Clinical trial results:
A Phase 3b Trial Investigating the Pharmacokinetics and Safety Profile of a Single Intravenous Dose of rFXIII in Paediatric (1 to less than 6 Years Old) Subjects with Congenital FXIII A-subunit Deficiency

Summary

EudraCT number	2009-016869-28
Trial protocol	GB
Global end of trial date	06 January 2012

Results information

Result version number	v1 (current)
This version publication date	15 March 2016
First version publication date	24 July 2015

Trial information

Trial identification

Sponsor protocol code	F13CD-3760 (mentor™4)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01230021
WHO universal trial number (UTN)	U1111-1116-2533

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	NOVO ALLE, Bagsvaerd, Denmark, 2880
Public contact	Global Clinical Registry, Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Global Clinical Registry, Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000185-PIP01-08
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	14 May 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 January 2012
Global end of trial reached?	Yes
Global end of trial date	06 January 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterise the pharmacokinetics of rFXIII in paediatric subjects (1 to less than 6 years old) with congenital FXIII A-subunit deficiency following a single intravenous dose administration by measuring the area under the concentration vs. time curve (AUC0-30 Days) (IU×h/mL)

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki and ICH Good Clinical Practice.

Background therapy:

Monthly prophylactic treatment with a FXIII containing product (Fibrogammin®P/Corifact®) prior to inclusion in the trial

Evidence for comparator:

Not applicable

Actual start date of recruitment	09 November 2010
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 Kingdom: 3
Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	Israel: 1
Worldwide total number of subjects	6
EEA total number of subjects	3

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)	1
Children (2-11 years)	5
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Three countries were included in this trial−Israel(1 site), United Kingdom(2 sites) and the United States (2 sites).

Pre-assignment

Screening details:

Between screening and treatment with trial drug the children were assessed for eligibility. If eligible, the children were treated with one single dose of FXIII. The trial was not randomised.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not Applicable

Arms

Arm title	Recombinant factor XIII

Arm description:

One single dose of 35 IU/kg rFXIII was administered as an intravenous (i.v.) injection to each child. The trial included one screening visit, one treatment visit (including pharmacokinetics (PK) assessments up to 24 hours) and 4 follow-up visits (at 7, 14, 21 and 30 days after dosing). Blood samples for PK assessments were drawn pre-dose and up to 30 days after dosing.

Arm type	Experimental
Investigational medicinal product name	Recombinant Factor XIII (rFXIII)
Investigational medicinal product code	NN1841
Other name	Recombinant Factor XIII (rFXIII)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous injection of a single dose of recombinant factor XIII, 35 IU/kg bodyweight. The reconstituted and diluted rFXIII was given as a slow i.v. injection at a rate not exceeding 1−2 mL/min.

Number of subjects in period 1	Recombinant factor XIII
Started	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall period
Reporting group description:	
One single dose of 35 IU/kg rFXIII was administered as an intravenous (i.v.) injection to each child. The trial included one screening visit, one treatment visit (including pharmacokinetics (PK) assessments up to 24 hours) and 4 follow-up visits (at 7, 14, 21 and 30 days after dosing). Blood samples for PK assessments were drawn pre-dose and up to 30 days after dosing	

Reporting group values	Overall period	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	1	1	
Children (2-11 years)	5	5	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	2.67		
standard deviation	± 1.03	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	3	3	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	6	6	
Unknown or not reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Native Hawaiian or other Pacific Islander	0	0	
Black or African American	1	1	
White	2	2	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Recombinant factor XIII

Reporting group description:

One single dose of 35 IU/kg rFXIII was administered as an intravenous (i.v.) injection to each child. The trial included one screening visit, one treatment visit (including pharmacokinetics (PK) assessments up to 24 hours) and 4 follow-up visits (at 7, 14, 21 and 30 days after dosing). Blood samples for PK assessments were drawn pre-dose and up to 30 days after dosing.

Primary: Area Under the Concentration vs. Time Curve (AUC)

End point title	Area Under the Concentration vs. Time Curve (AUC)[1]

End point description:

A measure of the exposure. Blood samples for the PK assessment were drawn pre-dose and up to 30 days after dosing. The PK of FXIII in children was assessed after a single i.v. dose of rFXIII 35 IU/kg.

End point type	Primary

End point timeframe:

At pre-dose, 30 minutes, 24 hours, 7, 14, 21 and 30 days after dosing

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: There were no statistical analysis for this endpoint.The evaluation of the endpoint was descriptive through summary and listings.

End point values	Recombinant factor XIII			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: IU*h/mL				
arithmetic mean (standard deviation)	250.25 (± 31.19)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected and reported during the entire trial period; that is from day 0 (the treatment day) to day 30 (last follow-up visit).

Adverse event reporting additional description:

Safety analysis population including all 6 children exposed to FXIII. All 6 children were exposed to one dose of trial product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Recombinant Factor XIII

Reporting group description:

One single dose of 35 IU/kg rFXIII was administered as an intravenous (i.v.) injection to each child. The trial included one screening visit, one treatment visit (including pharmacokinetics (PK) assessments up to 24 hours) and 4 follow-up visits (at 7, 14, 21 and 30 days after dosing). Blood samples for PK assessments were drawn pre-dose and up to 30 days after dosing

Serious adverse events	Recombinant Factor XIII		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (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	Recombinant Factor XIII		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain in extremity			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2011	In this substantial protocol amendment: The title of the trial has been changed to include the name MentorTM 4. The name MentorTM 4 has been assigned to the trial to enhance recollection of the trial by accompanying the trial impact number with a name reference. In addition, a word mark will be placed on the front page.The protocol specifies a number of laboratory parameters to be assessed during the trial. The local laboratories for this trial operate according to standard operating procedures for each type of laboratory assessment. As a result of these standard procedures the local laboratories may provide analyses not requested in the protocol but produced in connection with the requested analyses. Such data will not be transferred to the trial database, but may be reported to the investigator according to specifications in the laboratory standard operating procedures and requirements. The investigator must review all laboratory results for concomitant illnesses and adverse events and report these according to the protocol. Consequently this discrepancy compromises neither subject safety, nor the safety reporting in the trial. This amendment will allow for these additional analyses to be reported to the investigator by the local laboratories. The text in Appendix C (Whole blood volume rule) regarding prioritization of blood samples has been deleted as this text is only applicable for the NN1841-3835 trial (safety extension trial to F13CD-3760) where pre- and post-dose blood samples are taken.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/23834599