4
upper limit	113.4

Secondary: Change in TG- lag time at 1 hour

End point title	Change in TG- lag time at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	17		
Units: minutes				
median (inter-quartile range (Q1-Q3))	-1.33 (-5.61 to 0.44)	-0.45 (-0.88 to 0.33)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	4.27

Secondary: Change in TG - lag time at 24 hours

End point title	Change in TG - lag time at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: minutes				
median (inter-quartile range (Q1-Q3))	-1.69 (-5.61 to 1.11)	0.34 (-0.22 to 2)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	2.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	6.31

Secondary: Change in TG- time to peak at 1 hour	
End point title	Change in TG- time to peak at 1 hour
End point description:	

End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	17		
Units: minutes				
median (inter-quartile range (Q1-Q3))	-2.83 (-9.56 to 0.61)	0.67 (-0.89 to 2)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	PCC per protocol v FFP per protocol
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	7.88

Secondary: Change in TG- time to peak at 24 hours	
End point title	Change in TG- time to peak at 24 hours
End point description:	

End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: minutes				
median (inter-quartile range (Q1-Q3))	-3.44 (-9.33 to 1.89)	1.11 (-0.67 to 3.22)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	4.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	10.39

Secondary: Change in Free PS antigen at 1 hour

End point title	Change in Free PS antigen at 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
1 hour	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	16		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	8.35 (4.4 to 11.7)	13 (6.55 to 16.05)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	PCC per protocol v FFP per protocol

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	10.23

Secondary: Change in Free PS antigen at 24 hours

End point title	Change in Free PS antigen at 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
24 hours	

End point values	FFP per protocol	PCC per protocol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	13		
Units: IU/dL				
median (inter-quartile range (Q1-Q3))	15.6 (-2.1 to 24.55)	12.2 (4.6 to 19.3)		

Statistical analyses

Statistical analysis title	Difference in change between treatment groups
Comparison groups	FFP per protocol v PCC per protocol
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.88
upper limit	10.68

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from one hour after receiving study intervention until 90 days following intervention or death, whichever occurs first.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Fresh Frozen Plasma (FFP) Safety population

Reporting group description:

All consenting patients who bled and received FFP regardless of whether they were randomised.

Reporting group title	Prothrombin Complex Concentrate (PCC) Safety population

Reporting group description:

All consenting patients who bled and received PCC regardless of whether they were randomised.

Serious adverse events	Fresh Frozen Plasma (FFP) Safety population	Prothrombin Complex Concentrate (PCC) Safety population	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 26 (34.62%)	5 / 29 (17.24%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Investigations			
Raised INR			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Lacunar infarction			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 26 (7.69%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord ischaemia			

subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute right ventricular failure			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve incompetence			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Heart failure			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Malaise			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Multiorgan failure			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Haemothorax			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fresh Frozen Plasma (FFP) Safety population	Prothrombin Complex Concentrate (PCC) Safety population	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 26 (80.77%)	22 / 29 (75.86%)	

Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 26 (7.69%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Thrombosis			
subjects affected / exposed	2 / 26 (7.69%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Thrombophlebitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Haematoma			
subjects affected / exposed	1 / 26 (3.85%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Epistaxis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Haemorrhage			
subjects affected / exposed	1 / 26 (3.85%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Peripheral artery aneurysm			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Tracheostomy			
subjects affected / exposed	1 / 26 (3.85%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
Cardiac pacemaker insertion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	2 / 26 (7.69%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Asthenia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 29 (3.45%)	
occurrences (all)	1	1	

Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	14 / 26 (53.85%)	14 / 29 (48.28%)	
occurrences (all)	15	15	
Atelectasis			
subjects affected / exposed	5 / 26 (19.23%)	2 / 29 (6.90%)	
occurrences (all)	5	2	
Lower respiratory tract infection			
subjects affected / exposed	1 / 26 (3.85%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Hypoxia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Pneumothorax			
subjects affected / exposed	0 / 26 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	3	
Respiratory failure			
subjects affected / exposed	1 / 26 (3.85%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 26 (3.85%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Transaminases increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Blood lactic acid increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Lactic acidosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Thoracic cavity drainage			

subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	2	
Cardiac perforation			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	4 / 26 (15.38%)	1 / 29 (3.45%)	
occurrences (all)	4	1	
Pulmonary oedema			
subjects affected / exposed	1 / 26 (3.85%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Nervous system disorders			
Meningioma			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Seizure			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Eye disorders			
Microvascular cranial nerve palsy			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 26 (3.85%)	5 / 29 (17.24%)	
occurrences (all)	1	5	
Melaena			

subjects affected / exposed	0 / 26 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 26 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Anuria			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Acute on chronic liver failure			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Polyuria			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Cholecystitis acute			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Sepsis			
subjects affected / exposed	2 / 26 (7.69%)	2 / 29 (6.90%)	
occurrences (all)	2	2	
Pneumonia			
subjects affected / exposed	2 / 26 (7.69%)	3 / 29 (10.34%)	
occurrences (all)	2	3	
Bacterial infection			

subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Escherichia bacteraemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Enterococcus test positive			
subjects affected / exposed	0 / 26 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	4 / 26 (15.38%)	0 / 29 (0.00%)	
occurrences (all)	4	0	
Hyperkalaemia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Hypernatraemia			
subjects affected / exposed	2 / 26 (7.69%)	2 / 29 (6.90%)	
occurrences (all)	2	2	
Hypokalaemia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			
subjects affected / exposed	1 / 26 (3.85%)	2 / 29 (6.90%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2019	Additional exclusion criteria (ECMO, any other reason clinician deems unsuitable), clarification of endpoints and analysis, qualitative research manual, updated IMP label
06 January 2020	Addition of a meeting at the end of the study where participants will be invited to hear study results and asked for their feedback on study recruitment procedures and outcome measures, to inform the large trial

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This is a feasibility/pilot study with the aim of determining the recruitment rate for a larger-scale trial and assessing trial procedures. It was not statistically powered to compare FFP and PCC in terms of effectiveness or safety.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31815658