



Clinical trial results:

An Open-Label Study to Evaluate Prophylaxis Treatment, and to Characterize the Efficacy, Safety, and Pharmacokinetics of B-Domain Deleted Recombinant Factor VIII Albumin Free (Moroctocog Alfa [AF-CC]) in Children With Hemophilia A

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-005575-17 |
| Trial protocol | ES DE AT IT |
| Global end of trial date | 18 April 2018 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v2 (current) |
| This version publication date | 06 January 2019 |
| First version publication date | 10 October 2018 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 3082B2-313 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00543439 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

Paediatric regulatory details

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|--|-----|
| 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 | 13 August 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 April 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that moroctocog alfa prophylaxis reduces annualized bleeding rates relative to on-demand (OD) therapy. Enrollment into the OD cohort has been closed.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 11 December 2007 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Poland: 15 |
| Country: Number of subjects enrolled | Turkey: 11 |
| Country: Number of subjects enrolled | Oman: 10 |
| Country: Number of subjects enrolled | Jordan: 6 |
| Country: Number of subjects enrolled | United States: 6 |
| Country: Number of subjects enrolled | Romania: 5 |
| Country: Number of subjects enrolled | Mexico: 3 |
| Country: Number of subjects enrolled | New Zealand: 3 |
| Country: Number of subjects enrolled | Argentina: 2 |
| Country: Number of subjects enrolled | Austria: 2 |
| Country: Number of subjects enrolled | Colombia: 1 |
| Country: Number of subjects enrolled | Croatia: 1 |
| Worldwide total number of subjects | 65 |
| EEA total number of subjects | 23 |

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) | 5 |
| Children (2-11 years) | 59 |
| Adolescents (12-17 years) | 1 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects for 1 of the sites, were excluded from efficacy and safety analysis due to data integrity issues, however were reported in subject disposition and baseline. Out of 66 enrolled subjects, 65 were treated (started Period 1). Period 1 and Period 2 both were post-baseline.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Moroctocog alfa (AF-CC), OD Cohort: OD Therapy Then RP Therapy |

Arm description:

Subjects who consented for pharmacokinetic assessment received single 50 international units per kilogram [IU/kg] infusion of AF-CC on Day 1 prior start of study treatment. Period 1: subjects were treated with on-demand (OD) therapy intravenous (IV) infusion of AF-CC for 6 months(Day 1 up to Month 6)prescribed by investigator based on current recommendations for OD therapy with licensed product Xyntha (Minor bleeding: repetition of IV infusion of AF-CC,20-40 IU/kg, every 12-24 hours (hr) until resolved for atleast 1 day, depending upon severity of bleeding episode; Moderate bleeding: repetition of IV infusion of AF-CC,30-60 IU/kg, every 12-24 hr for 3-4 days/until adequate local hemostasis achieved; Major bleeding: repetition of IV infusion of AF-CC,60-100 IU/kg, every 8-24 hr until bleeding resolved).Then in Period 2 subjects received IV infusion of AF-CC at 25 IU/kg once in 2 days up to 12 months (Month 7 to Month 18) as RP therapy and if required were treated with OD IV infusion.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Moroctocog alfa (AF-CC) |
| Investigational medicinal product code | |
| Other name | Xyntha |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

First period: Subjects were treated with moroctocog alfa (AF-CC) IV infusion for 6 months as prescribed by investigator based on current recommendations for on demand treatment with licensed product Xyntha.

| | |
|------------------|--|
| Arm title | Moroctocog alfa (AF-CC), RP Cohort: RP 25IU/kg Then RP 45IU/kg |
|------------------|--|

Arm description:

Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg once in 2 days up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg, twice per week up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-------------------------|
| Investigational medicinal product name | Moroctocog alfa (AF-CC) |
| Investigational medicinal product code | |
| Other name | Xyntha |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

First period: Subjects received moroctocog alfa (AF-CC) infusion intravenously at 25 IU/kg, once in 2 days up to 12 months.

| | |
|------------------|--|
| Arm title | Moroctocog alfa(AF-CC), RP Cohort: RP 45 IU/kg Then RP 25IU/kg |
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Arm description:

Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg twice per week up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Moroctocog alfa (AF-CC) |
| Investigational medicinal product code | |
| Other name | Xyntha |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

First period: Subjects received 45 IU/kg moroctocog alfa (AF-CC) infusion intravenously twice per week up to 12 months.

| Number of subjects in period 1 | Moroctocog alfa (AF-CC), OD Cohort: OD Therapy Then RP Therapy | Moroctocog alfa (AF-CC), RP Cohort: RP 25IU/kg Then RP 45IU/kg | Moroctocog alfa(AF-CC), RP Cohort: RP 45 IU/kg Then RP 25IU/kg |
|---------------------------------------|--|--|--|
| Started | 9 | 29 | 27 |
| Completed | 9 | 26 | 25 |
| Not completed | 0 | 3 | 2 |
| Consent withdrawn by subject | - | 1 | - |
| Physician decision | - | - | 1 |
| Adverse Event | - | 2 | 1 |

Period 2

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|--|
| Arm title | Moroctocog alfa (AF-CC), OD Cohort: OD Therapy Then RP Therapy |
|------------------|--|

Arm description:

Subjects who consented for pharmacokinetic assessment received single 50 international units per kilogram [IU/kg] infusion of AF-CC on Day 1 prior start of study treatment. Period 1: subjects were treated with on-demand (OD) therapy intravenous (IV) infusion of AF-CC for 6 months (Day 1 up to Month 6) prescribed by investigator based on current recommendations for OD therapy with licensed product Xyntha (Minor bleeding: repetition of IV infusion of AF-CC, 20-40 IU/kg, every 12-24 hours (hr) until resolved for at least 1 day, depending upon severity of bleeding episode; Moderate bleeding: repetition of IV infusion of AF-CC, 30-60 IU/kg, every 12-24 hr for 3-4 days until adequate local hemostasis achieved; Major bleeding: repetition of IV infusion of AF-CC, 60-100 IU/kg, every 8-24 hr until bleeding resolved). Then in Period 2 subjects received IV infusion of AF-CC at 25 IU/kg once in 2 days up to 12 months (Month 7 to Month 18) as RP therapy and if required were treated with OD IV infusion.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Moroctocog alfa (AF-CC) |
| Investigational medicinal product code | |
| Other name | Xyntha |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Second period: Subjects received 25 IU/kg moroctocog alfa (AF-CC) infusion intravenously once in 2 days up to 12 months.

| | |
|------------------|--|
| Arm title | Moroctocog alfa, RP Cohort: RP 25 IU/kg Then RP 45 IU/kg |
|------------------|--|

Arm description:

Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg once in 2 days up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg, twice per week up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Moroctocog alfa (AF-CC) |
| Investigational medicinal product code | |
| Other name | Xyntha |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Second period: Subjects received 45 IU/kg moroctocog alfa (AF-CC) infusion intravenously twice per week up to 12 months.

| | |
|------------------|--|
| Arm title | Moroctocog alfa (AF-CC), RP Cohort: RP 45 IU/kg Then RP 25 IU/kg |
|------------------|--|

Arm description:

Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg twice per week up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Moroctocog alfa (AF-CC) |
| Investigational medicinal product code | |
| Other name | Xyntha |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Second period: Subjects received 25 IU/kg moroctocog alfa (AF-CC) infusion intravenously once in 2

days up to 12 months.

| Number of subjects in period 2 | Moroctocog alfa (AF-CC), OD Cohort: OD Therapy Then RP Therapy | Moroctocog alfa, RP Cohort: RP 25 IU/kg Then RP 45 IU/kg | Moroctocog alfa(AF-CC), RP Cohort: RP 45 IU/kg Then RP 25IU/kg |
|--------------------------------|--|--|--|
| | | | |
| Started | 9 | 26 | 25 |
| Completed | 8 | 25 | 23 |
| Not completed | 1 | 1 | 2 |
| Adverse Event | - | 1 | 1 |
| Protocol deviation | 1 | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Moroctocog alfa (AF-CC), OD Cohort: OD Therapy Then RP Therapy |
|-----------------------|--|

Reporting group description:

Subjects who consented for pharmacokinetic assessment received single 50 international units per kilogram [IU/kg] infusion of AF-CC on Day 1 prior start of study treatment. Period 1: subjects were treated with on-demand (OD) therapy intravenous (IV) infusion of AF-CC for 6 months (Day 1 up to Month 6) prescribed by investigator based on current recommendations for OD therapy with licensed product Xyntha (Minor bleeding: repetition of IV infusion of AF-CC, 20-40 IU/kg, every 12-24 hours (hr) until resolved for at least 1 day, depending upon severity of bleeding episode; Moderate bleeding: repetition of IV infusion of AF-CC, 30-60 IU/kg, every 12-24 hr for 3-4 days/until adequate local hemostasis achieved; Major bleeding: repetition of IV infusion of AF-CC, 60-100 IU/kg, every 8-24 hr until bleeding resolved). Then in Period 2 subjects received IV infusion of AF-CC at 25 IU/kg once in 2 days up to 12 months (Month 7 to Month 18) as RP therapy and if required were treated with OD IV infusion.

| | |
|-----------------------|--|
| Reporting group title | Moroctocog alfa (AF-CC), RP Cohort: RP 25IU/kg Then RP 45IU/kg |
|-----------------------|--|

Reporting group description:

Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg once in 2 days up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg, twice per week up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months.

| | |
|-----------------------|---|
| Reporting group title | Moroctocog alfa (AF-CC), RP Cohort: RP 45 IU/kg Then RP 25IU/kg |
|-----------------------|---|

Reporting group description:

Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg twice per week up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months.

| Reporting group values | Moroctocog alfa (AF-CC), OD Cohort: OD Therapy Then RP Therapy | Moroctocog alfa (AF-CC), RP Cohort: RP 25IU/kg Then RP 45IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP 45 IU/kg Then RP 25IU/kg |
|--|--|--|---|
| Number of subjects | 9 | 29 | 27 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 2 | 3 |
| Children (2-11 years) | 9 | 27 | 23 |
| Adolescents (12-17 years) | 0 | 0 | 1 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |

| | | | |
|---|---------------|---------------|---------------|
| Age Continuous Units: years arithmetic mean standard deviation | 4.7 ± 1.05 | 4.4 ± 1.84 | 4.1 ± 2.28 |
| Sex: Female, Male Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 9 | 29 | 27 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 8 | 24 | 22 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 1 | 5 | 5 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 65 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 5 | | |
| Children (2-11 years) | 59 | | |
| Adolescents (12-17 years) | 1 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age Continuous Units: years arithmetic mean standard deviation | - | | |
| Sex: Female, Male Units: Subjects | | | |
| Female | 0 | | |
| Male | 65 | | |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 0 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 0 | | |
| White | 54 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 11 | | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Moroctocog alfa (AF-CC), OD Cohort: OD Therapy Then RP Therapy |
| Reporting group description: Subjects who consented for pharmacokinetic assessment received single 50 international units per kilogram [IU/kg] infusion of AF-CC on Day 1 prior start of study treatment. Period 1: subjects were treated with on-demand (OD) therapy intravenous (IV) infusion of AF-CC for 6 months(Day 1 up to Month 6)prescribed by investigator based on current recommendations for OD therapy with licensed product Xyntha (Minor bleeding: repetition of IV infusion of AF-CC,20-40 IU/kg, every 12-24 hours (hr) until resolved for atleast 1 day, depending upon severity of bleeding episode; Moderate bleeding: repetition of IV infusion of AF-CC,30-60 IU/kg, every 12-24 hr for 3-4 days/until adequate local hemostasis achieved; Major bleeding: repetition of IV infusion of AF-CC,60-100 IU/kg, every 8-24 hr until bleeding resolved).Then in Period 2 subjects received IV infusion of AF-CC at 25 IU/kg once in 2 days up to 12 months (Month 7 to Month 18) as RP therapy and if required were treated with OD IV infusion. | |
| Reporting group title | Moroctocog alfa (AF-CC), RP Cohort: RP 25IU/kg Then RP 45IU/kg |
| Reporting group description: Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg once in 2 days up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg, twice per week up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months. | |
| Reporting group title | Moroctocog alfa(AF-CC), RP Cohort: RP 45 IU/kg Then RP 25IU/kg |
| Reporting group description: Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg twice per week up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months. | |
| Reporting group title | Moroctocog alfa (AF-CC), OD Cohort: OD Therapy Then RP Therapy |
| Reporting group description: Subjects who consented for pharmacokinetic assessment received single 50 international units per kilogram [IU/kg] infusion of AF-CC on Day 1 prior start of study treatment. Period 1: subjects were treated with on-demand (OD) therapy intravenous (IV) infusion of AF-CC for 6 months(Day 1 up to Month 6)prescribed by investigator based on current recommendations for OD therapy with licensed product Xyntha (Minor bleeding: repetition of IV infusion of AF-CC,20-40 IU/kg, every 12-24 hours (hr) until resolved for atleast 1 day, depending upon severity of bleeding episode; Moderate bleeding: repetition of IV infusion of AF-CC,30-60 IU/kg, every 12-24 hr for 3-4 days/until adequate local hemostasis achieved; Major bleeding: repetition of IV infusion of AF-CC,60-100 IU/kg, every 8-24 hr until bleeding resolved).Then in Period 2 subjects received IV infusion of AF-CC at 25 IU/kg once in 2 days up to 12 months (Month 7 to Month 18) as RP therapy and if required were treated with OD IV infusion. | |
| Reporting group title | Moroctocog alfa, RP Cohort: RP 25 IU/kg Then RP 45 IU/kg |
| Reporting group description: Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg once in 2 days up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg, twice per week up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months. | |
| Reporting group title | Moroctocog alfa(AF-CC), RP Cohort: RP 45 IU/kg Then RP 25IU/kg |

Reporting group description:

Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort. In Period 1 subjects for routine prophylaxis therapy, received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg twice per week up to 12 months (Day 1 up to Month 12). Period 1 was followed by Period 2 where subjects received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days up to 12 months (Month 13 up to Month 24) as routine prophylaxis therapy. Subjects were treated OD IV infusion up to 12 months.

| | |
|----------------------------|--|
| Subject analysis set title | Moroctocog alfa (AF-CC), On Demand Cohort: On Demand Therapy |
|----------------------------|--|

| | |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

In Period 1, subjects for on-demand therapy were treated with IV infusion of moroctocog alfa (AF-CC) for 6 months (Day 1 up to Month 6) as prescribed by the investigator based on current recommendations for on-demand treatment with licensed product Xyntha (Minor bleeding: repetition of IV infusion of moroctocog alfa (AF-CC), 20-40 IU/kg, every 12-24 hours as necessary until resolved for at least 1 day, depending upon severity of bleeding episode; Moderate bleeding: repetition of IV infusion of Moroctocog alfa, 30-60 IU/kg, every 12-24 hours for 3-4 days or until adequate local hemostasis was achieved; Major bleeding: repetition of IV infusion of moroctocog alfa (AF-CC), 60-100 IU/kg, every 8-24 hours until bleeding was resolved).

| | |
|----------------------------|--|
| Subject analysis set title | Moroctocog alfa (AF-CC), On Demand Cohort: RP Therapy 25 IU/kg |
|----------------------------|--|

| | |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

In Period 2, subjects for on-demand cohort received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg once in 2 days up to 12 months (Month 7 up to Month 18) as routine prophylaxis therapy.

| | |
|----------------------------|--|
| Subject analysis set title | Moroctocog alfa (AF-CC): On Demand Therapy |
|----------------------------|--|

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|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

Subjects of either on demand cohort or routine prophylaxis cohort were treated for bleeds, as needed on demand, with IV infusion of moroctocog alfa (AF-CC) up to 24 months as prescribed by the investigator based on current recommendations for on-demand treatment with licensed product Xyntha (Minor bleeding: repetition of IV infusion of moroctocog alfa (AF-CC), 20-40 IU/kg, every 12-24 hours as necessary until resolved for at least 1 day, depending upon severity of bleeding episode; Moderate bleeding: repetition of IV infusion of moroctocog alfa (AF-CC), 30-60 IU/kg, every 12-24 hours for 3-4 days or until adequate local hemostasis was achieved; Major bleeding: repetition of IV infusion of moroctocog alfa (AF-CC), 60-100 IU/kg, every 8-24 hours until bleeding was resolved).

| | |
|----------------------------|---|
| Subject analysis set title | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 25 IU/kg |
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|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

Subjects of routine prophylaxis cohort, as routine prophylaxis therapy received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days up to 12 months as routine prophylaxis therapy for either Period 1 (Day 1 up to Month 12) or Period 2 (Month 13 up to Month 24) of the study.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | Moroctocog alfa (AF-CC): 50 IU/kg |
|----------------------------|-----------------------------------|

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|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects received a single 50 IU/kg infusion of moroctocog alfa (AF-CC) on Day 1 before initiation of moroctocog alfa (AF-CC) study treatment either in on demand cohort or routine prophylaxis cohort.

| | |
|----------------------------|---------------------------------------|
| Subject analysis set title | Moroctocog alfa (AF-CC): All Subjects |
|----------------------------|---------------------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

All subjects who received moroctocog alfa-(AF-CC) 50 IU/kg for PK assessment on Day 1 prior start of study treatment and as on demand or routine prophylaxis treatment (25 and 45 IU/kg).

| | |
|----------------------------|---|
| Subject analysis set title | Moroctocog alfa (AF-CC) RP Cohort: RP therapy |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

Subjects received moroctocog alfa (AF-CC) in routine prophylaxis cohort as RP 45 IU/kg, twice per week up to 12 months either in Period 1 (Day 1 up to Month 12) or Period 2 (Month 13 up to Month 24); and as RP 25 IU/kg, once in 2 days up to 12 months either in Period 1 (Day 1 up to Month 12) or Period 2 (Month 13 up to Month 24).

| | |
|---|--|
| Subject analysis set title | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects randomized to the routine prophylaxis cohort, in which IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg, twice per week up to 12 months as routine prophylaxis therapy would be assigned for either Period 1 (Day 1 up to Month 12) or Period 2 (Month 13 up to Month 24) of the study. | |
| Subject analysis set title | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| Subjects of routine prophylaxis cohort received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days up to 12 months as routine prophylaxis therapy each for either Period 1 (Day 1 up to Month 12) or Period 2 (Month 13 up to Month 24) of the study. And subjects of on demand cohort for Period 2 of the study, received IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days as routine prophylaxis therapy up to 12 months (Month 7 up to Month 18). | |
| Subject analysis set title | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| Subjects of routine prophylaxis cohort, received IV infusion of moroctocog alfa (AF-CC) at 45 IU/kg, twice per week up to 12 months as routine prophylaxis therapy each for either Period 1 (Day 1 up to Month 12) or Period 2 (Month 13 up to Month 24) of the study. | |
| Subject analysis set title | Moroctocog alfa (AF-CC): All Subjects |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| All subjects who received moroctocog alfa-(AF-CC) 50 IU/kg for PK assessment on Day 1 prior start of study treatment and as on demand or routine prophylaxis treatment (25 and 45 IU/kg). | |
| Subject analysis set title | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects randomized to routine prophylaxis cohort to receive IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days up to 12 months as routine prophylaxis therapy for either Period 1 (Day 1 up to Month 12) or Period 2 (Month 13 up to Month 24) of the study. And subjects randomized to on demand cohort for Period 2 of the study, to receive IV infusion of moroctocog alfa (AF-CC) at 25 IU/kg, once in 2 days as routine prophylaxis therapy up to 12 months (Month 7 up to Month 18). | |

Primary: Mean Annualized Bleed Rate (ABR) by Treatment: On Demand Cohort

| | |
|--|---|
| End point title | Mean Annualized Bleed Rate (ABR) by Treatment: On Demand Cohort |
| End point description: | |
| ABR for each subject was calculated as the number of bleeds requiring administration of moroctocog alfa (AF-CC) divided by the total therapy duration (in days), then multiplied by 365.25 (days in a year). Intent-to-treat (ITT) analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form. Here, "Overall Number of Subjects Analysed" signifies subjects who were evaluable for this end point. | |
| End point type | Primary |
| End point timeframe: | |
| Day 1 up to Month 6 (OD Cohort, OD Therapy, Period 1); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2) | |

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Moroctocog alfa (AF-CC), On Demand Cohort: On Demand Therapy | Moroctocog alfa (AF-CC), On Demand Cohort: RP Therapy 25 IU/kg | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 9 | 8 | | |
| Units: Bleeds per year | | | | |
| arithmetic mean (standard deviation) | 47.0 (\pm 32.2) | 1.5 (\pm 2.2) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | OD Cohort: OD therapy versus RP therapy 25 IU/kg |
| Statistical analysis description: | |
| Ratio of the arithmetic means of the ABR for on demand cohort, on demand therapy to routine prophylaxis therapy 25 IU/kg was calculated. One-sided 95% CI for this ratio was reported. Number of subjects contributing to ratio of means and CI =9. | |
| Comparison groups | Moroctocog alfa (AF-CC), On Demand Cohort: On Demand Therapy v Moroctocog alfa (AF-CC), On Demand Cohort: RP Therapy 25 IU/kg |
| Number of subjects included in analysis | 17 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | = 0.002 ^[2] |
| Method | Paired t-test |
| Parameter estimate | Ratio of arithmetic means |
| Point estimate | 0.03 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | 0.08 |

Notes:

[1] - Field appearing in later section: "Number of subjects included in analysis", is an auto populated field from database (sum of number of subjects analysed for the reporting arms selected to report statistical data): which may not be the actual number of subjects contributing to statistical analysis.

[2] - Number of subjects contributing to P-value = 8.

Secondary: Mean Annualized Bleed Rate (ABR) by Treatment: Routine Prophylaxis Cohort

| | |
|---|---|
| End point title | Mean Annualized Bleed Rate (ABR) by Treatment: Routine Prophylaxis Cohort |
| End point description: | |
| ABR for each subject was calculated as the number of bleeds requiring administration of moroctocog alfa (AF-CC) divided by the total therapy duration (in days), then multiplied by 365.25 (days in a year). ITT analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form. Here, "Overall Number of Subjects Analysed" signifies subjects who were evaluable for this endpoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Month 24 (RP Cohort, Period 1 and Period 2) | |

| End point values | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 38 | 38 | | |
| Units: Bleeds per year | | | | |
| arithmetic mean (standard deviation) | 2.2 (± 4.1) | 3.3 (± 5.3) | | |

Statistical analyses

| Statistical analysis title | RP Cohort: RP 45 IU/kg versus RP 25 IU/kg |
|---|--|
| Statistical analysis description: | |
| Field appearing in later section: "Number of subjects included in analysis", is auto populated from database (sum of number of subjects analysed for reporting arms selected to report statistical data): which may not be actual number of subjects contributing to statistical analysis. Here, number of subjects contributing to statistical analysis =35. | |
| Comparison groups | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 25 IU/kg v Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg |
| Number of subjects included in analysis | 76 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[3] |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.03 |
| upper limit | 2.22 |

Notes:

[3] - 90% 2-sided CI for the mean difference in ABRs for the 2 prophylaxis regimens for ITT subjects was constructed using the t distribution with n-1 degrees of freedom (n equals the number of subjects) to assess the equivalence of the 2 regimens. Equivalence was demonstrated and the null hypothesis rejected if the limits of the 90% CI fell wholly within the interval of (-4, 4) bleeds per year.

Secondary: Mean of Moroctocog Alfa (AF-CC) Infusions Administered To Treat Bleeding Episode: All Subjects

| | |
|---|--|
| End point title | Mean of Moroctocog Alfa (AF-CC) Infusions Administered To Treat Bleeding Episode: All Subjects |
| End point description: | |
| In this end point, the mean of total number of moroctocog alfa (AF-CC) on-demand infusions administered to treat each bleeding episode was reported, regardless of subject cohort or period during which it occurred. ITT analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form. Here, "Overall Number of Subjects Analysed" signifies subjects who were evaluable for this endpoint. Number of bleeds analysed: Moroctocog alfa: All Subjects (562) | |
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Month 24 | |

| | | | | |
|--------------------------------------|---------------------------------------|--|--|--|
| End point values | Moroctocog alfa (AF-CC): All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 38 | | | |
| Units: Infusions | | | | |
| arithmetic mean (standard deviation) | 1.5 (± 1.38) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Treated Bleeds Classified on Basis of Response to First Infusion of Moroctocog Alfa (AF-CC) as On-Demand Treatment: OD Therapy (OD and RP Cohort)

| | |
|-----------------|---|
| End point title | Number of Treated Bleeds Classified on Basis of Response to First Infusion of Moroctocog Alfa (AF-CC) as On-Demand Treatment: OD Therapy (OD and RP Cohort) |
|-----------------|---|

End point description:

Number (no.) of bleeds treated reported on basis of response to first (1st) infusion of study drug, at 4-point scale: excellent, good, moderate, no response. Excellent: definite pain relief and improvement (DPRI) in bleeding signs within 8 hours (hr) after infusion, no additional infusion given; Good: DPRI in bleeding signs within 8 hr after infusion, at least 1 additional infusion given for complete resolution or with no additional infusion given; Moderate: probable or slight improvement starting after 8 hr following infusion, at least 1 additional infusion given for complete resolution; No Response: no improvement at all between infusions or during 24 hr interval following infusion or condition worsen. Bleeds in which response not recorded, reported as: Data Not Recorded. No. of 1st infusions not=total no. of bleeds if bleed was: missing start date/dose information or treated initially with non study FVIII. ITT analysis. Subjects Analysed=subjects evaluable. Bleeds analysed=559.

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

End point timeframe:

Day 1 up to Month 24

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | Moroctocog alfa (AF-CC): On Demand Therapy | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 38 | | | |
| Units: Bleeds | | | | |
| Excellent | 376 | | | |
| Good | 150 | | | |
| Moderate | 27 | | | |
| No Response | 2 | | | |
| Data Not Recorded | 4 | | | |

Statistical analyses

Secondary: Number of Treated Spontaneous Bleeds by Time Interval between Bleed Onset and Prior Moroctocog alfa (AF-CC) Prophylaxis Dose: Routine Prophylaxis Therapy

| | |
|-----------------|---|
| End point title | Number of Treated Spontaneous Bleeds by Time Interval between Bleed Onset and Prior Moroctocog alfa (AF-CC) Prophylaxis Dose: Routine Prophylaxis Therapy |
|-----------------|---|

End point description:

In this end point number of treated spontaneous bleeding episodes for following time intervals between bleed onset and prior moroctocog alfa (AF-CC) prophylaxis dose are reported: lesser than or equal to (\leq) 24 hours, greater than ($>$) 24 hours to \leq 48 hours, $>$ 48 hours to \leq 72 hours, $>$ 72 hours. For reporting arm: routine prophylaxis 25 IU/kg therapy, cumulative data for routine prophylaxis cohort (Day 1 up to Month 24, Period 1 and Period 2) and on demand cohort (Month 7 up to Month 18, Period 2) is reported. Analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form and only subjects who reported a spontaneous bleeding episode following a routine prophylaxis dose. Number of bleeds analysed: Moroctocog alfa, RP Therapy 45 IU/kg (28) and Moroctocog alfa: RP Therapy 25 IU/kg (18).

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

End point timeframe:

Day 1 up to Month 24 (RP Cohort, RP 25 IU/kg and 45 IU/kg, Period 1 and 2); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2)

| End point values | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg | | |
|---------------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 7 | 9 | | |
| Units: Bleeds | | | | |
| \leq 24 hours | 3 | 1 | | |
| $>$ 24 hours to \leq 48 hours | 6 | 4 | | |
| $>$ 48 hours to \leq 72 hours | 2 | 10 | | |
| $>$ 72 hours | 7 | 13 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Requiring Prophylaxis Regimen Escalation: Routine Prophylaxis Therapy

| | |
|-----------------|--|
| End point title | Number of Subjects Requiring Prophylaxis Regimen Escalation: Routine Prophylaxis Therapy |
|-----------------|--|

End point description:

During prophylaxis, criteria for prophylaxis regimen escalation are occurrence, over 4-week duration of (a) 2 or more spontaneous bleeds into a major joint and target joint, or (b) 3 or more spontaneous bleeds (consisting of joint bleeds and significant soft tissue/muscle or other site bleeds). If either criterion was met, subject was escalated to more intense prophylaxis regimen of 45 IU/kg, administered every other day. Subject who met dose escalation criteria while on prophylaxis regimen of 45 IU/kg, were escalated to higher intensity regimen designated by investigator. Significant spontaneous bleeds were those that led to transient or persistent loss of function. For reporting arm: routine prophylaxis 25

IU/kg therapy, cumulative data for RP cohort (Day 1 up to Month 24, Period 1 and Period 2) and OD cohort (Month 7 up to Month 18, Period 2) is reported. ITT analysis set. Overall Number of Subjects Analysed = subjects evaluable for this endpoint.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Month 24 (RP Cohort, RP 25 IU/kg and 45 IU/kg, Period 1 and 2); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2) | |

| End point values | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg | | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 48 | 39 | | |
| Units: Subjects | 1 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Routine Prophylaxis Dose (IU/kg) of Moroctocog alfa (AF-CC) Received: Routine Prophylaxis Therapy

| | |
|-----------------|--|
| End point title | Mean Routine Prophylaxis Dose (IU/kg) of Moroctocog alfa (AF-CC) Received: Routine Prophylaxis Therapy |
|-----------------|--|

End point description:

Mean RP dose (by weight) for each subject was calculated as his total moroctocog alfa (AF-CC) consumption (in IU) divided by weight (in kg). For reporting arm: routine prophylaxis 25 IU/kg therapy, cumulative data for routine prophylaxis cohort (Day 1 up to Month 24, Period 1 and Period 2) and on demand cohort (Month 7 up to Month 18, Period 2) is reported. ITT analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form. Here, "Overall Number of Subjects Analysed" signifies subjects who were evaluable for this end point.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Month 24 (RP Cohort, Period 1 and Period 2); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2) | |

| End point values | Moroctocog alfa (AF-CC), On Demand Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg |
|--------------------------------------|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 8 | 40 | 48 | 39 |
| Units: IU/kg | | | | |
| arithmetic mean (standard deviation) | 25 (± 4.6) | 26 (± 5.4) | 26 (± 5.2) | 46 (± 5.8) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean of Total Number Moroctocog alfa (AF-CC) Infusions Received: Routine Prophylaxis Therapy

| | |
|-----------------|--|
| End point title | Mean of Total Number Moroctocog alfa (AF-CC) Infusions Received: Routine Prophylaxis Therapy |
|-----------------|--|

End point description:

In this end point mean of total number of infusions of moroctocog alfa (AF-CC) received by subject is reported. For reporting arm: routine prophylaxis 25 IU/kg therapy, cumulative data for routine prophylaxis cohort (Day 1 up to Month 24, Period 1 and Period 2) and on demand cohort (Month 7 up to Month 18, Period 2) is reported. ITT analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form. Here, "Overall Number of Subjects Analysed" signifies subjects who were evaluable for this end point.

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

End point timeframe:

Day 1 up to Month 24 (RP Cohort, Period 1 and Period 2); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2)

| End point values | Moroctocog alfa (AF-CC), On Demand Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg |
|--------------------------------------|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 8 | 40 | 48 | 39 |
| Units: Infusions | | | | |
| arithmetic mean (standard deviation) | 170 (\pm 31.3) | 150 (\pm 37.0) | 154 (\pm 36.6) | 91 (\pm 22.4) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean of Total Number of Days Subjects Exposed to Moroctocog alfa (AF-CC): Routine Prophylaxis Therapy

| | |
|-----------------|---|
| End point title | Mean of Total Number of Days Subjects Exposed to Moroctocog alfa (AF-CC): Routine Prophylaxis Therapy |
|-----------------|---|

End point description:

For reporting arm: routine prophylaxis 25 IU/kg therapy, cumulative data for routine prophylaxis cohort (Day 1 up to Month 24, Period 1 and Period 2) and on demand cohort (Month 7 up to Month 18, Period 2) is reported. ITT analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form. Here, "Overall Number of Subjects Analysed" signifies subjects who were evaluable for this end point.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Month 24 (RP Cohort, Period 1 and Period 2); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2) | |

| End point values | Moroctocog alfa (AF-CC), On Demand Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg |
|--------------------------------------|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 8 | 40 | 48 | 39 |
| Units: Days | | | | |
| arithmetic mean (standard deviation) | 170 (± 31.3) | 150 (± 37.0) | 153 (± 36.5) | 91 (± 22.3) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean of Total Number of Infusions of Moroctocog alfa (AF-CC) Received per Week to Assess Compliance: Routine Prophylaxis Therapy

| | |
|-----------------|--|
| End point title | Mean of Total Number of Infusions of Moroctocog alfa (AF-CC) Received per Week to Assess Compliance: Routine Prophylaxis Therapy |
|-----------------|--|

End point description:

Subjects' compliance to their assigned prophylaxis regimen was measured by following: a) number of infusions received per week and b) dose received. In this end point mean of total number of infusions of moroctocog alfa (AF-CC) received by subjects per week is reported. For reporting arm: routine prophylaxis 25 IU/kg therapy, cumulative data for routine prophylaxis cohort (Day 1 up to Month 24, Period 1 and Period 2) and on demand cohort (Month 7 up to Month 18, Period 2) is reported. ITT analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form. Here, "Overall Number of Subjects Analysed" signifies subjects who were evaluable for this endpoint.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Month 24 (RP Cohort, RP 25 IU/kg and 45 IU/kg, Period 1 and 2); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2) | |

| End point values | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg | | |
|--------------------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 48 | 39 | | |
| Units: Infusions per week | | | | |
| arithmetic mean (standard deviation) | 3.3 (± 0.18) | 2.1 (± 0.81) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Phase Half Life (t_{1/2}) of Factor VIII (FVIII) Activity

| | |
|-----------------|--|
| End point title | Terminal Phase Half Life (t _{1/2}) of Factor VIII (FVIII) Activity |
|-----------------|--|

End point description:

Plasma decay half-life is the time measured for the FVIII activity to decrease by one half. Analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form, were in a non bleeding state, participated in a single pharmacokinetic (PK) assessment at the start of the study and for whom an adequate PK profile had been obtained.

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

End point timeframe:

0.5, 8, 24, 28 and 32 hours post dose on Day 1

| | | | | |
|--------------------------------------|-----------------------------------|--|--|--|
| End point values | Moroctocog alfa (AF-CC): 50 IU/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Hour | | | | |
| arithmetic mean (standard deviation) | 8.86 (± 2.3513) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) of Factor VIII Activity

| | |
|-----------------|--|
| End point title | Clearance (CL) of Factor VIII Activity |
|-----------------|--|

End point description:

Clearance is a measure of the volume of plasma from which FVIII activity is removed per unit time. It was reported in units milliliter per hour per kilogram (mL/hr/kg). Analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form, were in a non bleeding state, participated in a single PK assessment at the start of the study and for whom an adequate PK profile had been obtained.

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

End point timeframe:

0.5, 8, 24, 28 and 32 hours post dose on Day 1

| | | | | |
|---|--------------------------------------|--|--|--|
| End point values | Moroctocog alfa (AF-CC): 50 IU/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: mL/hr/kg | | | | |
| geometric mean (geometric coefficient of variation) | 5.822 (\pm 59) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Incremental Recovery of Factor VIII Activity

| | |
|--|--|
| End point title | Incremental Recovery of Factor VIII Activity |
| End point description: | |
| Incremental recovery was the increase in circulating factor VIII (FVIII) activity for every international unit (IU) of moroctocog alfa (AF-CC) administered per kilogram of body weight of subject. It was measured in international units per deciliter per international units per kilogram (IU/dL)/(IU/kg). Analysis population included all subjects for whom legal acceptable representative had signed informed consent/assent form, were in a non-bleeding state, participated in single PK assessment at start of the study and for whom an adequate PK profile had been obtained. Here, "n" signifies number of subjects evaluable at specified time point. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 1, Month 6 | |

| | | | | |
|--------------------------------------|--------------------------------------|--|--|--|
| End point values | Moroctocog alfa (AF-CC): 50 IU/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: (IU/dL)/(IU/kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1(n=6) | 1.4438 (\pm 0.6145) | | | |
| Month 6 (n=2) | 1.4148 (\pm 0.4046) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Concentration of Factor VIII Activity

| | |
|--|---|
| End point title | Maximum Concentration of Factor VIII Activity |
| End point description: | |
| Maximum concentration of FVIII activity was measured in international units per milliliter (IU/mL). Analysis population included all subjects for whom legal acceptable representative had signed informed | |

consent/assent form, were in a non-bleeding state, participated in single PK assessment at start of the study and for whom an adequate PK profile had been obtained.

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

End point timeframe:

0.5, 8, 24, 28 and 32 hours post dose on Day 1

| | | | | |
|--|---|--|--|--|
| End point values | Moroctocog alfa (AF-CC): 50 IU/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: IU/mL | | | | |
| geometric mean (geometric coefficient of variation) | 0.7005 (\pm 60) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Extrapolated Infinite Time (AUCinf) of Factor VIII Activity

| | |
|-----------------|--|
| End point title | Area Under the Curve From Time Zero to Extrapolated Infinite Time (AUCinf) of Factor VIII Activity |
|-----------------|--|

End point description:

Area under FVIII activity-time profile from time zero extrapolated to infinite time. AUCinf is reported in units: international units*hour per milliliter (IU*hour/mL). Analysis population included all subjects for whom legal acceptable representative had signed informed consent/assent form, were in a non-bleeding state, participated in single PK assessment at start of the study and for whom an adequate PK profile had been obtained.

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

End point timeframe:

0.5, 8, 24, 28 and 32 hours post dose on Day 1

| | | | | |
|--|---|--|--|--|
| End point values | Moroctocog alfa (AF-CC): 50 IU/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: IU*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | 9.02 (\pm 50) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Last Measurable Concentration (AUClast) of Factor VIII Activity

| | |
|-----------------|--|
| End point title | Area Under the Curve From Time Zero to Last Measurable Concentration (AUClast) of Factor VIII Activity |
|-----------------|--|

End point description:

Area under the FVIII activity-versus-time curve from time zero to the time of the last quantifiable concentration. Analysis population included all subjects for whom legal acceptable representative had signed informed consent/assent form, were in a non-bleeding state, participated in single PK assessment at start of the study and for whom an adequate PK profile had been obtained.

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

End point timeframe:

0.5, 8, 24, 28 and 32 hours post dose on Day 1

| | | | | |
|---|-----------------------------------|--|--|--|
| End point values | Moroctocog alfa (AF-CC): 50 IU/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: IU*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | 8.04 (± 46) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Steady-State Volume of Distribution (Vss) of Factor VIII Activity

| | |
|-----------------|---|
| End point title | Steady-State Volume of Distribution (Vss) of Factor VIII Activity |
|-----------------|---|

End point description:

Volume of distribution is defined as the theoretical volume in which the total amount of FVIII would need to be uniformly distributed to produce the observed plasma concentration of FVIII. Steady state volume of distribution (Vss) is the apparent volume of distribution at steady-state. Analysis population included all subjects for whom legal acceptable representative had signed informed consent/assent form, were in a non-bleeding state, participated in single PK assessment at start of the study and for whom an adequate PK profile had been obtained.

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

End point timeframe:

0.5, 8, 24, 28 and 32 hours post dose on Day 1

| | | | | |
|---|---|--|--|--|
| End point values | Moroctocog alfa (AF-CC): 50 IU/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Milliliter per kilogram | | | | |
| geometric mean (geometric coefficient of variation) | 78.38 (\pm 50) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Residence Time (MRT) of Factor VIII Activity

| | |
|-----------------|---|
| End point title | Mean Residence Time (MRT) of Factor VIII Activity |
|-----------------|---|

End point description:

MRT was calculated as $AUMC_{inf} / AUC_{inf-TI/2}$, where $AUMC_{inf}$ is the area under the moment curve from time zero to infinity and TI is the duration of infusion. Analysis population included all subjects for whom legal acceptable representative had signed informed consent/assent form, were in a non-bleeding state, participated in single PK assessment at start of the study and for whom an adequate PK profile had been obtained.

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

End point timeframe:

0.5, 8, 24, 28 and 32 hours post dose on Day 1

| | | | | |
|---|---|--|--|--|
| End point values | Moroctocog alfa (AF-CC): 50 IU/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 7 | | | |
| Units: Hour | | | | |
| geometric mean (geometric coefficient of variation) | 13.46 (\pm 33) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment Emergent Adverse Events (AEs) According to Severity

| | |
|-----------------|---|
| End point title | Number of Subjects with Treatment Emergent Adverse Events (AEs) According to Severity |
|-----------------|---|

End point description:

AE=untoward medical occurrence in clinical investigation subject administered product or medical device;event need not necessarily had causal relationship with treatment or usage.Treatment-emergent are events between first dose of study drug and up to 28 days after last dose of study drug(up to 25 months)that were absent before treatment or that worsened relative to pretreatment state.AEs were classified into following on basis of severity:mild=did not interfere with subject's usual function;moderate=interfered to someextentwith subject's usual function;severe=interfered significantly

subject's usual function;life threatening=AE required discontinuation of study drug,subject was at immediate risk of death.All subject in study receivedAF-CC.AEs were not collected separately for each intervention for subjects.All subjects were properly combined for analysis,regardless of regimen were following attime,regardless of OD or RP cohort.Safety analysis set.N=number of subjects evaluable.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Month 25 | |

| | | | | |
|-----------------------------|---------------------------------------|--|--|--|
| End point values | Moroctocog alfa (AF-CC): All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 49 | | | |
| Units: Subjects | | | | |
| Mild | 12 | | | |
| Moderate | 29 | | | |
| Severe | 8 | | | |
| Life threatening | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Related Adverse Events

| | |
|-----------------|--|
| End point title | Number of Subjects With Treatment-Related Adverse Events |
|-----------------|--|

End point description:

A treatment related AE is any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event had a causal relationship with the treatment or usage. All subjects in the study received moroctocog alfa-(AF-CC). Adverse events were not collected separately for each intervention for the subjects. All subjects were properly combined for the analysis and was regardless of the regimen they were following at the time, and regardless of OD or RP cohort. Analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form and were analysed for safety.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 up to Month 25 | |

| | | | | |
|-----------------------------|---------------------------------------|--|--|--|
| End point values | Moroctocog alfa (AF-CC): All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 51 | | | |
| Units: Subjects | 49 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Confirmed FVIII Inhibitor Development

| | |
|--|---|
| End point title | Number of Subjects With Confirmed FVIII Inhibitor Development |
| End point description: Confirmed FVIII inhibitors were defined as a neutralizing antibody to FVIII with a titer value of greater than or equal to (\geq) 0.6 Bethesda units (BU) per millimeter in a sample assayed using the Nijmegen assay at the central laboratory. Modified intent-to-treat (mITT) analysis population included all subjects for whom a legal acceptable representative had signed the informed consent/assent form and who received at least 1 dose of moroctocog alfa (AF-CC). Here, "Overall Number of Subjects Analysed" signifies those subjects who were evaluable for this end point. | |
| End point type | Secondary |
| End point timeframe: Day 1 up to Month 24 | |

| End point values | Moroctocog alfa (AF-CC): All Subjects | | | |
|-----------------------------|---------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 49 | | | |
| Units: Subjects | 3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Incidence of Less than Expected Therapeutic Effect (LETE): On Demand Therapy

| | |
|---|--|
| End point title | Number of Subjects With Incidence of Less than Expected Therapeutic Effect (LETE): On Demand Therapy |
| End point description: LETE occurs in on-demand setting if subject recorded 2 successive "No Response" ratings after 2 successive infusions of study drug. Infusions must have been administered within 24 hours of each other for treatment of same bleeding event in the absence of confounding factors (known presence or subsequent identification of a FVIII inhibitor, known inadequate dose for type and severity of bleed in opinion of investigator, delay of >4 hours between onset of bleed to infusion, delay of >24 hours before administration of a follow-up infusion, known compromised study drug, faulty administration of study drug, subject had an underlying, predisposing condition responsible for bleed in opinion of investigator. For reporting arm: routine prophylaxis 25 IU/kg therapy, cumulative data for RP cohort (Day 1 up to Month 24, Period 1 and Period 2) and OD cohort (Month 7 up to Month 18, Period 2) is reported. ITT analysis population. Number of Subjects Analysed = subjects evaluable for this endpoint. | |
| End point type | Secondary |
| End point timeframe: Day 1 up to Month 24 (RP Cohort, RP 25 IU/kg and 45 IU/kg, Period 1 and 2); Day 1 up to Month 6 (OD Cohort, OD Therapy, Period 1); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2) | |

| End point values | Moroctocog alfa (AF-CC), On Demand Cohort: On Demand Therapy | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 9 | 42 | 51 | |
| Units: Subjects | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Incidence of Less than Expected Therapeutic Effect (LETE): Routine Prophylaxis Therapy

| | |
|-----------------|--|
| End point title | Number of Subjects With Incidence of Less than Expected Therapeutic Effect (LETE): Routine Prophylaxis Therapy |
|-----------------|--|

End point description:

LETE in prophylaxis setting if there was spontaneous bleed within 48 hours after regularly scheduled prophylactic dose of study drug in absence of confounding factors (known presence or subsequent identification of a FVIII inhibitor, known inadequate prophylactic dose [a dose less than that prescribed in subject's regimen], known lack of adherence to the prescribed prophylaxis regimen, bleed occurs in a target joint identified at the start of the study, known compromised study drug, faulty administration of study drug, subject had an underlying, predisposing condition responsible for bleed in opinion of investigator. Therefore, LETE in prophylaxis setting was occurrence of a bleed. For reporting arm: routine prophylaxis 25 IU/kg therapy, cumulative data for RP cohort (Day 1 up to Month 24, Period 1 and Period 2) and OD cohort (Month 7 up to Month 18, Period 2) is reported. ITT analysis population. Number of Subjects Analysed = subjects evaluable for this endpoint.

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

End point timeframe:

Day 1 up to Month 24 (RP Cohort, RP 25 IU/kg and 45 IU/kg, Period 1 and 2); Month 7 up to Month 18 (OD Cohort, RP 25 IU/kg, Period 2)

| End point values | Moroctocog alfa (AF-CC), RP Cohort: RP Therapy 45 IU/kg | Moroctocog alfa (AF-CC), OD and RP Cohort: RP Therapy 25 IU/kg | | |
|-----------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 42 | 51 | | |
| Units: Subjects | 3 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Month 25

Adverse event reporting additional description:

Same event may appear both an AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as non-serious in another, or subjects may have experienced both SAE and NAE. All subjects in study received moroctocog alfa (AF-CC). AEs were not collected separately for each intervention for subjects.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Moroctocog alfa (AF-CC): All Subjects |
|-----------------------|---------------------------------------|

Reporting group description:

All subjects who received moroctocog alfa-(AF-CC) 50 IU/kg for PK assessment on Day 1 prior start of study treatment and as on demand or routine prophylaxis treatment (25 and 45 IU/kg).

| Serious adverse events | Moroctocog alfa (AF-CC): All Subjects | | |
|---|---------------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 51 (25.49%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Limb injury | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |

| | | | |
|--|----------------|--|--|
| Monoplegia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Seizure | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Factor VIII inhibition | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Catheter site rash | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Haemarthrosis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscle haemorrhage | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Torticollis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| | | | |
|---|---------------------------------------|--|--|
| Non-serious adverse events | Moroctocog alfa (AF-CC): All Subjects | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 49 / 51 (96.08%) | | |
| Surgical and medical procedures | | | |
| Tooth extraction | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | | |
| occurrences (all) | 4 | | |
| Central venous catheterisation | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|------------------|--|--|
| Pyrexia | | | |
| subjects affected / exposed | 24 / 51 (47.06%) | | |
| occurrences (all) | 56 | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | | |
| occurrences (all) | 4 | | |
| Catheter site discharge | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Catheter site haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Catheter site swelling | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |
| Allergy to arthropod bite | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 15 / 51 (29.41%) | | |
| occurrences (all) | 21 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 7 / 51 (13.73%) | | |
| occurrences (all) | 11 | | |
| Epistaxis | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | | |
| occurrences (all) | 6 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 4 | | |
| Upper respiratory tract congestion | | | |

| | | | |
|--|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 5 / 51 (9.80%) 7 | | |
| Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | | |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | | |
| Body temperature increased subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 3 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | | |
| Injury, poisoning and procedural complications Joint injury subjects affected / exposed occurrences (all) | 10 / 51 (19.61%) 19 | | |
| Limb injury subjects affected / exposed occurrences (all) | 10 / 51 (19.61%) 11 | | |
| Head injury subjects affected / exposed occurrences (all) | 7 / 51 (13.73%) 18 | | |
| Contusion subjects affected / exposed occurrences (all) | 5 / 51 (9.80%) 11 | | |
| Fall subjects affected / exposed occurrences (all) | 5 / 51 (9.80%) 8 | | |
| Face injury | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 3 / 51 (5.88%) | | |
| occurrences (all) | 3 | | |
| Laceration | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | | |
| occurrences (all) | 3 | | |
| Traumatic haematoma | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | | |
| occurrences (all) | 4 | | |
| Eye injury | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Injury | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Skin abrasion | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Arthropod bite | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Arthropod sting | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Foreign body in gastrointestinal tract | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 2 | | |
| Traumatic haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Cyanosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--------------------------------------|------------------|--|--|
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 7 / 51 (13.73%) | | |
| occurrences (all) | 13 | | |
| Restless legs syndrome | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 5 | | |
| Tympanic membrane hyperaemia | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Eye disorders | | | |
| Astigmatism | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 2 | | |
| Vitreous floaters | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 10 / 51 (19.61%) | | |
| occurrences (all) | 18 | | |
| Diarrhoea | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 7 / 51 (13.73%) | | |
| occurrences (all) | 7 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 6 / 51 (11.76%) | | |
| occurrences (all) | 6 | | |
| Toothache | | | |
| subjects affected / exposed | 6 / 51 (11.76%) | | |
| occurrences (all) | 6 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | | |
| occurrences (all) | 8 | | |
| Tooth loss | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | | |
| occurrences (all) | 4 | | |
| Constipation | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Dental caries | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Gingival swelling | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Lip haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Oral disorder | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | | |
| occurrences (all) | 3 | | |

| | | | |
|---|------------------|--|--|
| Swelling face | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 3 | | |
| Intertrigo | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Ecchymosis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 10 / 51 (19.61%) | | |
| occurrences (all) | 14 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 10 / 51 (19.61%) | | |
| occurrences (all) | 17 | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | | |
| occurrences (all) | 6 | | |
| Haemarthrosis | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | | |
| occurrences (all) | 4 | | |
| Joint swelling | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 3 | | |
| Osteochondrosis | | | |

| | | | |
|-----------------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 16 / 51 (31.37%) | | |
| occurrences (all) | 35 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 14 / 51 (27.45%) | | |
| occurrences (all) | 33 | | |
| Influenza | | | |
| subjects affected / exposed | 8 / 51 (15.69%) | | |
| occurrences (all) | 12 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 7 / 51 (13.73%) | | |
| occurrences (all) | 9 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | | |
| occurrences (all) | 11 | | |
| Varicella | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | | |
| occurrences (all) | 4 | | |
| Viral infection | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | | |
| occurrences (all) | 4 | | |
| Device related infection | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 7 | | |
| Eye infection | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Impetigo | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 4 | | |

| | | | |
|---|----------------|--|--|
| Laryngitis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 4 | | |
| Otitis media | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 2 | | |
| Body tinea | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Enterobiasis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | | |
| occurrences (all) | 1 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | | |
| occurrences (all) | 4 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 12 June 2007 | Duration of each treatment period (Period 1 and 2) was lengthened from 9 months per treatment period to 12 months per treatment period. |
| 31 August 2011 | Segment 1 for the OD cohort was shortened to 6 months duration from 12 months. Segment 2 for the OD cohort and Segments 1 and 2 for the RP cohort remained at 12 months duration. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported