



Clinical trial results: Efficacy and safety study of vWF SD-35-DH (WILFACTIN) in children under 6 years of age

Summary

EudraCT number	2004-005051-34
Trial protocol	BE
Global end of trial date	05 August 2014

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	22 February 2015

Trial information

Trial identification

Sponsor protocol code	42-73-305
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	WIL1-0305: WIL1-0305

Notes:

Sponsors

Sponsor organisation name	LFB Biotechnologies
Sponsor organisation address	3 Avenue des Tropiques , COURTABOEUF, France, 91930
Public contact	Françoise BRIDEY, LFB Biotechnologies, 33 169827010,
Scientific contact	Françoise BRIDEY, LFB Biotechnologies, 33 169827010,

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	04 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 August 2014
Global end of trial reached?	Yes
Global end of trial date	05 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main objective : to evaluate, in children presenting with inherited von Willebrand factor (VWF) deficiencies, the biological and clinical efficacy of WILFACTIN for the treatment of bleeding episodes and for the prevention of haemorrhages during surgery or invasive procedures when desmopressin is ineffective or contraindicated.

Protection of trial subjects:

Blood sampling usually done for laboratory testing presents a potential discomfort and the associated risks are slight pain at the site, feeling light-headed, bruising and, exceptionally, local infection as well as bleeding from the site of the puncture. However, all precautionary measures will be taken to minimize potential side effects in children.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Tunisia: 4
Worldwide total number of subjects	9
EEA total number of subjects	5

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	2

months)	
Children (2-11 years)	7
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:

9 patients were included at 5 study centers in Belgium, Greece, Poland and Tunisia.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	10 ^[1]
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Number of subjects completed	9
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Pre-assignment subject non-completion reasons

Reason: Number of subjects	selection criteria missing: 1
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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: 1 subject withdrawn after the pre-assignment period (1 selection criteria missing).

Period 1

Period 1 title	Inclusion visit
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Is this the baseline period?	Yes
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Allocation method	Not applicable
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Blinding used	Not blinded
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Arms

Arm title	Wilfactin treatment
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Wilfactin
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Investigational medicinal product code	vWF SD-35-DH
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Other name	
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Pharmaceutical forms	Powder and solvent for solution for infusion
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Routes of administration	Intravenous use
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Dosage and administration details:

No administration at inclusion.

Number of subjects in period 1	Wilfactin treatment
Started	9
Completed	9

Period 2

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

Arms

Arm title	Wilfactin treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Wilfactin
Investigational medicinal product code	vWF SD-35-DH
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 IU/kg by intravenous route

Number of subjects in period 2	Wilfactin treatment
Started	9
Completed	9

Period 3

Period 3 title	Efficacy period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Efficacy
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Wilfactin
Investigational medicinal product code	vWF SD-35-DH
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For surgical procedures and treatment of bleeding episodes

- when the recovery of von Willebrand factor is known: individualized dosing to provide plasma level of 100 % (VWF:RCo) ,
 - when recovery information of von Willebrand factor was not available: 60-100 IU/kg
- The treatment duration depends on the clinical status of the subject and the baseline blood levels of

VWF and factor VIII.

For long-term prophylaxis, 50 IU/kg once per week to 30 IU/kg every other day to minimize spontaneous bleeding episodes.

Number of subjects in period 3	Efficacy
Started	9
Completed	9

Baseline characteristics

Reporting groups

Reporting group title	Inclusion visit
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Reporting group description: -

Reporting group values	Inclusion visit	Total	
Number of subjects	9	9	
Age categorical			
Units: Subjects			
less than 6 years old	9	9	
Age continuous			
Units: years			
median	2		
full range (min-max)	0 to 5	-	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	5	5	

Subject analysis sets

Subject analysis set title	TTS
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Subject analysis set type	Full analysis
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Subject analysis set description:

Total Treated Set

Reporting group values	TTS		
Number of subjects	9		
Age categorical			
Units: Subjects			
less than 6 years old	9		
Age continuous			
Units: years			
median	2		
full range (min-max)	0 to 5		
Gender categorical			
Units: Subjects			
Female	4		
Male	5		

End points

End points reporting groups

Reporting group title	Wilfactin treatment
Reporting group description: -	
Reporting group title	Wilfactin treatment
Reporting group description: -	
Reporting group title	Efficacy
Reporting group description: -	
Subject analysis set title	TTS
Subject analysis set type	Full analysis
Subject analysis set description:	
Total Treated Set	

Primary: Percentage of Excellent/Good response

End point title	Percentage of Excellent/Good response ^[1]
End point description:	

End point type	Primary
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End point timeframe:

Hemostasis in bleeding episodes and surgical/invasive procedures was evaluated by the investigator at the end of the bleeding episode or course of 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: Descriptive analysis

End point values	Efficacy			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Four-point scale				
Excellent	49			
Good	43			
Moderate	8			
None	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:
throughout the study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.1
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Reporting groups

Reporting group title	Total Treated Set
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Reporting group description: -

Serious adverse events	Total Treated Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eyelid oedema			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hordeolum			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Total Treated Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	6		
Gingival injury			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	6		
Limb injury			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	6		
Traumatic haematoma			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	11		
Mouth injury			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	5		
Surgical and medical procedures			
Hepatitis A immunisation			
subjects affected / exposed	7 / 9 (77.78%)		
occurrences (all)	7		
Infections and infestations			

Bronchitis			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	9		
Dental caries			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	13		
Tonsillitis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 June 2007	To prolong the study recruitment period. To add a recovery study to be performed after 6 months for children with type 3 VWD. To extend the number of centres including the participation of other countries.
12 November 2007	To change the name of the sponsor (LFB BIOTECHNOLOGIES). To prolong the patient recruitment period (+ 6 month) and to add vWF inhibitor information in accordance with the guidelines on clinical investigation of human plasma derived von Willebrand factor products.
12 November 2007	To allow the patient to continue the IMP after 18 months follow-up under the same conditions if the product is registered but not yet commercialized. To specify the 2nd recovery study in the information patient sheet related to amendment n°4. To change the clinical project manager and extend the number of center and countries.
05 September 2008	To prolong the patient recruitment period; To update the procedure for SAE reporting; To add an interim analysis in Q2 2008.
15 March 2011	To prolong the recruitment period; To transfer storage and distribution to a sub-contractor; To clarify criteria for recovery study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported