



Clinical trial results:

A Phase 2a Multiple Dose “Basket Design” Study Of The Safety, Tolerability, And Pharmacologic Activity Of BT200 In Patients With Hereditary Bleeding Disorders

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2020-003807-32 |
| Trial protocol | AT |
| Global end of trial date | 24 August 2021 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 20 April 2022 |
| First version publication date | 20 April 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | BT200-02 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04677803 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Medical University of Vienna |
| Sponsor organisation address | Währinger Gürtel 18-20, Vienn, Austria, 1090 |
| Public contact | Dept. of Clinical Pharmacology, Medical University of Vienna, 0043 140400298190, klin-pharmakologie@meduniwien.ac.at |
| Scientific contact | Dept. of Clinical Pharmacology, Medical University of Vienna, 0043 140400298190, klin-pharmakologie@meduniwien.ac.at |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 31 May 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 May 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 August 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to obtain clinical proof of mechanism for BT200 in one or more hereditary bleeding disorders.

Protection of trial subjects:

Prior to any trial-related activity, the Investigator or an authorized physician gave the patient oral and written information about the trial in a form that the patient was able to read and to understand. A voluntary, signed and dated Informed Consent Form was to be obtained from the patient prior to any trial-related activity. The patient had to consent to participate after the nature, scope, and possible consequences of the clinical trial were explained in a form understandable to the patient. It was also explained to the patient that he/she was free to refuse to enter the study or to withdraw from it at any time for any reason without incurring any penalty or withholding of treatment on the part of the Investigator.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 22 December 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Austria: 26 |
| Worldwide total number of subjects | 26 |
| EEA total number of subjects | 26 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 25 |

| | |
|---------------------|---|
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Hereditary bleeding disorder
Congenital hemophilia A w/o inhibitors on a prophylactic treatment regimen
Heterozygous carriers of hem. A with subnormal FVIII levels
Von Willebrand disease (VWD) Type 1
VWD type IIb (also known as "VWD Type 2b" or "type 2B VWD")
VWD Type 3 under subst. therapy
Acquired von Willebrand Syndrome w/o spec inhib.

Pre-assignment

Screening details:

Patients underwent the Screening Visit within 28 days prior to dosing on Day 0. All patients were to be dosed with a subcutaneous (SC) injection of 3 mg BT200 on Days 0 and 4. Thereafter, doses of the weekly SC injections were to be titrated between 3 and 9 mg based on the patient's response.

Period 1

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

Arms

| | |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Hemophilia A Mild/Mod |

Arm description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

Hemophilia A: titration until largest possible increase in FVIII activity before PFA-100® CADP-CT increased to 150 seconds. No up-titration from 3 mg was foreseen in severe hemophilia patients on on-demand therapy.

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | BT200 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Injection |

Dosage and administration details:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

| | |
|------------------|---------------------|
| Arm title | Hemophilia A Severe |
|------------------|---------------------|

Arm description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

Hemophilia A: titration until largest possible increase in FVIII activity before PFA-100® CADP-CT increased to 150 seconds. No up-titration from 3 mg was foreseen in severe hemophilia patients on on-demand therapy.

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | BT200 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Injection |

Dosage and administration details:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

| | |
|------------------|-------------|
| Arm title | VWD Type 2b |
|------------------|-------------|

Arm description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

VWD type IIb: titration until normalization of platelet count and/or FVIII activity level

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | BT200 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Injection |

Dosage and administration details:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

| | |
|------------------|------------|
| Arm title | VWD Type 3 |
|------------------|------------|

Arm description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

VWD Type 3 under substitution therapy: titration only between 3 and 6 mg

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | BT200 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Injection |

Dosage and administration details:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

| | |
|------------------|------|
| Arm title | aVWS |
|------------------|------|

Arm description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance

below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

aVWS: titration until normalization of FVIII activity

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | BT200 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Injection |

Dosage and administration details:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

| Number of subjects in period 1 | Hemophilia A Mild/Mod | Hemophilia A Severe | VWD Type 2b |
|--------------------------------|-----------------------|---------------------|-------------|
| Started | 10 | 9 | 5 |
| Completed | 10 | 9 | 5 |
| Not completed | 0 | 0 | 0 |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | VWD Type 3 | aVWS |
|--------------------------------|------------|------|
| Started | 1 | 1 |
| Completed | 0 | 1 |
| Not completed | 1 | 0 |
| Lost to follow-up | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Hemophilia A Mild/Mod |
|-----------------------|-----------------------|

Reporting group description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

Hemophilia A: titration until largest possible increase in FVIII activity before PFA-100® CADP-CT increased to 150 seconds. No up-titration from 3 mg was foreseen in severe hemophilia patients on on-demand therapy.

| | |
|-----------------------|---------------------|
| Reporting group title | Hemophilia A Severe |
|-----------------------|---------------------|

Reporting group description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

Hemophilia A: titration until largest possible increase in FVIII activity before PFA-100® CADP-CT increased to 150 seconds. No up-titration from 3 mg was foreseen in severe hemophilia patients on on-demand therapy.

| | |
|-----------------------|-------------|
| Reporting group title | VWD Type 2b |
|-----------------------|-------------|

Reporting group description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

VWD type IIb: titration until normalization of platelet count and/or FVIII activity level

| | |
|-----------------------|------------|
| Reporting group title | VWD Type 3 |
|-----------------------|------------|

Reporting group description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

VWD Type 3 under substitution therapy: titration only between 3 and 6 mg

| | |
|-----------------------|------|
| Reporting group title | aVWS |
|-----------------------|------|

Reporting group description:

On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed.

aVWS: titration until normalization of FVIII activity

| Reporting group values | Hemophilia A Mild/Mod | Hemophilia A Severe | VWD Type 2b |
|--|-----------------------|---------------------|-------------|
| Number of subjects | 10 | 9 | 5 |
| 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 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 10 | 9 | 4 |
| From 65-84 years | 0 | 0 | 1 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 4 | 0 | 2 |
| Male | 6 | 9 | 3 |

| Reporting group values | VWD Type 3 | aVWS | Total |
|--|------------|------|-------|
| Number of subjects | 1 | 1 | 26 |
| 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 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 1 | 1 | 25 |
| From 65-84 years | 0 | 0 | 1 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 1 | 7 |
| Male | 1 | 0 | 19 |

Subject analysis sets

| | |
|----------------------------|----------------------|
| Subject analysis set title | Hemophilia A Overall |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Blood samples for the determination of plasma concentrations were collected on Days 0, 4, 7, 14, 21, 28, 35, 42, 49 and 56 (EOS Visit). On dosing days, the sample was collected prior to administration of IMP.

The concentration of BT200 which is required to produce a 2-fold increase in FVIIIc activity was calculated to be in the range from 368 to 508 ng/mL, and the concentration of BT200 which would be required to produce a 2-fold increase in the VWF Ag level was calculated to be in the range from 459 to 649 ng/mL. Both of these thresholds were readily achieved after 6 doses of BT200 in all disease entities. Comment: Type 1 (0 subjects), 3 (1 subject) and aVWS (1 subject) were not analyzed.

| | |
|----------------------------|----------------------|
| Subject analysis set title | VWD Type IIb Overall |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Blood samples for the determination of plasma concentrations were collected on Days 0, 4, 7, 14, 21, 28, 35, 42, 49 and 56 (EOS Visit). On dosing days, the sample was collected prior to administration of IMP.

The concentration of BT200 which is required to produce a 2-fold increase in FVIIIc activity was calculated to be in the range from 368 to 508 ng/mL, and the concentration of BT200 which would be required to produce a 2-fold increase in the VWF Ag level was calculated to be in the range from 459 to 649 ng/mL. Both of these thresholds were readily achieved after 6 doses of BT200 in

all disease entities.

| Reporting group values | Hemophilia A Overall | VWD Type IIb Overall | |
|---|----------------------|----------------------|--|
| Number of subjects | 17 | 5 | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 17 | 4 | |
| From 65-84 years | 0 | 1 | |
| 85 years and over | 0 | 0 | |
| Gender categorical Units: Subjects | | | |
| Female | 4 | 2 | |
| Male | 13 | 3 | |

End points

End points reporting groups

| | |
|--|-----------------------|
| Reporting group title | Hemophilia A Mild/Mod |
| Reporting group description: On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed. Hemophilia A: titration until largest possible increase in FVIII activity before PFA-100® CADP-CT increased to 150 seconds. No up-titration from 3 mg was foreseen in severe hemophilia patients on on-demand therapy. | |
| Reporting group title | Hemophilia A Severe |
| Reporting group description: On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed. Hemophilia A: titration until largest possible increase in FVIII activity before PFA-100® CADP-CT increased to 150 seconds. No up-titration from 3 mg was foreseen in severe hemophilia patients on on-demand therapy. | |
| Reporting group title | VWD Type 2b |
| Reporting group description: On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed. VWD type IIb: titration until normalization of platelet count and/or FVIII activity level | |
| Reporting group title | VWD Type 3 |
| Reporting group description: On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed. VWD Type 3 under substitution therapy: titration only between 3 and 6 mg | |
| Reporting group title | aVWS |
| Reporting group description: On Day 0 and Day 4 each patient was to receive a single SC injection of 3 mg of BT200. On Days 7, 14, 21, and 28, the BT200 dose was to be titrated between 3 mg and 9 mg using the guidance below. It was anticipated that dose adjustments were to be performed in 2-3 mg steps. The 9-mg dose was only to be applied on Day 21-28 under exceptional circumstances, e.g. if no relevant changes in PD and safety parameters were observed. aVWS: titration until normalization of FVIII activity | |
| Subject analysis set title | Hemophilia A Overall |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Blood samples for the determination of plasma concentrations were collected on Days 0, 4, 7, 14, 21, 28, 35, 42, 49 and 56 (EOS Visit). On dosing days, the sample was collected prior to administration of IMP. The concentration of BT200 which is required to produce a 2-fold increase in FVIIIc activity was calculated to be in the range from 368 to 508 ng/mL, and the concentration of BT200 which would be required to produce a 2-fold increase in the VWF Ag level was calculated to be in the range from 459 to 649 ng/mL. Both of these thresholds were readily achieved after 6 doses of BT200 in all disease entities. Comment: Type 1 (0 subjects), 3 (1 subject) and aVWS (1 subject) were not analyzed. | |

| | |
|----------------------------|----------------------|
| Subject analysis set title | VWD Type IIb Overall |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Blood samples for the determination of plasma concentrations were collected on Days 0, 4, 7, 14, 21, 28, 35, 42, 49 and 56 (EOS Visit). On dosing days, the sample was collected prior to administration of IMP.

The concentration of BT200 which is required to produce a 2-fold increase in FVIIIc activity was calculated to be in the range from 368 to 508 ng/mL, and the concentration of BT200 which would be required to produce a 2-fold increase in the VWF Ag level was calculated to be in the range from 459 to 649 ng/mL. Both of these thresholds were readily achieved after 6 doses of BT200 in all disease entities.

Primary: FVIIIc activity change from Baseline to Day 35

| | |
|-----------------|---|
| End point title | FVIIIc activity change from Baseline to Day 35 ^[1] |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to Day 35

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were performed for this endpoint

| End point values | Hemophilia A Overall | VWD Type IIb Overall | | |
|----------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 17 | 5 | | |
| Units: fold change from Baseline | | | | |
| arithmetic mean (standard error) | 5.29 (± 141.1) | 2.21 (± 24.0) | | |

Statistical analyses

No statistical analyses for this end point

Primary: FVIIIc Observed activity level at Day 35

| | |
|-----------------|---|
| End point title | FVIIIc Observed activity level at Day 35 ^[2] |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to Day 35

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were performed for this endpoint

| End point values | Hemophilia A Overall | VWD Type IIb Overall | | |
|----------------------------------|-------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 17 | 5 | | |
| Units: percent | | | | |
| arithmetic mean (standard error) | 26.5 (± 94.1) | 151 (± 26.7) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment Period

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Overall |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | Overall | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | Overall | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 26 (65.38%) | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Haemorrhage | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |

| | | | |
|--|---------------------|--|--|
| Injection site reaction subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 2 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Dysphonia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Haemoptysis subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 2 | | |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 2 | | |
| Psychiatric disorders Depression subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Sleep disorder subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Injury, poisoning and procedural complications Subcutaneous haematoma subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Cardiac disorders Tachycardia | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 3 / 26 (11.54%) 5 | | |
| Blood and lymphatic system disorders Lymphangiopathy subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Gastrointestinal haemorrhage subjects affected / exposed occurrences (all) Gingival bleeding subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Tongue haemorrhage subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 2 / 26 (7.69%) 2 2 / 26 (7.69%) 2 1 / 26 (3.85%) 1 3 / 26 (11.54%) 3 1 / 26 (3.85%) 1 1 / 26 (3.85%) 2 | | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|----------------------|--|--|
| Eczema subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Back pain subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Haemarthrosis subjects affected / exposed occurrences (all) | 3 / 26 (11.54%) 6 | | |
| Muscle haemorrhage subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 2 | | |
| Soft tissue haemorrhage subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Infections and infestations | | | |
| Conjunctivitis subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Tooth infection subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|---------------------|--|--|
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
|--|---------------------|--|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported