



Clinical trial results:

A Phase 3b, Prospective, Open-Label, Uncontrolled, Multicenter Study on Long-Term Safety and Efficacy of rVWF in Pediatric and Adult Subjects With Severe Von Willebrand Disease (VWD)

Summary

EudraCT number	2018-003453-16
Trial protocol	FR NL DE ES AT IT BE
Global end of trial date	30 January 2025

Results information

Result version number	v1 (current)
This version publication date	20 July 2025
First version publication date	20 July 2025

Trial information

Trial identification

Sponsor protocol code	SHP677-304
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03879135
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Ave, Lexington, MA, United States, 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.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	30 January 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main aim of this study is to check effectiveness of rVWF (vonicog alfa) prophylaxis based on the annualized bleeding rate (ABR) of spontaneous (not related to trauma) bleeding episodes in pediatric and adult participants during the first 12 months on study treatment.

Protection of trial subjects:

Each participant or their parents/guardians/legally authorized representatives signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Türkiye: 11
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	35
EEA total number of subjects	11

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)	8
Adolescents (12-17 years)	9
Adults (18-64 years)	17
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 23 investigative sites globally from 1 April 2019 to 30 January 2025.

Pre-assignment

Screening details:

38 subjects with diagnosis of Von Willebrand disease were enrolled. Only subjects who received treatment(N=35) were included in analysis. These subjects received rVWF(vonicog alfa), 50±10 IU/kg, IV infusion in either prophylaxis/OD cohorts. Some subjects received supportive treatment with ADVATE for treating BEs if deemed necessary by investigator.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Prophylaxis

Arm description:

Adult participants who transitioned from the phase 3 prophylaxis parent study 071301 (NCT02973087) received the same prophylactic dose, 50±10 IU/kg, IV infusion of vonicog alfa twice weekly as in parent study 071301.

Arm type	Experimental
Investigational medicinal product name	Vonicog alfa
Investigational medicinal product code	
Other name	BAX-111, SHP-677, TAK-577
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vonicog alfa, prophylactic dose 50±10 IU/kg, IV, infusion, twice weekly.

Arm title	Cohort 2: Prophylaxis
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Arm description:

Adult participants who transitioned from parent study 071301 (NCT02973087) with no clinically significant BE for the past 6 months started this continuation study at a lower dose/frequency of vonicog alfa once weekly or twice weekly prophylactic dose, 50±10 IU/kg, IV infusion compared to the dose received (50±10 IU/kg, IV infusion, thrice weekly) in parent study 071301.

Arm type	Experimental
Investigational medicinal product name	Vonicog alfa
Investigational medicinal product code	
Other name	BAX-111, SHP-677, TAK-577
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vonicog alfa, prophylactic dose 50±10 IU/kg, IV infusion, once weekly or twice weekly.

Arm title	Cohort 3: Prophylaxis
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Arm description:

Adolescent participants (aged 12 to <18 years) who transitioned from the phase 3 OD and surgery parent study 071102 (NCT02932618) switched from receiving vonicog alfa OD treatment to receiving prophylactic dose of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Arm type	Experimental
Investigational medicinal product name	Vonicog alfa
Investigational medicinal product code	
Other name	BAX-111, SHP-677, TAK-577
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vonicog alfa, prophylactic dose, 50±10 IU/kg, IV infusion once weekly or twice weekly .

Arm title	Cohort 4: Prophylaxis
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Arm description:

Newly enrolled adult and adolescent (aged 12 to <18 years) participants who switched from OD treatment with Von Willebrand Factor (VWF) products started 50±10 IU/kg, IV infusion once weekly prophylaxis with vonicog alfa in this continuation study.

Arm type	Experimental
Investigational medicinal product name	Vonicog alfa
Investigational medicinal product code	
Other name	BAX-111, SHP-677, TAK-577
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vonicog alfa prophylactic dose, 50±10 IU/kg, IV infusion, once weekly.

Arm title	Cohort 5: On Demand
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Arm description:

Pediatric participants of all ages from parent study 071102 (NCT02932618) continued receiving OD treatment of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Arm type	Experimental
Investigational medicinal product name	Vonicog alfa
Investigational medicinal product code	
Other name	BAX-111, SHP-677, TAK-577
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vonicog alfa, 50±10 IU/kg, IV infusion, once weekly or twice weekly.

Arm title	Cohort 6: On Demand
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Arm description:

Adult participants from parent study 071301 (NCT02973087) switched back from prophylactic treatment in study 071301 to OD treatment of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Arm type	Experimental
Investigational medicinal product name	Vonicog alfa
Investigational medicinal product code	
Other name	BAX-111, SHP-677, TAK-577
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vonicog alfa, 50±10 IU/kg, IV infusion once weekly or twice weekly.

Number of subjects in period 1	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis
Started	10	1	1
Completed	10	1	1
Not completed	0	0	0
Physician decision	-	-	-
Consent withdrawn by subject	-	-	-
Site Closed by Sponsor	-	-	-

Number of subjects in period 1	Cohort 4: Prophylaxis	Cohort 5: On Demand	Cohort 6: On Demand
Started	5	16	2
Completed	3	15	1
Not completed	2	1	1
Physician decision	1	-	-
Consent withdrawn by subject	-	-	1
Site Closed by Sponsor	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Prophylaxis
Reporting group description: Adult participants who transitioned from the phase 3 prophylaxis parent study 071301 (NCT02973087) received the same prophylactic dose, 50±10 IU/kg, IV infusion of vonicog alfa twice weekly as in parent study 071301.	
Reporting group title	Cohort 2: Prophylaxis
Reporting group description: Adult participants who transitioned from parent study 071301 (NCT02973087) with no clinically significant BE for the past 6 months started this continuation study at a lower dose/frequency of vonicog alfa once weekly or twice weekly prophylactic dose, 50±10 IU/kg, IV infusion compared to the dose received (50±10 IU/kg, IV infusion, thrice weekly) in parent study 071301.	
Reporting group title	Cohort 3: Prophylaxis
Reporting group description: Adolescent participants (aged 12 to <18 years) who transitioned from the phase 3 OD and surgery parent study 071102 (NCT02932618) switched from receiving vonicog alfa OD treatment to receiving prophylactic dose of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.	
Reporting group title	Cohort 4: Prophylaxis
Reporting group description: Newly enrolled adult and adolescent (aged 12 to <18 years) participants who switched from OD treatment with Von Willebrand Factor (VWF) products started 50±10 IU/kg, IV infusion once weekly prophylaxis with vonicog alfa in this continuation study.	
Reporting group title	Cohort 5: On Demand
Reporting group description: Pediatric participants of all ages from parent study 071102 (NCT02932618) continued receiving OD treatment of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.	
Reporting group title	Cohort 6: On Demand
Reporting group description: Adult participants from parent study 071301 (NCT02973087) switched back from prophylactic treatment in study 071301 to OD treatment of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.	

Reporting group values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis
Number of subjects	10	1	1
Age categorical			
Units: participants			
<6 years	0	0	0
>=6 to <12 years	0	0	0
>=12 to <18 years	0	0	1
>=18 years	10	1	0
Gender categorical			
Units: Subjects			
Female	4	1	0
Male	6	0	1
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	9	0	1
More than one race	0	0	0
Unknown or Not Reported	1	1	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	8	0	1
Unknown or Not Reported	1	1	0

Reporting group values	Cohort 4: Prophylaxis	Cohort 5: On Demand	Cohort 6: On Demand
Number of subjects	5	16	2
Age categorical			
Units: participants			
<6 years	0	3	0
>=6 to <12 years	0	5	0
>=12 to <18 years	2	6	0
>=18 years	3	2	2
Gender categorical			
Units: Subjects			
Female	2	9	1
Male	3	7	1
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	4	14	2
More than one race	0	1	0
Unknown or Not Reported	1	1	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	5	14	2
Unknown or Not Reported	0	1	0

Reporting group values	Total		
Number of subjects	35		
Age categorical			
Units: participants			
<6 years	3		
>=6 to <12 years	5		
>=12 to <18 years	9		
>=18 years	18		
Gender categorical			
Units: Subjects			
Female	17		

Male	18		
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Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	30		
More than one race	1		
Unknown or Not Reported	4		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	30		
Unknown or Not Reported	3		

End points

End points reporting groups

Reporting group title	Cohort 1: Prophylaxis
Reporting group description: Adult participants who transitioned from the phase 3 prophylaxis parent study 071301 (NCT02973087) received the same prophylactic dose, 50±10 IU/kg, IV infusion of vonicog alfa twice weekly as in parent study 071301.	
Reporting group title	Cohort 2: Prophylaxis
Reporting group description: Adult participants who transitioned from parent study 071301 (NCT02973087) with no clinically significant BE for the past 6 months started this continuation study at a lower dose/frequency of vonicog alfa once weekly or twice weekly prophylactic dose, 50±10 IU/kg, IV infusion compared to the dose received (50±10 IU/kg, IV infusion, thrice weekly) in parent study 071301.	
Reporting group title	Cohort 3: Prophylaxis
Reporting group description: Adolescent participants (aged 12 to <18 years) who transitioned from the phase 3 OD and surgery parent study 071102 (NCT02932618) switched from receiving vonicog alfa OD treatment to receiving prophylactic dose of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.	
Reporting group title	Cohort 4: Prophylaxis
Reporting group description: Newly enrolled adult and adolescent (aged 12 to <18 years) participants who switched from OD treatment with Von Willebrand Factor (VWF) products started 50±10 IU/kg, IV infusion once weekly prophylaxis with vonicog alfa in this continuation study.	
Reporting group title	Cohort 5: On Demand
Reporting group description: Pediatric participants of all ages from parent study 071102 (NCT02932618) continued receiving OD treatment of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.	
Reporting group title	Cohort 6: On Demand
Reporting group description: Adult participants from parent study 071301 (NCT02973087) switched back from prophylactic treatment in study 071301 to OD treatment of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.	

Primary: Spontaneous Annualized Bleeding Rate (sABR)

End point title	Spontaneous Annualized Bleeding Rate (sABR) ^{[1][2]}
End point description: sABR was derived as [number of treated bleeds] / [duration in years]. Bleeds with unknown causality were considered as spontaneous. Bleeds were categorized based on the investigator assessment of cause. sABR during the first 12 months of prophylactic treatment with rVWF (vonicog alfa) was reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug. '99999' denotes that standard deviation was not estimable for a single participant.	
End point type	Primary
End point timeframe: Up to 12 months	

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: Only descriptive analysis was planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: spontaneous bleeds per year				
arithmetic mean (standard deviation)	1.430 (\pm 2.3894)	1.040 (\pm 99999)	0.000 (\pm 99999)	3.022 (\pm 2.4746)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Based on Severity of TEAEs

End point title	Number of Participants Based on Severity of TEAEs
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End point description:

An AE is defined as any untoward medical occurrence in a participant administered IP that does not necessarily have a causal relationship with the treatment. TEAE was defined as any AE that started after the first administration of study drug in this continuation study. Severity of TEAEs was determined by following definitions: Mild: No limitation of usual activities; Moderate: Some limitation of usual activities and may required therapeutic intervention; Severe: Inability to carry out usual activities with sequelae, which required therapeutic intervention. Number of participants with TEAEs based on severity of TEAEs were reported. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants				
Mild	7	1	1	4
Moderate	7	0	0	3
Severe	3	0	0	1

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants				
Mild	14	2		
Moderate	11	1		
Severe	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Treatment emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of participants with Treatment emergent Adverse Events (TEAEs) and Serious TEAEs
End point description: AE: any untoward medical occurrence in participant administered a pharmaceutical product; untoward medical occurrence does not necessarily have a causal relationship with this treatment. AE can therefore be any unfavorable & unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with use of medicinal (investigational) product whether or not it is related to medicinal product. TEAE: any AE that started after first administration of study drug in this continuation study. Serious TEAEs: any untoward medical occurrence that: results in death, is life-threatening, requires inpatient hospitalization/prolongation of existing hospitalization, results in persistent/significant disability/incapacity, leads to a congenital anomaly/birth defect in offspring of participant/ is medically important. SAS: all participants who received any amount of vonicog alfa as obtained from study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.	
End point type	Secondary
End point timeframe: Up to 5.8 years	

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants				
TEAEs	8	1	1	4
Serious TEAEs	3	0	0	1

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants				
TEAEs	15	2		
Serious TEAEs	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Based on Causality of TEAEs

End point title	Number of Participants Based on Causality of TEAEs
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End point description:

An AE is defined as any untoward medical occurrence in a participant administered IP that does not necessarily have a causal relationship with the treatment. TEAE was defined as any AE that started after the first administration of study drug in this continuation study. A physician/investigator made the assessment of relationship to investigational product for each AE. Number of participants with TEAEs based on causality were reported. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Neutralizing Antibodies to von Willebrand factor (VWF)

End point title	Number of Participants who Developed Neutralizing Antibodies to von Willebrand factor (VWF)
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End point description:

Three functional VWF assays for von Willebrand factor collagen binding (VWF:CB), von Willebrand factor: Ristocetin Cofactor (VWF:RCO) and von Willebrand factor VIII B (VWF:FVIIIB) were used to test the presence of neutralizing anti-VWF antibodies. Neutralizing antibodies to VWF:RCO, VWF:CB and VWF:FVIIIB activities were measured by assays based on the Bethesda assay established for quantitative analysis of FVIII inhibitors (Nijmegen modification of the Bethesda assay). Only confirmed neutralizing anti -VWF antibodies were considered inhibitors. Number of participants who developed neutralizing antibodies to rVWF were assessed. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Hypersensitivity Reactions

End point title	Number of Participants With Hypersensitivity Reactions
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End point description:

Hypersensitivity (also called hypersensitivity reaction or intolerance) defined as undesirable reactions produced by the normal immune system, including allergies and autoimmunity. Potential hypersensitivity events were identified by broad search criteria and then medically assessed. Number of participants with hypersensitivity reactions as TEAEs of special interest was calculated. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
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Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Thromboembolic Events

End point title	Number of Participants With Thromboembolic Events
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End point description:

Thromboembolism defined as formation of a clot (thrombus) in a blood vessel that breaks loose, is carried by the blood stream and could plug another vessel. Number of participants with thromboembolic events as TEAEs of special interest were reported. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Total Binding Antibodies to von Willebrand factor (VWF)

End point title	Number of Participants who Developed Total Binding Antibodies to von Willebrand factor (VWF)
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End point description:

The presence of total binding anti-VWF antibodies was determined by an enzyme-linked immunosorbent assay (ELISA) employing polyclonal anti-human Immunoglobulin (Ig) antibodies (IgG, IgM and IgA). Number of participants who developed of total binding antibodies to rVWF were assessed. The SAS

consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
End point timeframe:	
Up to 5.8 years	

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Neutralizing Antibodies to Factor VIII (FVIII)

End point title	Number of Participants who Developed Neutralizing Antibodies to Factor VIII (FVIII)
End point description:	
Three functional VWF assays for von Willebrand factor collagen binding (VWF:CB), von Willebrand factor: Ristocetin Cofactor (VWF:RCO) and von Willebrand factor VIII B (VWF:FVIII B) were used to test the presence of neutralizing anti-VWF antibodies. Neutralizing antibodies to VWF:RCO, VWF:CB and VWF:FVIII B activities was measured by assays based on the Bethesda assay established for quantitative analysis of FVIII inhibitors (Nijmegen modification of the Bethesda assay). Only confirmed neutralizing anti -VWF antibodies were considered inhibitors. Number of participants who developed neutralizing antibodies to FVIII were assessed. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.	
End point type	Secondary
End point timeframe:	
Up to 5.8 years	

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Binding Antibodies to Chinese hamster ovary (CHO) proteins

End point title	Number of Participants who Developed Binding Antibodies to Chinese hamster ovary (CHO) proteins
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End point description:

Total Ig antibodies (IgG, IgA, IgM) against CHO protein were analyzed using ELISA. Number of participants who developed binding antibodies to CHO proteins were assessed. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Total Binding Antibodies to Factor VIII (FVIII)

End point title	Number of Participants who Developed Total Binding Antibodies to Factor VIII (FVIII)
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End point description:

Binding antibodies against FVIII were analyzed using a proprietary enzyme immunoassay. Number of participants who developed of total binding antibodies to FVIII were assessed. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Binding Antibodies to Mouse Immunoglobulin G (IgG)

End point title	Number of Participants who Developed Binding Antibodies to Mouse Immunoglobulin G (IgG)
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End point description:

Detection and quantification of IgG antibodies originating from human plasma that were directed against mouse-IgG (HAMA: human anti- mouse antibodies) were assessed using ELISA (Medac, Hamburg, Germany). Number of participants who developed binding antibodies to Mouse IgG were assessed. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Develop Binding Antibodies to recombinant Furin (rFurin)

End point title	Number of Participants who Develop Binding Antibodies to recombinant Furin (rFurin)
End point description: Total Ig antibodies (IgG, IgA, IgM) against human furin were analyzed using ELISA. Number of participants who developed binding antibodies to rFurin were assessed. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.	
End point type	Secondary
End point timeframe: Up to 5.8 years	

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Vital Signs

End point title	Number of Participants With Clinically Significant Changes in Vital Signs
End point description: Vital signs included blood pressure (systolic and diastolic), pulse rate, respiratory rate and body temperature. Number of participants with clinically significant change from baseline in vital signs were assessed. The SAS consisted of all participants who received any amount of vonicog alfa as obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF.	
End point type	Secondary
End point timeframe: Up to 5.8 years	

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Laboratory Parameters

End point title	Number of Participants With Clinically Significant Changes in Laboratory Parameters
End point description: Clinical laboratory parameters included serum chemistry, hematology and urinalysis assessments. Number of participants with clinically significant change from baseline in clinical laboratory parameters were assessed. The SAS consisted of all participants who received any amount of vonicog alfa as	

obtained from the study drug administration eDiary, study drug administration details eCRF, or PK infusion eCRF. '9999' denotes that no postbaseline results were collected for any urinalysis parameters in the OD cohorts.

End point type	Secondary
End point timeframe:	
Up to 5.8 years	

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants				
Serum Chemistry	0	0	0	0
Hematology	0	0	0	0
Urinalysis	0	0	0	0

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: participants				
Serum Chemistry	0	0		
Hematology	0	0		
Urinalysis	9999	9999		

Statistical analyses

No statistical analyses for this end point

Secondary: Spontaneous Annualized Bleeding Rate (sABR) Under Prophylactic Treatment

End point title	Spontaneous Annualized Bleeding Rate (sABR) Under Prophylactic Treatment ^[3]
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End point description:

sABR was derived as [number of treated bleeds] / [duration in years]. Bleeds with unknown causality were considered as spontaneous. Bleeds were categorized based on the investigator assessment of cause. sABR during prophylaxis treatment with rVWF (vonicog alfa) while enrolled in the study were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug. '99999' denotes that standard deviation was not estimable for a single participant.

End point type	Secondary
End point timeframe:	
Up to 5.8 years	

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: spontaneous bleeds per year				
arithmetic mean (standard deviation)	1.122 (± 2.1084)	0.330 (± 99999)	0.000 (± 99999)	2.110 (± 1.9954)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Categorized Based on Spontaneous Annualized Bleeding Rate (sABR)

End point title	Number of Participants Categorized Based on Spontaneous Annualized Bleeding Rate (sABR) ^[4]
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End point description:

The sABR was the number of spontaneous bleeds divided by the observation period in years, where an observation period = (date of completion/termination-date of first dose+1)/365.2425. sABR was categorized based on number of BEs as 0, greater than (>) 0 through 2, >2 through 5, >5 during the prophylactic treatment with rVWF (vonicog alfa). Bleeding at multiple locations related to the same injury was counted as single BE. BEs of unknown cause were counted as spontaneous bleeds. Number of participants categorized based on sABR during prophylactic treatment with rVWF (vonicog alfa) were reported. The FAS consisted of all participants who satisfied all entry criteria and received any amount of study drug.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants				
0 bleeds/year	5	0	1	0
>0 to ≤2 bleeds/year	3	1	0	3
>2 to ≤5 bleeds/year	1	0	0	1
>5 bleeds/year	1	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Categorized Based on Weekly Number of Infusions

End point title	Number of Participants Categorized Based on Weekly Number of Infusions ^[5]
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End point description:

Categorized as ≥ 0 to < 1 infusion per week, ≥ 1 to < 2 infusions per week, ≥ 2 to < 3 infusions per week, ≥ 3 infusions per week. The number of participants categorized based on number of infusions per week during prophylactic treatment with rVWF (vonicog alfa) were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants				
≥ 0 to < 1	1	0	0	0
≥ 1 to < 2	6	1	1	5
≥ 2 to < 3	3	0	0	0
≥ 3	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Bleeding Event on Prophylaxis Treatment

End point title	Time to First Bleeding Event on Prophylaxis Treatment ^[6]
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End point description:

Time to event estimates and confidence intervals obtained from Kaplan-Meier analysis. Participants with 0 bleeds during each study period were censored at the date of the last day in that study period. The FAS consisted of all participants who satisfied all entry criteria and received any amount of study drug. Subjects analysed is the number of participants with event. '9' and '99999' indicates that the lower and upper limit of 95% Confidence interval (CI) was not estimable due to censoring.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	1	0 ^[7]	5
Units: days				
median (confidence interval 95%)	172 (5 to 99999)	141 (9 to 99999)	(to)	88 (9 to 99999)

Notes:

[7] - No participants with data were available for analyses.

Statistical analyses

No statistical analyses for this end point

Secondary: Spontaneous Annualized Bleeding Rate (sABR) by Location of Bleeding

End point title	Spontaneous Annualized Bleeding Rate (sABR) by Location of Bleeding ^[8]
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End point description:

sABR was derived as [number of treated bleeds] / [duration in years]. sABR for BEs based on location of bleeding: Skin, Muscle, Mucosal Nasal, Mucosal Oral, Joint, Gastrointestinal (GI), Menstrual/Heavy Menstrual, Venipuncture Site, Soft Tissue, Body Cavity, Hematuria, Central Nervous System (CNS) and Other, while on prophylactic treatment with rVWF (vonicog alfa) were reported. The FAS consisted of all participants who satisfied all entry criteria and received any amount of study drug. 'n' is the number of participants with data available for analyses for the specified category. 'n' denotes the number of participants with data available for analyses for the specified category. '999' denotes mean was not estimable as number of participants analysed was zero. '99999' indicates that standard deviation was not estimable for a single participant.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: bleeds per year				
arithmetic mean (standard deviation)				
Skin (n=10,1,1,5)	0.033 (± 0.1044)	0.000 (± 99999)	0.000 (± 99999)	0.000 (± 0.0000)
Muscle (n=10,1,1,5)	0.000 (± 0.0000)	0.000 (± 99999)	0.000 (± 99999)	0.068 (± 0.1521)
Mucosal, Nasal (n=10,1,1,5)	0.199 (± 0.3542)	0.000 (± 99999)	0.000 (± 99999)	0.068 (± 0.1521)
Mucosal, Oral (n=10,1,1,5)	0.268 (± 0.7358)	0.330 (± 99999)	0.000 (± 99999)	0.268 (± 0.5993)
Joint (n=10,1,1,5)	0.067 (± 0.2119)	0.000 (± 99999)	0.000 (± 99999)	1.370 (± 2.3644)
GI (n=10,1,1,5)	0.000 (± 0.0000)	0.000 (± 99999)	0.000 (± 99999)	0.136 (± 0.3041)
Menstrual/Heavy Menstrual (n=2,1,0,2)	2.770 (± 3.9174)	0.000 (± 99999)	999 (± 99999)	0.500 (± 0.7071)
Venipuncture Site (n=10,1,1,5)	0.000 (± 0.0000)	0.000 (± 99999)	0.000 (± 99999)	0.000 (± 0.0000)
Soft Tissue (n=10,1,1,5)	0.000 (± 0.0000)	0.000 (± 99999)	0.000 (± 99999)	0.000 (± 0.0000)
Body Cavity (n=10,1,1,5)	0.000 (± 0.0000)	0.000 (± 99999)	0.000 (± 99999)	0.000 (± 0.0000)

Hematuria (n=10,1,1,5)	0.000 (± 0.0000)	0.000 (± 99999)	0.000 (± 99999)	0.000 (± 0.0000)
CNS (n=10,1,1,5)	0.000 (± 0.0000)	0.000 (± 99999)	0.000 (± 99999)	0.000 (± 0.0000)
Other (n=10,1,1,5)	0.067 (± 0.1413)	0.000 (± 99999)	0.000 (± 99999)	0.068 (± 0.1521)

Statistical analyses

No statistical analyses for this end point

Secondary: Average Number of Infusions Per Week During Prophylactic Treatment

End point title	Average Number of Infusions Per Week During Prophylactic Treatment ^[9]
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End point description:

Average number of infusions per week during prophylactic treatment with rVWF (vonicog alfa) were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug. '99999' denotes that standard deviation was not estimable for a single participant.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: infusions per week				
arithmetic mean (standard deviation)	1.87 (± 0.351)	1.01 (± 99999)	1.14 (± 99999)	1.38 (± 0.372)

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of Infusions During Prophylactic Treatment

End point title	Total Number of Infusions During Prophylactic Treatment ^[10]
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End point description:

Total number of infusions during prophylactic treatment with rVWF (vonicog alfa) were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug. '99999' denotes that standard deviation was not estimable for a single participant.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: infusions				
arithmetic mean (standard deviation)	287.8 (± 53.42)	157.0 (± 99999)	177.0 (± 99999)	159.2 (± 41.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved Transfusion-free Maintenance of Hemoglobin Levels

End point title	Number of Participants who Achieved Transfusion-free Maintenance of Hemoglobin Levels ^[11]
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End point description:

Transfusion free maintenance of hemoglobin levels during prophylactic treatment with rVWF (vonicog alfa) were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: participants	8	1	1	5

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Ferritin Levels Over Time

End point title	Change From Baseline in Ferritin Levels Over Time ^[12]
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End point description:

Change from baseline in ferritin levels over time during prophylactic treatment with rVWF (vonicog alfa) were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any

amount of study drug. Subjects analysed are the number of participants with data available for analysis at Baseline. 'n' denotes the number of participants with data available for analyses at the specified timepoint.

End point type	Secondary
End point timeframe:	
Up to 5.8 years	

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	0 ^[13]	0 ^[14]	5
Units: picomole per liter (pmol/L)				
arithmetic mean (standard deviation)				
Baseline (n=2,0,0,5)	148.5 (± 171.83)	()	()	90.8 (± 110.82)
Month 1 (n=2,0,0,5)	11.0 (± 18.38)	()	()	-31.0 (± 44.89)
Month 2 (n=2,0,0,5)	0.0 (± 1.41)	()	()	-43.8 (± 59.60)
Month 3 (n=2,0,0,4)	-18.5 (± 21.92)	()	()	-33.3 (± 64.57)
Month 6 (n=2,0,0,5)	2.0 (± 2.83)	()	()	-16.6 (± 19.88)
Month 9 (n=2,0,0,5)	58.5 (± 91.22)	()	()	-12.8 (± 53.05)
Month 12 (n=2,0,0,4)	19.0 (± 26.87)	()	()	-27.0 (± 27.51)
Month 15 (n=2,0,0,3)	5.5 (± 13.44)	()	()	-25.7 (± 80.16)
Month 18 (n=2,0,0,3)	18.0 (± 46.67)	()	()	-49.7 (± 52.56)
Month 21 (n=2,0,0,5)	37.5 (± 64.35)	()	()	-59.3 (± 50.16)
Month 24 (n=2,0,0,5)	12.0 (± 26.87)	()	()	-53.3 (± 91.22)
Month 27 (n=2,0,0,5)	34.0 (± 60.81)	()	()	-54.0 (± 55.56)
Month 30(n=2,0,0,3)	46.5 (± 77.07)	()	()	-70.7 (± 70.12)
Month 33 (n=2,0,0,3)	71.5 (± 106.77)	()	()	-21.3 (± 114.00)
End of Study (n=2,0,0,5)	38.5 (± 48.79)	()	()	-27.6 (± 52.46)

Notes:

[13] - No participants were analysed.

[14] - No participants were analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Total Weight Adjusted Consumption of Recombinant Von Willebrand Factor (rVWF) (Vonico Alfa) Per Participant During Prophylactic Treatment

End point title	Total Weight Adjusted Consumption of Recombinant Von
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End point description:

For each participant, the body weight-adjusted dose (IU/kg) was derived as the number of units of rVWF infused (IU) divided by the last available body weight (kilogram [kg]) prior to the infusion. Total weight adjusted consumption of rVWF (vonicog alfa) per participant during prophylactic treatment with rVWF (vonicog alfa) was reported as International Units per kilogram (IU/kg). The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug. '99999' denotes that standard deviation was not estimable for a single participant.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the prophylaxis cohort.

End point values	Cohort 1: Prophylaxis	Cohort 2: Prophylaxis	Cohort 3: Prophylaxis	Cohort 4: Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	1	1	5
Units: IU/kg				
arithmetic mean (standard deviation)	14953.497 (± 3349.4461)	9992.460 (± 99999)	9270.620 (± 99999)	9171.746 (± 1505.5667)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Hemostatic Efficacy Rating

End point title	Overall Hemostatic Efficacy Rating ^[16]
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End point description:

.Hemostatic efficacy for treatment of BEs was rated on 4-point Likert scale as:excellent=full relief of pain&cessation of objective signs of bleeding after single infusion,no additional infusion is required for control of bleeding&administration of further infusion to maintain hemostasis would not affect scoring;good=definite pain relief&/or improvement in signs of bleeding after single infusion,possibly requires >2 infusions for complete resolution&administration of further infusion to maintain hemostasis would not affect scoring;fair=probable&/or slight relief of pain&slight improvement in signs of bleeding after single infusion,required multiple infusions for complete resolution;none=no improvement of signs/symptoms or conditions worsen.Missing=number of unique BEs without any overall hemostatic efficacy rating at resolution of breakthrough BE. Analysis Population: FAS. Subjects analysed is the number of participants with treated bleeding episodes.

End point type	Secondary
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End point timeframe:

Initial 12 months of study

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the On Demand cohort.

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	2		
Units: bleeding episodes				
number (not applicable)				
Excellent	74	21		
Good	1	0		
Fair	0	0		
None	0	0		
Missing	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Infusions of Vonicog Alfa

End point title	Number of Infusions of Vonicog Alfa ^[17]
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End point description:

Number of infusions of rVWF (vonicog alfa) utilized to treat BEs during OD treatment while enrolled in the study were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the On Demand cohort.

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: infusions				
arithmetic mean (standard deviation)	1.1 (± 0.65)	1.2 (± 0.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Infusions of ADVATE

End point title	Number of Infusions of ADVATE ^[18]
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End point description:

Number of infusions of ADVATE (rFVIII, octocog alfa) utilized to treat BEs during OD treatment while enrolled in the study were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug. Subjects analysed is the number of participants with ADVATE-treated bleeding episodes.

End point type	Secondary
End point timeframe:	
Up to 5.8 years	
Notes:	
[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.	
Justification: This endpoint is only applicable for the arms in the On Demand cohort.	

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: infusions				
arithmetic mean (standard deviation)	1.1 (± 0.25)	1.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Weight-adjusted Consumption of Vonicog alfa per Bleeding Episode

End point title	Weight-adjusted Consumption of Vonicog alfa per Bleeding Episode ^[19]
End point description:	
Weight-adjusted consumption (IU/kg) was derived as the total units infused (IU) divided by the last available body weight (kg) prior to the infusion. Weight-adjusted consumption of rVWF (vonicog alfa) per bleeding episode during OD treatment while enrolled in the study were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug.	
End point type	Secondary
End point timeframe:	
Up to 5.8 years	
Notes:	
[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.	
Justification: This endpoint is only applicable for the arms in the On Demand cohort.	

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: IU/kg per bleeding episode				
arithmetic mean (standard deviation)	56.109 (± 33.1312)	61.713 (± 26.6936)		

Statistical analyses

No statistical analyses for this end point

Secondary: Weight-adjusted Consumption of ADVATE per Bleeding Episode

End point title	Weight-adjusted Consumption of ADVATE per Bleeding
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End point description:

Weight-adjusted consumption (IU/kg) was derived as the total units infused (IU) divided by the last available body weight (kg) prior to the infusion. Weight-adjusted consumption of ADVATE (rFVIII, octocog alfa) per bleeding episode during OD treatment while enrolled in the study were reported. The FAS consisted of all participants who satisfied all the entry criteria and received any amount of study drug. Subjects analysed is the number of participants with ADVATE-treated bleeding episodes.

End point type	Secondary
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End point timeframe:

Up to 5.8 years

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable for the arms in the On Demand cohort.

End point values	Cohort 5: On Demand	Cohort 6: On Demand		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: IU/kg per bleeding episode				
arithmetic mean (standard deviation)	39.217 (\pm 11.0752)	35.175 (\pm 2.2274)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 5.8 years

Adverse event reporting additional description:

The SAS consisted of all participants who received any amount of rVWF as obtained from the IP administration eDiary, Study Drug Administration Details eCRF or Pharmacokinetic Infusion eCRF.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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Reporting groups

Reporting group title	Cohort 2: Prophylaxis: Adult ≥ 18 years
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Reporting group description:

Adult participants who transitioned from parent study 071301 (NCT02973087) with no clinically significant BE for the past 6 months started this continuation study at a lower dose/frequency of vonicog alfa once weekly or twice weekly prophylactic dose, 50 ± 10 IU/kg, IV infusion compared to the dose received (50 ± 10 IU/kg, IV infusion, thrice weekly) in parent study 071301.

Reporting group title	Cohort 1: Prophylaxis: Adult ≥ 18 years
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Reporting group description:

Adult participants who transitioned from the phase 3 prophylaxis parent study 071301 (NCT02973087) received the same prophylactic dose, 50 ± 10 IU/kg, IV infusion of vonicog alfa twice weekly as in parent study 071301.

Reporting group title	Cohort 4: Prophylaxis: Pediatric 12 to < 18 years
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Reporting group description:

Newly enrolled adolescent (aged 12 to < 18 years) participants who switched from OD treatment with VWF products started 50 ± 10 IU/kg, IV infusion once weekly prophylaxis with vonicog alfa in this continuation study.

Reporting group title	Cohort 3: Prophylaxis: Pediatric 12 to < 18 years
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Reporting group description:

Adolescent participants (aged 12 to < 18 years) who transitioned from the phase 3 OD and surgery parent study 071102 (NCT02932618) switched from receiving vonicog alfa OD treatment to receiving prophylactic dose of vonicog alfa 50 ± 10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Reporting group title	Cohort 4: Prophylaxis: Adult ≥ 18 years
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Reporting group description:

Newly enrolled adult participants who switched from OD treatment with VWF products started 50 ± 10 IU/kg, IV infusion once weekly prophylaxis with vonicog alfa in this continuation study.

Reporting group title	Cohort 5: On Demand: Pediatric < 6 years
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Reporting group description:

Pediatric participants of < 6 years of age from Parent Study 071102/NCT02932618 continued receiving OD treatment of vonicog alfa 50 ± 10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Reporting group title	Cohort 5: On Demand: Pediatric 6 to < 12 years
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Reporting group description:

Pediatric participants of 6 to < 12 years age from parent study 071102 (NCT02932618) continued receiving OD treatment of vonicog alfa 50 ± 10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Reporting group title	Cohort 5: On Demand: Pediatric 12 to < 18 years
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Reporting group description:

Pediatric participants of 12 to < 18 years of age from parent study 071102 (NCT02932618) continued receiving OD treatment of vonicog alfa 50 ± 10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Reporting group title	Cohort 5: On Demand: Adult ≥ 18 years
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Reporting group description:

Adult Participants from Parent Study 071102/NCT02932618 continued receiving OD treatment of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Reporting group title	Cohort 6: On Demand: Adult ≥18 years
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Reporting group description:

Adult participants from parent study 071301 (NCT02973087) switched back from prophylactic treatment in Study 071301 to OD treatment of vonicog alfa 50±10 IU/kg, IV infusion, once weekly or twice weekly in this continuation study.

Serious adverse events	Cohort 2: Prophylaxis: Adult ≥18 years	Cohort 1: Prophylaxis: Adult ≥18 years	Cohort 4: Prophylaxis: Pediatric 12 to <18 years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	3 / 10 (30.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			

subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Medical device site extravasation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus infection			

subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 3: Prophylaxis: Pediatric 12 to <18 years	Cohort 4: Prophylaxis: Adult ≥18 years	Cohort 5: On Demand: Pediatric <6 years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Medical device site extravasation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus infection			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 5: On Demand: Pediatric 6 to <12 years	Cohort 5: On Demand: Pediatric 12 to <18 years	Cohort 5: On Demand: Adult ≥18 years
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Medical device site extravasation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus infection			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 6: On Demand: Adult ≥18 years		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibula fracture			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Medical device site extravasation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronavirus infection			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 2: Prophylaxis: Adult ≥18 years	Cohort 1: Prophylaxis: Adult ≥18 years	Cohort 4: Prophylaxis: Pediatric 12 to <18 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	8 / 10 (80.00%)	2 / 2 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion site rash			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			

subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	1 / 2 (50.00%)
occurrences (all)	0	1	2
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Dysmenorrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Catarrh			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 1 (100.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			

subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Respiratory tract congestion subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Product issues Device malfunction subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Investigations Anti factor VIII antibody positive subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Blood triglycerides increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	2 / 10 (20.00%) 2	0 / 2 (0.00%) 0
Serum ferritin decreased subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 2	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0

Arthropod sting			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Bone contusion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Chest injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 1 (0.00%)	2 / 10 (20.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Fall			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Epicondylitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Fracture displacement			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 1 (0.00%)	2 / 10 (20.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0

Meniscus injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	2
Limb injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Spinal compression fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Stress fracture			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Traumatic haematoma			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Lymphatic malformation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Palpitations			

subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	1 / 2 (50.00%) 1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 1 (100.00%)	3 / 10 (30.00%)	2 / 2 (100.00%)
occurrences (all)	1	5	12
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Eosinophilia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Astigmatism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	2 / 10 (20.00%) 3	0 / 2 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 10 (10.00%) 2	0 / 2 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1	1 / 10 (10.00%) 1	1 / 2 (50.00%) 1
Angular cheilitis subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Dental caries subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 10 (10.00%) 3	0 / 2 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 10 (10.00%) 2	0 / 2 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1	1 / 2 (50.00%) 1
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1	0 / 2 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0
Faeces discoloured subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1	0 / 2 (0.00%) 0
Haematochezia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0	0 / 2 (0.00%) 0

Enteritis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 1 (0.00%)	2 / 10 (20.00%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Tooth deposit			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Bile duct stone			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Haemobilia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Cholelithiasis			

subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hepatomegaly			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Perioral dermatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Skin disorder			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Ecchymosis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Petechiae			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nephrolithiasis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Arthralgia			

subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Haemophilic arthropathy			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	1 / 1 (100.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	2	0	2
Joint effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	1 / 2 (50.00%)
occurrences (all)	0	2	1
Tendonitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Croup infectious			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Coronavirus infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 1 (100.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 1 (100.00%)	0 / 10 (0.00%)	1 / 2 (50.00%)
occurrences (all)	2	0	2
Otitis media			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Pharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Tracheobronchitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Viral rhinitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Iron deficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Obesity			

subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 10 (10.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Zinc deficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 10 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 3: Prophylaxis: Pediatric 12 to <18 years	Cohort 4: Prophylaxis: Adult ≥18 years	Cohort 5: On Demand: Pediatric <6 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	2 / 3 (66.67%)	3 / 3 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Varicose vein			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infusion site rash			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Pyrexia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 3 (33.33%) 1	2 / 3 (66.67%) 2
Reproductive system and breast disorders Intermenstrual bleeding subjects affected / exposed occurrences (all) Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Atelectasis subjects affected / exposed occurrences (all) Asthma subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Catarrh subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Pleural effusion subjects affected / exposed occurrences (all) Respiratory tract congestion	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0	0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 0 / 3 (0.00%) 1 1 / 3 (33.33%) 0	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 2 / 3 (66.67%) 5 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0

subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Product issues Device malfunction subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Investigations Anti factor VIII antibody positive subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Blood triglycerides increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Serum ferritin decreased subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 2	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Arthropod sting subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1

Bone contusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest injury			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epicondylitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fracture displacement			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Head injury			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Infusion related reaction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Limb injury			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stress fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Traumatic haematoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sunburn			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Congenital, familial and genetic disorders			
Lymphatic malformation			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Eosinophilia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Ear and labyrinth disorders Cerumen impaction subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Ear pain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Astigmatism subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Conjunctivitis allergic subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0

Abdominal distension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Angular cheilitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Enteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	3 / 3 (100.00%)
occurrences (all)	0	1	5
Tooth deposit			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bile duct stone			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemobilia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cholelithiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatomegaly			

subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Perioral dermatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemophilic arthropathy			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Joint effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	1 / 1 (100.00%)	2 / 3 (66.67%)	3 / 3 (100.00%)
occurrences (all)	1	2	3
Conjunctivitis bacterial			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Croup infectious			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2

Coronavirus infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Onychomycosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Rhinitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Tracheobronchitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Viral rhinitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Obesity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Zinc deficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 5: On Demand: Pediatric 6 to <12 years	Cohort 5: On Demand: Pediatric 12 to <18 years	Cohort 5: On Demand: Adult ≥18 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	6 / 6 (100.00%)	1 / 2 (50.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion site rash			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast			

disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	4
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Catarrh			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Product issues Device malfunction subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Investigations Anti factor VIII antibody positive subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
Blood triglycerides increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Serum ferritin decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Arthropod sting subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Bone contusion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0

Chest injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Epicondylitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Fracture displacement			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	1	1	0

Road traffic accident subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
Skin laceration subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Spinal compression fracture subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Stress fracture subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Traumatic haematoma subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Wound subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Sunburn subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Congenital, familial and genetic disorders Lymphatic malformation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Cardiac disorders Bundle branch block right subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0

Headache subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	1 / 2 (50.00%) 3
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Eosinophilia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	1 / 2 (50.00%) 1
Ear and labyrinth disorders			
Cerumen impaction subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Ear pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Eye disorders			
Cataract subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Astigmatism subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
Conjunctivitis allergic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	1 / 2 (50.00%) 1
Abdominal distension subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0

Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Angular cheilitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Enteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Irritable bowel syndrome subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
Salivary hypersecretion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
Tooth deposit subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1	0 / 2 (0.00%) 0
Hepatobiliary disorders Cholecystitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Bile duct stone subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Haemobilia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Cholelithiasis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Hepatomegaly subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0	0 / 2 (0.00%) 0
Skin and subcutaneous tissue disorders			

Dermatitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Perioral dermatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Haemophilic arthropathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Joint effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	1 / 2 (50.00%)
occurrences (all)	1	0	1
Tendonitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	1 / 5 (20.00%)	3 / 6 (50.00%)	1 / 2 (50.00%)
occurrences (all)	1	3	1
Conjunctivitis bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Croup infectious			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Coronavirus infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0

Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Periodontitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Otitis media acute			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Tracheobronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 5 (60.00%)	1 / 6 (16.67%)	1 / 2 (50.00%)
occurrences (all)	3	2	3
Viral rhinitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 2 (50.00%)
occurrences (all)	0	1	1
Obesity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Zinc deficiency			

subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Cohort 6: On Demand: Adult ≥18 years		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Varicose vein			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Infusion site rash			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Intermenstrual bleeding			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dysmenorrhoea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Asthma			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Catarrh			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Respiratory tract congestion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Product issues Device malfunction subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Investigations Anti factor VIII antibody positive subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) Blood triglycerides increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) SARS-CoV-2 test positive subjects affected / exposed occurrences (all) Serum ferritin decreased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all) Arthropod sting subjects affected / exposed occurrences (all) Bone contusion subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		

Chest injury			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Epicondylitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Fracture displacement			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Infusion related reaction			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Joint injury			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Meniscus injury			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Road traffic accident subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Skin laceration subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Spinal compression fracture subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Stress fracture subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Traumatic haematoma subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Wound subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Sunburn subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Congenital, familial and genetic disorders Lymphatic malformation subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Cardiac disorders Bundle branch block right subjects affected / exposed occurrences (all) Palpitations subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		

Headache subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Eosinophilia subjects affected / exposed occurrences (all) Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Ear and labyrinth disorders Cerumen impaction subjects affected / exposed occurrences (all) Ear pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Eye disorders Cataract subjects affected / exposed occurrences (all) Astigmatism subjects affected / exposed occurrences (all) Conjunctivitis allergic subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 1 / 2 (50.00%) 1 0 / 2 (0.00%) 0		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		

Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Angular cheilitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Faeces discoloured			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Haematochezia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Enteritis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Irritable bowel syndrome subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Salivary hypersecretion subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Toothache subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Tooth deposit subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Hepatobiliary disorders Cholecystitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Bile duct stone subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Haemobilia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Cholelithiasis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Hepatomegaly subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Skin and subcutaneous tissue disorders			

Dermatitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Perioral dermatitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Skin disorder subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Ecchymosis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Petechiae subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Arthralgia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Haemophilic arthropathy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Muscle spasms			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Joint effusion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tendonitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Conjunctivitis bacterial			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Croup infectious			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Coronavirus infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Laryngitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Onychomycosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Periodontitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Otitis media acute			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tracheobronchitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Viral rhinitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vitamin B12 deficiency			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Iron deficiency			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	4		
Obesity			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Zinc deficiency			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 May 2019	The following change was made as per protocol amendment 01: 1. Requirement of human leukocyte antigen genotyping was removed from screening. 2. Pregnant Partner reporting was added.
19 May 2020	The following change was made as per protocol amendment 03: Wording was included to provide for additional interim analyses to be performed as needed to support submissions to health authorities.
20 December 2021	The following changes were made as per protocol amendment 4: 1. Updated Sponsor name to Takeda. 2. The time for completion of the study was extended to December 2025. 3. The total sample size was updated to include up to 71 pediatric and adult subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported