



Clinical trial results: EFFICACY AND SAFETY STUDY OF vWF SD-35-DH (WILFACTIN) IN PATIENTS UNDER LONG-TERM PROPHYLAXIS

Summary

EudraCT number	2005-001746-17
Trial protocol	BE PL
Global end of trial date	17 July 2012

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	04 July 2015

Trial information

Trial identification

Sponsor protocol code	42-73-406
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LFB Biotechnologies
Sponsor organisation address	3 Avenue des Tropiques, Les Ulis, COURTABOEUF, France, 91930
Public contact	Global Clinical Development Leader, LFB Biotechnologies, 33 169825656,
Scientific contact	Global Clinical Development Leader, LFB Biotechnologies, 33 169825656,

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	17 January 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 July 2012
Global end of trial reached?	Yes
Global end of trial date	17 July 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of vWF SD-35-DH (WILFACTIN) in a long-term prophylaxis treatment regimen for the prevention of haemorrhages.

Protection of trial subjects:

Blood sampling usually done for laboratory testing presents a potential discomfort and the possible 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2005
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Tunisia: 6
Worldwide total number of subjects	10
EEA total number of subjects	4

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)	3

Adolescents (12-17 years)	2
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	10
Number of subjects completed	8

Pre-assignment subject non-completion reasons

Reason: Number of subjects	screening failure: 2
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Period 1

Period 1 title	Prophylaxis study follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

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

Dosage and administration details:

Individualized dose for long-term prophylaxis regimen according to historical profile of recurrent bleeding.

- 60 IU/kg in subjects with a predisposition to "mucosal" bleeds:
 - twice per week if VWF:RCo level at 48 hours post-infusion was > 10 IU/dL at the time of the recovery test.
 - 3 times per week if VWF:RCo level at 48 hours post-infusion was < 10 IU/dL
- 40 IU/kg in subjects with a predisposition to 'non-mucosal' bleeds:
 - twice per week if FVIII:C level at 48 hours post-infusion was >20 IU/dL at the time of the recovery test
 - 3 times per week if FVIII:C level at 48 hours post-infusion was <20 IU/dL

Number of subjects in period 1 ^[1]	WILFACTIN
Started	8
Completed	7
Not completed	1
Adverse event, non-fatal	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One subject not completed the baseline period because of a not fatal adverse event.

Baseline characteristics

Reporting groups

Reporting group title	Prophylaxis study follow-up
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Reporting group description: -

Reporting group values	Prophylaxis study follow-up	Total	
Number of subjects	8	8	
Age categorical			
Units: Subjects			
Children (2-11 years)	3	3	
12-64 years	5	5	
Age continuous			
Units: years			
median	16		
full range (min-max)	11 to 57	-	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	7	7	

Subject analysis sets

Subject analysis set title	Total Treated Set
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Eight subjects received study drug and were included in the safety population or TTS

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

Seven subjects completed the study and were included in the FAS. One subject was excluded from the efficacy analyses because he withdrew prematurely after the first administration of the study drug.

Reporting group values	Total Treated Set	FAS set	
Number of subjects	8	7	
Age categorical			
Units: Subjects			
Children (2-11 years)	3	3	
12-64 years	5	4	
Age continuous			
Units: years			
median	16	16	
full range (min-max)	11 to 57	11 to 45	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	7	6	

End points

End points reporting groups

Reporting group title	WILFACTIN
Reporting group description: -	
Subject analysis set title	Total Treated Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Eight subjects received study drug and were included in the safety population or TTS	
Subject analysis set title	FAS set
Subject analysis set type	Full analysis
Subject analysis set description:	
Seven subjects completed the study and were included in the FAS. One subject was excluded from the efficacy analyses because he withdrew prematurely after the first administration of the study drug.	

Primary: Reduction of haemorrhages

End point title	Reduction of haemorrhages ^[1]
End point description:	
All breakthrough bleeding episodes requiring VWF treatment or not were analysed.	
End point type	Primary
End point timeframe:	
ABR calculated at the end of the study compared with historical ABR the year before prophylaxis	

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 analyse

End point values	FAS set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Annual bleeding rate (ABR)				
median (full range (min-max))	81.9 (-11.9 to 99.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All included subjects (8) received at least one infusion; all were included in the safety analysis. Subjects were followed after the first infusion (recovery test) between 0 and 54.8 months (median: 27.3 months).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	safety group
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Reporting group description: -

Serious adverse events	safety group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	1 / 8 (12.50%)		
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	safety group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)		
Investigations			
Seroconversion test positive	Additional description: Not related Seroconversion were post-vaccinal (2 after hepatitis A vaccine and 1 after hepatitis B vaccine)		
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			

Gingival injury subjects affected / exposed occurrences (all)	Additional description: not related		
	2 / 8 (25.00%)		
	4		
Joint injury subjects affected / exposed occurrences (all)	Additional description: not related		
	2 / 8 (25.00%)		
	2		
Bite subjects affected / exposed occurrences (all)	Additional description: not related		
	1 / 8 (12.50%)		
	3		
Limb injury subjects affected / exposed occurrences (all)	Additional description: not related		
	2 / 8 (25.00%)		
	2		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)			
	Additional description: Mild events possibly related to the study drug. Dizziness symptoms occurred twice for a total of 116 administered infusions (the 40th and 41st infusion). They resolved without corrective treatment and the patient recovered without sequelae.		
	1 / 8 (12.50%)		
	2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)			
	Additional description: not related		
	2 / 8 (25.00%)		
	2		
Gastrointestinal disorders Loose tooth subjects affected / exposed occurrences (all)			
	Additional description: not related		
	1 / 8 (12.50%)		
	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2006	MSI for information. To increase the number of patients
18 December 2006	To allow the patients at the study end to continue the study drug up to the commercialisation. Add details regarding the bleeding episodes as inclusion criteria.
13 June 2007	Addition of a new center Dr El Khorassani, Maroc and LFB status = LFB SA
26 November 2007	Prolong study recruitment period (+ 6 months), extend the number of centres (countries: Tunisia and Poland). To change the sponsor name (LFB BIOTECHNOLOGIES) .
03 September 2008	This amendment concerns the Study Protocol. The main objective is the following: -to prolong the patient recruitment period, -to update the procedure for reporting Serious Adverse Events (SAE), -to add an intermediary analysis in Q4 2008, -to specify change of clinical development director, -to specify change of clinical project manager, -It also includes the correction of typing errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported