Clinical trial results:
A RANDOMISED, MULTICENTRE, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY ON THE EFFICACY AND SAFETY OF A THERAPEUTIC STRATEGY OF POST PARTUM HAEMORRHAGE COMPARING EARLY ADMINISTRATION OF HUMAN FIBRINOGEN VERSUS PLACEBO IN PATIENTS TREATED WITH INTRAVENOUS PROSTAGLANDINS FOLLOWING VAGINAL DELIVERY.

Summary

EudraCT number	2013-002484-26
Trial protocol	FR
Global end of trial date	06 August 2018

Results information

Result version number	v1 (current)
This version publication date	18 June 2020
First version publication date	18 June 2020

Trial information

Trial identification

Sponsor protocol code	FIDEL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02155725
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LFB Biomédicaments
Sponsor organisation address	3, Avenue des tropiques, LES ULIS, France, 91940
Public contact	Medical Director france, LFB Biomédicaments, 33 169827229, zitounis@lfb.fr
Scientific contact	Medical Director france, LFB Biomédicaments, 33 169827229, zitounis@lfb.fr

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	20 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 August 2018
Global end of trial reached?	Yes
Global end of trial date	06 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the benefits of a therapeutic strategy that associates an early administration of human fibrinogen concentrate in the management of PPH on the reduction of bleeding after the initiation of prostaglandins intravenous infusion.

Protection of trial subjects:

This study was conducted in compliance with good clinical practice (GCP) as described in the International Conference on Harmonisation (ICH) document "Guidance for Industry-E6 Good Clinical Practice: Consolidated Guidance". These practices were consistent with the principles stated in the Declaration of Helsinki. All other applicable regulations were followed.
Due to the context of emergency, consent was obtained after a concise information from the patient or a member of her family or a reliable person, depending on the patient's level of consciousness. In all cases, as soon as the patient regained competence, she received full information about the study and a post-inclusion consent to continue the study was requested.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 April 2014
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	France: 448
Worldwide total number of subjects	448
EEA total number of subjects	448

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)	448
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 10 April 2014 and 20 June 2018, 448 patients from 30 sites signed an informed consent.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	448
Number of subjects completed	437

Pre-assignment subject non-completion reasons

Reason: Number of subjects	treated with another IMP: 1
Reason: Number of subjects	not treated: 5
Reason: Number of subjects	no emergency consent signed: 2
Reason: Number of subjects	no post inclusion consent signed: 1
Reason: Number of subjects	refused to continue the study: 2

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Clottafact group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Clottafact
Investigational medicinal product code	
Other name	Fibrinogen concentrate
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fibrinogen: 3g; 2 vials of 1.5g/100 mL, each vial of powder will be reconstituted with 100 mL of sterile water for injection.
Route of administration: IV administration with a flow rate ≤ 20 mL/min

Arm title	Placebo group

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo: 2 vials of 100 mL, each vial of powder will be reconstituted with 100 mL of sterile water for injection.
Route of administration: IV administration with a flow rate ≤ 20 mL/min

Number of subjects in period 1[1]	Clottafact group	Placebo group
Started	224	213
Completed	224	213

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 448 patients from 30 sites signed an informed consent but only 437 patients included after the pre-assigment period.

Period 2

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

Blinding implementation details:

During this follow-up period, no new randomisation for the patients, but the blind is maintained.

Arms

Are arms mutually exclusive?	Yes
Arm title	Clottafact group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Clottafact
Investigational medicinal product code	
Other name	Fibrinogen concentrate
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

No injection during this period.

Arm title	Placebo group

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
No injection during this period

Number of subjects in period 2	Clottafact group	Placebo group
Started	224	213
Completed	207	202
Not completed	17	11
Patient refusal to continue	3	-
Consent withdrawn by subject	-	5
Last visit not done	10	4
Protocol deviation	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Clottafact group
Reporting group description: -	
Reporting group title	Placebo group
Reporting group description: -	

Reporting group values	Clottafact group	Placebo group	Total
Number of subjects	224	213	437
Age categorical Units: Subjects			
Adults (18-64 years)	224	213	437
Age continuous Units: years			
arithmetic mean	30.5	30.3	
standard deviation	± 5.6	± 5.4	-
Gender categorical Units: Subjects			
Female	224	213	437
Male	0	0	0

End points

End points reporting groups

Reporting group title	Clottafact group
Reporting group description: -	
Reporting group title	Placebo group
Reporting group description: -	
Reporting group title	Clottafact group
Reporting group description: -	
Reporting group title	Placebo group
Reporting group description: -	
Subject analysis set title	PP Set Clottafact
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients with no missing data for the primary criterion.	
Subject analysis set title	PP Set Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients with no missing data for the primary criterion.	
Subject analysis set title	ITT Set Clottafact
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients treated with Clottafact.	
Subject analysis set title	ITT Set Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients treated with Placebo.	
Subject analysis set title	FAS Set Clottafact
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients treated with Clottafact of the ITT Set with no missing data for the primary criteria.	
Subject analysis set title	FAS Set Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients treated with Placebo of the ITT Set with no missing data for the primary criteria.	

Primary: Failure rate of PPH management

End point title	Failure rate of PPH management

End point description:

The primary efficacy variable is a binary (Failure versus Success) composite endpoint.
Failure is defined when a patient:
- loses at least 4 g/dL of Hb compared to the reference Hb level ,
AND/OR
- requires the transfusion of at least 2 units of packed RBCs.

End point type	Primary

End point timeframe:

Evaluation of the two criteria that form the primary endpoint within the 48 h following the administration of IMP.

End point values	PP Set Clottafact	PP Set Placebo	FAS Set Clottafact	FAS Set Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	195[1]	193[2]	220[3]	210[4]
Units: number of patients with failure	75	80	88	89

Notes:

[1] - 38,5 % of patients in failure

[2] - 41,5 % of patients in failure

[3] - 40,0 % of patients in failure

[4] - 42,4 % of patients in failure

Statistical analyses

Statistical analysis title	Failure rate

Statistical analysis description:

Logistic regression adjusting for baseline fibrinogen level and centre.

Comparison groups	FAS Set Clottafact v FAS Set Placebo
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9563
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.9889
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6633
upper limit	1.4744

Secondary: Patients with at least administration of 2 units of RBCs

End point title	Patients with at least administration of 2 units of RBCs

End point description:

Considering failure as the fact of requiring at least 2 units of RBCs.

End point type	Secondary

End point timeframe:

from H0 to Day 2

End point values	FAS Set Clottafact	FAS Set Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220[5]	210[6]		
Units: number of patients	51	52		

Notes:

[5] - 23,4 % of patients with administration of at least 2 RBCs.

[6] - 25,0 % of patients with administration of at least 2 RBCs.

Statistical analyses

Statistical analysis title	Failure on the adminidtration of RBCs
Statistical analysis description:	
Failure on individual component of the primary endpoint defined as administration of 2 units of RBCs	
Comparison groups	FAS Set Clottafact v FAS Set Placebo
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9786
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.0064
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6321
upper limit	1.6022

Secondary: Patients with lost of at least 4 g/dL of Hb

End point title	Patients with lost of at least 4 g/dL of Hb
End point description:	
Considering failure as the fact of having lost at least 4 g/dL of Hb.	
End point type	Secondary
End point timeframe:	
From reference value to Day 2	

End point values	FAS Set Clottafact	FAS Set Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220[7]	210[8]		
Units: number of patients	42	41		

Notes:

[7] - 19,1 % of patients with lost of at least 4 g/dL of Hb.

[8] - 19,5 % of patients with lost of at least 4 g/dL of Hb.

Statistical analyses

Statistical analysis title	Failure on the loss of Hb
Statistical analysis description: Failure on individual component of the primary endpoint defined as a loss of at least 4 g/dL of Hb	
Comparison groups	FAS Set Clottafact v FAS Set Placebo
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9474
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.0169
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6177
upper limit	1.6741

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse events are reported from the inclusion to the end of the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Clottafact group
Reporting group description: -	
Reporting group title	Placebo group

Reporting group description: -

Serious adverse events	Clottafact group	Placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 224 (4.46%)	10 / 213 (4.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure ambulatory increased			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood uric acid increased			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aneurysm			

subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 224 (0.45%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
HELLP syndrome			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Postpartum haemorrhage			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retained placenta or membranes			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Broad ligament haematoma			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			

subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haematoma			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine necrosis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine rupture			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute fatty liver of pregnancy			
subjects affected / exposed	0 / 224 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychological trauma			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Amniotic cavity infection			

subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis decidual			
subjects affected / exposed	1 / 224 (0.45%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Clottafact group	Placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	95 / 224 (42.41%)	106 / 213 (49.77%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 224 (1.34%)	6 / 213 (2.82%)	
occurrences (all)	3	6	
Hypotension			
subjects affected / exposed	5 / 224 (2.23%)	4 / 213 (1.88%)	
occurrences (all)	5	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 224 (0.89%)	3 / 213 (1.41%)	
occurrences (all)	3	3	
Headache			

subjects affected / exposed	5 / 224 (2.23%)	7 / 213 (3.29%)	
occurrences (all)	6	8	
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	2 / 224 (0.89%)	5 / 213 (2.35%)	
occurrences (all)	2	5	
Influenza like illness			
subjects affected / exposed	0 / 224 (0.00%)	3 / 213 (1.41%)	
occurrences (all)	0	3	
Oedema peripheral			
subjects affected / exposed	4 / 224 (1.79%)	6 / 213 (2.82%)	
occurrences (all)	4	6	
Pyrexia			
subjects affected / exposed	11 / 224 (4.91%)	12 / 213 (5.63%)	
occurrences (all)	11	12	
Malaise			
subjects affected / exposed	2 / 224 (0.89%)	4 / 213 (1.88%)	
occurrences (all)	2	4	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 224 (1.79%)	1 / 213 (0.47%)	
occurrences (all)	4	1	
Constipation			
subjects affected / exposed	9 / 224 (4.02%)	4 / 213 (1.88%)	
occurrences (all)	9	4	
Haemorrhoids			
subjects affected / exposed	21 / 224 (9.38%)	29 / 213 (13.62%)	
occurrences (all)	21	29	
Nausea			
subjects affected / exposed	0 / 224 (0.00%)	4 / 213 (1.88%)	
occurrences (all)	0	4	
Vomiting			
subjects affected / exposed	1 / 224 (0.45%)	4 / 213 (1.88%)	
occurrences (all)	1	4	
Reproductive system and breast disorders			

Metrorrhagia			
subjects affected / exposed	6 / 224 (2.68%)	3 / 213 (1.41%)	
occurrences (all)	6	3	
Nipple disorder			
subjects affected / exposed	0 / 224 (0.00%)	4 / 213 (1.88%)	
occurrences (all)	0	4	
Oedema genital			
subjects affected / exposed	2 / 224 (0.89%)	5 / 213 (2.35%)	
occurrences (all)	2	5	
Uterine pain			
subjects affected / exposed	4 / 224 (1.79%)	0 / 213 (0.00%)	
occurrences (all)	4	0	
Vulval oedema			
subjects affected / exposed	0 / 224 (0.00%)	4 / 213 (1.88%)	
occurrences (all)	0	4	
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	3 / 224 (1.34%)	0 / 213 (0.00%)	
occurrences (all)	3	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 224 (1.34%)	1 / 213 (0.47%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 224 (1.34%)	4 / 213 (1.88%)	
occurrences (all)	3	4	
Infections and infestations			
Endometritis decidual			
subjects affected / exposed	4 / 224 (1.79%)	5 / 213 (2.35%)	
occurrences (all)	4	5	
Puerperal pyrexia			
subjects affected / exposed	7 / 224 (3.13%)	4 / 213 (1.88%)	
occurrences (all)	7	4	
Urinary tract infection			

subjects affected / exposed occurrences (all)	4 / 224 (1.79%) 4	0 / 213 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2015	In a purpose to facilitate the emergency procedure, the information sheet and the informed consent have been simplified in terms of both content and form, without modifying the meaning and the purpose of the provided information.
21 December 2017	The purpose of this amendment was to update the patient information leaflet (emergency and post-inclusion) according to the new version of the Clottafact SPC .
29 March 2018	The purpose of this amendment is to update the patient information leaflet (emergency and post-inclusion) according to the new version of the Clottafact SPC.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 February 2018	Interruption of inclusions due to IMP shortage	19 March 2018

Notes:

Limitations and caveats

None reported