



Clinical trial results:

BAX326 (recombinant Factor IX): Evaluation of Safety, Immunogenicity, and Hemostatic Efficacy in Previously Treated Patients with Severe (FIX level < 1%) or Moderately Severe (FIX level 1-2 %) Hemophilia B - A Continuation Study

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2010-022726-33 |
| Trial protocol | BG CZ GB DE SE PL ES IT IE |
| Global end of trial date | 29 June 2017 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 05 January 2018 |
| First version publication date | 05 January 2018 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 251001 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01286779 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Baxalta, now part of Shire |
| Sponsor organisation address | Industriestrasse 67, Vienna, Austria, 1221 |
| Public contact | Study Physician, Baxalta, now part of Shire, ClinicalTransparency@shire.com |
| Scientific contact | Study Physician, Baxalta, now part of Shire, ClinicalTransparency@shire.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001139-PIP01-11 |
| 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 | 29 June 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 June 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 June 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Further evaluate safety of BAX326 in terms of IP-related AEs as well as clinically significant changes in routine laboratory parameters and vital signs. Further evaluate the hemostatic efficacy of BAX326 in the prevention and routine prophylaxis of acute bleeding episodes using various dose regimens. Further evaluate the hemostatic efficacy of BAX326 in the management of acute bleeding episodes. Further evaluate the immunogenicity of BAX326 for up to 100 exposure days to BAX326. Monitor IR of BAX326 over time. Evaluate changes in health related quality of life (HR QoL), patient activity level and health resource use.

Protection of trial subjects:

This study was conducted in accordance with the study protocol, the International Conference on Harmonisation Guideline for Good Clinical Practice E6 (ICH GCP, April 1996), Title 21 of the US Code of Federal Regulations (US CFR), the European Clinical Trial Directive (2001/20/EC and 2005/28/EC), and applicable national and local regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 12 April 2011 |
| 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 | Bulgaria: 10 |
| Country: Number of subjects enrolled | Czech Republic: 2 |
| Country: Number of subjects enrolled | Ireland: 2 |
| Country: Number of subjects enrolled | Italy: 4 |
| Country: Number of subjects enrolled | Poland: 22 |
| Country: Number of subjects enrolled | Romania: 12 |
| Country: Number of subjects enrolled | Sweden: 1 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | India: 1 |
| Country: Number of subjects enrolled | Japan: 3 |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | Taiwan: 6 |
| Country: Number of subjects enrolled | Argentina: 2 |
| Country: Number of subjects enrolled | Brazil: 1 |
| Country: Number of subjects enrolled | Chile: 5 |
| Country: Number of subjects enrolled | Colombia: 4 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Russian Federation: 18 |
| Country: Number of subjects enrolled | Ukraine: 21 |
| Worldwide total number of subjects | 117 |
| EEA total number of subjects | 55 |

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) | 21 |
| Adolescents (12-17 years) | 5 |
| Adults (18-64 years) | 89 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Enrollment was conducted at 40 clinical sites in 18 countries. A total of 117 participants were enrolled. Of these, 65 participants transitioned from BAX326 pivotal study, 20 participants transitioned from BAX326 pediatric study and 32 participant were newly recruited.

Pre-assignment

Screening details:

Of 117 enrolled participants, 115 received treatment with IP. All 85 participants who transitioned from the pivotal/pediatric studies continued to receive IP in this study. Of the 32 newly recruited participants, 30 received treatment with IP. 1 participant did not meet the entry criteria and 1 participant discontinued the study prior treatment.

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 117 |
| Number of subjects completed | 115 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---|
| Reason: Number of subjects | Subject discontinued the study prior treatment: 1 |
| Reason: Number of subjects | Screen failure: 1 |

Period 1

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

Arms

| | |
|-----------|---------------|
| Arm title | Overall study |
|-----------|---------------|

Arm description:

Participants treated with BAX 326

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Rixubis |
| Investigational medicinal product code | BAX 326 |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Treatment with BAX326 is at the discretion of the investigator and consists of either prophylaxis or on-demand. Newly recruited subjects receive prophylactic treatment only. Standard Prophylaxis with twice weekly infusions of 50 IU/kg (range 40-60 IU/kg) which may be increased to 75 IU/kg in subjects ≥ 12 years of age; range 40-80 IU/kg in subjects < 12 years of age. Modified Prophylaxis is determined by the investigator and dose can be increased up to 100 IU/kg, if applicable. PK-tailored Prophylaxis is based on subject's individual PK. The maximum dose is 120 IU/kg.

| Number of subjects in period 1^[1] | Overall study |
|---|----------------------|
| Started | 115 |
| Completed | 96 |
| Not completed | 19 |
| Consent withdrawn by subject | 9 |
| Physician decision | 2 |
| Participant moved to another country | 1 |
| Discontinued by sponsor | 1 |
| Participant had scheduled surgery | 1 |
| Protocol deviation | 5 |

Notes:

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

Justification: Of 117 enrolled participants (who signed informed consent), 115 received treatment with investigational product. 1 participant did not meet the entry criteria and 1 participant discontinued the study prior treatment.

Baseline characteristics

Reporting groups

| | |
|-----------------------------------|---------------|
| Reporting group title | Overall study |
| Reporting group description: | |
| Participants treated with BAX 326 | |

| Reporting group values | Overall study | Total | |
|--------------------------------|---------------|-------|--|
| Number of subjects | 115 | 115 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 29.6 | | |
| standard deviation | ± 16.39 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 115 | 115 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Race White | 99 | 99 | |
| Race Black or African American | 1 | 1 | |
| Race Asian | 10 | 10 | |
| Race Other | 5 | 5 | |

Subject analysis sets

| | |
|---|-------------------------|
| Subject analysis set title | Full analysis set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Comprises all participants who are exposed to any amount of investigational product. | |
| Subject analysis set title | Standard prophylaxis |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants treated with BAX 326 with twice weekly prophylactic infusions of 50 IU/kg | |
| Subject analysis set title | Modified prophylaxis |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants treated with BAX 326 with prophylactic treatment determined by the investigator. The dose could be increased up to 100 IU/kg if indicated. | |
| Subject analysis set title | PK-tailored prophylaxis |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants treated with BAX 326 with PK tailored prophylaxis based on participant's individual PK with maximum dose of 120 IU/kg. | |
| Subject analysis set title | Overall prophylaxis |

| | |
|---|-----------------------------------|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All participants who received BAX 326 as prophylactic regimen (standard prophylaxis, modified prophylaxis and PK-tailored prophylaxis) | |
| Subject analysis set title | On-demand |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All participants who received BAX 326 as on-demand regimen. | |
| Subject analysis set title | Pharmacokinetic full analysis set |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Comprises all participants from the full analysis set who underwent an abbreviated PK study. | |

| Reporting group values | Full analysis set | Standard prophylaxis | Modified prophylaxis |
|------------------------------------|-------------------|----------------------|----------------------|
| Number of subjects | 115 | 108 | 26 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Age continuous Units: years arithmetic mean standard deviation | 29.6 ± 16.39 | 28.9 ± 16.19 | 32.3 ± 17.76 |
| Gender categorical Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 115 | 108 | 26 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Race White | 99 | 95 | 23 |
| Race Black or African American | 1 | 1 | 0 |
| Race Asian | 10 | 7 | 1 |
| Race Other | 5 | 5 | 2 |

| Reporting group values | PK-tailored prophylaxis | Overall prophylaxis | On-demand |
|------------------------------------|-------------------------|---------------------|-----------|
| Number of subjects | 3 | 110 | 13 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Age continuous Units: years arithmetic mean standard deviation | 43.0 ± 18.52 | 29.1 ± 16.28 | 36.6 ± 11.64 |
| Gender categorical Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 3 | 110 | 13 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Race White | 0 | 95 | 12 |

| | | | |
|--------------------------------|---|---|---|
| Race Black or African American | 0 | 1 | 0 |
| Race Asian | 3 | 9 | 1 |
| Race Other | 0 | 5 | 0 |

| | | | |
|-------------------------------|-----------------------------------|--|--|
| Reporting group values | Pharmacokinetic full analysis set | | |
| Number of subjects | 6 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------------------|---------|--|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 38.5 | | |
| standard deviation | ± 12.77 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | | |
| Male | 6 | | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Race White | 2 | | |
| Race Black or African American | 0 | | |
| Race Asian | 4 | | |
| Race Other | 0 | | |

End points

End points reporting groups

| | |
|---|-----------------------------------|
| Reporting group title | Overall study |
| Reporting group description: | |
| Participants treated with BAX 326 | |
| Subject analysis set title | Full analysis set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Comprises all participants who are exposed to any amount of investigational product. | |
| Subject analysis set title | Standard prophylaxis |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants treated with BAX 326 with twice weekly prophylactic infusions of 50 IU/kg | |
| Subject analysis set title | Modified prophylaxis |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants treated with BAX 326 with prophylactic treatment determined by the investigator. The dose could be increased up to 100 IU/kg if indicated. | |
| Subject analysis set title | PK-tailored prophylaxis |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants treated with BAX 326 with PK tailored prophylaxis based on participant's individual PK with maximum dose of 120 IU/kg. | |
| Subject analysis set title | Overall prophylaxis |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| All participants who received BAX 326 as prophylactic regimen (standard prophylaxis, modified prophylaxis and PK-tailored prophylaxis) | |
| Subject analysis set title | On-demand |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| All participants who received BAX 326 as on-demand regimen. | |
| Subject analysis set title | Pharmacokinetic full analysis set |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Comprises all participants from the full analysis set who underwent an abbreviated PK study. | |

Primary: Adverse events possibly or probably related to the investigational product

| | |
|---|---|
| End point title | Adverse events possibly or probably related to the investigational product ^[1] |
| End point description: | |
| Possibly or probably related adverse events that occurred during or after first BAX326 infusion. | |
| End point type | Primary |
| End point timeframe: | |
| Assessed (based on patient diary) every 3 months until study completion. | |
| 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: Per protocol, only descriptive statistics were collected for this endpoint. | |

| End point values | Overall study | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 115 | | | |
| Units: Adverse Events | | | | |
| Related adverse events | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment of bleeding episodes: Number of infusions per bleeding episode

| | |
|--|--|
| End point title | Treatment of bleeding episodes: Number of infusions per bleeding episode |
| End point description: Infusions of BAX326 that were required until bleed resolution. | |
| End point type | Secondary |
| End point timeframe: Throughout the study from screening to study completion | |

| End point values | Overall study | Standard prophylaxis | Modified prophylaxis | PK-tailored prophylaxis |
|--------------------------------------|-----------------|----------------------|----------------------|-------------------------|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 115 | 108 | 26 | 3 |
| Units: Number of infusions | | | | |
| arithmetic mean (standard deviation) | | | | |
| Number of infusions | 1.8 (± 1.65) | 2.1 (± 2.12) | 1.9 (± 1.41) | 1.3 (± 0.46) |

| End point values | Overall prophylaxis | On-demand | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 110 | 13 | | |
| Units: Number of infusions | | | | |
| arithmetic mean (standard deviation) | | | | |
| Number of infusions | 2.0 (± 2.01) | 1.5 (± 0.79) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment of bleeding episodes: Overall hemostatic efficacy rating at resolution of bleed

| | |
|--|---|
| End point title | Treatment of bleeding episodes: Overall hemostatic efficacy rating at resolution of bleed |
| End point description: | |
| Excellent: Full relief of pain and cessation of objective signs of bleeding after a single infusion. No additional infusion is required for the control of bleeding. Administration of further infusion would not affect the scoring. Good: Definite pain relief and/or improvement in signs of bleeding after a single infusion. Possibly requires more than 1 infusion for complete resolution. Fair: Probable and/or slight relief of pain and slight improvement in signs of bleeding after a single infusion. Required more than 1 infusion for complete resolution. None: No improvement or condition worsens. | |
| End point type | Secondary |
| End point timeframe: | |
| Throughout the study from screening to study completion. | |

| End point values | Overall study | Standard prophylaxis | Modified prophylaxis | PK-tailored prophylaxis |
|-----------------------------|-----------------|----------------------|----------------------|-------------------------|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 115 | 108 | 26 | 3 |
| Units: Bleeding episodes | | | | |
| Excellent | 341 | 168 | 51 | 0 |
| Good | 650 | 281 | 40 | 0 |
| Fair | 115 | 90 | 17 | 6 |
| None | 6 | 3 | 0 | 2 |

| End point values | Overall prophylaxis | On-demand | | |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 110 | 13 | | |
| Units: Bleeding episodes | | | | |
| Excellent | 219 | 122 | | |
| Good | 321 | 329 | | |
| Fair | 113 | 2 | | |
| None | 5 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized bleed rate during prophylaxis treatment

| | |
|---|--|
| End point title | Annualized bleed rate during prophylaxis treatment |
| End point description: | |
| Annualized bleed rate (ABR) was calculated as (number of bleeding episodes / observed treatment period in days) * 365.25. The ABR was calculated for participants with an observation period of at least 3 months with BAX326 on the specified treatment regimen. | |
| End point type | Secondary |
| End point timeframe: | |
| For Prophylactic treatment the period from first to last prophylactic infusion is considered. | |

| End point values | Standard prophylaxis | Modified prophylaxis | PK-tailored prophylaxis | Overall prophylaxis |
|-------------------------------|----------------------|----------------------|-------------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 106 | 22 | 2 | 108 |
| Units: Annualized bleed rate | | | | |
| median (full range (min-max)) | 1.3 (0.0 to 78.7) | 1.4 (0.0 to 34.6) | 1.9 (0.5 to 3.3) | 1.3 (0.0 to 52.2) |

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of BAX 326: Number of infusions per month and per year

| | |
|-----------------|--|
| End point title | Consumption of BAX 326: Number of infusions per month and per year |
|-----------------|--|

End point description:

The number of infusions consumed per month and per year for the prophylactic and on-demand treatment regimens.

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

End point timeframe:

Throughout the study from screening to study completion.

| End point values | Standard prophylaxis | Modified prophylaxis | PK-tailored prophylaxis | Overall prophylaxis |
|--------------------------------------|----------------------|----------------------|-------------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 108 | 26 | 3 | 110 |
| Units: Number of infusions | | | | |
| arithmetic mean (standard deviation) | | | | |
| Number of infusions per month | 8.5 (± 1.25) | 10.8 (± 4.34) | 4.0 (± 0.60) | 8.4 (± 1.38) |
| Number of infusions per year | 101.8 (± 15.03) | 130.2 (± 52.13) | 48.3 (± 7.23) | 101.1 (± 16.50) |

| End point values | On-demand | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 13 | | | |
| Units: Number of infusions | | | | |
| arithmetic mean (standard deviation) | | | | |
| Number of infusions per month | 3.6 (± 2.44) | | | |
| Number of infusions per year | 43.1 (± 29.28) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of BAX 326: Weight adjusted consumption per month and per year

| | |
|-----------------|--|
| End point title | Consumption of BAX 326: Weight adjusted consumption per month and per year |
|-----------------|--|

End point description:

The weight adjusted consumption of BAX 326 per month and per year for the prophylactic and on-demand treatment regimens.

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

End point timeframe:

Throughout the study from screening to study completion.

| End point values | Standard prophylaxis | Modified prophylaxis | PK-tailored prophylaxis | Overall prophylaxis |
|---|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 108 | 26 | 3 | 110 |
| Units: IU/kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| Weight adjusted BAX 326 consumption per month | 462.3 (\pm 102.05) | 684.4 (\pm 337.70) | 250.9 (\pm 41.37) | 464.2 (\pm 111.46) |
| Weight adjusted BAX 326 consumption per year | 5547.8 (\pm 1224.65) | 8212.4 (\pm 4052.36) | 3010.3 (\pm 496.44) | 5570.7 (\pm 1337.53) |

| End point values | On-demand | | | |
|---|-------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 13 | | | |
| Units: IU/kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| Weight adjusted BAX 326 consumption per month | 199.8 (\pm 124.18) | | | |
| Weight adjusted BAX 326 consumption per year | 2397.4 (\pm 1490.22) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of BAX326: Weight adjusted consumption per bleeding episode

| | |
|-----------------|---|
| End point title | Consumption of BAX326: Weight adjusted consumption per bleeding episode |
|-----------------|---|

End point description:

The weight adjusted consumption of BAX 326 per bleeding episode for the prophylactic and on-demand treatment regimens. Only infusions required until the resolution of bleed are considered.

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

End point timeframe:

Throughout the study from screening to study completion.

| End point values | Standard prophylaxis | Modified prophylaxis | PK-tailored prophylaxis | Overall prophylaxis |
|--------------------------------------|----------------------|----------------------|-------------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 108 | 26 | 3 | 110 |
| Units: IU/kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| IU/kg | 124.2 (± 140.70) | 114.8 (± 99.41) | 67.4 (± 34.39) | 122.0 (± 134.02) |

| End point values | On-demand | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 13 | | | |
| Units: IU/kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| IU/kg | 82.6 (± 48.21) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Development of inhibitory and total binding antibodies to FIX

| | |
|-----------------|---|
| End point title | Development of inhibitory and total binding antibodies to FIX |
|-----------------|---|

End point description:

Testing for inhibitory and total binding antibodies to FIX. Development during study means negative at screening and positive at any subsequent visit. Treatment emergent means more than 2-dilution increase as compared to the pre-study titer at screening.

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

End point timeframe:

Laboratory assessment for immunology were done at screening, at exposure day 1, at week 4 (± 1 week), at month 3 (±1 week), thereafter, every 3 months (± 1 week) and at study completion/termination.

| End point values | Overall study | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 115 | | | |
| Units: Participants | | | | |
| Inhibitory antibody to FIX | 0 | | | |
| Total binding antibody to FIX-develop.during study | 0 | | | |
| Total binding antibody to FIX-treatment emergent | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Development of antibodies to Chinese Hamster Ovary Proteins (CHO proteins) and rFurin

| | |
|-----------------|---|
| End point title | Development of antibodies to Chinese Hamster Ovary Proteins (CHO proteins) and rFurin |
|-----------------|---|

End point description:

Testing for antibodies to CHO proteins and rFurin. Development during study means negative at screening and positive at any subsequent visit. Treatment emergent means more than 2-dilution increase as compared to the pre-study titer at screening.

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

End point timeframe:

Laboratory assessment for immunology were done at screening, at exposure day 1, at week 4 (\pm 1 week), at month 3 (\pm 1 week), thereafter, every 3 months (\pm 1 week) and at study completion/termination.

| End point values | Overall study | | | |
|---|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 115 | | | |
| Units: Participants | | | | |
| Antibodies to CHO | 0 | | | |
| Antibodies to rFurin - development during study | 4 | | | |
| Antibodies to rFurin - treatment emergent | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of severe allergic reactions and thrombotic events

| | |
|-----------------|---|
| End point title | Occurrence of severe allergic reactions and thrombotic events |
|-----------------|---|

End point description:

The occurrence of severe allergic reactions and thrombotic events was assessed.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Throughout the study from screening to study completion. | |

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Overall study | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 115 | | | |
| Units: Participants | | | | |
| Severe allergic reactions | 0 | | | |
| Thrombotic events | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical significant changes in routine laboratory parameters and vital signs

| | |
|-----------------|---|
| End point title | Clinical significant changes in routine laboratory parameters and vital signs |
|-----------------|---|

End point description:

Hematology panel consists of complete blood count (hemoglobin, hematocrit, erythrocytes, leukocytes) with differential (ie, basophils, eosinophils, lymphocytes, monocytes, neutrophils), mean corpuscular volume, mean corpuscular hemoglobin concentration and platelet count. Clinical chemistry panel consists of sodium, potassium, chloride, bicarbonate, total protein, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, alkaline phosphatase, blood urea nitrogen, creatinine and glucose. Vital signs include body temperature, respiratory rate, pulse rate, supine systolic and diastolic blood pressure.

CS = clinically significant, NCS = not clinically significant

Change from Screening to End of Study is reported.

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

End point timeframe:

Measurements at screening and at study completion/termination are included in the analysis.

| | | | | |
|---|-----------------|--|--|--|
| End point values | Overall study | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 115 | | | |
| Units: Participants | | | | |
| Hematology: Change from normal to abnormal CS | 2 | | | |
| Hematology: Change from abnormal NCS to abnormal CS | 1 | | | |
| Chemistry: Change from normal to abnormal, CS | 1 | | | |
| Chemistry: Change from abnormal NCS to abnormal CS | 3 | | | |
| Change in vital signs | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Incremental Recovery (IR) over time

| | |
|-----------------|---|
| End point title | Pharmacokinetics: Incremental Recovery (IR) over time |
|-----------------|---|

End point description:

PK infusion with investigational product was administered after a wash out period of at least 5 days. Incremental recovery is calculated as $IR_{30min} = (C_{30min} [IU/dL] - C_{pre-infusion} [IU/dL]) / \text{dose per kg body weight [IU/kg]}$ where C_{30min} and $C_{pre-infusion}$ relate to the unadjusted concentration values. All subjects treated with investigational product were included in this analysis.

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

End point timeframe:

IR over time was analysed at Baseline and at Completion/Termination visit within 30 minutes pre-infusion and at 30 (\pm 5) minutes post-infusion.

| End point values | Overall study | | | |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 110 ^[2] | | | |
| Units: (IU/dL)/(IU/kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 0.85 (\pm 0.207) | | | |
| End of study | 0.85 (\pm 0.286) | | | |
| Change from baseline to end of study | -0.005 (\pm 0.259) | | | |

Notes:

[2] - n=110 at baseline, n=108 at end of study, n=104 for change

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Area under the plasma concentration versus time curve from time 0 to infinity (AUC 0- ∞)

| | |
|-----------------|--|
| End point title | Pharmacokinetics: Area under the plasma concentration versus time curve from time 0 to infinity (AUC 0- ∞) |
|-----------------|--|

End point description:

After a wash out period of at least 5 days PK infusion with investigational product was administered. AUC 0- ∞ is defined as $AUC_{0-t} + C_t / \lambda_z$, where t is the time of last quantifiable concentration, C_t is the last quantifiable concentration.

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

End point timeframe:

PK assessments were done within 30 minutes pre-infusion and post-infusion at 30 minutes, 9 hours, 24 hours, 48 hours and 72 hours

| | | | | |
|--------------------------------------|-----------------------------------|--|--|--|
| End point values | Pharmacokinetic full analysis set | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 6 | | | |
| Units: IU*hr/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| IU*hr/dL | 1335.56 (± 299.83) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Elimination phase half-life (T1/2)

| | |
|--|--|
| End point title | Pharmacokinetics: Elimination phase half-life (T1/2) |
| End point description: PK infusion with investigational product was administered after a wash out period of at least 5 days. Elimination phase half-life is calculated as $T_{1/2} = \log e(2) / \lambda_z$ where the elimination rate constant (λ_z) will be obtained by log e - linear fitting using least squares deviation to at least the last 3 quantifiable concentrations above pre-infusion level. | |
| End point type | Secondary |
| End point timeframe: PK assessments were done within 30 minutes pre-infusion and post-infusion at 30 minutes, 9 hours, 24 hours, 48 hours and 72 hours | |

| | | | | |
|--------------------------------------|-----------------------------------|--|--|--|
| End point values | Pharmacokinetic full analysis set | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 6 | | | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | | | | |
| hours | 28.52 (± 4.12) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Mean residence time (MRT)

| | |
|---|---|
| End point title | Pharmacokinetics: Mean residence time (MRT) |
| End point description: PK infusion with investigational product was administered after a wash out period of at least 5 days. | |

Mean residence time is calculated as total area under the moment curve divided by the total area under the curve. $MRT = (AUMC_{0-\infty} [h^2 \cdot IU/dL]) / (AUC_{0-\infty} [h \cdot IU/dL]) - TI/2$ where $AUMC_{0-\infty}$ is determined in a similar manner as $AUC_{0-\infty}$ and TI represents infusion duration in hours.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| PK assessments were done within 30 minutes pre-infusion and post-infusion at 30 minutes, 9 hours, 24 hours, 48 hours and 72 hours | |

| | | | | |
|--------------------------------------|-----------------------------------|--|--|--|
| End point values | Pharmacokinetic full analysis set | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 6 | | | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | | | | |
| hours | 29.97 (± 2.72) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Systemic Clearance (CL)

| | |
|---|---|
| End point title | Pharmacokinetics: Systemic Clearance (CL) |
| End point description: | |
| PK infusion with investigational product was administered after a wash out period of at least 5 days. Systemic clearance is calculated as the dose in IU/kg divided by the total AUC. $CL = \text{Dose} [IU/kg] / AUC_{0-\infty} [h \cdot IU/dL]$ | |
| End point type | Secondary |
| End point timeframe: | |
| PK assessments were done within 30 minutes pre-infusion and post-infusion at 30 minutes, 9 hours, 24 hours, 48 hours and 72 hours | |

| | | | | |
|--------------------------------------|-----------------------------------|--|--|--|
| End point values | Pharmacokinetic full analysis set | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 6 | | | |
| Units: dL/kg/hours | | | | |
| arithmetic mean (standard deviation) | | | | |
| dL/kg/hours | 0.06 (± 0.014) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Volume of distribution at steady state (Vss)

| | |
|-----------------|--|
| End point title | Pharmacokinetics: Volume of distribution at steady state (Vss) |
|-----------------|--|

End point description:

PK infusion with investigational product was administered after a wash out period of at least 5 days. Apparent steady state volume of distribution is calculated as $V_{ss} = CL * MRT$ CL=Systemic Clearance and MRT=Mean residence time

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

End point timeframe:

PK assessments were done within 30 minutes pre-infusion and post-infusion at 30 minutes, 9 hours, 24 hours, 48 hours and 72 hours

| End point values | Pharmacokinetic full analysis set | | | |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 6 | | | |
| Units: dL/kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| dL/kg | 1.78 (± 0.42) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Incremental recovery (IR)

| | |
|-----------------|---|
| End point title | Pharmacokinetics: Incremental recovery (IR) |
|-----------------|---|

End point description:

PK infusion with investigational product was administered after a wash out period of at least 5 days. Incremental recovery is calculated as $IR_{30min} = (C_{30min} [IU/dL] - C_{pre-infusion} [IU/dL]) / \text{dose per kg body weight [IU/kg]}$ where C_{30min} and $C_{pre-infusion}$ relate to the unadjusted concentration values.

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

End point timeframe:

IR assessments were done within 30 minutes pre-infusion and post-infusion at 30 (± 5) minutes.

| End point values | Pharmacokinetic full analysis set | | | |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 6 | | | |
| Units: (IU/dL)/(IU/kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| (IU/dL)/(IU/kg) | 0.85 (± 0.196) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in health related quality of life (HR QoL) based on questionnaire SF-36

| | |
|-----------------|---|
| End point title | Changes in health related quality of life (HR QoL) based on questionnaire SF-36 |
|-----------------|---|

End point description:

The SF-36 is a validated, generic HR QoL instrument, measuring physical, emotional, social functioning as well as overall general health, suitable for subjects of 17 years of age or older. Higher scores indicate better health status. The Change in health related quality of life is analyzed from baseline to study completion. Only newly recruited subjects are included in the analysis of change as baseline values were not reported for transitioning subjects. Only subjects who received prophylaxis treatment are included.

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

End point timeframe:

Baseline at exposure day 1 and at study completion/termination.

| End point values | Overall prophylaxis | | | |
|---------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 24 | | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| SF-36 Bodily Pain | 6.7 (± 12.66) | | | |
| SF-36 General Health | 3.2 (± 9.32) | | | |
| SF-36 Mental Health | 0.7 (± 14.72) | | | |
| SF-36 Mental Health Component Score | 0.8 (± 12.08) | | | |
| SF-36 Physical Functioning | 4.2 (± 10.46) | | | |
| SF-36 Physical Health Component Score | 5.7 (± 8.43) | | | |
| SF-36 Role-Emotional | 2.3 (± 11.57) | | | |
| SF-36 Role-Physical | 4.5 (± 10.28) | | | |
| SF-36 Social Functioning | 4.5 (± 11.67) | | | |
| SF-36 Vitality | 2.0 (± 8.87) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in health related quality of life using the Peds QL

| | |
|-----------------|---|
| End point title | Changes in health related quality of life using the Peds QL |
|-----------------|---|

End point description:

The Peds QL is a generic HR QoL instrument designed specifically for a pediatric population. It captures following domains: general health/activities, feelings/emotional, social functioning, school functioning. Higher scores indicate better quality of life. The Change in health related quality of life is analyzed from baseline to study completion. Only newly recruited subjects are included in the analysis of change as baseline values were not reported for transitioning subjects. Only subjects who received prophylaxis treatment are included.

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

End point timeframe:

Baseline at exposure day 1 and at study completion/termination.

| End point values | Overall prophylaxis | | | |
|---|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: Change from baseline to end of study | | | | |
| arithmetic mean (standard deviation) | | | | |
| Peds-QL Physical Health Summary Score | -2.3 (± 18.47) | | | |
| Peds-QL Psychosocial Health Summary Score | 3.8 (± 5.99) | | | |
| Peds-QL Total Score | 1.6 (± 10.14) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in health related quality of life (HR QoL) based on questionnaire Haemo-QoL and Haem-A-QoL

| | |
|-----------------|--|
| End point title | Changes in health related quality of life (HR QoL) based on questionnaire Haemo-QoL and Haem-A-QoL |
|-----------------|--|

End point description:

The Haemo-QoL and Haem-A-QoL instruments have been developed and used in hemophilia A patients. As a hemophilia-specific instrument, this measure assesses very specific aspects of dealing with hemophilia. The areas covered by this instrument are: physical health, sports/leisure, school/work, dealing with hemophilia, and outlook for the future. For both instruments higher scores indicate worse quality of life.

The Change in health related quality of life is analyzed from baseline to study completion. Only newly recruited subjects are included in the analysis of change as baseline values were not reported for transitioning subjects. Only subjects who received prophylaxis treatment are included.

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

End point timeframe:

Baseline at exposure day 1 and at study completion/termination.

| End point values | Overall prophylaxis | | | |
|---|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 16 ^[3] | | | |
| Units: Change from baseline to end of study | | | | |
| arithmetic mean (standard deviation) | | | | |
| Haem-A-QoL Total Score | -3.0 (± 9.45) | | | |
| Haemo-QoL Total Score | -0.7 (± 99.999) | | | |

Notes:

[3] - n=16 for Haem-A-QoL and n=1 for Haemo-QoL - Dispersion not applicable as n=1, entered as 99.999

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in health related quality of life (HR QoL) based on questionnaire EQ-5D and pain score.

| | |
|-----------------|---|
| End point title | Changes in health related quality of life (HR QoL) based on questionnaire EQ-5D and pain score. |
|-----------------|---|

End point description:

The EQ-5D captures overall HR QoL (physical, mental and social functioning). A health utility score can be calculated from this measure, adult and proxy versions available. General pain assessment are done through a visual analog scale (VAS). For the EQ-5D Index score and EQ-5D VAS score, a higher score represents better quality of life. For the pain scale, a higher score indicates worse pain.

The Change in health related quality of life is analyzed from baseline to study completion. Only newly recruited subjects are included in the analysis of change as baseline values were not reported for transitioning subjects. Only subjects who received prophylaxis treatment are included.

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

End point timeframe:

Baseline at exposure day 1 and at study completion/termination.

| End point values | Overall prophylaxis | | | |
|---|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 26 ^[4] | | | |
| Units: Change from baseline to end of study | | | | |
| arithmetic mean (standard deviation) | | | | |
| EQ-5D Total Index | 0.0 (± 0.13) | | | |
| EQ-5D VAS | 5.1 (± 21.75) | | | |
| Pain Score | -8.0 (± 36.62) | | | |

Notes:

[4] - n=26 for EQ-5D Total Index, n=25 for EQ-5D VAS, n=24 for Pain Score

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the entire study period from screening to completion/termination. Overall 6 years and 2 months.

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

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | N/A |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | BAX 326 |
|-----------------------|---------|

Reporting group description:

Participants treated with BAX 326

| Serious adverse events | BAX 326 | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 115 (7.83%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Brain contusion | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Extradural hematoma | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Head injury | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Scroctal haematoma | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Nervous system disorders | | | |
| Seizure | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Duodenal ulcer hemorrhage | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Testicular appendage torsion | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal colic | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Corneal abscess | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 115 (0.87%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|---|-------------------|--|--|
| Non-serious adverse events | BAX 326 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 63 / 115 (54.78%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | | |
| occurrences (all) | 6 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | | |
| occurrences (all) | 20 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 14 / 115 (12.17%) | | |
| occurrences (all) | 23 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 11 / 115 (9.57%) | | |
| occurrences (all) | 15 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | | |
| occurrences (all) | 6 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 15 / 115 (13.04%) | | |
| occurrences (all) | 48 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | | |
| occurrences (all) | 8 | | |

| | | | |
|-----------------------------------|-------------------|--|--|
| Influenza | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | | |
| occurrences (all) | 8 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 25 / 115 (21.74%) | | |
| occurrences (all) | 55 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | | |
| occurrences (all) | 8 | | |
| Rhinitis | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | | |
| occurrences (all) | 15 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 11 / 115 (9.57%) | | |
| occurrences (all) | 17 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 07 December 2011 | Enrollment opened to pediatric subjects who participated in BAX326 pediatric study 251101 (to enable pediatric subjects to continue to receive BAX326 after completion of the pediatric study); other changes made due to the inclusion of pediatric subjects: <ul style="list-style-type: none">- 80 IU/kg stated as upper end of dose range for pediatric subjects- Anticipated IR of 0.7 [IU/dL]/[IU/kg] stated for pediatric subjects for calculation of the required number of units to treat a bleeding episode- Separate analyses between adult and pediatric subjects, if applicable |
| 31 July 2013 | <ul style="list-style-type: none">- Enrollment opened to at least 25 subjects naïve to BAX326 (per regulatory authority request).- Addition of PK-tailored prophylactic administration of BAX326 as an additional prophylactic treatment option.- Clarification provided that newly recruited subjects had to receive prophylactic treatment.- IR for calculating dose for subjects ≥ 12 years of age updated from 0.8 to 0.9 (based on PK data of BAX326 pivotal protocol 250901) -> Formula changed to: 'body weight (kg) x desired FIX rise (% or (IU/dL)) x 1.1 IU/kg' (previously 1.3 IU/kg)- Addition of TGA testing for the following new exploratory objective: "To correlate pre-infusion TGA parameters with pre-infusion FIX levels and spontaneous breakthrough bleeds in a subset of subjects receiving twice weekly standard or modified prophylactic treatment, including PK-tailored prophylaxis" (to evaluate whether and which TGA parameters, in particular endogenous thrombin potential (ETP) and/or peak thrombin generation may be a better parameter to monitor the adequacy of prophylactic treatment instead of FIX activity trough levels and/or clinical outcome); TGA testing was only to be performed in subjects ≥ 12 years of age |
| 19 October 2015 | <ul style="list-style-type: none">- Term "Cohort 1" introduced for subjects who were previously treated in BAX326 Studies 250901 or 251101; term "Cohort 2" introduced for newly recruited, BAX326 naïve subjects- Maximum dose of 120 IU/kg introduced for PK-tailored prophylaxis |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported