



Clinical trial results:

A Phase 1, Prospective, Uncontrolled, Open-label, Multicenter, Dose-escalation Study Evaluating the Safety and Pharmacokinetics in Hereditary TTP (Thrombotic Thrombocytopenic Purpura)

Summary

EudraCT number	2012-003221-19
Trial protocol	AT DE GB PL Outside EU/EEA
Global end of trial date	22 February 2016

Results information

Result version number	v1 (current)
This version publication date	28 August 2016
First version publication date	28 August 2016

Trial information

Trial identification

Sponsor protocol code	281101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02216084
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Baxalta Innovations GmbH
Sponsor organisation address	Industriestrasse 67, Vienna, Austria, 1220
Public contact	Clinical Trial Registries and Results Disclosure, Baxalta Innovations GmbH, ClinicalTrialsDisclosure@baxalta.com
Scientific contact	Clinical Trial Registries and Results Disclosure, Baxalta Innovations GmbH, ClinicalTrialsDisclosure@baxalta.com
Sponsor organisation name	Baxalta US Inc.
Sponsor organisation address	One Baxter Way, Westlake Village, United States, CA 91362-3811
Public contact	Clinical Trial Registries and Results Disclosure, Baxalta US Inc., ClinicalTrialsDisclosure@baxalta.com
Scientific contact	Clinical Trial Registries and Results Disclosure, Baxalta US Inc., ClinicalTrialsDisclosure@baxalta.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001160-PIP01-11
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	No

1901/2006 apply to this trial?

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 February 2016
Global end of trial reached?	Yes
Global end of trial date	22 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of BAX930 following single infusions at doses of 5, 20 and 40 U/kg body weight, including the occurrence of adverse events (serious and non-serious adverse events) and formation of binding and inhibitory antibodies to BAX930.

Protection of trial subjects:

This study was conducted in accordance with the protocol, the International Conference of Harmonization 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 applicable national and local regulatory requirements.

Subjects were to be recruited to the next dose level only after short-term safety had been demonstrated and reviewed by an independent Data Monitoring Committee at the preceding dose level

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2014
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	Austria: 3
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	Switzerland: 1
Worldwide total number of subjects	16
EEA total number of subjects	12

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)	2
Adults (18-64 years)	14
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Nine sites participated in the study. All sites enrolled subjects. Subjects were to be recruited to the next dose level only after short-term safety had been demonstrated and reviewed by an independent DMC. Reenrollment of subjects completing treatment in cohort 1/2 into cohort 3 would have been possible but no subject was reenrolled across cohorts

Pre-assignment

Screening details:

A total of 16 subjects were enrolled in the study, across 9 study sites, of which 15 subjects received the investigational product and completed the study. 1 subject discontinued the study before treatment due to Sponsor Decision, Patient not dosed during time period required by protocol.

Pre-assignment period milestones

Number of subjects started	16
Number of subjects completed	15

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Patient not dosed during time period per protocol: 1
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Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose Cohort 1 (5 U/kg)

Arm description:

Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 5 U/kg bodyweight

Arm type	Experimental
Investigational medicinal product name	BAX930
Investigational medicinal product code	
Other name	rADAMTS13
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

5 U/kg bodyweight

Arm title	Dose Cohort 2 (20 U/kg)
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Arm description:

Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 20 U/kg bodyweight

Arm type	Experimental
Investigational medicinal product name	BAX930
Investigational medicinal product code	
Other name	rADAMTS13
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

20 U/kg bodyweight

Arm title	Dose Cohort 3 (40 U/kg)
Arm description:	
Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 40 U/kg bodyweight	
Arm type	Experimental
Investigational medicinal product name	BAX930
Investigational medicinal product code	
Other name	rADAMTS13
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous bolus use
Dosage and administration details:	
40 U/kg bodyweight	

Number of subjects in period 1^[1]	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)
Started	3	3	9
Completed	3	3	9

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: A total of 16 subjects were enrolled in the study, across 9 study sites, of which 15 subjects received the investigational product and completed the study. 1 subject discontinued the study before treatment due to 'Sponsor Decision, Patient not dosed during time period required by protocol'.

Baseline characteristics

Reporting groups

Reporting group title	Dose Cohort 1 (5 U/kg)
Reporting group description:	
Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 5 U/kg bodyweight	
Reporting group title	Dose Cohort 2 (20 U/kg)
Reporting group description:	
Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 20 U/kg bodyweight	
Reporting group title	Dose Cohort 3 (40 U/kg)
Reporting group description:	
Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 40 U/kg bodyweight	

Reporting group values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)
Number of subjects	3	3	9
Age categorical			
Units: Subjects			
Adults (18-65 years)	3	3	7
Adolescents (12-17 years)	0	0	2
Gender categorical			
Units:			
Male	1	1	5
Female	2	2	4

Reporting group values	Total		
Number of subjects	15		
Age categorical			
Units: Subjects			
Adults (18-65 years)	13		
Adolescents (12-17 years)	2		
Gender categorical			
Units:			
Male	7		
Female	8		

Subject analysis sets

Subject analysis set title	Pharmacokinetic full analysis set (PK-FAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects who received at least one dose of the investigational product and provided at least 4 valid data points from scheduled PK timepoints after start of dosing with BAX 930.	
Subject analysis set title	Pharmacokinetic per protocol set (PK-PPS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects in the PK-FAS with no major protocol deviations or events that could have affected the integrity of the PK data.	
Subject analysis set title	Safety analysis set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of the investigational product.

Reporting group values	Pharmacokinetic full analysis set (PK-FAS)	Pharmacokinetic per protocol set (PK-PPS)	Safety analysis set (SAF)
Number of subjects	15	15	15
Age categorical Units: Subjects			
Adults (18-65 years)	13	13	13
Adolescents (12-17 years)	2	2	2
Gender categorical Units:			
Male	7	7	7
Female	8	8	8

End points

End points reporting groups

Reporting group title	Dose Cohort 1 (5 U/kg)
Reporting group description:	
Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 5 U/kg bodyweight	
Reporting group title	Dose Cohort 2 (20 U/kg)
Reporting group description:	
Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 20 U/kg bodyweight	
Reporting group title	Dose Cohort 3 (40 U/kg)
Reporting group description:	
Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 40 U/kg bodyweight	
Subject analysis set title	Pharmacokinetic full analysis set (PK-FAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects who received at least one dose of the investigational product and provided at least 4 valid data points from scheduled PK timepoints after start of dosing with BAX 930.	
Subject analysis set title	Pharmacokinetic per protocol set (PK-PPS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects in the PK-FAS with no major protocol deviations or events that could have affected the integrity of the PK data.	
Subject analysis set title	Safety analysis set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who received at least one dose of the investigational product.	

Primary: Occurrence of Adverse Events (serious and non-serious AEs) and formation of binding and inhibitory antibodies to BAX 930

End point title	Occurrence of Adverse Events (serious and non-serious AEs) and formation of binding and inhibitory antibodies to BAX 930 ^[1]
End point description:	
To evaluate the safety of BAX930 following single infusion at doses 5, 20 and 40 U/kg bodyweight.	
End point type	Primary
End point timeframe:	
Up to 28 (+/- 3) days after investigational product infusion.	

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	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	Safety analysis set (SAF)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	3	9	15
Units: Number of events				
Treatment Emergent Adverse Events (TEAEs)	17	9	13	39
Severe TEAEs	0	0	0	0
TEAEs Related to Investigational Product	0	0	5	5
TEAEs Related to Study Procedure	0	1	3	4

Treatment Emergent Serious Adverse Events (TESAEs)	0	0	0	0
TEAEs Leading to Discontinuation of Study	0	0	0	0
TEAEs Leading to Discont./Interrup. of IP	0	0	0	0
TEAEs Leading to Death	0	0	0	0
Breakthrough TEAEs	0	0	0	0
TESAEs Related to Investigational Product	0	0	0	0
Positive Anti-ADAMTS13-antibodies (neutralizing)	0	0	0	0
Positive Anti-BAX930-antibodies (binding)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Incremental Recovery (IR) for ADAMTS13 activity

End point title	PK Parameter: Incremental Recovery (IR) for ADAMTS13 activity
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End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type	Secondary
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End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: U/mL*kg/U				
geometric mean (geometric coefficient of variation)				
Technozym Assay	0.0169 (± 5.5)	0.0176 (± 33.7)	0.0205 (± 22.7)	
FRETs-VWF73 Assay	0.0153 (± 20.1)	0.02 (± 34.1)	0.0232 (± 14.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Incremental Recovery (IR) for ADAMTS13 antigen

End point title	PK Parameter: Incremental Recovery (IR) for ADAMTS13 antigen
End point description: PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3. The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).	
End point type	Secondary
End point timeframe: Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.	

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: µg/mL*kg/µg				
geometric mean (geometric coefficient of variation)	0.018 (± 6.5)	0.0241 (± 35.8)	0.0244 (± 16.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Maximum concentration following infusion (Cmax) for ADAMTS13 activity

End point title	PK Parameter: Maximum concentration following infusion (Cmax) for ADAMTS13 activity
End point description: PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3. The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).	
End point type	Secondary
End point timeframe: Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.	

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: U/mL				
geometric mean (geometric coefficient of variation)				
Technozym Assay	0.087 (± 4.6)	0.35 (± 34.5)	0.837 (± 20.5)	
FRET5-VWF73 Assay	0.079 (± 22.2)	0.398 (± 35.3)	0.948 (± 15.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Maximum concentration following infusion (C_{max}) for ADAMTS13 antigen

End point title	PK Parameter: Maximum concentration following infusion (C _{max}) for ADAMTS13 antigen
End point description: PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3. The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).	
End point type	Secondary
End point timeframe: Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.	

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: µg/mL				
geometric mean (geometric coefficient of variation)	0.065 (± 3.6)	0.323 (± 37.1)	0.672 (± 14.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Maximum time to reach C_{max} (t_{max})

End point title	PK Parameter: Maximum time to reach C _{max} (t _{max})
End point description: PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3. The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).	
End point type	Secondary
End point timeframe: Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.	

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: hours				
median (full range (min-max))				
ADAMTS13 Technozym	0.25 (0.25 to 0.52)	0.55 (0.28 to 0.97)	0.3 (0.25 to 0.58)	
ADAMTS13 FRETS-VWF73	1 (0.52 to 1)	0.33 (0.25 to 0.53)	0.37 (0.22 to 0.58)	
ADAMTS13:Ag	0.25 (0.25 to 0.52)	0.55 (0.53 to 0.97)	0.3 (0.22 to 1.12)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Terminal or disposition half-life (t_{1/2})

End point title	PK Parameter: Terminal or disposition half-life (t _{1/2})
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End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type	Secondary
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End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[2]	3	7	
Units: hours				
geometric mean (geometric coefficient of variation)				
ADAMTS13 Technozym	88.6 (± 108)	59.6 (± 21.2)	60.7 (± 19.6)	
ADAMTS13 FRETS-VWF73	999999 (± 999999)	42.1 (± 46.7)	59.2 (± 23.6)	
ADAMTS13:Ag	86.3 (± 40.9)	57.1 (± 32.6)	66.2 (± 20.5)	

Notes:

[2] - For ADAMTS13 FRETS-VWF73 n=1. PK Parameter estimation not possible. 999999 was entered.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Mean residence time (MRT(0-inf))

End point title	PK Parameter: Mean residence time (MRT(0-inf))
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End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type	Secondary
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End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[3]	3	7	
Units: hours				
geometric mean (geometric coefficient of variation)				
ADAMTS13 Technozym	133.992 (± 115.4)	87.849 (± 28.7)	83.936 (± 24.8)	
ADAMTS13 FRETS-VWF73	999999 (± 999999)	58.464 (± 43.2)	84.178 (± 31.9)	
ADAMTS13:Ag	123.954 (± 49.7)	81.415 (± 41.5)	86.27 (± 23.7)	

Notes:

[3] - For ADAMTS13 FRETS-VWF73 n=1. PK Parameter estimation not possible. 999999 was entered.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Systemic clearance (CL)

End point title	PK Parameter: Systemic clearance (CL)
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End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type	Secondary
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End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[4]	3	7	
Units: mL/h				
geometric mean (geometric coefficient of variation)				
ADAMTS13 Technozym	39.4 (± 126.9)	61.6 (± 42.4)	67.4 (± 28.2)	
ADAMTS13 FRETS-VWF73	999999 (± 999999)	70.2 (± 33.2)	62 (± 33.6)	

ADAMTS13:Ag	46.9 (\pm 50)	49.2 (\pm 48.3)	61.5 (\pm 32.9)	
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Notes:

[4] - For ADAMTS13 FRETS-VWF73 n=1. PK Parameter estimation not possible. 999999 was entered.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Steady state volume of distribution(Vss)

End point title	PK Parameter: Steady state volume of distribution(Vss)
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End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type	Secondary
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End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[5]	3	7	
Units: mL				
geometric mean (geometric coefficient of variation)				
ADAMTS13 Technozym	5280 (\pm 14.2)	5410 (\pm 26.7)	5650 (\pm 33.5)	
ADAMTS13 FRETS-VWF73	999999 (\pm 999999)	4110 (\pm 33.3)	5220 (\pm 19.3)	
ADAMTS13:Ag	5810 (\pm 35.2)	4010 (\pm 36)	5300 (\pm 30.5)	

Notes:

[5] - For ADAMTS13 FRETS-VWF73 n=1. PK Parameter estimation not possible. 999999 was entered.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Area under the plasma-time concentration curve from zero to infinity (AUC(0-inf)) for ADAMTS13 activity

End point title	PK Parameter: Area under the plasma-time concentration curve from zero to infinity (AUC(0-inf)) for ADAMTS13 activity
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End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type	Secondary
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End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[6]	3	7	
Units: U*h/mL				
geometric mean (geometric coefficient of variation)				
ADAMTS13 Technozym	7.94 (± 81.1)	21.7 (± 17.4)	48.9 (± 28.5)	
ADAMTS13 FRETS-VWF73	999999 (± 999999)	19.1 (± 24.8)	53.1 (± 24.6)	

Notes:

[6] - For ADAMTS13 FRETS-VWF73 n=1. PK Parameter estimation not possible. 999999 was entered.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Area under the plasma-time concentration curve from zero to infinity (AUC(0-inf)) for ADAMTS13 antigen

End point title	PK Parameter: Area under the plasma-time concentration curve from zero to infinity (AUC(0-inf)) for ADAMTS13 antigen
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End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type	Secondary
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End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: µg*h/mL				
geometric mean (geometric coefficient of variation)	4.66 (± 20.7)	18.3 (± 9.4)	36 (± 29.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Area under the plasma-time concentration curve from zero to the last measured timepoint (AUC(0-t)) for ADAMTS13 activity

End point title	PK Parameter: Area under the plasma-time concentration curve from zero to the last measured timepoint (AUC(0-t)) for
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End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type Secondary

End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: U*h/mL				
geometric mean (geometric coefficient of variation)				
ADAMTS13 Technozym	6.12 (± 35.4)	20.3 (± 23.6)	46.6 (± 26.4)	
ADAMTS13 FRETS-VWF73	0.325 (± 440.6)	15.3 (± 31.3)	47.8 (± 25.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Area under the plasma-time concentration curve from zero to the last measured timepoint (AUC(0-t)) for ADAMTS13 antigen

End point title PK Parameter: Area under the plasma-time concentration curve from zero to the last measured timepoint (AUC(0-t)) for ADAMTS13 antigen

End point description:

PK parameter were evaluated after a single infusion of BAX930 in Cohorts 1, 2 and 3.

The population consisted of adult subjects only (2 adolescent subjects are not included due to sparse PK sampling scheme).

End point type Secondary

End point timeframe:

Pharmacokinetic samples were taken within 1 hour pre-infusion and up to 288 (+/- 4) hours post-infusion.

End point values	Dose Cohort 1 (5 U/kg)	Dose Cohort 2 (20 U/kg)	Dose Cohort 3 (40 U/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: µg*h/mL				
geometric mean (geometric coefficient of variation)	4.03 (± 11.2)	17.2 (± 12.7)	34.1 (± 27.2)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For each subject from first exposure of BAX930 until completion visit (28 +/- 3 days). Overall study period (all subjects) was 1 year and 5 months.

Adverse event reporting additional description:

The population consisted of subjects who received at least one dose of BAX930.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Dose Cohort 1 (5 U/kg)
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Reporting group description:

Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 5 U/kg bodyweight

Reporting group title	Dose Cohort 3 (40 U/kg)
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Reporting group description:

Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 40 U/kg bodyweight

Reporting group title	Dose Cohort 2 (20 U/kg)
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Reporting group description:

Subjects will receive a single pharmacokinetic infusion of BAX930 with dosage of 20 U/kg bodyweight

Serious adverse events	Dose Cohort 1 (5 U/kg)	Dose Cohort 3 (40 U/kg)	Dose Cohort 2 (20 U/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Dose Cohort 1 (5 U/kg)	Dose Cohort 3 (40 U/kg)	Dose Cohort 2 (20 U/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	7 / 9 (77.78%)	2 / 3 (66.67%)
Investigations			
Hemoglobin Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Von Willebrand's Factor Activity Decreased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Von Willebrand's Factor Antigen Decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	1 / 3 (33.33%)
occurrences (all)	6	0	3
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Paraesthesia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Facial Paresis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Visual Field Defect			
subjects affected / exposed	1 / 3 (33.33%)	0 / 9 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Feeling Hot			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oedema Peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 9 (11.11%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			

Vertigo subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 9 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 2	0 / 3 (0.00%) 0
Abdominal Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 3 (33.33%) 1
Flatulence subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 3 (0.00%) 0
Gastroesophageal Reflux Disease subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 9 (11.11%) 1	0 / 3 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 3 (33.33%) 1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 9 (0.00%) 0	0 / 3 (0.00%) 0
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 3 (33.33%) 1
Urticaria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 9 (0.00%) 0	1 / 3 (33.33%) 1
Musculoskeletal and connective tissue disorders			
Muscle Tightness subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 9 (0.00%) 0	0 / 3 (0.00%) 0
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	2 / 9 (22.22%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 July 2015	Exclusion criterion 5 corrected to reflect autoimmune disorders instead of hematological disorders; Excl. 6 clarified which subjects with neurological events may be included in the study; Excl. 12 updated to clarify the use of hydrocortisone administration; Excl. 17 updated to clarify the reference was to mental disorder and not any disorder; section 6.2 Clinical condition/indication updated; 6.5 Evaluation of anticipated risks and benefits of the IP to human subjects updated; 8.6 Study Stopping rules - stopping rule was added; added that IgE antibodies to be performed for any subject experiencing allergic reactions; under medications text was added to clarify the FFP administration timepoints; added that at screening CD4 levels were to be tested for all subjects; clarify the start of recording of AEs and which AEs and SAEs were not to be included in the analysis; clarified timepoints for weight/height measurements; clarified periods during which FFP and ADAMTS13 containing products were to be withheld; Cardiac troponin I biomarker added to flowdiagram; Bicarbonate, protein, albumin added to assessments; updates according new protocol template for text in sections: withdrawal and completion/discontinuation, SAEs, urgent safety measures and nonmedical complaints

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported