Clinical trial results:
A Phase 2, Randomized, Open-label (with Blinded Plasminogen Activator and Placebo Control Groups) Study to Evaluate the Effects of Different Intra-thrombus Infusion Regimens of Plasmin (Human) Compared to Plasminogen Activator and Placebo in Patients With Acute Lower Extremity Native Artery or Bypass Graft Occlusion

Summary

EudraCT number	2010-019760-36
Trial protocol	SK HU DE BE ES CZ BG
Global end of trial date	03 September 2014

Results information

Result version number	v1 (current)
This version publication date	30 December 2016
First version publication date	30 December 2016

Trial information

Trial identification

Sponsor protocol code	T05018-2004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01222117
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Grifols Therapeutics Inc.
Sponsor organisation address	79 TW Alexander Drive - Research Triangle Park, Durham, United States, NC 27709
Public contact	Kecia Courtney Grifols Therapeutics Inc. 79 TW Alexander Drive Research Triangle Park, NC 27709, Grifols Therapeutics Inc., Kecia.courtney@grifols.com
Scientific contact	Kecia Courtney Grifols Therapeutics Inc. 79 TW Alexander Drive Research Triangle Park, NC 27709, Grifols Therapeutics Inc., Kecia.courtney@grifols.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 January 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of this Phase 2 study was to optimize Plasmin delivery by comparing different delivery regimens in patients with peripheral arterial occlusion. The study included a blinded plasminogen activator treatment group and a blinded plasminogen activator placebo group. The study also assessed safety and tolerability of Plasmin at 150 and 250 mg doses.

Protection of trial subjects:

Any subject might be released to rescue/standard of care should any of the following conditions occured during study drug treatment:
1. Clinical deterioration
2. Rethrombosis or embolization
3. For treatment group M only, inability to successfully place and inflate the BOC before the study drug treatment

In treatment groups I, J, and M, if the event ischemia worsened beyond SVS IIa (ischemia related signs or symptoms), the BOC balloon was to be deflated at the Investigator's discretion, and the Plasmin infusion continued at the Investigator's discretion.
At EOT, all subjects were released to standard of care and, if necessary, further thrombus debulking (other CDT, mechanical thrombectomy or surgical thrombectomy).
Procedures Consistent with Plasmin Success:
Where warranted, correction of the underlying culprit lesion was to occur with focal surgical procedures defined as:
- Angioplasty and/or stenting
- Focal endarterectomy
- Patch angioplasty
- Segmental graft placement
- No intervention (eg, anticoagulant therapy)
- Aspiration thrombectomy

Procedures Consistent with Plasmin Failure:
If a focal surgical procedure was insufficient or not indicated, then major procedures must be instituted and might include the following:
- Operative thrombectomy/embolectomy
- Operative graft placement or replacement
- Mechanical device thrombectomy (excluding aspiration thrombectomy)
- Major amputation (ankle or above)
- Profundaplasty

If distal embolization was suspected during treatment, the investigator should have used his or her clinical judgment as to whether the clinical condition of the subject warranted a release to standard of care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 December 2010
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	Poland: 5
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Slovakia: 40
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Bulgaria: 5
Country: Number of subjects enrolled	Czech Republic: 45
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	United States: 5
Country: Number of subjects enrolled	Peru: 4
Country: Number of subjects enrolled	India: 4
Country: Number of subjects enrolled	Serbia: 43
Country: Number of subjects enrolled	Ukraine: 2
Worldwide total number of subjects	174
EEA total number of subjects	116

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	95
From 65 to 84 years	77
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	241[1]
Number of subjects completed	174

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Adverse event, non-fatal: 1
Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	Physician decision: 4
Reason: Number of subjects	Study entry criteria not met: 57
Reason: Number of subjects	Other: 4

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 241 subjects were screened, a total of 174 subjects were randomized into the study; 67 subjects were screen failures

Period 1

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

Blinding implementation details:

Blinded Plasminogen Activator (PA) and Placebo Control Groups. Unblinded pharmacist would prepare and dispense PA or placebo (as assigned by the IVR-IWR System) for infusion. Information about the dose and the volume of the control group (PA or placebo) would be provided to the investigator after randomization. Subjects in the blinded control groups (group E and group F) were to receive the same total volume of PA or placebo and there was no visible difference between PA and placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	Plasmin Open-label Treatment Group A

Arm description:

Open-label 150 mg Plasmin administered without initial proximal pulse; 5-hour infusion using 10 mL/hour infusion rate

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

5-hour infusion (10 mL/h), 150 mg Plasmin in 75 mL, pulse, possible repositioning after 2-hour arteriogram without balloon occlusion catheter.

Plasmin: Plasmin prepared in 0.9% saline for injection

Arm title	Plasmin Open-label Treatment Group B

Arm description:

Open-label 150 mg Plasmin administered with initial proximal pulse; 5-hour infusion using 15 mL/hour infusion rate

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

5-hour infusion (15 mL/h), 150 mg Plasmin in 75 mL, initial proximal pulse, possible repositioning after 2-hour arteriogram without balloon occlusion catheter.
Plasmin: Plasmin prepared in 0.9% saline for injection

Arm title	Plasmin Open-label Treatment Group C

Arm description:

Open-label 150 mg Plasmin administered with proximal pulse; 5 hour infusion using 30 mL/hour infusion rate

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

5-hour infusion (30 mL/h), 150 mg Plasmin in 150 mL, pulse, possible repositioning after 2-hour without balloon occlusion catheter.
Plasmin: Plasmin prepared in 0.9% saline for injection

Arm title	Plasmin Open-label Treatment Group D

Arm description:

Open-label 150 mg Plasmin administered with proximal pulse; 2-hour infusion using 35 mL/hour infusion rate

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

2-hour infusion (35 mL/h), 150 mg Plasmin in 75 mL, pulse, without balloon occlusion catheter.
Plasmin: Plasmin prepared in 0.9% saline for injection

Arm title	Plasminogen Activator Blinded Group E

Arm description:

Plasminogen Activator administered for five hours at a dose and volume according to the Investigator's

clinical judgement/standard practice

Arm type	Active comparator
Investigational medicinal product name	Plasminogen activator
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

Plasminogen Activator administered for 5 hours at a dose and volume according to the Investigator's clinical judgement/standard practice
Plasminogen Activator: Plasminogen activator used according to the Investigator's clinical judgment.

Arm title	PA Placebo Blinded Treatment Arm F

Arm description:

PA placebo (normal saline for injection) administered for 5 hours at a dose and volume according to the Investigator's clinical judgement/standard practice for PA administration

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

PA placebo (normal saline for injection) administered for 5 hours at a dose and volume according to the Investigator's clinical judgement/standard practice for PA administration

Placebo: Normal saline for injection at the same volume as the plasminogen activator.

Arm title	Plasmin Open-label Treatment Group G

Arm description:

Open-label 150 mg Plasmin administered without pulsing; 5-hour infusion using 60 mL/hour infusion rate

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

5-hour infusion (60 mL/h), 150 mg Plasmin in 300 mL, no pulse, no repositioning without balloon occlusion catheter.
Plasmin: Plasmin prepared in 0.9% saline for injection

Arm title	Plasmin Open-label Treatment Group H

Arm description:

Open-label 150 mg Plasmin administered without pulsing; 2-hour infusion using 75 mL/hour infusion rate

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

2-hour infusion (75 mL/h), 150 mg Plasmin in 150 mL, no pulse, without balloon occlusion catheter.
Plasmin: Plasmin prepared in 0.9% saline for injection

Arm title	Plasmin Open-label Treatment Group I

Arm description:

Open-label 150 mg Plasmin administered without pulsing; 5-hour infusion using 30 mL/hour infusion rate with balloon occlusion catheter

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

5-hour infusion (30 mL/h), 150 mg Plasmin in 150 mL, no pulse, with balloon occlusion catheter.
Plasmin: Plasmin prepared in 0.9% saline for injection

Arm title	Plasmin Open-label Treatment Group J

Arm description:

Open-label 150 mg Plasmin administered without pulsing; 2-hour infusion using 35 mL/hour infusion rate with balloon occlusion catheter

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

2-hour infusion (35 mL/h), 150 mg Plasmin in 75 mL, no pulse, with balloon occlusion catheter.
Plasmin: Plasmin prepared in 0.9% saline for injection

Arm title	Plasmin Open-label Treatment Group M

Arm description:

Open-label 250 mg Plasmin administered without pulsing; 5-hour infusion using 30 mL/hour infusion rate with balloon occlusion catheter

Arm type	Experimental
Investigational medicinal product name	Plasmin (Human)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

5-hour infusion (30 mL/h), 250 mg Plasmin in 150 mL, no pulse, with balloon occlusion catheter.
Plasmin: Plasmin prepared in 0.9% saline for injection

Number of subjects in period 1	Plasmin Open-label Treatment Group A	Plasmin Open-label Treatment Group B	Plasmin Open-label Treatment Group C
Started	20	20	22
Completed	17	19	22
Not completed	3	1	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	1	-	-
Death	1	-	-
Lost to follow-up	-	1	-
balloon occlusion catheter not inflated	-	-	-

Number of subjects in period 1	Plasmin Open-label Treatment Group D	Plasminogen Activator Blinded Group E	PA Placebo Blinded Treatment Arm F
Started	20	9	10
Completed	19	8	9
Not completed	1	1	1
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	-
Death	-	1	1
Lost to follow-up	-	-	-
balloon occlusion catheter not inflated	-	-	-

Number of subjects in period 1	Plasmin Open-label Treatment Group G	Plasmin Open-label Treatment Group H	Plasmin Open-label Treatment Group I
Started	13	12	23
Completed	13	12	20
Not completed	0	0	3
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	2
Death	-	-	-
Lost to follow-up	-	-	-
balloon occlusion catheter not inflated	-	-	1

Number of subjects in period 1	Plasmin Open-label Treatment Group J	Plasmin Open-label Treatment Group M
Started	19	6
Completed	17	6
Not completed	2	0
Consent withdrawn by subject	-	-
Adverse event, non-fatal	-	-
Death	-	-
Lost to follow-up	-	-
balloon occlusion catheter not inflated	2	-

Baseline characteristics

Reporting groups

Reporting group title	Plasmin Open-label Treatment Group A

Reporting group description:

Open-label 150 mg Plasmin administered without initial proximal pulse; 5-hour infusion using 10 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group B

Reporting group description:

Open-label 150 mg Plasmin administered with initial proximal pulse; 5-hour infusion using 15 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group C

Reporting group description:

Open-label 150 mg Plasmin administered with proximal pulse; 5 hour infusion using 30 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group D

Reporting group description:

Open-label 150 mg Plasmin administered with proximal pulse; 2-hour infusion using 35 mL/hour infusion rate

Reporting group title	Plasminogen Activator Blinded Group E

Reporting group description:

Plasminogen Activator administered for five hours at a dose and volume according to the Investigator's clinical judgement/standard practice

Reporting group title	PA Placebo Blinded Treatment Arm F

Reporting group description:

PA placebo (normal saline for injection) administered for 5 hours at a dose and volume according to the Investigator's clinical judgement/standard practice for PA administration

Reporting group title	Plasmin Open-label Treatment Group G

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 5-hour infusion using 60 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group H

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 2-hour infusion using 75 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group I

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 5-hour infusion using 30 mL/hour infusion rate with balloon occlusion catheter

Reporting group title	Plasmin Open-label Treatment Group J

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 2-hour infusion using 35 mL/hour infusion rate with balloon occlusion catheter

Reporting group title	Plasmin Open-label Treatment Group M

Reporting group description:

Open-label 250 mg Plasmin administered without pulsing; 5-hour infusion using 30 mL/hour infusion rate with balloon occlusion catheter

Reporting group values	Plasmin Open-label Treatment Group A	Plasmin Open-label Treatment Group B	Plasmin Open-label Treatment Group C
Number of subjects	20	20	22
Age categorical Units: Subjects			
<65 years	12	10	10
>=65 years	8	10	12
Gender categorical Units: Subjects			
Female	3	3	5
Male	17	17	17
Region of Enrollment Units: Subjects			
Czech Republic	4	4	3
Romania	0	0	3
Belgium	3	1	3
United states	1	1	1
Poland	0	1	1
Slovakia	3	2	4
Serbia	6	7	3
Bulgaria	1	1	2
Peru	1	0	0
Germany	0	0	1
India	1	2	1
Ukraine	0	1	0

Reporting group values	Plasmin Open-label Treatment Group D	Plasminogen Activator Blinded Group E	PA Placebo Blinded Treatment Arm F
Number of subjects	20	9	10
Age categorical Units: Subjects			
<65 years	10	5	5
>=65 years	10	4	5
Gender categorical Units: Subjects			
Female	7	0	3
Male	13	9	7
Region of Enrollment Units: Subjects			
Czech Republic	5	1	1
Romania	0	0	0
Belgium	2	2	2
United states	1	1	0
Poland	2	0	0
Slovakia	1	1	0
Serbia	4	4	6
Bulgaria	0	0	0
Peru	3	0	0
Germany	2	0	0
India	0	0	0
Ukraine	0	0	1

Reporting group values	Plasmin Open-label Treatment Group G	Plasmin Open-label Treatment Group H	Plasmin Open-label Treatment Group I
Number of subjects	13	12	23
Age categorical Units: Subjects			
<65 years	8	7	13
>=65 years	5	5	10
Gender categorical Units: Subjects			
Female	2	3	7
Male	11	9	16
Region of Enrollment Units: Subjects			
Czech Republic	5	5	9
Romania	0	0	0
Belgium	1	0	1
United states	0	0	0
Poland	1	0	0
Slovakia	2	2	11
Serbia	4	5	1
Bulgaria	0	0	1
Peru	0	0	0
Germany	0	0	0
India	0	0	0
Ukraine	0	0	0

Reporting group values	Plasmin Open-label Treatment Group J	Plasmin Open-label Treatment Group M	Total
Number of subjects	19	6	174
Age categorical Units: Subjects			
<65 years	12	3	95
>=65 years	7	3	79
Gender categorical Units: Subjects			
Female	5	1	39
Male	14	5	135
Region of Enrollment Units: Subjects			
Czech Republic	7	1	45
Romania	0	0	3
Belgium	0	0	15
United states	0	0	5
Poland	0	0	5
Slovakia	9	5	40
Serbia	3	0	43
Bulgaria	0	0	5
Peru	0	0	4
Germany	0	0	3
India	0	0	4
Ukraine	0	0	2

End points

End points reporting groups

Reporting group title	Plasmin Open-label Treatment Group A

Reporting group description:

Open-label 150 mg Plasmin administered without initial proximal pulse; 5-hour infusion using 10 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group B

Reporting group description:

Open-label 150 mg Plasmin administered with initial proximal pulse; 5-hour infusion using 15 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group C

Reporting group description:

Open-label 150 mg Plasmin administered with proximal pulse; 5 hour infusion using 30 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group D

Reporting group description:

Open-label 150 mg Plasmin administered with proximal pulse; 2-hour infusion using 35 mL/hour infusion rate

Reporting group title	Plasminogen Activator Blinded Group E

Reporting group description:

Plasminogen Activator administered for five hours at a dose and volume according to the Investigator's clinical judgement/standard practice

Reporting group title	PA Placebo Blinded Treatment Arm F

Reporting group description:

PA placebo (normal saline for injection) administered for 5 hours at a dose and volume according to the Investigator's clinical judgement/standard practice for PA administration

Reporting group title	Plasmin Open-label Treatment Group G

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 5-hour infusion using 60 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group H

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 2-hour infusion using 75 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group I

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 5-hour infusion using 30 mL/hour infusion rate with balloon occlusion catheter

Reporting group title	Plasmin Open-label Treatment Group J

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 2-hour infusion using 35 mL/hour infusion rate with balloon occlusion catheter

Reporting group title	Plasmin Open-label Treatment Group M

Reporting group description:

Open-label 250 mg Plasmin administered without pulsing; 5-hour infusion using 30 mL/hour infusion rate with balloon occlusion catheter

Primary: Proportion of Subjects With >50% Thrombolysis

End point title	Proportion of Subjects With >50% Thrombolysis[1]

End point description:

The proportion of subjects with >50% thrombolysis at the end of treatment compared to baseline by arteriography.

In groups A-D, G and H, 7 subjects were excluded (EOT arteriogram missing or not read, did not receive >=90% of dose). In groups I and J, 11 subjects were excluded (BOC not inserted/appropriately inflated, missing an arteriogram). In group F, 1 subject was not dosed and 4 subjects were excluded (did not receive >=90% of dose).

End point type	Primary

End point timeframe:

5 hours (Treatment Groups A, B, C, G, I, M) or 2 hours (Treatment Groups D, H, J)

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: No statistical analysis provided for The Proportion of Subjects With >50% Thrombolysis

End point values	Plasmin Open-label Treatment Group A	Plasmin Open-label Treatment Group B	Plasmin Open-label Treatment Group C	Plasmin Open-label Treatment Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	19	21	19
Units: Number of subjects	7	9	17	9

End point values	Plasminogen Activator Blinded Group E	PA Placebo Blinded Treatment Arm F	Plasmin Open-label Treatment Group G	Plasmin Open-label Treatment Group H
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	5	12	12
Units: Number of subjects	8	2	8	8

End point values	Plasmin Open-label Treatment Group I	Plasmin Open-label Treatment Group J	Plasmin Open-label Treatment Group M	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	6	
Units: Number of subjects	11	6	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Major and Minor Bleeding Events, Deaths, Adverse Events, Serious Adverse Events, and Abnormal Laboratory Values as a Measure of Safety and Tolerability

End point title	Incidence of Major and Minor Bleeding Events, Deaths, Adverse Events, Serious Adverse Events, and Abnormal Laboratory Values as a Measure of Safety and Tolerability

End point description:

The incidence of major and minor bleeding events, deaths, adverse events, serious adverse events, and abnormal laboratory values as a measure of safety and tolerability.

Subjects were excluded from the safety population if they did not receive any dose of Plasmin (groups I and J) or placebo (group F).

End point type	Secondary

End point timeframe:

30 days

End point values	Plasmin Open-label Treatment Group A	Plasmin Open-label Treatment Group B	Plasmin Open-label Treatment Group C	Plasmin Open-label Treatment Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	22	20
Units: Number of subjects				
Adverse events	16	12	18	14
Serious adverse events	10	4	6	4
Major bleeding events	3	1	1	0
Minor bleeding events	1	4	2	4
Deaths	1	0	0	0
Abnormal laboratory values	3	2	3	0

End point values	Plasminogen Activator Blinded Group E	PA Placebo Blinded Treatment Arm F	Plasmin Open-label Treatment Group G	Plasmin Open-label Treatment Group H
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	13	12
Units: Number of subjects				
Adverse events	7	8	9	7
Serious adverse events	2	5	4	3
Major bleeding events	1	1	0	0
Minor bleeding events	3	3	6	1
Deaths	1	1	0	0
Abnormal laboratory values	1	2	2	0

End point values	Plasmin Open-label Treatment Group I	Plasmin Open-label Treatment Group J	Plasmin Open-label Treatment Group M	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	17	6	
Units: Number of subjects				
Adverse events	14	10	3	
Serious adverse events	7	2	0	
Major bleeding events	2	0	0	
Minor bleeding events	6	2	2	
Deaths	0	0	0	
Abnormal laboratory values	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

December 09 2010 - September 03 2014

Adverse event reporting additional description:

Subjects were excluded from the safety population if they did not receive any dose of Plasmin (groups I and J) or placebo (group F)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Plasmin Open-label Treatment Group A

Reporting group description:

Open-label 150 mg Plasmin administered without initial proximal pulse; 5-hour infusion using 10 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group B

Reporting group description:

Open-label 150 mg Plasmin administered with initial proximal pulse; 5-hour infusion using 15 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group C

Reporting group description:

Open-label 150 mg Plasmin administered with proximal pulse; 5 hour infusion using 30 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group D

Reporting group description:

Open-label 150 mg Plasmin administered with proximal pulse; 2-hour infusion using 35 mL/hour infusion rate

Reporting group title	Plasminogen Activator Blinded Group E

Reporting group description:

Plasminogen Activator administered for five hours at a dose and volume according to the Investigator's clinical judgement/standard practice

Reporting group title	PA Placebo Blinded Treatment Arm F

Reporting group description:

PA placebo (normal saline for injection) administered for 5 hours at a dose and volume according to the Investigator's clinical judgement/standard practice for PA administration

Reporting group title	Plasmin Open-label Treatment Group G

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 5-hour infusion using 60 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group H

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 2-hour infusion using 75 mL/hour infusion rate

Reporting group title	Plasmin Open-label Treatment Group I

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 5-hour infusion using 30 mL/hour infusion rate with balloon occlusion catheter

Reporting group title	Plasmin Open-label Treatment Group J

Reporting group description:

Open-label 150 mg Plasmin administered without pulsing; 2-hour infusion using 35 mL/hour infusion rate with balloon occlusion catheter

Reporting group title	Plasmin Open-label Treatment Group M

Reporting group description:

Open-label 250 mg Plasmin administered without pulsing; 5-hour infusion using 30 mL/hour infusion rate with balloon occlusion catheter

Serious adverse events	Plasmin Open-label Treatment Group A	Plasmin Open-label Treatment Group B	Plasmin Open-label Treatment Group C
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 20 (50.00%)	4 / 20 (20.00%)	6 / 22 (27.27%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Vascular graft thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia postoperative			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Operative haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anastomotic haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reocclusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	4 / 20 (20.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral embolism			
subjects affected / exposed	4 / 20 (20.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral arterial stenosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial thrombosis limb			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic limb pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reperfusion injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Peroneal nerve palsy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Vessel puncture site reaction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Puncture site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Plasmin Open-label Treatment Group D	Plasminogen Activator Blinded Group E	PA Placebo Blinded Treatment Arm F
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 20 (20.00%)	2 / 9 (22.22%)	5 / 9 (55.56%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Vascular graft thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia postoperative			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Operative haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anastomotic haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reocclusion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	3 / 9 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral embolism			

subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral arterial stenosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial thrombosis limb			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic limb pain			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reperfusion injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Peroneal nerve palsy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Vessel puncture site reaction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Catheter site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Puncture site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Plasmin Open-label Treatment Group G	Plasmin Open-label Treatment Group H	Plasmin Open-label Treatment Group I
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 13 (30.77%)	3 / 12 (25.00%)	7 / 21 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Vascular graft thrombosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia postoperative			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Operative haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anastomotic haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reocclusion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral embolism			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	3 / 21 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral arterial stenosis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial thrombosis limb			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic limb pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reperfusion injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Peroneal nerve palsy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Vessel puncture site reaction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Puncture site haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Plasmin Open-label Treatment Group J	Plasmin Open-label Treatment Group M	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Injury, poisoning and procedural complications			
Vascular graft thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia postoperative			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft thrombosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Operative haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reocclusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral arterial stenosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial thrombosis limb			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic limb pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reperfusion injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Peroneal nerve palsy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Vessel puncture site reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Multi-organ failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Puncture site haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Plasmin Open-label Treatment Group A	Plasmin Open-label Treatment Group B	Plasmin Open-label Treatment Group C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 20 (70.00%)	11 / 20 (55.00%)	18 / 22 (81.82%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Peripheral embolism			
subjects affected / exposed	4 / 20 (20.00%)	2 / 20 (10.00%)	6 / 22 (27.27%)
occurrences (all)	4	2	7
Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Hypertension			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Arterial thrombosis limb			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Femoral artery embolism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ischaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ischaemic limb pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Extremity necrosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Femoral artery aneurysm			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Iliac artery stenosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Intermittent claudication			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Labile blood pressure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Peripheral artery aneurysm			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Peripheral artery dissection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Peripheral ischaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0

Reperfusion injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Infusion related reaction			
subjects affected / exposed	5 / 20 (25.00%)	2 / 20 (10.00%)	5 / 22 (22.73%)
occurrences (all)	6	2	6
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	3 / 22 (13.64%)
occurrences (all)	0	1	3
Puncture site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Infusion site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Complication of device removal			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Device leakage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Local swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Disorientation			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Restlessness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Blood glucose increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Haematocrit decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood fibrinogen decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Red blood cell count decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Reocclusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Graft complication			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Graft thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vascular graft complication			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vascular graft thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Cardiac failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Presyncope			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Hypercoagulation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Thrombocytopenia			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Anaemia of chronic disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Lymphocytosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Neutrophilia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Retinal artery embolism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Renal failure acute			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Renal failure			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Dysuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nephropathy toxic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oliguria			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Renal failure chronic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	1 / 22 (4.55%)
occurrences (all)	3	3	1
Back pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Groin pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Graft infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Post procedural infection			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	2	1	0
Acidosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Plasmin Open-label Treatment Group D	Plasminogen Activator Blinded Group E	PA Placebo Blinded Treatment Arm F
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 20 (70.00%)	7 / 9 (77.78%)	8 / 9 (88.89%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Peripheral embolism			
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	2	1	1

Haematoma			
subjects affected / exposed	2 / 20 (10.00%)	3 / 9 (33.33%)	1 / 9 (11.11%)
occurrences (all)	2	3	1
Hypertension			
subjects affected / exposed	3 / 20 (15.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Arterial thrombosis limb			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Femoral artery embolism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Ischaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ischaemic limb pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Extremity necrosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Femoral artery aneurysm			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Iliac artery stenosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Intermittent claudication			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Labile blood pressure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Peripheral artery aneurysm			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Peripheral artery dissection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Peripheral ischaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Reperfusion injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Infusion related reaction			
subjects affected / exposed	6 / 20 (30.00%)	2 / 9 (22.22%)	4 / 9 (44.44%)
occurrences (all)	7	2	4
Pyrexia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	2	0	2
Puncture site haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Infusion site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Catheter site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Chest pain			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Complication of device removal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Device leakage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injection site haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Puncture site pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dyspnoea			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Disorientation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Mental status changes			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood glucose increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Haematocrit decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood fibrinogen decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Reocclusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Graft complication			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Graft thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vascular graft complication			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vascular graft thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Hypercoagulation			
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Anaemia of chronic disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Lymphocytosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Neutrophilia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Retinal artery embolism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Skin discolouration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal failure acute			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Renal failure			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nephropathy toxic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oliguria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal failure chronic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Groin pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Infections and infestations			
Graft infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Post procedural infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Acidosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Non-serious adverse events	Plasmin Open-label Treatment Group G	Plasmin Open-label Treatment Group H	Plasmin Open-label Treatment Group I

Total subjects affected by non-serious adverse events subjects affected / exposed	9 / 13 (69.23%)	7 / 12 (58.33%)	14 / 21 (66.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Lung neoplasm malignant subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	0 / 21 (0.00%) 0
Vascular disorders Peripheral embolism subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	0 / 12 (0.00%) 0	4 / 21 (19.05%) 5
Haematoma subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 4	1 / 12 (8.33%) 1	0 / 21 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0	0 / 21 (0.00%) 0
Arterial thrombosis limb subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0	2 / 21 (9.52%) 4
Femoral artery embolism subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	1 / 21 (4.76%) 1
Hypotension subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0	0 / 21 (0.00%) 0
Ischaemia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0	1 / 21 (4.76%) 1
Ischaemic limb pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0	1 / 21 (4.76%) 1
Extremity necrosis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	0 / 21 (0.00%) 0
Femoral artery aneurysm			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Iliac artery stenosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Intermittent claudication			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Labile blood pressure			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Peripheral artery aneurysm			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Peripheral artery dissection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Peripheral ischaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Reperfusion injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Infusion related reaction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Puncture site haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Oedema peripheral			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Infusion site haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Complication of device removal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Device leakage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Investigations			

Haemoglobin decreased			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Haematocrit decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood fibrinogen decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Reocclusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	4 / 21 (19.05%)
occurrences (all)	0	0	4
Graft complication			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Graft thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Vascular graft complication			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Vascular graft thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Presyncope			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Hypercoagulation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Anaemia of chronic disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Lymphocytosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Neutrophilia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Retinal artery embolism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Intra-abdominal haematoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Renal failure acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Nephropathy toxic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Oliguria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Renal failure chronic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Back pain			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Graft infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Post procedural infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Acidosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Plasmin Open-label Treatment Group J	Plasmin Open-label Treatment Group M	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 17 (58.82%)	3 / 6 (50.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Peripheral embolism			
subjects affected / exposed	3 / 17 (17.65%)	0 / 6 (0.00%)	
occurrences (all)	4	0	
Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Arterial thrombosis limb			
subjects affected / exposed	1 / 17 (5.88%)	2 / 6 (33.33%)	
occurrences (all)	1	2	
Femoral artery embolism			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Ischaemia			

subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Ischaemic limb pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Extremity necrosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Femoral artery aneurysm			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Iliac artery stenosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Intermittent claudication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Labile blood pressure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Peripheral artery aneurysm			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Peripheral artery dissection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Peripheral ischaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Reperfusion injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Infusion related reaction			

subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Puncture site haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Oedema peripheral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Infusion site haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Catheter site haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Chest discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Complication of device removal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Device leakage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Injection site haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Injection site haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Local swelling			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Puncture site pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Vessel puncture site haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Disorientation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Mental status changes			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Restlessness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood glucose increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood pressure increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Haematocrit decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood cholesterol increased			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood fibrinogen decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood potassium decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Red blood cell count decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Reocclusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Graft complication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Graft thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Vascular graft complication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Vascular graft thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Cardiac failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypercoagulation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Anaemia of chronic disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Leukocytosis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Lymphocytosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Lymphopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Neutrophilia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Retinal artery embolism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Intra-abdominal haematoma			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Skin discolouration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Renal failure acute			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Renal failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Nephropathy toxic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Oliguria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Proteinuria			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Renal failure chronic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 17 (5.88%)	2 / 6 (33.33%)	
occurrences (all)	2	2	
Back pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Groin pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Graft infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Post procedural infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Postoperative wound infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Acidosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypercholesterolaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rhabdomyolysis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2010	-Changes in the Study Design and Assignment of Subject Number -Changes in the Subject Population -Changes in the Imaging Procedures -Changes in the Infusion Catheter Procedures -Changes in the Anticoagulation Procedures -Change in the Rescue/Release to Standard of Care - Changes in assessments Additional changes were made in the protocol for clarification, consistency, and administrative reasons.
07 July 2011	- Changes in Efficacy Objective - Changes in Inclusion/Exclusion Criteria - Changes in Imaging Procedures - Changes in Anticoagulation Procedures - Changes in Serious Adverse Events (SAE) Reporting Additional changes were made in the protocol for clarification, consistency, and administrative reasons.
10 January 2012	- Study Design Added 30 subjects and 2 additional Plasmin treatment groups that provided new treatment regimens for consideration for future studies. There was no change in the Plasmin dose. The 2 new treatment groups employed simplified procedures (removing pulsing and only maintaining continuous infusion for the whole treatment duration, 5 hours or 2 hours) to administer Plasmin. The 2 Plasmin treatment groups were also designed to further explore the effect of infusion rate on thrombolysis. Enrollment of additional 30 subjects (approximately) after the completion of the first approximately 100 subjects (treatment groups A to F): • Two additional open-label Plasmin treatment groups were added: G and H. • Thirty subjects were randomized into treatment groups G and H at a 1:1 ratio without stratification by age. • There was no restriction on number of subjects with native artery. • Plasmin treatment group G: No pulsing, 5-hour continuous infusion at 60 mL/hour • Plasmin treatment group H: No pulsing, 2-hour continuous infusion at 75 mL/hour Infusion Catheter Procedures • For treatment groups G and H, the position of the catheter within the thrombus was based on the alignment of the proximal radiopaque marker with the proximal margin of the clot. • There was no pulsing of Plasmin and no reposition of the infusion catheter during the infusion. - DMC The DMC remained active during the course of the entire study. - Sponsor Name Change Talecris Biotherapeutics, Inc., became a subsidiary of Grifols Inc. as the result of the acquisition of Talecris Biotherapeutics Holding Company by Grifols S.A.

11 June 2012	Study Design Added 30 subjects and 2 additional Plasmin treatment groups to evaluate new treatment regimens for consideration of future studies. There was no change in the Plasmin dose. The 2 new treatment groups employed the Balloon Occlusion Catheter (BOC) for the duration of Plasmin administration (5 hours or 2 hours). Enrollment of 30 additional subjects (approximately) after completion of approximately 130 subjects in treatment groups A to H: • Two additional open-label Plasmin treatment groups were added: I and J. • Thirty subjects were randomized into treatment groups I and J at a 1:1 ratio without stratification by age. • There was no restriction on number of subjects with a native artery occlusion. • Plasmin treatment group I: No pulsing, 5-hour continuous infusion with BOC at 30 mL/hour • Plasmin treatment group J: No pulsing, 2-Hour continuous infusion with at 35 mL/hour Infusion Catheter Procedures • For treatment groups I and J, the position of the catheter within the thrombus was based on the need to position the BOC at the distal margin of the clot. • There was no pulsing of Plasmin and no repositioning of the infusion catheter during the infusion.
24 June 2013	Three additional open-label Plasmin treatment groups were planned to evaluate the effects of the increased dose of Plasmin from 150 to 250 mg. Two of these treatment groups (K and L) were planned to evaluate effects of 250 mg Plasmin for 5 or 15 h. One treatment group (M) employed the Balloon occlusion catheter (BOC) for the duration of Plasmin administration (5 h). The intention was to evenly distribute the subjects across the 3 treatment groups. However, if a treatment group was not implemented, the remaining subjects could be re-allocated to the remaining treatment groups. Enrollment of approximately 45 additional subjects after completion of approximately 160 subjects in Groups A to J: Three additional open-label 250 mg Plasmin treatment groups were added: K, L, and M. Subjects in treatment groups K or L were planned to be randomized in a 1:1 with stratification by occluded lower extremity blood vessel type (native artery versus graft). Plasmin treatment group K: 250 mg Plasmin, no pulsing, 5-h continuous infusion at 30 mL/h Plasmin treatment group L: 250 mg Plasmin, no pulsing, 15-h continuous infusion at 30 mL/h Plasmin treatment group M: 250 mg Plasmin, unblinded, no pulsing, 5-hour continuous infusion with BOC at 30 mL/h -Infusion Catheter Procedures Treatment groups K and L: the position of the catheter within the thrombus was planned to be based on the alignment of the proximal radiopaque marker with the proximal margin of the clot. Treatment group M: the position of the catheter within the thrombus was based on the need to position the BOC at the distal margin of the clot. There was no pulsing of Plasmin and no reposition of the infusion catheter during the infusion for these treatment arms. Prior to subject enrollment, treatment groups K and L were not implemented; 6 subjects enrolled into treatment group M only. Treatment groups K and L were planned to be implemented only if treatment group M showed an improvement in thrombolytic activity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported