# Clinical trial results:
# EFFICACY AND SAFETY STUDY OF FACTANE 200 IU/ml ADMINISTERED BY CONTINUOUS INFUSION IN SEVERE HAEMOPHILIA A PATIENTS DURING MAJOR SURGICAL PROCEDURES

## Summary

| | |
|---|---|
| EudraCT number | 2010-023666-46 |
| Trial protocol | PL |
| Global end of trial date | 31 July 2012 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 06 January 2017 |
| First version publication date | 06 January 2017 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | F8VR-1006 |

### 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, COURTABOEUF, France, 91958 |
| 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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 27 February 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 July 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 July 2012 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of FACTANE 200 IU/ml administered by continuous infusion for the perioperative and postoperative prophylaxis of bleeding during major surgical procedures in severe haemophilia A patients.

Protection of trial subjects:

LFB has developed a new concentration to improve patient comfort by supplying the product in a smaller volume: FACTANE 200 IU/mL contains approximately 1000 IU of factor VIII in 5 mL of solution. Continuous infusion, through a catheter placed in a vein in the arm, is also advantageous in that it avoids repeat injections and minimises pain and injury in the vein due to many needle punctures. The study was conducted in accordance with the with the principles laid down in the Declaration of Helsinki, the ICH guidelines for Good Clinical Practice (GCP) and all applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 12 March 2012 |
| 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 | Poland: 4 |
| Worldwide total number of subjects | 4 |
| 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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 4 |
| From 65 to 84 years | 0 |

| | |
|---|---|
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

In total, four (4) subjects have been enrolled by in single center in Poland (Warsaw) between 12 March 2012 and 28 May 2012

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 4 |
| Number of subjects completed | 4 |

### Period 1

| | |
|---|---|
| Period 1 title | Preoperative pharmacokinetic study |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | FACTANE |

Arm description: -

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | FACTANE |
| Investigational medicinal product code | F8VR |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Pharmacokinetic study before the surgical procedure:
Single weight-adjusted dose (50 IU/kg) administered by bolus at a rate of 4mL/min

| **Number of subjects in period 1** | FACTANE |
|---|---|
| Started | 4 |
| Completed | 4 |

## Period 2

| | |
|---|---|
| Period 2 title | Surgery by continuous infusion |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| **Arm title** | FACTANE |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | FACTANE |
| Investigational medicinal product code | F8VR |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

- Preoperative loading dose administered by IV bolus at a rate of 4 mL/min. The loading dose was to be administered to reach circulating FVIII levels between 80 and 120 IU/dL according to the following formula:

Loading dose (IU) = patient's weight (kg) × desired level (IU/dL) × 1 / patient's incremental recovery at T15 min ([IU/dL]/[IU/kg]).

- Continuous infusion dose immediately after bolus injection: H0 (D0). The infusion rate was calculated based on the patient's clearance and the desired FVIII level as follows:

Infusion rate (IU/kg/h) = clearance (mL/h/kg) × desired FVIII level (IU/mL).

The desired FVIII levels were to be: 80 to 120 IU/dL from D0 to D6 and 30 to 80 IU/dL from D7 to the end of the continuous infusion (Dn).

| **Number of subjects in period 2** | FACTANE |
|---|---|
| Started | 4 |
| Completed | 4 |

## Period 3

| | |
|---|---|
| Period 3 title | Follow-up period |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

## Arms

| **Arm title** | FACTANE |
|---|---|
| Arm description: - | |
| Arm type | Active comparator |
| Investigational medicinal product name | Factor 8 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

after continuous infusion, the patient had to be treated with his usual factor VIII concentrate.

| **Number of subjects in period 3** | FACTANE |
|---|---|
| Started | 4 |
| Completed | 4 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Preoperative pharmacokinetic study |
|---|---|

Reporting group description: -

| Reporting group values | Preoperative pharmacokinetic study | Total | |
|---|---|---|---|
| Number of subjects | 4 | 4 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 4 | 4 | |
| Age continuous<br>Units: years | | | |
| median | 39 | | |
| full range (min-max) | 37 to 43 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 4 | 4 | |

### 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 | 4 | | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 4 | | |
| Age continuous<br>Units: years | | | |
| median | 39 | | |
| full range (min-max) | 37 to 43 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | | |
| Male | 4 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | FACTANE |
| Reporting group description: - | |
| Reporting group title | FACTANE |
| Reporting group description: - | |
| Reporting group title | FACTANE |
| Reporting group description: - | |
| Subject analysis set title | TTS |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Total Treated Set | |

### Primary: Hemostatic efficacy

| | |
|---|---|
| End point title | Hemostatic efficacy[1] |

End point description:

Efficacy was assessed based on the number of 'responder' patients. A patient was considered as a 'responder' if he obtained an 'excellent' or 'good' score in 3 successive haemostasis assessments:
• 6 hours after the start of the surgery (by the surgeon),
• on the day of drain tube removal (or on D2 if there was no drain) (by the surgeon),
• on D7 (by the Investigator).

Haemostasis was evaluated using the following scale: 'excellent', 'good', 'moderate', 'none'.
- 'excellent': haemostasis similar to that of a non-bleeding disorder patient during the same surgery
- 'good': slight oozing at surgical incision,
- 'moderate': mild, but controlled bleeding,
- 'none': severe, uncontrolled bleeding.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Haemostatic efficacy was rated at 3 time-points after start of surgery (D0): H6, day of drain removal, D7

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 | TTS | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: number of 'responder' patients | | | | |
| excellent/good | 4 | | | |
| moderate/none | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: patient with inhibitor

| | |
|---|---|
| End point title | patient with inhibitor |

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:
during the study

| **End point values** | TTS | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: number | 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 | 15.0 |

### 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 | 2 / 4 (50.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| postoperative anaemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| circulatory collapse | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| 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 | Total treated Set | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Anaemia postoperative | Additional description: Not related | | |
| subjects affected / exposed | 3 / 4 (75.00%) | | |
| occurrences (all) | 3 | | |
| Vascular disorders | | | |
| Haematoma | Additional description: Note related | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Catheter site inflammation | Additional description: Not related | | |
| subjects affected / exposed | 3 / 4 (75.00%) | | |
| occurrences (all) | 4 | | |
| Pyrexia | Additional description: Not related | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Haemarthrosis | Additional description: Note related | | |
| subjects affected / exposed | 4 / 4 (100.00%) | | |
| occurrences (all) | 14 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported