



## Clinical trial results:

### A 12-week, Multicenter, Pharmacokinetic and Safety Study of Human Plasma-Derived Factor XIII Concentrate in Subjects with Congenital Factor XIII Deficiency

### Estudio de 12 semanas, multicéntrico, de farmacocinética y seguridad del concentrado de factor XIII derivado del plasma humano en sujetos con deficiencia congénita de factor XIII

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2009-010387-41   |
| Trial protocol           | ES               |
| Global end of trial date | 24 February 2010 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 13 July 2016   |
| First version publication date | 06 August 2015 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | BI71023_2002 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00883090 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                  |
|------------------------------|----------------------------------------------------------------------------------|
| Sponsor organisation name    | CSL Behring LLC                                                                  |
| Sponsor organisation address | 1020 First Avenue, King of Prussia, United States, 19406-0901                    |
| Public contact               | Clinical Trial Disclosure Manager, CSL Behring,<br>clinicaltrials@cslbehring.com |
| Scientific contact           | Clinical Trial Disclosure Manager, CSL Behring,<br>clinicaltrials@cslbehring.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                       | 04 May 2010      |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 24 February 2010 |
| 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 generate steady-state PK Factor XIII data in subjects with congenital Factor XIII deficiency.

Protection of trial subjects:

This study was carried out in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice guidelines and standard operating procedures for clinical research and development at CSL Behring (CSLB).

The study protocol and all amendments were approved by the Independent Ethics Committee(s) (IECs) / Institutional Review Board(s) (IRBs) of the participating centers.

Before undergoing screening procedures for possible enrollment into the study, subjects were informed, in an understandable form, about the nature, scope, and possible consequences of the study. The investigator was responsible for obtaining a subject's written informed consent to participate in the study.

Background therapy: -

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 18 May 2009 |
| 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 | Spain: 5          |
| Country: Number of subjects enrolled | United States: 10 |
| Worldwide total number of subjects   | 15                |
| 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 months)  | 0 |
| Children (2-11 years)                     | 3 |

|                           |    |
|---------------------------|----|
| Adolescents (12-17 years) | 2  |
| Adults (18-64 years)      | 10 |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Eligible subjects had documented congenital FXIII deficiency requiring prophylactic treatment with a FXIII containing product. Males and females of any age with congenital FXIII deficiency could participate in the study.

### Pre-assignment

Screening details:

At the Screening Visit, blood for determination of viral markers, serum aspartate transaminase (AST) and alanine transaminase (ALT) levels, and, if female of childbearing potential, pregnancy testing was obtained.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|           |             |
|-----------|-------------|
| Arm title | Factor XIII |
|-----------|-------------|

Arm description:

Subjects received 40 U/kg of Factor XIII per administration every 28 days for 3 doses administered as a bolus IV injection.

|                                        |                                               |
|----------------------------------------|-----------------------------------------------|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | Factor XIII Concentrate (Human)               |
| Investigational medicinal product code | B17023                                        |
| Other name                             | Fibrogammin® P, Cluvot®                       |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intravenous use                               |

Dosage and administration details:

Subjects received 40 U/kg of Factor XIII Concentrate (Human) per administration every 28 days for 3 doses administered as a bolus intravenous (IV) injection at 250 U/minute (when reconstituted 250 U/minute equals 4mL/minute).

| Number of subjects in period 1    | Factor XIII |
|-----------------------------------|-------------|
| Started                           | 15          |
| Treated                           | 14          |
| Completed                         | 13          |
| Not completed                     | 2           |
| Consent withdrawn by subject      | 1           |
| Sponsor's administrative decision | 1           |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Factor XIII |
|-----------------------|-------------|

Reporting group description:

Subjects received 40 U/kg of Factor XIII per administration every 28 days for 3 doses administered as a bolus IV injection.

| Reporting group values                                | Factor XIII | Total |  |
|-------------------------------------------------------|-------------|-------|--|
| Number of subjects                                    | 15          | 15    |  |
| Age categorical                                       |             |       |  |
| Units: Subjects                                       |             |       |  |
| Age continuous                                        |             |       |  |
| Based on the safety population of 14 treated subjects |             |       |  |
| Units: years                                          |             |       |  |
| arithmetic mean                                       | 24          |       |  |
| standard deviation                                    | ± 12.55     | -     |  |
| Gender categorical                                    |             |       |  |
| Units: Subjects                                       |             |       |  |
| Female                                                | 7           | 7     |  |
| Male                                                  | 8           | 8     |  |

## End points

### End points reporting groups

|                                                                                                                                                             |             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|
| Reporting group title                                                                                                                                       | Factor XIII |
| Reporting group description:<br>Subjects received 40 U/kg of Factor XIII per administration every 28 days for 3 doses administered as a bolus IV injection. |             |

### Primary: Peak FXIII Concentration at Steady State

|                        |                                                         |
|------------------------|---------------------------------------------------------|
| End point title        | Peak FXIII Concentration at Steady State <sup>[1]</sup> |
| End point description: |                                                         |

|                                  |         |
|----------------------------------|---------|
| End point type                   | Primary |
| End point timeframe:<br>12 weeks |         |

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: No formal testing of hypotheses was performed.

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | Factor XIII       |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 13 <sup>[2]</sup> |  |  |  |
| Units: IU/mL                         |                   |  |  |  |
| arithmetic mean (standard deviation) | 0.9 (± 0.2)       |  |  |  |

Notes:

[2] - The PK population comprised all subjects in the safety population who completed the study.

### Statistical analyses

No statistical analyses for this end point

### Primary: Trough FXIII Concentration at Steady State

|                        |                                                           |
|------------------------|-----------------------------------------------------------|
| End point title        | Trough FXIII Concentration at Steady State <sup>[3]</sup> |
| End point description: |                                                           |

|                                  |         |
|----------------------------------|---------|
| End point type                   | Primary |
| End point timeframe:<br>12 weeks |         |

Notes:

[3] - 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: No formal testing of hypotheses was performed.

| End point values                     | Factor XIII       |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 13 <sup>[4]</sup> |  |  |  |
| Units: IU/mL                         |                   |  |  |  |
| arithmetic mean (standard deviation) | 0.05 (± 0.05)     |  |  |  |

Notes:

[4] - PK population

## Statistical analyses

No statistical analyses for this end point

### Primary: Time to Peak Concentration

|                 |                                           |
|-----------------|-------------------------------------------|
| End point title | Time to Peak Concentration <sup>[5]</sup> |
|-----------------|-------------------------------------------|

End point description:

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

End point timeframe:

12 weeks

Notes:

[5] - 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: No formal testing of hypotheses was performed.

| End point values                     | Factor XIII       |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 13 <sup>[6]</sup> |  |  |  |
| Units: hours                         |                   |  |  |  |
| arithmetic mean (standard deviation) | 1.7 (± 1.44)      |  |  |  |

Notes:

[6] - PK population

## Statistical analyses

No statistical analyses for this end point

### Primary: Incremental Recovery

|                 |                                     |
|-----------------|-------------------------------------|
| End point title | Incremental Recovery <sup>[7]</sup> |
|-----------------|-------------------------------------|

End point description:

Incremental recovery is defined as the maximum (peak) FXIII activity (IU/mL) obtained after infusion, per dose of FXIII (IU/kg) administered.

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

End point timeframe:

12 weeks

Notes:

[7] - 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: No formal testing of hypotheses was performed.

| End point values                     | Factor XIII       |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 13 <sup>[8]</sup> |  |  |  |
| Units: IU/mL/IU/kg                   |                   |  |  |  |
| arithmetic mean (standard deviation) | 0.02 (± 0.01)     |  |  |  |

Notes:

[8] - PK population

## Statistical analyses

No statistical analyses for this end point

### Primary: Terminal Half-life

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Terminal Half-life <sup>[9]</sup> |
|-----------------|-----------------------------------|

End point description:

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

End point timeframe:

12 weeks

Notes:

[9] - 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: No formal testing of hypotheses was performed.

| End point values                     | Factor XIII        |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| Subject group type                   | Reporting group    |  |  |  |
| Number of subjects analysed          | 13 <sup>[10]</sup> |  |  |  |
| Units: days                          |                    |  |  |  |
| arithmetic mean (standard deviation) | 6.6 (± 2.29)       |  |  |  |

Notes:

[10] - PK population

## Statistical analyses

No statistical analyses for this end point

### Primary: Area Under the Curve at Steady State

|                 |                                                      |
|-----------------|------------------------------------------------------|
| End point title | Area Under the Curve at Steady State <sup>[11]</sup> |
|-----------------|------------------------------------------------------|

End point description:

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

End point timeframe:

12 weeks

Notes:

[11] - 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: No formal testing of hypotheses was performed.

| End point values                     | Factor XIII        |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| Subject group type                   | Reporting group    |  |  |  |
| Number of subjects analysed          | 13 <sup>[12]</sup> |  |  |  |
| Units: IU*hr/mL                      |                    |  |  |  |
| arithmetic mean (standard deviation) | 184 (± 65.78)      |  |  |  |

Notes:

[12] - PK Population

## Statistical analyses

No statistical analyses for this end point

### Primary: Clearance

|                 |                           |
|-----------------|---------------------------|
| End point title | Clearance <sup>[13]</sup> |
|-----------------|---------------------------|

End point description:

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

End point timeframe:

12 weeks

Notes:

[13] - 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: No formal testing of hypotheses was performed.

| End point values                     | Factor XIII        |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| Subject group type                   | Reporting group    |  |  |  |
| Number of subjects analysed          | 13 <sup>[14]</sup> |  |  |  |
| Units: mL/hr/kg                      |                    |  |  |  |
| arithmetic mean (standard deviation) | 0.25 (± 0.09)      |  |  |  |

Notes:

[14] - PK population

## Statistical analyses

No statistical analyses for this end point

### Primary: Volume of Distribution at Steady State

|                 |                                                        |
|-----------------|--------------------------------------------------------|
| End point title | Volume of Distribution at Steady State <sup>[15]</sup> |
|-----------------|--------------------------------------------------------|

End point description:

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

End point timeframe:

12 weeks

Notes:

[15] - 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: No formal testing of hypotheses was performed.

| End point values                     | Factor XIII        |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| Subject group type                   | Reporting group    |  |  |  |
| Number of subjects analysed          | 13 <sup>[16]</sup> |  |  |  |
| Units: mL/kg                         |                    |  |  |  |
| arithmetic mean (standard deviation) | 51.1 (± 12.61)     |  |  |  |

Notes:

[16] - PK population

## Statistical analyses

No statistical analyses for this end point

### Primary: Mean Residence Time

|                 |                                     |
|-----------------|-------------------------------------|
| End point title | Mean Residence Time <sup>[17]</sup> |
|-----------------|-------------------------------------|

End point description:

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

End point timeframe:

12 weeks

Notes:

[17] - 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: No formal testing of hypotheses was performed.

| End point values                     | Factor XIII        |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| Subject group type                   | Reporting group    |  |  |  |
| Number of subjects analysed          | 13 <sup>[18]</sup> |  |  |  |
| Units: days                          |                    |  |  |  |
| arithmetic mean (standard deviation) | 10 (± 3.45)        |  |  |  |

Notes:

[18] - PK population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Adverse Events

|                 |                                            |
|-----------------|--------------------------------------------|
| End point title | Number of Participants with Adverse Events |
|-----------------|--------------------------------------------|

End point description:

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

End point timeframe:

16 weeks

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | Factor XIII        |  |  |  |
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 14 <sup>[19]</sup> |  |  |  |
| Units: participants         | 8                  |  |  |  |

Notes:

[19] - The safety population comprised all subjects who received a dose of Factor XIII.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Clinically Significant Laboratory Safety Parameter Values

|                 |                                                                                       |
|-----------------|---------------------------------------------------------------------------------------|
| End point title | Number of Participants with Clinically Significant Laboratory Safety Parameter Values |
|-----------------|---------------------------------------------------------------------------------------|

End point description:

Number of participants with clinically significant laboratory safety parameter values. The laboratory safety parameters measured included serum chemistries, hematology and urinalysis.

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

End point timeframe:

16 weeks

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | Factor XIII        |  |  |  |
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 14 <sup>[20]</sup> |  |  |  |
| Units: participants         | 0                  |  |  |  |

Notes:

[20] - Safety population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Clinically Significant Vital Signs

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Number of Participants with Clinically Significant Vital Signs |
|-----------------|----------------------------------------------------------------|

End point description:

Number of participants with clinically significant vital signs. The vital signs measured included blood pressure, pulse rate and temperature. Clinically significant changes in vital signs were to be reported as adverse events.

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

End point timeframe:

16 weeks

|                             |                    |  |  |  |
|-----------------------------|--------------------|--|--|--|
| <b>End point values</b>     | Factor XIII        |  |  |  |
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 14 <sup>[21]</sup> |  |  |  |
| Units: participants         | 0                  |  |  |  |

Notes:

[21] - safety population

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The time frame for adverse event (AE) reporting was up to 16 weeks and comprised the time from giving written informed consent (during screening) to 28 days after the last administration of study treatment.

Adverse event reporting additional description:

Reporting group is comprised of all subjects treated with Factor FXIII Concentrate (Human) (FXIII).

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Factor XIII |
|-----------------------|-------------|

Reporting group description:

Subjects received 40 U/kg of Factor XIII per administration every 28 days for 3 doses administered as a bolus IV injection.

| Serious adverse events                            | Factor XIII    |  |  |
|---------------------------------------------------|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 14 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | Factor XIII     |  |  |
|-------------------------------------------------------|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 8 / 14 (57.14%) |  |  |
| Investigations                                        |                 |  |  |
| Fibrin D dimer increased                              |                 |  |  |
| subjects affected / exposed                           | 1 / 14 (7.14%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Prothrombin increased                                 |                 |  |  |
| subjects affected / exposed                           | 1 / 14 (7.14%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Thrombin-antithrombin III complex increased           |                 |  |  |

|                                                                                                                                                                                                                                                                                                                                                        |                                                                                                      |  |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                       | 1 / 14 (7.14%)<br>1                                                                                  |  |  |
| Injury, poisoning and procedural complications<br>Ankle injury<br>subjects affected / exposed<br>occurrences (all)<br><br>Bruising of arm<br>subjects affected / exposed<br>occurrences (all)<br><br>Contusion of knee<br>subjects affected / exposed<br>occurrences (all)<br><br>Contusion of toe<br>subjects affected / exposed<br>occurrences (all) | 1 / 14 (7.14%)<br>1<br><br>1 / 14 (7.14%)<br>1<br><br>1 / 14 (7.14%)<br>1<br><br>1 / 14 (7.14%)<br>1 |  |  |
| Reproductive system and breast disorders<br>Penile adhesion<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                        | 1 / 14 (7.14%)<br>1                                                                                  |  |  |
| Skin and subcutaneous tissue disorders<br>Ecchymosis<br>subjects affected / exposed<br>occurrences (all)<br><br>Rash<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                               | 1 / 14 (7.14%)<br>1<br><br>1 / 14 (7.14%)<br>1                                                       |  |  |
| Infections and infestations<br>Acute bronchitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Flu<br>subjects affected / exposed<br>occurrences (all)<br><br>Infected sebaceous cyst<br>subjects affected / exposed<br>occurrences (all)                                                                                                  | 2 / 14 (14.29%)<br>2<br><br>1 / 14 (7.14%)<br>1<br><br>1 / 14 (7.14%)<br>1                           |  |  |

|                                                                                                               |                     |  |  |
|---------------------------------------------------------------------------------------------------------------|---------------------|--|--|
| Tinea corporis<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 14 (7.14%)<br>1 |  |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 14 (7.14%)<br>1 |  |  |
| Metabolism and nutrition disorders<br>Borderline diabetes<br>subjects affected / exposed<br>occurrences (all) | 1 / 14 (7.14%)<br>1 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 04 February 2009 | <p>The dose for all 3 treatments was calculated based on screening weight rather than baseline weight</p> <p>Updated the inclusion criteria to include males and females of any age with congenital Factor XIII deficiency</p> <p>The AE reporting requirement was changed from 30 days to 28 days</p> <p>Removed the requirement to collect further information if any AEs were experienced after discontinuing participation in the study</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 09 July 2009     | <p>The number of subjects planned for enrollment was updated to "approximately 15"</p> <p>An inclusion criterion was changed from "Eligible subjects will have been diagnosed with severe congenital Factor XIII deficiency (&lt;10 U/dL at diagnosis)" to "Eligible subjects will have documented congenital Factor XIII deficiency that requires prophylactic treatment with a Factor XIII containing product"</p> <p>Updated the inclusion criteria to include receipt of full hepatitis B vaccination and/or was hepatitis B surface antibody positive</p> <p>Excluded subjects with known or suspected to have antibodies towards Factor XIII</p> <p>Removed the following exclusion criterion: "Negative serology for hepatitis B and has not received a full hepatitis B vaccination"</p> <p>Updated the PK statistical analysis to include calculation with and without adjustment for any unknown remaining endogenous Factor XIII levels</p> <p>Added guidance for subjects who experienced a bleeding event requiring additional dosing with a Factor XIII-containing product</p> <p>Added guidance for subjects who were actively bleeding at the time of Dose 3 (main PK visit)</p> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported