# 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 |

**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 minimizes 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] |
| Number of subjects completed | 9 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | selection criteria missing: 1 |

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-assigment period (1 selection criteria missing).

### Period 1

| | |
|---|---|
| Period 1 title | Inclusion visit |
| Is this the baseline period? | Yes |
| 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:

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 |
|---|---|

Reporting group description: -

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

### Subject analysis sets

| Subject analysis set title | TTS |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:
Total Treated Set

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 11.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Total Treated Set |

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<br>subjects affected / exposed<br>occurrences (all) | 4 / 9 (44.44%)<br>9 | | |
| Dental caries<br>subjects affected / exposed<br>occurrences (all) | 3 / 9 (33.33%)<br>5 | | |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 4 / 9 (44.44%)<br>13 | | |
| Tonsillitis<br>subjects affected / exposed<br>occurrences (all) | 2 / 9 (22.22%)<br>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 recuitment period.<br>To add a recovery study to be performed after 6 months for children with type 3 VWD.<br>To extand the number of centres including the participation of other countries. |
| 12 November 2007 | To change the name of the sponsor (LFB BIOTECHNOLOGIES ).<br>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.<br>To specify the 2nd recovery study in the information patient sheet related to amendment n°4.<br>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 storageand 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