Clinical trial results:
Clinical Study to Investigate the Pharmacokinetics, Efficacy, Safety, and Immunogenicity of Wilate in Previously Treated Pediatric Patients with Severe Hemophilia A

Summary

EudraCT number	2017-001531-40
Trial protocol	Outside EU/EEA
Global end of trial date	02 November 2018

Results information

Result version number	v1 (current)
This version publication date	30 November 2020
First version publication date	30 November 2020

Trial information

Trial identification

Sponsor protocol code	WIL-30

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Octapharma AG
Sponsor organisation address	Seidenstrasse 2, Lachen, Switzerland, CH-8853
Public contact	VP, Clinical R&D Haematology, Octapharma AG, +41 554512189, cristina.solomon@octapharma.com
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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	16 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the FVIII:C pharmacokinetics (PK) for Wilate in previously treated patients (PTP) with severe hemophilia A aged 1 to <12 years.

Protection of trial subjects:

This trial was conducted in accordance to the principles of ICH- GCP, ensuring that the rights, safety and well-being of patients are protected and in consistency with the Declaration of Helsinki and national regulatory requirements. Inclusion and exclusion criteria were carefully defined in order to protect subjects from contraindications, interactions with other medication and risk factors associated with the investigational medicinal product. Throughout the study safety was assessed, such as of monitoring of AEs, SAEs and concomitant medications.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	22 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 3
Country: Number of subjects enrolled	Ukraine: 7
Worldwide total number of subjects	10
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	10
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male patients with documented diagnosis of Severe Haemophilia A were screened according to predefined in- and exclusion criteria.

Period 1

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

Arms

Arm title	Wilate

Arm description:

The dosage and frequency of Wilate treatment during the study was determined by the individual patient's clinical situation. Dose (and duration) of treatment for breakthrough BEs was dependent on the location and extent of bleeding and on the clinical condition of the patient.Two patients underwent surgeries treated with Wilate.

Arm type	Experimental
Investigational medicinal product name	Wilate
Investigational medicinal product code	
Other name	HUMAN COAGULATION FACTOR VIII, VON WILLEBRAND FACTOR COMPLEX
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The dosage and frequency of Wilate treatment during the study was determined by the individual patient's clinical situation. In the 2-day PK Assessment Phase performed before the start of the Prophylactic Treatment, Wilate was administered to all patients as a single dose of 50 ± 5 IU kg BW. In the Prophylactic Treatment Phase, Wilate was to be administered every 2 to 3 days at a dose of 20–40 IU/kg Wilate/kg BW for 6 months (+2 weeks) and at least 50 EDs. In case of unacceptably frequent spontaneous breakthrough BEs the dose of Wilate was to be increased by approximately 5 IU/kg.

Number of subjects in period 1	Wilate
Started	10
Completed	9
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
1 - <6 years	5	5	
6 -<12 years	5	5	
Age continuous Units: years			
median	7		
full range (min-max)	2 to 11	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	10	10	

End points

End points reporting groups

Reporting group title	Wilate

Reporting group description:

The dosage and frequency of Wilate treatment during the study was determined by the individual patient's clinical situation. Dose (and duration) of treatment for breakthrough BEs was dependent on the location and extent of bleeding and on the clinical condition of the patient.Two patients underwent surgeries treated with Wilate.

Subject analysis set title	SAF Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety (SAF) set included all patients who received at least one infusion of IMP

Subject analysis set title	PK Set
Subject analysis set type	Full analysis

Subject analysis set description:

The PK set includes all patients for whom a valid Wilate PK profile was obtained.

Subject analysis set title	PP Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PP set, i.e., a subset of the FAS, excludes patients with major protocol deviations that may have an impact on the evaluation of the efficacy outcome parameters.
Of the patients in the PP population, only 8 patients had evaluable bleeding events. Five of these patients were aged 1-<6 years, and 3 aged 6-<12 years.

Subject analysis set title	SURG Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The surgery (SURG) set is a subset of the FAS, containing all patients who underwent a surgical procedure treated with Wilate during their Prophylactic Treatment Phase.

Subject analysis set title	PK Set 1-<6 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

patients in PK Set aged 1-<6 years

Subject analysis set title	PK Set 6-<12 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

patients in PK Set aged 6-<12 years

Subject analysis set title	FAS Set 1 to <6 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

FAS Set 1 to <6 years

Subject analysis set title	FAS Set 6 to <12 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

FAS Set 6 to <12 years

Subject analysis set title	FAS Set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) defined according to the intention-to-treat (ITT) principle will include all enrolled subjects who received at least one infusion of IMP (after the initial PK visit).

Subject analysis set title	PP Set 1-<6 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients in the PP population aged 1-<6 years.
Of the patients in the PP population, only 8 patients had evaluable bleeding events. Five of these patients were aged 1-<6 years, and 3 aged 6-<12 years

Subject analysis set title	PP Set 6-<12 Years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients in the PP population aged 6-<12 years.
Of the patients in the PP population, only 8 patients had evaluable bleeding events. Five of these patients were aged 1-<6 years, and 3 aged 6-<12 years

Primary: Pharmacokinetic (PK) Assessment (Area Under the Curve (AUC) of FVIII:C

End point title	Pharmacokinetic (PK) Assessment (Area Under the Curve (AUC) of FVIII:C[1]

End point description:

PK assessments of the factor VIII coagulant activity (FVIII:C) for Wilate were determined using the one-stage (OS) assay. The units of measure to calculate AUC is hours (h) x international units (IU)/decilitre (dL).

End point type	Primary

End point timeframe:

0h, 0.25h, 1h, 6h, 24h and 48 h after the end of injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: h*IU/dL				
arithmetic mean (standard deviation)	720.3 (± 277.3)	768.8 (± 288.5)	671.9 (± 289.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) Assessment (Area Under the Curve [AUC] Normalised (AUCNorm)) of FVIII:C for Wilate

End point title	Pharmacokinetic (PK) Assessment (Area Under the Curve [AUC] Normalised (AUCNorm)) of FVIII:C for Wilate[2]

End point description:

PK assessments of the factor VIII coagulant activity (FVIII:C) for Wilate were determined using the one-stage (OS) assay. The mean area under the curve normalised for the administered dose (AUCnorm) was calculated for Wilate. The units of measure used were AUC divided by dose.

End point type	Primary

End point timeframe:

0h, 0.25h, 1h, 6h, 24h and 48 h after end of injection

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: h*kg*IU/dL/IU				
arithmetic mean (standard deviation)	14.41 (± 5.55)	15.38 (± 5.77)	13.44 (± 5.79)	

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) Assessment (Maximum Plasma Concentration) for FVIII:C

End point title	Pharmacokinetic (PK) Assessment (Maximum Plasma Concentration) for FVIII:C[3]

End point description:

PK assessments of FVIII:C were determined using the one-stage (OS) assays. The maximum plasma concentration of FVIII:C was calculated based on the FVIII:C values measured in the patients participating in the PK study. Units of measure for maximum plasma concentration are international units (IU)/ decilitre (dL)

End point type	Primary

End point timeframe:

0h, 0.25h, 1h, 6h, 24h and 48 h after the end of injection

Notes:

[3] - 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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: IU/dL				
arithmetic mean (standard deviation)	80.99 (± 20.94)	83.0 (± 16.5)	78.94 (± 26.56)	

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) Assessment (Half-life (h)) of FVIII:C

End point title	Pharmacokinetic (PK) Assessment (Half-life (h)) of FVIII:C[4]

End point description:

PK assessments of the factor VIII coagulant activity (FVIII:C) for Wilate were determined using the one-stage (OS) assay. The units of measure to calculate half-life is hours.

End point type	Primary

End point timeframe:

0h, 0.25h, 1h, 6h, 24h and 48 h after the end of injection

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: hours				
arithmetic mean (standard deviation)	8.82 (± 1.97)	8.28 (± 1.51)	9.35 (± 2.40)	

Statistical analyses

No statistical analyses for this end point

Primary: harmacokinetic (PK) Assessment (Time to Reach Maximum Plasma Concentration (Tmax)) of FVIII:C

End point title	harmacokinetic (PK) Assessment (Time to Reach Maximum Plasma Concentration (Tmax)) of FVIII:C[5]

End point description:

PK assessments of the factor VIII coagulant activity (FVIII:C) for Wilate were determined using the one-stage (OS) assay. The units of measure to calculate Tmax is hours (h).

End point type	Primary

End point timeframe:

48 h after the end of injection

Notes:

[5] - 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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: hours				
arithmetic mean (standard deviation)	0.25 (± 0.00)	0.25 (± 0.00)	0.25 (± 0.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) Assessment (Mean Residence Time (MRT)) of FVIII:C

End point title	Pharmacokinetic (PK) Assessment (Mean Residence Time (MRT)) of FVIII:C[6]

End point description:

PK assessments of the factor VIII coagulant activity (FVIII:C) for Wilate were determined using the one-stage (OS) assay. The units of measure to calculate MRT is hours.

End point type	Primary

End point timeframe:

48 h after the end of injection

Notes:

[6] - 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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: hour				
arithmetic mean (standard deviation)	12.01 (± 2.88)	11.47 (± 2.34)	12.56 (± 3.53)	

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) Assessment (Volume of Distribution (Vd)) of FVIII:C

End point title	Pharmacokinetic (PK) Assessment (Volume of Distribution (Vd)) of FVIII:C[7]

End point description:

PK assessments of the factor VIII coagulant activity (FVIII:C) for Wilate were determined using the one-stage (OS) assay. The units of measure to calculate Vd is decilitre (dL)/ kilograms (kg).

End point type	Primary

End point timeframe:

0h, 0.25h, 1h, 6h, 24h and 48 h after the end of injection

Notes:

[7] - 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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: dL/kg				
arithmetic mean (standard deviation)	0.933 (± 0.384)	0.784 (± 0.177)	1.081 (± 0.494)	

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) Assessment (Clearance) of FVIII:C

End point title	Pharmacokinetic (PK) Assessment (Clearance) of FVIII:C[8]

End point description:

PK assessments of the factor VIII coagulant activity (FVIII:C) for Wilate were determined using the one-stage (OS) assay. The units of measure to calculate clearance are decilitre (dL)/ hours (h)/ kilograms (kg).

End point type	Primary

End point timeframe:

0h, 0.25h, 1h, 6h, 24h and 48 h after the end of injection

Notes:

[8] - 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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: dL/h/kg				
arithmetic mean (standard deviation)	0.084 (± 0.053)	0.071 (± 0.019)	0.098 (± 0.074)	

Statistical analyses

No statistical analyses for this end point

Primary: Incremental In Vivo Recovery (IVR) of FVIII:C

End point title	Incremental In Vivo Recovery (IVR) of FVIII:C[9]

End point description:

The incremental IVR was determined from all patients at baseline was determined using the one-stage (OS) assay (standardised to 50 IU/kg).
The units of measure to calculate IVR is kilograms (kg) / deciliter (dL).

End point type	Primary

End point timeframe:

48 h after the end of injection

Notes:

[9] - 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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	FAS Set 1 to <6 years	FAS Set 6 to <12 years	FAS Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	5	10	
Units: kg/dL				
arithmetic mean (standard deviation)	1.65 (± 0.33)	1.57 (± 0.53)	1.61 (± 0.42)	

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy of prophylactic treatment with Wilate based on Total Annualized Bleeding Rate (TABR)

End point title	Efficacy of prophylactic treatment with Wilate based on Total Annualized Bleeding Rate (TABR)

End point description:

The total number of bleeding events (BEs) in the time period between the first dose of IMP and the study completion visit, divided by the duration (in years) between the first dose of IMP and the study completion visit. Surgery periods, and BEs occurring within these periods, will be excluded from the calculation of TABR.

End point type	Secondary

End point timeframe:

6 months

End point values	FAS Set 1 to <6 years	FAS Set 6 to <12 years	FAS Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	5	10	
Units: Bleeding events per year				
arithmetic mean (standard deviation)	6.47 (± 6.61)	10.62 (± 9.06)	8.54 (± 7.79)	

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy of prophylactic treatment with Wilate based on Spontaneous Annualized Bleeding Rate (SABR)

End point title	Efficacy of prophylactic treatment with Wilate based on Spontaneous Annualized Bleeding Rate (SABR)

End point description:

The SABR was calculated in analogy to the TABR. The total number of spontaneous bleeding events (BEs) in the time period between the first dose of IMP and the study completion visit, divided by the duration (in years) between the first dose of IMP and the study completion visit. Surgery periods, and BEs occurring within these periods, will be excluded from the calculation of the SABR.

End point type	Secondary

End point timeframe:

6 months

End point values	FAS Set 1 to <6 years	FAS Set 6 to <12 years	FAS Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	5	10	
Units: Spontaneous bleeding events per year				
arithmetic mean (standard deviation)	2.70 (± 2.93)	1.20 (± 2.68)	1.95 (± 2.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy of Wilate in the Treatment of Breakthrough Bleeding Events (BEs)

End point title	Efficacy of Wilate in the Treatment of Breakthrough Bleeding Events (BEs)

End point description:

The proportion of BEs successfully treated with Wilate was assessed by the patient (together with the investigator in case of on-site treatment) in a patient diary. The treatment efficacy for all BEs was assessed using a pre-defined four-point scale: 'excellent', 'good', 'moderate', 'none'. 'Excellent' was defined as "Abrupt pain relief and/or unequivocal improvement in objective signs of bleeding within approximately 8 hours after a single injection" (best outcome); 'good 'was defined as "definite pain relief and/or improvement in signs of bleeding within approximately 8-12 hours after an injection, requiring up to 2 injections for complete resolution". All efficacy ratings assessed as either 'excellent' or 'good' were considered 'successfully treated'. 'Moderate' was defined as "probable or slight beneficial effect within approximately 12 hours after the first injection" and 'none' defined as "no improvement within 12 hours, or worsening of symptoms".

End point type	Secondary

End point timeframe:

6 months

End point values	PP Set	PP Set 1-<6 years	PP Set 6-<12 Years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	5	3	
Units: Bleeding Events				
number (not applicable)				
Excellent	16	7	9	
Good	17	9	8	
Moderate	2	1	1	
None	0	0	0	
Total Number of BE	35	17	18	

Statistical analyses

No statistical analyses for this end point

Secondary: Wilate Consumption Data: Average Dose of Wilate Per Week of Study

End point title	Wilate Consumption Data: Average Dose of Wilate Per Week of Study

End point description:

The average consumption of Wilate per week of the study (IU/kg) for all patients receiving prophylaxis. The analysis was performed in the full analysis (FAS) population (total: n=10). The FAS comprised 5 patients were aged 1-<6 years and 5 were aged 6-<12 years.

End point type	Secondary

End point timeframe:

6 months

End point values	FAS Set 1 to <6 years	FAS Set 6 to <12 years	FAS Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	5	10	
Units: IU/kg per week				
arithmetic mean (standard deviation)	58.52 (± 14.85)	68.08 (± 19.02)	63.30 (± 16.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incremental in Vivo Recovery (IVR) of Wilate Over Time

End point title	Incremental in Vivo Recovery (IVR) of Wilate Over Time

End point description:

The rise in FVIII:C activity in IU/dl per unit dose administered in IU/kg was determined for all patients at baseline, 3 and 6 months, using the one-stage (OS) assay. (Standardised to 50 IU/kg).
The analysis was performed in the full analysis (FAS) population (total: n=10). The FAS comprised 5 patients were aged 1-<6 years and 5 were aged 6-<12 years.

End point type	Secondary

End point timeframe:

Baseline, and 3 and 6 months of treatment

End point values	FAS Set 1 to <6 years	FAS Set 6 to <12 years	FAS Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	5	10	
Units: kg/dL				
arithmetic mean (standard deviation)				
Baseline	1.65 (± 0.33)	1.57 (± 0.53)	1.61 (± 0.42)	
3 months	1.55 (± 0.14)	1.56 (± 0.57)	1.56 (± 0.39)	
6 months	1.63 (± 0.24)	1.32 (± 0.45)	1.48 (± 0.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: Association Between ABO Blood Type and the FVIII:C Half-life of Wilate (OS Assay)

End point title	Association Between ABO Blood Type and the FVIII:C Half-life of Wilate (OS Assay)

End point description:

Analysis of variance (ANOVA) was used in an exploratory sense to assess a possible association between the ABO blood type and the FVIII:C half-life of Wilate. This was analysed by calculating the mean square in a one-stage (OS) assay.
The analysis was performed for the PK population which included all patients who underwent PK assessment during the study (total: n=10). The PK population comprised 5 patients aged 1-<6 years and 5 aged 6-<12 years.

End point type	Secondary

End point timeframe:

6 months

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: p-value (ANOVA)				
number (not applicable)				
Mean square	0.922	0.185	6.100	
p-value	0.8273	0.9593	0.3752	

Statistical analyses

No statistical analyses for this end point

Secondary: Association Between VWF:Ag Concentration and the FVIII:C Half-life of Wilate

End point title	Association Between VWF:Ag Concentration and the FVIII:C Half-life of Wilate

End point description:

Analysis of variance (ANOVA) was used in an exploratory sense to assess a possible association between VWF:Ag with the FVIII:C half-life of Wilate. This was analysed by calculating the mean square in a one-stage (OS) assay.

End point type	Secondary

End point timeframe:

6 months

End point values	PK Set	PK Set 1-<6 years	PK Set 6-<12 years	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	5	5	
Units: p-value (ANOVA)				
number (not applicable)				
Mean Square	0.003	0.121	0.006	
P-Value	0.9791	0.8536	0.9791	

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity of Wilate: Number of Participants With FVIII Inhibitor Activity at 6 Months

End point title	Immunogenicity of Wilate: Number of Participants With FVIII Inhibitor Activity at 6 Months

End point description:

FVIII inhibitor activity was determined at each study visit: screening, PK, Day 14 visit, Day 30 visit, 3 Months visit and 6 Months visit before injection (estimated along with 95% Pearson-Clopper CIs)

End point type	Secondary

End point timeframe:

6 months

End point values	SAF Set			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: number of subjects				
number (confidence interval 95%)	0 (0 to 30.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Virus Safety Measured by the Number With Parvovirus B19 Seroconversions Between Baseline (BL) and End of Study

End point title	Virus Safety Measured by the Number With Parvovirus B19 Seroconversions Between Baseline (BL) and End of Study

End point description:

Virus safety was evaluated by taking a plasma sample for parvovirus B19 antibody testing before the first injection of Wilate at the PK visit. All patients negative at screening were tested again at the Study Completion visit. The number of Parvovirus B19 seroconversions between BL and end of study was recorded

End point type	Secondary

End point timeframe:

6 month

End point values	FAS Set			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: number of subjects				
number (not applicable)	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Throughout the Study	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	Safety Population (SAF)

Reporting group description: -

Serious adverse events	Safety Population (SAF)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Safety Population (SAF)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)		
Investigations			
Parvovirus B19 test positive			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Varicella			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported