Clinical trial results:
EFFICACY AND SAFETY STUDY OF FACTANE 200 IU/ml ADMINISTERED BY CONTINUOUS INFUSION IN SEVERE HAEMOPHILIA A PATIENTS DURING MAJOR SURGICAL PROCEDURES

Summary

EudraCT number	2010-023666-46
Trial protocol	PL
Global end of trial date	31 July 2012

Results information

Result version number	v1 (current)
This version publication date	06 January 2017
First version publication date	06 January 2017

Trial information

Trial identification

Sponsor protocol code	F8VR-1006

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LFB Biotechnologies
Sponsor organisation address	3 Avenue des Tropiques, COURTABOEUF, France, 91958
Public contact	Global Clinical Development Leader, LFB Biotechnologies, 33 169825656,
Scientific contact	Global Clinical Development Leader, LFB Biotechnologies, 33 169825656,

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	27 February 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2012
Global end of trial reached?	Yes
Global end of trial date	31 July 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of FACTANE 200 IU/ml administered by continuous infusion for the perioperative and postoperative prophylaxis of bleeding during major surgical procedures in severe haemophilia A patients.

Protection of trial subjects:

LFB has developed a new concentration to improve patient comfort by supplying the product in a smaller volume: FACTANE 200 IU/mL contains approximately 1000 IU of factor VIII in 5 mL of solution. Continuous infusion, through a catheter placed in a vein in the arm, is also advantageous in that it avoids repeat injections and minimises pain and injury in the vein due to many needle punctures. The study was conducted in accordance with the with the principles laid down in the Declaration of Helsinki, the ICH guidelines for Good Clinical Practice (GCP) and all applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

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)	4
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total, four (4) subjects have been enrolled by in single center in Poland (Warsaw) between 12 March 2012 and 28 May 2012

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	4
Number of subjects completed	4

Period 1

Period 1 title	Preoperative pharmacokinetic study
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	FACTANE

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	FACTANE
Investigational medicinal product code	F8VR
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pharmacokinetic study before the surgical procedure:
Single weight-adjusted dose (50 IU/kg) administered by bolus at a rate of 4mL/min

Number of subjects in period 1	FACTANE
Started	4
Completed	4

Period 2

Period 2 title	Surgery by continuous infusion
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	FACTANE

Arm description: -

Arm type	Experimental
Investigational medicinal product name	FACTANE
Investigational medicinal product code	F8VR
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

- Preoperative loading dose administered by IV bolus at a rate of 4 mL/min. The loading dose was to be administered to reach circulating FVIII levels between 80 and 120 IU/dL according to the following formula:

Loading dose (IU) = patient's weight (kg) × desired level (IU/dL) × 1 / patient's incremental recovery at T15 min ([IU/dL]/[IU/kg]).

- Continuous infusion dose immediately after bolus injection: H0 (D0). The infusion rate was calculated based on the patient's clearance and the desired FVIII level as follows:

Infusion rate (IU/kg/h) = clearance (mL/h/kg) × desired FVIII level (IU/mL).

The desired FVIII levels were to be: 80 to 120 IU/dL from D0 to D6 and 30 to 80 IU/dL from D7 to the end of the continuous infusion (Dn).

Number of subjects in period 2	FACTANE
Started	4
Completed	4

Period 3

Period 3 title	Follow-up period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	FACTANE
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Factor 8
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

after continuous infusion, the patient had to be treated with his usual factor VIII concentrate.

Number of subjects in period 3	FACTANE
Started	4
Completed	4

Baseline characteristics

Reporting groups

Reporting group title	Preoperative pharmacokinetic study

Reporting group description: -

Reporting group values	Preoperative pharmacokinetic study	Total	
Number of subjects	4	4	
Age categorical Units: Subjects			
Adults (18-64 years)	4	4	
Age continuous Units: years			
median	39		
full range (min-max)	37 to 43	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	4	4	

Subject analysis sets

Subject analysis set title	TTS
Subject analysis set type	Full analysis

Subject analysis set description:
Total Treated Set

Reporting group values	TTS		
Number of subjects	4		
Age categorical Units: Subjects			
Adults (18-64 years)	4		
Age continuous Units: years			
median	39		
full range (min-max)	37 to 43		
Gender categorical Units: Subjects			
Female	0		
Male	4		

End points

End points reporting groups

Reporting group title	FACTANE
Reporting group description: -	
Reporting group title	FACTANE
Reporting group description: -	
Reporting group title	FACTANE
Reporting group description: -	
Subject analysis set title	TTS
Subject analysis set type	Full analysis
Subject analysis set description:	
Total Treated Set	

Primary: Hemostatic efficacy

End point title	Hemostatic efficacy[1]

End point description:

Efficacy was assessed based on the number of 'responder' patients. A patient was considered as a 'responder' if he obtained an 'excellent' or 'good' score in 3 successive haemostasis assessments:
• 6 hours after the start of the surgery (by the surgeon),
• on the day of drain tube removal (or on D2 if there was no drain) (by the surgeon),
• on D7 (by the Investigator).

Haemostasis was evaluated using the following scale: 'excellent', 'good', 'moderate', 'none'.
- 'excellent': haemostasis similar to that of a non-bleeding disorder patient during the same surgery
- 'good': slight oozing at surgical incision,
- 'moderate': mild, but controlled bleeding,
- 'none': severe, uncontrolled bleeding.

End point type	Primary

End point timeframe:

Haemostatic efficacy was rated at 3 time-points after start of surgery (D0): H6, day of drain removal, D7

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: Descriptive analysis

End point values	TTS			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: number of 'responder' patients				
excellent/good	4			
moderate/none	0			

Statistical analyses

No statistical analyses for this end point

Secondary: patient with inhibitor

End point title	patient with inhibitor

End point description:

End point type	Secondary

End point timeframe:
during the study

End point values	TTS			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: number	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Total treated Set

Reporting group description: -

Serious adverse events	Total treated Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
postoperative anaemia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
circulatory collapse			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Total treated Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Injury, poisoning and procedural complications			

Anaemia postoperative	Additional description: Not related		
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	3		
Vascular disorders			
Haematoma	Additional description: Note related		
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Catheter site inflammation	Additional description: Not related		
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	4		
Pyrexia	Additional description: Not related		
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Haemarthrosis	Additional description: Note related		
subjects affected / exposed	4 / 4 (100.00%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported