Clinical trial results:
A Multi-centre, Open-label Trial Evaluating Efficacy, Safety and Pharmacokinetics of Turoctocog Alfa Pegol (N8-GP) When used for Treatment and Prophylaxis of Bleeding Episodes in Previously Treated Chinese Patients with Haemophilia A

Summary

EudraCT number	2020-003001-58
Trial protocol	Outside EU/EEA
Global end of trial date	28 December 2022

Results information

Result version number	v1 (current)
This version publication date	13 July 2023
First version publication date	13 July 2023

Trial information

Trial identification

Sponsor protocol code	NN7088-4595

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05082116
WHO universal trial number (UTN)	U1111-1235-5905

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/, clinicaltrials@novonordisk.com

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical efficacy of turoctocog alfa pegol (N8-GP) in bleeding prophylaxis (number of bleeding episodes during prophylaxis) in Chinese adolescent and adult patients with severe haemophilia A previously treated with other antihemophilic factor (FVIII) products

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki [64th World Medical Association (WMA) 2013] and International Council for Harmonisation Good Clinical Practice, including archiving of essential documents, (2016) and 21 Code of Federal Regulations (CFR) 312.120.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	27 September 2021
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	China: 36
Worldwide total number of subjects	36
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)	13
Adults (18-64 years)	23
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 36 Chinese subjects with a severe haemophilia A were recruited in this trial. The trial was conducted at 8 sites in China mainland.

Pre-assignment

Screening details:

A total of 38 subjects were screened for the trial, of which 2 were screen failures and 36 subjects completed the study treatment.

Period 1

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

Blinding implementation details:

Not Applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Adolescents (12-17 years)

Arm description:

Subjects with haemophilia A aged 12-17 years with greater than or equal to (≥) 150 exposure days to other FVIII product received one single bolus dose of 50 international unit per Kilogram (IU/kg) of turoctocog alfa pegol (N8-GP), administered intravenously (IV) every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Arm type	Experimental
Investigational medicinal product name	N8-GP rFVIII
Investigational medicinal product code	
Other name	Turoctocog alfa pegol
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects with haemophilia A aged 12-17 years with ≥150 exposure days to other FVIII product received one single bolus dose of 50 IU/kg of N8-GP, administered IV every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Arm title	Adults (18-70 years)

Arm description:

Subjects with haemophilia A aged 18-70 years with ≥150 exposure days to other FVIII product received one single bolus dose of 50 IU/kg of turoctocog alfa pegol (N8-GP), administered IV every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Arm type	Experimental
Investigational medicinal product name	N8-GP rFVIII
Investigational medicinal product code	
Other name	Turoctocog alfa pegol
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects with haemophilia A aged 18-70 years with ≥150 exposure days to other FVIII product received one single bolus dose of 50 IU/kg of N8-GP, administered IV every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to

the severity and location of the bleeding episode.

Number of subjects in period 1	Adolescents (12-17 years)	Adults (18-70 years)
Started	13	23
Full analysis set	13	23
Safety analysis set	13	23
Pharmacokinetic (PK) analysis set	4 [1]	11 [2]
Completed	13	23

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left. Either resolve this issue or provide a justification.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left. Either resolve this issue or provide a justification.

Baseline characteristics

Reporting groups	
Reporting group title	Adolescents (12-17 years)

Reporting group description:

Subjects with haemophilia A aged 12-17 years with greater than or equal to (≥) 150 exposure days to other FVIII product received one single bolus dose of 50 international unit per Kilogram (IU/kg) of turoctocog alfa pegol (N8-GP), administered intravenously (IV) every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Reporting group title	Adults (18-70 years)

Reporting group description:

Subjects with haemophilia A aged 18-70 years with ≥150 exposure days to other FVIII product received one single bolus dose of 50 IU/kg of turoctocog alfa pegol (N8-GP), administered IV every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Reporting group values	Adolescents (12-17 years)	Adults (18-70 years)	Total
Number of subjects	13	23	36
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)	13	0	13
Adults (18-64 years)	0	23	23
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	13.7	28.7	
standard deviation	± 1.7	± 9.2	-
Gender Categorical Units: Subjects			
Female	0	0	0
Male	13	23	36

End points

End points reporting groups

Reporting group title	Adolescents (12-17 years)

Reporting group description:

Subjects with haemophilia A aged 12-17 years with greater than or equal to (≥) 150 exposure days to other FVIII product received one single bolus dose of 50 international unit per Kilogram (IU/kg) of turoctocog alfa pegol (N8-GP), administered intravenously (IV) every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Reporting group title	Adults (18-70 years)

Reporting group description:

Subjects with haemophilia A aged 18-70 years with ≥150 exposure days to other FVIII product received one single bolus dose of 50 IU/kg of turoctocog alfa pegol (N8-GP), administered IV every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Primary: Number of Bleeding Episodes

End point title	Number of Bleeding Episodes

End point description:

Number of bleeding episodes per year data is reported. Annualised bleeding rate (ABR) is the number of bleeding episodes per year. Results were based on the full analysis set (FAS) which included all participants exposed to N8-GP in this trial.

End point type	Primary

End point timeframe:

From start of treatment until visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	23		
Units: Bleeds per subject per year				
median (inter-quartile range (Q1-Q3))	0.00 (0.00 to 1.63)	0.00 (0.00 to 1.83)		

Statistical analyses

Statistical analysis title	N8-GP Prophylaxis

Statistical analysis description:

The analysis is based on a Poisson regression model allowing for over-dispersion. For subjects withdrawing prematurely, the log planned treatment duration is used as offset; for completers, the log actual treatment duration is used.

Comparison groups	Adolescents (12-17 years) v Adults (18-70 years)

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Poisson regression
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	5.23

Secondary: Haemostatic Effect of N8-GP When used for Treatment of Bleeding Episodes, Assessed on a Four-point Scale for Haemostatic Response (Excellent, Good, Moderate and None)

End point title	Haemostatic Effect of N8-GP When used for Treatment of Bleeding Episodes, Assessed on a Four-point Scale for Haemostatic Response (Excellent, Good, Moderate and None)

End point description:

Haemostatic effect of N8-GP for treatment of bleeding episodes was assessed by 4-point response scale: none, moderate, good or excellent. Evaluation during trial was done by subject and/or parent(s)/caregiver within approximately 8 hours after a single injection as follows: Excellent: Abrupt pain relief and/or clear improvement in objective signs of bleeding within approximately 8 hrs after a single injection; Good: Definite pain relief and/or improvement in signs of bleeding within approximately 8 hrs after a single injection, but possibly requiring more than one injection for complete resolution; Moderate: Probable or slight beneficial effect within approximately 8 hours after the first injection, but usually requiring more than one injection; None: No improvement, or worsening of symptoms. Results were based on the FAS which included all participants exposed to N8-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment until visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	23		
Units: Bleeding Episodes				
Excellent	18	22		
Good	3	6		
Moderate	3	0		
None	0	0		
Missing	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of N8-GP for Treatment of Bleeding Episodes

End point title	Consumption of N8-GP for Treatment of Bleeding Episodes

End point description:

The mean number of injections of N8-GP used for treatment of a bleed from start to stop of a bleed was reported and it was measured in international units per kilogram per bleed (IU/kg/bleed). Results were based on the FAS which included all subjects exposed to N8-GP in this trial

End point type	Secondary

End point timeframe:

From start of treatment until visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	23		
Units: IU/kg/bleed				
arithmetic mean (standard deviation)	66.7 (± 28.2)	56.2 (± 13.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of N8-GP for Prophylaxis

End point title	Consumption of N8-GP for Prophylaxis

End point description:

The mean consumption of N8-GP for prophylaxis per year per subject was reported and it was measured in international units per kilogram per year (IU/kg/year). Results were based on the FAS which included all subjects exposed to N8-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment until visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	23		
Units: IU/kg/year				
arithmetic mean (standard deviation)	4909.5 (± 252.0)	4873.9 (± 237.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: FVIII Trough Activity During Prophylaxis

End point title	FVIII Trough Activity During Prophylaxis

End point description:

Trough levels of FVIII was reported for all subjects who received prophylaxis treatment. Chromogenic assay was performed with N8-GP product specific standard (PSS) as a calibrator. Data of Visit 7 is presented. Results were based on the FAS which included all subjects exposed to N8-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment (excluding the first exposure) until visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	23		
Units: International unit per milliliter(IU/mL)				
geometric mean (geometric coefficient of variation)	0.02 (± 107.93)	0.03 (± 85.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Serious Adverse Events (SAEs)

End point title	Number of Serious Adverse Events (SAEs)

End point description:

A serious adverse event (SAE) is defined as any untoward medical occurrence that at any dose results in death, or is life-threatening, or requires inpatient hospitalization or causes prolongation of existing hospitalization results in persistent or significant disability/incapacity, or may have caused a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage. All presented SAEs are treatment-emergent. A treatment-emergent adverse event was defined as an event with onset after first N8-GP administration.Results were based on the SAS which included all subjects exposed to N8-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment until end of trial

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	23		
Units: Events	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Adverse Events (AEs)

End point title	Number of Adverse Events (AEs)

End point description:

An adverse event (AE) was defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a product, whether or not considered related to the product. All presented AEs are treatment-emergent. A treatment-emergent adverse event was defined as an event with onset after first N8-GP administration. Results were based on the safety analysis set (SAS) which included all subjects exposed to N8-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment until end of trial

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	23		
Units: Events	7	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence Rate of Confirmed FVIII Inhibitors ≥0.6 BU

End point title	Incidence Rate of Confirmed FVIII Inhibitors ≥0.6 BU

End point description:

A subject was said to have FVIII-inhibitors if two consecutive tests, preferably within 2 weeks, were positive (greater than or equal to (≥) 0.6 bethesda unit (BU)). For the calculation of the inhibitor rate the numerator was included for all subjects with neutralising antibodies while the denominator was included for all subjects with a minimum of 50 exposures plus any patients with less than 50 exposures but with neutralising inhibitor. Results were based on the FAS which included all subjects exposed to N8-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment until visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Inhibitory rate				
number (not applicable)	0.00	0.00		

Statistical analyses

No statistical analyses for this end point

Secondary: FVIII activity 30 min Post-injection (C30min)

End point title	FVIII activity 30 min Post-injection (C30min)

End point description:

FVIII plasma activity was measured after 30 mins of injection. This was measured at two time points Visit 2a and visit 7 during the study. Chromogenic assay was performed. The Pharmacokinetic (PK) analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data. Here, n= number of subjects from the respective arms analysed for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 30 min ± 5 min post-injection at visit 2a, Steady-state: 30 min ± 5 min post-injection at visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	11		
Units: IU/mL				
geometric mean (geometric coefficient of variation)				
Visit 2a (n= 4, 10)	1.178 (± 24.531)	1.196 (± 27.304)		
Visit 7 (n= 3, 11)	1.557 (± 0.646)	1.302 (± 21.521)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incremental Recovery (IR)

End point title	Incremental Recovery (IR)

End point description:

Incremental recovery was defined as the dose-normalised activity recorded 30 min after end of injection. This was measured at two time points Visit 2a and visit 7 during the study. Chromogenic assay was performed. PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for respective arm. Here, n = number of subjects from the respective arms analysed for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 30 min ± 5 min post-injection at visit 2a, Steady-state: 30 min ± 5 min post-injection at

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	11		
Units: (IU/mL)/(IU/kg)				
geometric mean (geometric coefficient of variation)				
Visit 2a (n= 4, 10)	0.023 (± 28.107)	0.023 (± 28.367)		
Visit 7 (n= 3, 11)	0.029 (± 1.443)	0.024 (± 23.535)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Curve (AUC)

End point title	Area under the Curve (AUC)

End point description:

Area under the plasma activity versus time profile from time zero to infinity (AUC0-inf) and area under the plasma activity versus time profile from time zero to 96 hours (AUC0-96h) were measured at the time points Visit 2a and visit 7 respectively during the study. It is the measure of total plasma exposure. Chromogenic assay was performed. PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data. Here, n= number of subjects from the respective arms analysed for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 0−inf post-injection at visit 2a, Steady-state: 0−96 h post-injection at visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	11		
Units: h*(IU/mL)				
geometric mean (geometric coefficient of variation)				
Visit 2a (n= 4, 10)	31.556 (± 20.100)	33.650 (± 26.123)		
Visit 7 (n= 3, 11)	36.428 (± 4.251)	36.398 (± 27.168)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-life (t½)

End point title	Terminal Half-life (t½)

End point description:

t½ = ln(2) / λz, where λz is the terminal elimination rate constant. The terminal elimination rate constant was estimated using linear regression on the terminal part of the log (activity) versus time profile. This was measured at Visit 2a and visit 7 during the study. Chromogenic assay was performed. PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data. Here, n= number of subjects from the respective arms analysed for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 0−96 h post-injection at visit 2a, Steady-state: 0−96 h post-injection at visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	11		
Units: hour (h)				
geometric mean (geometric coefficient of variation)				
Visit 2a (n= 4, 10)	19.106 (± 14.019)	20.200 (± 20.422)		
Visit 7 (n= 3, 11)	17.729 (± 5.568)	20.238 (± 18.882)		

Statistical analyses

No statistical analyses for this end point

Secondary: FVIII Trough Activity 96 h Post-injection (C96h)

End point title	FVIII Trough Activity 96 h Post-injection (C96h)

End point description:

FVIII plasma activity was measured after 96 h of injection. This was measured at two time points Visit 2a and visit 7 during the study. Chromogenic assay was performed. PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data. Here, n= number of subjects from the respective arms analysed for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 96 h ± 8 h post-injection at visit 2a, Steady-state: 96 h ± 8 h post-injection at visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	11		
Units: IU/mL				
geometric mean (geometric coefficient of variation)				
Visit 2a (n= 4, 10)	0.033 (± 36.048)	0.039 (± 44.608)		
Visit 7 (n= 3, 11)	0.032 (± 14.616)	0.045 (± 58.020)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL)

End point title	Clearance (CL)

End point description:

Total plasma clearance (CL) of drug after intravenous administration was reported. Clearance was calculated using the formula CL= Dose / AUC0-inf for single dose and CL= Dose / AUC0-96 h for steady state. This was measured at two time points Visit 2a and visit 7 during the study. Chromogenic assay was performed. PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data. Here, n= number of subjects from the respective arms analysed for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 0−96 h post-injection at visit 2a, Steady-state: 0−96 h post-injection at visit 7

End point values	Adolescents (12-17 years)	Adults (18-70 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	11		
Units: milliliter per hour per kilogram (mL/h/kg)				
geometric mean (geometric coefficient of variation)				
Visit 2a (n= 4, 10)	1.636 (± 17.092)	1.550 (± 29.123)		
Visit 7 (n= 3, 11)	1.434 (± 4.488)	1.434 (± 25.335)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of treatment until end of trial

Adverse event reporting additional description:

All presented AEs are TEAEs. A treatment-emergent adverse event was defined as an event with onset after first N8-GP administration. Results were based on the SAS which included all subjects exposed to N8-GP in this trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Adults (18-70 years)

Reporting group description:

Subjects with haemophilia A aged 18-70 years with ≥150 exposure days to other FVIII product received one single bolus dose of 50 IU/kg of N8-GP, administered IV every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Reporting group title	Adolescents (12-17 years)

Reporting group description:

Subjects with haemophilia A aged 12-17 years with ≥150 exposure days to other FVIII product received one single bolus dose of 50 IU/kg of N8-GP, administered IV every 4th day (96 hours) or twice weekly (investigator's discretion). All bleeds were to be treated with doses between 20-75 IU/kg according to the severity and location of the bleeding episode.

Serious adverse events	Adults (18-70 years)	Adolescents (12-17 years)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Adults (18-70 years)	Adolescents (12-17 years)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 23 (17.39%)	7 / 13 (53.85%)	
Investigations			
Weight decreased			
subjects affected / exposed	2 / 23 (8.70%)	1 / 13 (7.69%)	
occurrences (all)	3	1	

Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Medication error			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 23 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Infections and infestations			
Influenza			

subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 23 (4.35%)	1 / 13 (7.69%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 13 (0.00%)	
occurrences (all)	2	0	

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