Clinical trial results:
A Post Authorization Safety Surveillance Study of Xyntha in Usual Care Settings

Summary

EudraCT number	2008-002456-24
Trial protocol	Outside EU/EEA
Global end of trial date	22 August 2011

Results information

Result version number	v1 (current)
This version publication date	30 May 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	3082B2-4418

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00765726
WHO universal trial number (UTN)	-
Other trial identifiers	alias: B1831003

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc. , 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc. , 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	15 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?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate factor VIII (FVIII) inhibitor development, defined as an inhibitor titer of greater than or equal to (>=)0.6 Bethesda units (BU) using the Nijmegen modification of the Bethesda assay and confirmed by the central laboratory, in subjects treated with Xyntha in usual use.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 February 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: 7
Country: Number of subjects enrolled	New Zealand: 5
Worldwide total number of subjects	12
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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	3
Adults (18-64 years)	9
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total number of subjects screened were 14, out of which 12 were enrolled in the study. The study was conducted in New Zealand and United States which started on 12 Feb 2009 and study was terminated by sponsor because the sponsor had ongoing studies collecting similar safety data.

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	Xyntha

Arm description:

Xyntha [moroctocog alfa albumin free cell culture (AF-CC)] administered intravenously (IV) at a dose and frequency prescribed by the treating physician as per local standard of care for up to 2 years.

Arm type	Experimental
Investigational medicinal product name	Xyntha
Investigational medicinal product code	
Other name	Moroctocog alfa albumin free cell culture (AF-CC)
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Xyntha administered IV at a dose and frequency prescribed by the treating physician as per local standard of care for up to 2 years.

Number of subjects in period 1	Xyntha
Started	12
Completed	3
Not completed	9
Consent withdrawn by subject	1
Discontinuation of study by sponsor	8

Baseline characteristics

Reporting groups	
Reporting group title	Xyntha

Reporting group description:

Xyntha [moroctocog alfa albumin free cell culture (AF-CC)] administered intravenously (IV) at a dose and frequency prescribed by the treating physician as per local standard of care for up to 2 years.

Reporting group values	Xyntha	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	30		
standard deviation	± 13.6	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	12	12	

End points

End points reporting groups

Reporting group title	Xyntha

Reporting group description:

Xyntha [moroctocog alfa albumin free cell culture (AF-CC)] administered intravenously (IV) at a dose and frequency prescribed by the treating physician as per local standard of care for up to 2 years.

Primary: Percentage of Subjects With Factor VIII (FVIII) Inhibitor Development

End point title	Percentage of Subjects With Factor VIII (FVIII) Inhibitor Development[1]

End point description:

FVIII inhibitor development was defined as an inhibitor titer of more than or equal to 0.6 Bethesda Units (BU) using the Nijmegen modification of the Bethesda assay and confirmed by the central laboratory. Safety analysis population included all enrolled subjects who had taken at least 1 dose of the study medication.

End point type	Primary

End point timeframe:

Month 24 or early withdrawal

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: Only descriptive data was planned to be reported for this endpoint.

End point values	Xyntha			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: subjects				
number (confidence interval 95%)	0 (0 to 0.27)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 30 days after last dose of study drug.

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as nonserious in another, or 1 subject may have experienced both serious, nonserious event during study. EU BR specific AE tables were generated separately as per EU format using latest coding.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Xyntha

Reporting group description:

Xyntha [moroctocog alfa albumin free cell culture (AF-CC)] administered intravenously (IV) at a dose and frequency prescribed by the treating physician as per local standard of care for up to 2 years.

Serious adverse events	Xyntha		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Drug effect incomplete			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Tooth impacted			
subjects affected / exposed	1 / 12 (8.33%)		
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	Xyntha		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 12 (75.00%)		
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Varicose vein			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Painful erection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Corneal abrasion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Head injury			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Incision site hypoaesthesia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Procedural pain			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Stress fracture			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Tooth fracture			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Fanconi syndrome			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nausea			

subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Tongue discolouration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Toothache			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Dermatitis contact			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	6		
Arthropathy			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		

Haemarthrosis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Osteomalacia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Osteoporosis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Pain in jaw			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Herpes zoster			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 July 2008	1.Immunogenicity section had revisions related to care of subject that developed inhibitor and the type of assay that the inhibitor testing would be done on. 2.Information addition: Investigator to review the infusion log for evaluation of AEs, SAEs and events of special circumstances. 3.Addition of instruction to safety section that the 'Investigator must continue to follow subjects after final study visit with ongoing inhibitors until inhibitor resolved or stabilized, which ever occurred first.' 4. Addition of Visit 7 – Follow up call, 30 days after Study Completion, to ask about how the subject is feeling and concomitant medications. 5. Concomitant medications were revised: -Addition of 'Immune tolerance induction therapy with other Factor VIII products is not acceptable'. -Addition of cyclosporins and anti-TNF agents as immunomodulatory therapy that was not permitted.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was discontinued because the sponsor had ongoing studies collecting similar safety data.

Notes: