



Clinical trial results:

A Phase 1, Open-label, Single-dose, Non-randomized Study to Evaluate Pharmacokinetics, Pharmacodynamics, and Safety of Betrixaban in Pediatric Patients

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2018-002562-40 |
| Trial protocol | GB |
| Global end of trial date | 08 October 2019 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v2 (current) |
| This version publication date | 04 November 2022 |
| First version publication date | 30 April 2021 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 16-021 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03346083 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Portola Pharmaceuticals, LLC, a wholly owned subsidiary of Alexion Pharmaceuticals, Inc. |
| Sponsor organisation address | 121 Seaport Boulevard, Boston, MA, United States, 02210 |
| Public contact | European Clinical Trial Information, Alexion Europe SAS, +33 14710615, clinicaltrials.eu@alexion.com |
| Scientific contact | European Clinical Trial Information, Alexion Europe SAS, +33 14710615, clinicaltrials.eu@alexion.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001834-PIP02-16 |
| 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 | 08 October 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 October 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 October 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

This trial was a Phase 1, open-label, multicenter study of the pharmacokinetics (PK), pharmacodynamics (PD), and safety of a single dose of betrixaban in pediatric participants at risk of venous thromboembolism (VTE). This study was to be conducted in 2 parts: Part 1 and Part 2. Part 1 (the initial opening of the study) was conducted in 21 adolescent participants (12 to < 18 years of age) who were assessed to be at risk for VTE. Participants in Part 1 received either 40 or 80 milligrams (mg) of study drug. The PK and PD data from Part 1 was to be used for dose determination for the next youngest age group using population PK and physiological-based PK modeling and simulation. Following analysis of Part 1 data, Part 2 of the study was to commence and enroll 12 participants 2 to < 12 years of age. However, after completion of Part 1 and prior to initiating Part 2, the Sponsor decided to cease developing betrixaban, prompting early study closure.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 14 March 2017 |
| 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 | United Kingdom: 1 |
| Country: Number of subjects enrolled | Russian Federation: 14 |
| Country: Number of subjects enrolled | United States: 4 |
| Country: Number of subjects enrolled | Ukraine: 2 |
| Worldwide total number of subjects | 21 |
| EEA total number of subjects | 0 |

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) | 21 |
| 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:

After a screening period of up to 30 days, eligible participants who had provided assent and for whom a parent or legal guardian had provided signed informed consent entered the hospital, clinical research unit, or Phase 1 unit on Day -1. Those who were already inpatients remained hospitalized.

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Overall (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 | Cohort 1: Betrixaban 40 mg |

Arm description:

Participants received a single, oral dose of betrixaban at 40 mg in a fed state, and had 10 PK blood sampling time points.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Betrixaban |
| Investigational medicinal product code | |
| Other name | PRT054021 |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Betrixaban was administered as a single oral dose of 40 mg.

| | |
|------------------|----------------------------|
| Arm title | Cohort 2: Betrixaban 80 mg |
|------------------|----------------------------|

Arm description:

Participants received a single, oral dose of betrixaban at 80 mg in a fed state, and had 5 PK sampling time points.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Betrixaban |
| Investigational medicinal product code | |
| Other name | PRT054021 |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Betrixaban was administered as a single oral dose of 80 mg.

| Number of subjects in period 1 | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg |
|--|-------------------------------|-------------------------------|
| Started | 3 | 18 |
| Received At Least 1 Dose Of Study Drug | 3 | 18 |
| Evaluated Through Day 7 Follow-up | 3 | 18 |
| Completed | 3 | 18 |

Baseline characteristics

Reporting groups

| | |
|--|----------------------------|
| Reporting group title | Cohort 1: Betrixaban 40 mg |
| Reporting group description: Participants received a single, oral dose of betrixaban at 40 mg in a fed state, and had 10 PK blood sampling time points. | |
| Reporting group title | Cohort 2: Betrixaban 80 mg |
| Reporting group description: Participants received a single, oral dose of betrixaban at 80 mg in a fed state, and had 5 PK sampling time points. | |

| Reporting group values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | Total |
|---|-------------------------------|-------------------------------|-------|
| Number of subjects | 3 | 18 | 21 |
| 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) | 3 | 18 | 21 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical Units: Subjects | | | |
| Female | 2 | 9 | 11 |
| Male | 1 | 9 | 10 |
| Race Units: Subjects | | | |
| White | 3 | 15 | 18 |
| Black or African American | 0 | 2 | 2 |
| Other | 0 | 1 | 1 |
| Ethnicity Units: Subjects | | | |
| Not Hispanic or Latino | 3 | 17 | 20 |
| Hispanic or Latino | 0 | 0 | 0 |
| Unknown | 0 | 1 | 1 |

End points

End points reporting groups

| | |
|--|----------------------------|
| Reporting group title | Cohort 1: Betrixaban 40 mg |
| Reporting group description: Participants received a single, oral dose of betrixaban at 40 mg in a fed state, and had 10 PK blood sampling time points. | |
| Reporting group title | Cohort 2: Betrixaban 80 mg |
| Reporting group description: Participants received a single, oral dose of betrixaban at 80 mg in a fed state, and had 5 PK sampling time points. | |

Primary: Area Under The Plasma Concentration–time Curve From 0 To Infinity (AUC(0-inf)) Of Betrixaban

| | |
|---|---|
| End point title | Area Under The Plasma Concentration–time Curve From 0 To Infinity (AUC(0-inf)) Of Betrixaban ^[1] |
| End point description: Following the Sponsor's decision to cease developing betrixaban, data for AUC(0-inf) were not collected. After completion of Part 1 of the study and prior to initiating Part 2, the Sponsor decided to stop developing betrixaban and closed the study early. Therefore, data for this Outcome Measure were not collected. | |
| End point type | Primary |
| End point timeframe: Up to 6 days post dose | |

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: Endpoint was summarized descriptively.

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|--------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[2] | 0 ^[3] | | |
| Units: mg/L/h | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[2] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

[3] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) Of Betrixaban

| | |
|-----------------|---|
| End point title | Maximum Observed Plasma Concentration (Cmax) Of Betrixaban ^[4] |
|-----------------|---|

End point description:

Data reported as "0.200" indicates that the data are below the lower limit of quantification. The evaluable PK population included all participants who received the study drug and had sufficient blood samples through Day 3 to compute either Cmax or total AUC assessments with the extrapolated portion of the AUC(0-inf) less than 30%. The Lower Limit and Upper Limit Cmax data are reported here as only

individual participant data are available. Below "0.99999" indicates that no data is available.

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

End point timeframe:

Up to 6 days post dose

Notes:

[4] - 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: Endpoint was summarized descriptively.

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|---------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 ^[5] | 18 ^[6] | | |
| Units: mg/L | | | | |
| geometric mean (full range (min-max)) | 0.99999 (0.200 to 2.57) | 0.99999 (0.200 to 48.5) | | |

Notes:

[5] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

[6] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: AUC To The Last Measurable Concentration Above The Quantitation Limit (AUC(0-last)) Of Betrixaban

| | |
|-----------------|---|
| End point title | AUC To The Last Measurable Concentration Above The Quantitation Limit (AUC(0-last)) Of Betrixaban |
|-----------------|---|

End point description:

Following the Sponsor's decision to cease developing betrixaban, data for AUC(0-last) were not collected. After completion of Part 1 of the study and prior to initiating Part 2, the Sponsor decided to stop developing betrixaban and closed the study early. Therefore, data for this Outcome Measure were not collected.

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

End point timeframe:

Up to 6 days post dose

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|--------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[7] | 0 ^[8] | | |
| Units: mg/L/h | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[7] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

[8] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Plasma Half-life ($t_{1/2}$) Of Betrixaban

| | |
|-----------------|---|
| End point title | Terminal Plasma Half-life ($t_{1/2}$) Of Betrixaban |
|-----------------|---|

End point description:

Following the Sponsor's decision to cease developing betrixaban, data for $t_{1/2}$ were not collected. After completion of Part 1 of the study and prior to initiating Part 2, the Sponsor decided to stop developing betrixaban and closed the study early. Therefore, data for this Outcome Measure were not collected.

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

End point timeframe:

Up to 6 days post dose

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|--------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[9] | 0 ^[10] | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[9] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

[10] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Maximum Observed Plasma Concentration (Tmax) Of Betrixaban

| | |
|-----------------|--|
| End point title | Time To Maximum Observed Plasma Concentration (Tmax) Of Betrixaban |
|-----------------|--|

End point description:

The Tmax that the highest (maximum) Cmax of betrixaban was observed per group up to Day 6 (120 hours) post dosing is reported. The evaluable PK population included all participants who received the study drug and had sufficient blood samples through Day 3 to compute either Cmax or total AUC assessments with the extrapolated portion of the AUC(0-inf) less than 30%.

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

End point timeframe:

Up to 6 days post dose

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|--------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[11] | 0 ^[12] | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[11] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

[12] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Total Body Clearance Of Betrixaban From Plasma (CL)

| | |
|-----------------|--|
| End point title | Apparent Total Body Clearance Of Betrixaban From Plasma (CL) |
|-----------------|--|

End point description:

Following the Sponsor's decision to cease developing betrixaban, data for CL were not collected. After completion of Part 1 of the study and prior to initiating Part 2, the Sponsor decided to stop developing betrixaban and closed the study early. Therefore, data for this Outcome Measure were not collected.

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

End point timeframe:

Up to 6 days post dose

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|--------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[13] | 0 ^[14] | | |
| Units: mg/h | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[13] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

[14] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume Of Distribution (Vd) Of Betrixaban

| | |
|-----------------|--|
| End point title | Apparent Volume Of Distribution (Vd) Of Betrixaban |
|-----------------|--|

End point description:

Following the Sponsor's decision to cease developing betrixaban, data for Vd were not collected. After completion of Part 1 of the study and prior to initiating Part 2, the Sponsor decided to stop developing betrixaban and closed the study early. Therefore, data for this Outcome Measure were not collected.

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

End point timeframe:

Up to 6 days post dose

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|--------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[15] | 0 ^[16] | | |
| Units: L/kg | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[15] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

[16] - Following the Sponsor's decision to cease developing betrixaban, PK parameters were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline In Thrombin Level At Day 6

| | |
|--|---|
| End point title | Percent Change From Baseline In Thrombin Level At Day 6 |
| End point description: | |
| Following the Sponsor's decision to cease developing betrixaban, data for thrombin levels were not collected. After completion of Part 1 of the study and prior to initiating Part 2, the Sponsor decided to stop developing betrixaban and closed the study early. Therefore, data for this Outcome Measure were not collected. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Day 6 | |

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|--------------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[17] | 0 ^[18] | | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[17] - Following the Sponsor's decision to cease developing betrixaban, PD parameters were not calculated.

[18] - Following the Sponsor's decision to cease developing betrixaban, PD parameters were not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number Of Participants With Treatment-related Adverse Events

| | |
|---|--|
| End point title | Number Of Participants With Treatment-related Adverse Events |
| End point description: | |
| A treatment-related adverse event was any undesirable event or any untoward medical occurrence that occurs to a participant during the course of a study, or the protocol-defined time after study termination. An Investigator qualified in medicine made the determination of relationship to the investigational product for each adverse event (Unrelated, Unlikely Related, Possibly Related, or Probably Related). If the relationship between the adverse event and the investigational product was determined to be "possible" or "probable", the event was considered to be related to the investigational product for the purposes of expedited regulatory reporting. One participant experienced a mild study- | |

drug-related headache that resolved in less than 2 hours. A summary of serious and all other non-serious adverse events, regardless of causality, is located in the Reported Adverse Events module. Safety population: all participants enrolled in Part 1 of the study who received study drug.

| | |
|------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to 7 days post dose | |

| End point values | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | | |
|-----------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 18 | | |
| Units: Participants | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 7 days post dose.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------|
| Reporting group title | Cohort 1: Betrixaban 40 mg |
|-----------------------|----------------------------|

Reporting group description:

Participants received a single, oral dose of betrixaban at 40 mg in a fed state, and had 10 PK blood sampling time points.

| | |
|-----------------------|----------------------------|
| Reporting group title | Cohort 2: Betrixaban 80 mg |
|-----------------------|----------------------------|

Reporting group description:

Participants received a single, oral dose of betrixaban at 80 mg in a fed state, and had 5 PK sampling time points.

| Serious adverse events | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | |
|---|-------------------------------|-------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 18 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Cohort 1: Betrixaban 40 mg | Cohort 2: Betrixaban 80 mg | |
|---|-------------------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 5 / 18 (27.78%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 18 (5.56%) | |
| occurrences (all) | 0 | 1 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 18 (5.56%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac disorders | | | |

| | | | |
|--|--|--|--|
| Bradycardia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 | 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1 | |
| Infections and infestations Sinusitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 18 (5.56%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 12 July 2017 | 1. Redundantly emphasized protocol requirement for a subsequent protocol amendment and ethics approval prior to the commencement of Part 2 (ages 2–12 years) and again prior to the commencement of Part 3 (ages 28 days to 2 years) to specify age appropriate blood sampling volumes and time points following review of data from the previous age cohorts. It is intended that a reduction of blood sampling time points and therefore volumes will be possible during the study of progressively younger age groups by selecting the most informative time points based on data review. 2. Provided additional guidance to minimize pain and discomfort to pediatric participants during blood sampling. Sampling may occur via intravenous catheter or butterfly needle followed by saline flush. For participants with pre-existing central venous catheter or access devices (that is, central line, central venous line, or central venous access catheter) sampling may occur via these access points. |
| 06 April 2018 | 1. Reduced size of Cohort 1 (40 mg) from 12 participants to 3 participants. Cohort 1 will serve as the single cohort containing 10 PK time points per participant. This rich sampling schedule will serve as the basis for bridging to pediatric PK from adult PK. To minimize the number of participants subjected to a rich sampling schedule, Cohort 2 (80 mg) will employ a sparse sampling schedule consisting of 5 PK time points per participant that will be combined to compile a complete average plasma concentration time course. The overall reduction of sampling time points is intended to minimize pain and discomfort to pediatric participants. Part 1 of the study will now consist of: - Cohort 1: Single dose, 40 mg, fed (n=3), rich PK sampling - Cohort 2: Single dose, 80 mg, fed (n=18), sparse PK sampling Following review of safety data from Cohort 1 (40 mg), the Sponsor may authorize continued enrollment into Cohort 2 (80 mg). 2. Reduced the number of PK sampling from 10 to 5 blood sampling time points to minimize pain and discomfort to pediatric participants. Participants in Cohort 2 will be assigned 1 of 3 blood sampling sequences. In aggregate, sequences will cover the majority of PK sampling time points. PK sampling sequences are described as: - Sequence A: predose, 1, 3, 12, and 120 h post-dose - Sequence B: predose, 0.5, 2, 4, and 24 h post-dose - Sequence C: predose, 2, 3, 12, and 24 h post-dose 3. Removed the study of the youngest age group (28 days to 2 years old) from this protocol, which was previously referred to as Part 3 of the study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

After completion of Part 1 and prior to initiating Part 2, the Sponsor decided to cease developing betrixaban, prompting early study closure.

Notes: