Clinical trial results:
A Prospective, Multicenter, Open Enrollment Study of Human Plasma-Derived Factor XIII Concentrate in Subjects With Congenital Factor XIII Deficiency

Summary

EudraCT number	2014-003764-20
Trial protocol	Outside EU/EEA
Global end of trial date	22 August 2011

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	BI71023_3002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00945906
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring LLC
Sponsor organisation address	1020 First Avenue, King of Prussia, United States, 19406-0901
Public contact	Clinical Trial Disclosure Manager, CSL Behring, clinicaltrials@cslbehring.com
Scientific contact	Clinical Trial Disclosure Manager, CSL Behring, clinicaltrials@cslbehring.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 December 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of the study are to provide FXIII Concentrate (Human) to patients in the United States until the product becomes commercially available in the United States as well as to collect additional long-term safety data in this population.

Protection of trial subjects:

This study was carried out in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice guidelines, and standard operating procedures for clinical research and development at CSL Behring (CSLB).
The study protocol and all amendments were approved by the Independent Ethics Committee(s) (IECs) / Institutional Review Board(s) (IRBs) of the participating centers.
Before undergoing screening procedures for possible enrollment into the study, subjects were informed, in an understandable form, about the nature, scope, and possible consequences of the study. The investigator was responsible for obtaining a subject's written informed consent to participate in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2009
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	United States: 61
Worldwide total number of subjects	61
EEA total number of subjects	0

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)	4
Children (2-11 years)	15

Adolescents (12-17 years)	15
Adults (18-64 years)	27
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who were enrolled in pharmacokinetic (PK) Study BI71023_2002 or Phase 3b Study B171023_3001 were offered enrollment in this study. Enrollment was also offered to subjects who were enrolled in a clinical study conducted under BB-IND 5986 or not currently participating in any other study.

Pre-assignment

Screening details:

Eligible subjects were males or females of any age with documented congenital Factor XIII deficiency that required prophylactic treatment with a Factor XIII-containing product.
Sixty-one subjects were screened, enrolled, and received at least 1 dose of Factor XIII Concentrate (Human) in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Factor XIII

Arm description:

Subjects were administered FXIII Concentrate (Human) by intravenous (IV) infusion approximately every 28 days to maintain a trough FXIII level of approximately 5 to 20%.

Arm type	Experimental
Investigational medicinal product name	Factor XIII Concentrate (Human)
Investigational medicinal product code	BI71023
Other name	Cluvot, Fibrogammin®, Corifact®
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects who did not complete PK Study BI71023_2002 or receive at least 3 doses of the investigational medicinal product in the Phase 3b Study BI71023_3001 received Factor XIII Concentrate (Human) at a dose of 40 U/kg by intravenous infusion. Subjects who were enrolled in a clinical study conducted under BB-IND 5986 received Factor XIII Concentrate at a dose of 40 U/kg by intravenous infusion. For all other subjects and all doses after Baseline (Day 0), the dose was guided by the individual subject's most recent (pre-infusion) trough Factor XIII activity levels, with the objective of dosing every 28 days (4 weeks) to maintain a trough Factor XIII activity level of approximately 5 to 20%.

Number of subjects in period 1	Factor XIII
Started	61
Completed	54
Not completed	7
Consent withdrawn by subject	1
'Did not want to return for last visit '	2
Moved to another country	2
Unable to return for last visit	2

Baseline characteristics

Reporting groups	
Reporting group title	Factor XIII
Reporting group description:	
Subjects were administered FXIII Concentrate (Human) by intravenous (IV) infusion approximately every 28 days to maintain a trough FXIII level of approximately 5 to 20%.	

Reporting group values	Factor XIII	Total	
Number of subjects	61	61	
Age categorical Units: Subjects			
< 16 years	29	29	
16 to <65 years	32	32	
>= 65 years	0	0	
Age continuous Units: years			
arithmetic mean	18.5		
standard deviation	± 12.48	-	
Gender categorical Units: Subjects			
Female	26	26	
Male	35	35	

End points

End points reporting groups

Reporting group title	Factor XIII

Reporting group description:

Subjects were administered FXIII Concentrate (Human) by intravenous (IV) infusion approximately every 28 days to maintain a trough FXIII level of approximately 5 to 20%.

Primary: Adverse Events

End point title	Adverse Events[1]

End point description:

Number of subjects with any treatment-emergent adverse event (AE), treatment-related AE or serious AE (SAE). Treatment-related AEs are defined as AEs whose relationship to treatment is related, or possibly related and AEs with missing relationship.

End point type	Primary

End point timeframe:

After the first infusion until study completion. Study completion is up to 2 years or until Factor XIII Concentrate (Human) is commercially available in the USA.

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: Statistical analyses were not performed in this study.

End point values	Factor XIII			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: subjects				
Any treatment-emergent AE	42			
Treatment-emergent and related AE	2			
Serious AE	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology and Chemistry Testing

End point title	Hematology and Chemistry Testing

End point description:

Number of participants with treatment-emergent clinically significant hematology and/or chemistry laboratory parameter values.

End point type	Secondary

End point timeframe:

After the first infusion and at the end-of-study (or withdrawal) visit.

End point values	Factor XIII			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: subjects				
Clinically significant hematology test result	1			
Clinically significant chemistry test result	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Factor XIII Antibody Testing

End point title	Factor XIII Antibody Testing

End point description:

Number of participants with serum Factor XIII antibodies.

End point type	Secondary

End point timeframe:

Before the first infusion, then every 48 weeks, at the end-of-study (or withdrawal) visit and after a bleeding episode requiring treatment with a Factor XIII -containing product.

End point values	Factor XIII			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: subjects				
Subjects with Factor XIII antibodies	1			
Subjects without Factor XIII antibodies	60			

Statistical analyses

No statistical analyses for this end point

Secondary: Factor XIII Concentration

End point title	Factor XIII Concentration

End point description:

Trough Factor XIII concentration.

End point type	Secondary

End point timeframe:

Before the first infusion, at 24 and 48 weeks after the first infusion, and at the end-of-study (or withdrawal) visit.

End point values	Factor XIII			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: IU/mL				
arithmetic mean (standard deviation)				
Baseline (n=35)	0.0987 (± 0.03695)			
Week 4 (n = 28)	0.1177 (± 0.03484)			
Week 8 (n = 8)	0.1238 (± 0.02973)			
Week 12 (n = 8)	0.1075 (± 0.03196)			
Week 16 (n = 4)	0.1025 (± 0.04573)			
Week 20 (n = 5)	0.116 (± 0.03578)			
Week 24 (n = 41)	0.1341 (± 0.03346)			
Week 28 (n = 3)	0.1667 (± 0.06658)			
Week 32 (n = 2)	0.095 (± 0.02121)			
Week 36 (n = 3)	0.1083 (± 0.07489)			
Week 40 (n = 3)	0.0933 (± 0.04509)			
Week 44 (n = 1)	0.05 (± 0)			
Week 48 (n = 13)	0.1246 (± 0.02961)			
Week 72 (n = 2)	0.14 (± 0.01414)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With at Least One Bleeding Episode

End point title	Number of Subjects With at Least One Bleeding Episode

End point description:

Number of subjects with at least one bleeding episode at any time after the first infusion in the study, and the number of subjects with at least one bleeding episode requiring Factor XIII treatment.

End point type	Secondary

End point timeframe:

After the first infusion until study completion. Study completion is up to 2 years or until Factor XIII Concentrate (Human) is commercially available in the USA.

End point values	Factor XIII			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: subjects				
At least one bleeding episode (after treatment)	10			
At least one bleeding episode requiring treatment	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of Bleeding Episodes

End point title	Total Number of Bleeding Episodes

End point description:

Number of bleeding episodes at any time after the first infusion in the study.

End point type	Secondary

End point timeframe:

After the first infusion until study completion. Study completion is up to 2 years or until Factor XIII Concentrate (Human) is commercially available in the USA.

End point values	Factor XIII			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Bleeding episodes	14			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the first infusion until study completion. Study completion is up to 2 years or until Factor XIII Concentrate (Human) is commercially available in the USA.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Factor XIII

Reporting group description:

Subjects were administered FXIII Concentrate (Human) by intravenous (IV) infusion approximately every 28 days to maintain a trough FXIII level of approximately 5 to 20%.

Serious adverse events	Factor XIII		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 61 (3.28%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Factor XIII inhibition			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pelvic inflammatory disease			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Factor XIII		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 61 (31.15%)		
Injury, poisoning and procedural complications			
Bruising			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	5		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	6 / 61 (9.84%)		
occurrences (all)	7		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 61 (8.20%)		
occurrences (all)	5		
Infections and infestations			
Upper respiratory infection			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	5		

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