



Clinical trial results:

Routine Prophylaxis Treatment Versus On-demand Treatment for Children With Severe Hemophilia A: Comparison of All Bleeding Events in Chinese Hemophilia Patients

Summary

EudraCT number	2014-001362-10
Trial protocol	Outside EU/EEA
Global end of trial date	03 January 2014

Results information

Result version number	v1
This version publication date	12 July 2016
First version publication date	04 April 2015

Trial information

Trial identification

Sponsor protocol code	BAY14-2222/16287
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01810666
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer HealthCare AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com
Scientific contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.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	27 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 January 2014
Global end of trial reached?	Yes
Global end of trial date	03 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the effect of three times a week prophylaxis on all bleeds compared to on-demand treatment in Chinese children with severe hemophilia A.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization (ICH) guideline E6: Good Clinical Practice (GCP).

An informed consent form explaining the procedures of the study including the potential hazards was reviewed and approved by the IEC/IRB before its use. Before entering the study, the informed assent/consent form was read by and explained to all subjects or their legally authorized representative. Each subject/ legally authorized representative had ample opportunity to ask questions and was assured of the right to withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision.

Only after the legal representatives of subjects voluntarily signed the informed consent form and the subject voluntarily signed the informed assent form, if adequate, was he able to enter the study. If the subject was not capable of providing a signature, an oral statement of consent could have been given in the presence of a witness. Each subject or representative received a signed and dated copy of the informed assent/ consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2013
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	China: 30
Worldwide total number of subjects	30
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)	14
Adolescents (12-17 years)	16
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subject recruitment period was between 20-Mar-2013 to 28-Jun-2013.

Pre-assignment

Screening details:

Of 33 participants who were screened for inclusion in the study, 30 were enrolled and received treatment.

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	Rec. factor VIII on-demand followed by prophylaxis
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Arm description:

Participants received Recombinant Factor VIII (Rec. factor VIII) on-demand treatment for 12 weeks followed by a 12 weeks prophylaxis treatment phase. The dose and mode of prophylaxis treatment was 25 IU/Kg, 3 times/per week. The dose in on-demand treatment was decided by physician according to the package insert or the current standard of care.

Arm type	Experimental
Investigational medicinal product name	Recombinant Factor VIII (Kogenate FS, BAY14-2222)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Intravenous use

Dosage and administration details:

Participants received on-demand treatment for 12 weeks followed by a 12 weeks prophylaxis treatment phase. The dose and mode of prophylaxis treatment was 25 IU/Kg, 3 times/per week. The dose in ondemand treatment was decided by physician according to the package insert or the current standard of care.

Number of subjects in period 1	Rec. factor VIII on-demand followed by prophylaxis
Started	30
Completed	30

Baseline characteristics

Reporting groups

Reporting group title	Overall study
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Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	30	30	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	10		
standard deviation	± 3.9	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	30	30	
Race			
Units: Subjects			
Asian	30	30	
Target Joint for Bleeds			
Units: Subjects			
No	8	8	
Yes	22	22	
Number of Target Joint			
Units: Subjects			
None	8	8	
One	16	16	
Two	6	6	
Prior FVIII Treatment			
Units: Subjects			
On Demand	30	30	
Baseline weight			
Units: kg			
arithmetic mean	41.42		
standard deviation	± 19.02	-	
Baseline body mass index			
Units: kg/m2			
arithmetic mean	18.65		
standard deviation	± 4.16	-	
Number of Bleeds in Last 3 Months			
Units: Bleeds			
arithmetic mean	12.4		
standard deviation	± 8.71	-	
Number of Joint Bleeds in Last 3 Months			
Units: Bleeds			

arithmetic mean	8.73		
standard deviation	± 8.07	-	

End points

End points reporting groups

Reporting group title	Rec. factor VIII on-demand followed by prophylaxis
Reporting group description: Participants received Recombinant Factor VIII (Rec. factor VIII) on-demand treatment for 12 weeks followed by a 12 weeks prophylaxis treatment phase. The dose and mode of prophylaxis treatment was 25 IU/Kg, 3 times/per week. The dose in on-demand treatment was decided by physician according to the package insert or the current standard of care.	

Primary: Difference of annualized number of all bleeds between on-demand and prophylaxis period

End point title	Difference of annualized number of all bleeds between on-demand and prophylaxis period ^[1]
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End point description:

Annualized bleedings period 1 minus period 2 ITT analysis set.

End point type	Primary
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End point timeframe:

Week 1-12 (on-demand treatment) and 13-24 (prophylactic treatment)

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: 2-sided Hodges Lehmann estimates for median 95% CI Annualized bleedings period 1 minus period 2 ITT analysis set.

End point values	Rec. factor VIII on-demand followed by prophylaxis			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Bleeds				
median (confidence interval 95%)	56 (48.8 to 62.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Difference of annualized number of joint bleeds between on-demand and prophylaxis period

End point title	Difference of annualized number of joint bleeds between on-demand and prophylaxis period
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End point description:

Annualized joint bleedings period 1 minus period 2 ITT analysis set.

End point type	Secondary
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End point timeframe:

Week 1-12 (on-demand treatment) and 13-24 (prophylactic treatment)

End point values	Rec. factor VIII on-demand followed by prophylaxis			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Bleeds				
median (confidence interval 95%)	37.71 (30.42 to 46.02)			

Statistical analyses

No statistical analyses for this end point

Secondary: Difference of intra-individual change of joint function during each period assessed by the Hemophilia Joint Health Score between on-demand and prophylaxis period

End point title	Difference of intra-individual change of joint function during each period assessed by the Hemophilia Joint Health Score between on-demand and prophylaxis period
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End point description:

Hemophilia Joint Health Score(HJHS) ranges from 0 to 124. Higher values in the HJHS represent worse situation for the subject. 2-sided Hodges Lehmann estimates for median 95% CI HJHS values difference of changes ITT analysis set.

End point type	Secondary
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End point timeframe:

From baseline to Week 12 (on-demand treatment) and Week 24 (prophylactic treatment)

End point values	Rec. factor VIII on-demand followed by prophylaxis			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Scores on scale				
median (confidence interval 95%)	-3 (-5 to 0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first treatment through 3 days after the last dose of study drug, up to 6 months

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Recombinant Factor VIII (Kogenate FS, BAY14-2222)
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Reporting group description: -

Serious adverse events	Recombinant Factor VIII (Kogenate FS, BAY14-2222)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Recombinant Factor VIII (Kogenate FS, BAY14-2222)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2012	Protocol amendment 01, dated 30 JUL 2012 The study design was re- evaluated and several key changes were made to the original protocol, including updates on secondary objectives, population selection criteria, and updates on study procedures.
08 March 2013	Protocol amendment 02, dated 08 MAR 2013 The evaluation of joint function by Physical examination score was excluded via this amendment. According to the original protocol, joint function was to be evaluated by Hemophilia Joint Health Score (HJHS) (for subjects ≥ 4 years) or Physical examination score (if age of the children < 4 years) as used in JOS. However, Physical examination score was not a well validated evaluation tool, and it was confirmed that HJHS could be applied to children under 4 years old. Therefore only HJHS was to be used to evaluate joint function for all subjects in this study. In order to minimize the risk of joint bleeding, injection of Kogenate® FS could be administered before the joint evaluation at the discretion of the investigator as per this protocol amendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported