Clinical trial results:
A Double-Blind, Randomized, Crossover Study of the Recovery of FACTANE 100 versus 200 IU/ml followed by an Open-Label Safety Study of FACTANE 200 IU/ml in Previously Treated Patients With Severe (FVIII: C<1%) Haemophilia A

Summary

EudraCT number	2009-013227-28
Trial protocol	FR
Global end of trial date	25 November 2010

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-0624

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	30 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 November 2010
Global end of trial reached?	Yes
Global end of trial date	25 November 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Recovery Study Part
The primary objective of this clinical research part is to compare the recovery of FACTANE 200 IU/ml with FACTANE 100 IU/ml, when given as a 4 ml/minute intravenous bolus injection.
Safety Study Part
The primary objective of this clinical research part is to assess the safety of FACTANE 200 IU/ml for at least 9 injections or 3 months whichever is sooner during standard-of-care treatment (on-demand, prophylaxis).

Protection of trial subjects:

Precautions taken to minimise inconveniencies and potential pain for patients during the recovery study part:
- The patient is managed by his usual medical team.
- The injections are performed by the nursing staff of the haemophilia treatment centre experienced in the management of haemophilia.
- The number of blood samples is restricted to six (before and after each IMP injection during the 3 visits for the recovery tests).

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 January 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	12
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

13 patients with severe haemophilia A patients (FVIII <1 IU/dl (%)) were included between 12/01/2010 and 25/11/2010 in France.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	12[1]
Number of subjects completed	12

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: 12 subjects included in the recovery study part.
13 subjects included in the safety period.

Period 1

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

Blinding implementation details:

Randomisation by complete block was used to assign patients to one of the two sequences: FACTANE 100 IU/ml - FACTANE 200 IU/ml and FACTANE 200 IU/ml - FACTANE 100 IU/ml. The number of patients in each block was balanced.

Arms

Arm title	FACTANE 100 or 200 IU/ml

Arm description:

Patients received FACTANE 100 IU/ml then FACTANE 200 IU/ml during a crossover study with active experimental product

Arm type	Active comparator
Investigational medicinal product name	FACTANE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

PK cohort included a randomized, blinded dual crossover design, in which subjects received a single dose each of FACTANE 100 IU/ml (25-50 IU/kg) and FACTANE 200 IU/ml (25-50 IU/kg) in random order (3-day washout)

Number of subjects in period 1[2]	FACTANE 100 or 200 IU/ml
Started	12
Completed	12

Notes:

[2] - 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: 12 subjects included in the recovery study part.
13 subjects included in the safety period.

Period 2

Period 2 title	Safety assessment period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	FACTANE 200 IU/ml

Arm description:

Safety study part all patients received FACTANE 200 IU/ml

Arm type	Experimental
Investigational medicinal product name	FACTANE 200 IU/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

FACTANE 200 IU/ml: dose varied by subject and therapeutic situation

Number of subjects in period 2	FACTANE 200 IU/ml
Started	12
Completed	13

Joined	1
no recovery period	1

Baseline characteristics

Reporting groups

Reporting group title	Recovery Study

Reporting group description: -

Reporting group values	Recovery Study	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
Adults (18-64 years)	12	12	
From 65-84 years	0	0	
Age continuous Units: years			
median	28.7		
full range (min-max)	22.2 to 60.8	-	
Gender categorical Units: Subjects			
Male	12	12	

Subject analysis sets

Subject analysis set title	Efficacy population
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects included in the Efficacy population (Per Protocol Population) who received FACTANE 100 UI/ml and FACTANE 200 UI/ml in crossover study.

Subject analysis set title	Safety population (TTS)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the safety population TTS (Total treated Set)

Reporting group values	Efficacy population	Safety population (TTS)	
Number of subjects	12	13	
Age categorical Units: Subjects			
Adults (18-64 years)	12	12	
From 65-84 years	0	1	
Age continuous Units: years			
median	28.7	29	
full range (min-max)	22.2 to 60.8	22.2 to 72.7	
Gender categorical Units: Subjects			
Male	12	13	

End points

End points reporting groups

Reporting group title	FACTANE 100 or 200 IU/ml
Reporting group description:	
Patients received FACTANE 100 IU/ml then FACTANE 200 IU/ml during a crossover study with active experimental product	
Reporting group title	FACTANE 200 IU/ml
Reporting group description:	
Safety study part all patients received FACTANE 200 IU/ml	
Subject analysis set title	Efficacy population
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects included in the Efficacy population (Per Protocol Population) who received FACTANE 100 UI/ml and FACTANE 200 UI/ml in crossover study.	
Subject analysis set title	Safety population (TTS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects in the safety population TTS (Total treated Set)	

Primary: FVIII incremental recovery

End point title	FVIII incremental recovery[1]
End point description:	
The primary endpoint of the 'Recovery Study' part was determination of the equivalence of the test drug (FACTANE 200 IU/ml) and the reference drug (FACTANE 100 IU/ml) evaluated using the concentration at 15 minutes post injection (CT15) normalised by the dose injected (expressed by IU/kg or incremental recovery	
End point type	Primary
End point timeframe:	
FVIII recovery for FVIII activity measured by one-stage clotting assay.	

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	Efficacy population			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: %/IU/kg				
median (full range (min-max))				
FACTANE 100 IU/ml	2.24 (1.76 to 2.89)			
FACTANE 200 IU/ml	2.21 (1.66 to 2.88)			

Statistical analyses

No statistical analyses for this end point

Primary: Long term tolerance of FACTANE 200 IU/ml (investigator's assessment

scale)

End point title	Long term tolerance of FACTANE 200 IU/ml (investigator's assessment scale)[2]

End point description:

Investigator's assessment of the global safety of FACTANE 200IU/ml according to the same scale: "very good/good", "satisfactory/unsatisfactory".

End point type	Primary

End point timeframe:

The primary objective of the safety part was to assess the long-term tolerance of FACTANE 200 IU/ml, when administered for at least 9 injections or 3 months whichever is sooner.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analysis

End point values	Safety population (TTS)			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: percentage				
very good /good	100			
satisfactory / unsatisfactory	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study, during part I (recovery study) and part II (safety study).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

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	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	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	3 / 13 (23.08%)		
Nervous system disorders			
Headache	Additional description: not related with the IMP.		
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	3		
Gastrointestinal disorders			
Dysgeusia	Additional description: possible relationship with the use of IMP (either FACTANE 100 IU/ml or FACTANE 200IU/ml)		
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 February 2010	The main objectives of this amendment are the following: - to extend the inclusion period, - to specify the changes of the Clinical Project Manager, - to homogenize information regarding the number of patients, - to describe the procedure for the management of non evaluable data (recovery part)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported