Clinical trial results:
CLINICAL STUDY TO INVESTIGATE THE EFFICACY, PHARMACOKINETICS, IMMUNOGENICITY AND SAFETY OF WILATE IN SEVERE VON WILLEBRAND DISEASE PATIENTS UNDER THE AGE OF 6 YEARS

Summary

EudraCT number	2020-004344-28
Trial protocol	CZ DE
Global end of trial date	16 December 2024

Results information

Result version number	v1 (current)
This version publication date	07 August 2025
First version publication date	07 August 2025

Trial information

Trial identification

Sponsor protocol code	WIL-33

Additional study identifiers

ISRCTN number	ISRCTN11217735
ClinicalTrials.gov id (NCT number)	NCT04953884
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 011303

Notes:

Sponsors

Sponsor organisation name	Octapharma Pharmazeutika Produktionsges.m.b.H
Sponsor organisation address	Oberlaaerstr. 235, Vienna, Austria, 1100
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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	13 June 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to determine the efficacy of wilate in the prophylactic treatment of up to 12 paediatric patients (eight evaluable) with severe VWD (defined as screening von Willebrand factor ristocetin cofactor activity [VWF:RCo] <20%) under the age of 6 years, for a period of 12 months.

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 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 monitoring of adverse events, vital signs, bleeding episodes and concomitant medication.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Moldova, Republic of: 1
Country: Number of subjects enrolled	North Macedonia: 1
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Ukraine: 2
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	12
EEA total number of subjects	5

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)	2
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:

Children under the age of 6 years with severe von Willebrand disease (VWD) requiring substitution therapy with a VWF-containing product were screened according to predefined in- and exclusion criteria.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Wilate

Arm description:

The VWF/FVIII concentrate wilate, produced from the plasma of human donors, is presented as a powder and solvent for intravenous injection containing nominally 500 IU (international units) or 1000 IU human VWF and human FVIII per vial. Dosing was chosen based on the European Summary of Product Characteristics [16] and adjusted in line with the well described lower IVR and shorter half-life of coagulation factor concentrates in young children.

Arm type	Experimental
Investigational medicinal product name	Wilate
Investigational medicinal product code	
Other name	Wilate 500
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

For the PK assessment, a single dose of 80 IU/kg BW wilate was administered, based on the BW measured at the beginning of the visit. The exact dose was calculated according to the nominal potency, with 70–85 IU/kg BW as the acceptable range. IVR assessments were performed following administration of a prophylactic dose, except for baseline IVR, which was done following administration of a single dose of 80 (70–85) IU/kg BW for the PK assessment. In case of unacceptably frequent breakthrough bleeding episodes (BEs) (i.e. two or more BEs within a 30-day period or one major BE), the dose of wilate was to be increased by ~5 IU/kg BW (depending on the vial size of the additional vial(s) that needed to be injected) and/or the treatment frequency increased.

Number of subjects in period 1	Wilate
Started	12
Completed	11
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Period

Reporting group description: -

Reporting group values	Overall Period	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
1 year	2	2	
2-3 years	8	8	
4-5 years	2	2	
Gender categorical Units: Subjects			
Female	6	6	
Male	6	6	

End points

End points reporting groups

Reporting group title	Wilate

Reporting group description:

The VWF/FVIII concentrate wilate, produced from the plasma of human donors, is presented as a powder and solvent for intravenous injection containing nominally 500 IU (international units) or 1000 IU human VWF and human FVIII per vial. Dosing was chosen based on the European Summary of Product Characteristics [16] and adjusted in line with the well described lower IVR and shorter half-life of coagulation factor concentrates in young children.

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

Subject analysis set description:

The safety set (SAF) that included all patients who received at least one dose of wilate.

Subject analysis set title	Full Analysis 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, which included all enrolled patients who received at least one dose of wilate after the PK visit.

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol (PP) set, i.e., a subset of the FAS, which excluded patients with major protocol deviations that may have an impacted the evaluation of the primary study outcome parameter(s)

Subject analysis set title	BEs (all BEs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Bleeding episodes in patients during prophylaxe. (FAS)

Subject analysis set title	TABR -mean (all BEs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Total annualized bleeding rate (FAS)

Subject analysis set title	BEs (treated BEs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Bleeding episodes in patients treated with wilate (FAS)

Subject analysis set title	TABR - mean (treated BEs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Total annualized bleeding rate in patients treated with wilate (FAS)

Subject analysis set title	BEs (all BEs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Bleeding episodes in patients during prophylaxis. (PP)

Subject analysis set title	TABR - mean (all BEs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Total Annual bleeding Rate (PP)

Subject analysis set title	BEs (treated BEs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Bleeding episodes in patients treated with wilate (PP)

Subject analysis set title	TABR - mean (treated BEs)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Bleeding episodes in patients treated with wilate (PP)

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

Subject analysis set description:

The PK-PP set was a subset of the PK set excluding subjects with a major protocol deviation regarding PK dosing.

Subject analysis set title	Surgery Set (SURG)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The surgery set (SURG) was 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	VWF:RCo, N=10
Subject analysis set type	Sub-group analysis

Subject analysis set description:

VWF:RCo

Subject analysis set title	FVIII OS, N=8
Subject analysis set type	Sub-group analysis

Subject analysis set description:

FVIII OS

Subject analysis set title	VWF:RCo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

VWF ristocetin cofactor assay.

Subject analysis set title	FVIII (OS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

FVIII one stage

Subject analysis set title	FAS (N=12) [47 BEs]
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy Assessment of Treatment of BEs with wilate in FAS (N=12)[47 BEs]

Subject analysis set title	PP (N=8) [18 BEs]
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy Assessment of Treatment of BEs with wilate in PP (N=8) [18 BEs]

Subject analysis set title	FAS (N=10), 47 BEs
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Consumption of wilate for the Treatment of BEs FAS (N=10), 47 BEs

Subject analysis set title	PP (N=7), 18 BEs
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Consumption of wilate for the Treatment of BEs; PP (N=7), 18 BEs

Subject analysis set title	Dose per Inj. (IU/kg)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Dose per Inj. (IU/kg)

Subject analysis set title	Dose per ED (IU/kg)

Subject analysis set type	Sub-group analysis
Subject analysis set description: Dose per ED (IU/kg)	
Subject analysis set title	15 min after PK infusion
Subject analysis set type	Sub-group analysis
Subject analysis set description: 15 min after PK infusion	
Subject analysis set title	24 h after PK infusion
Subject analysis set type	Sub-group analysis
Subject analysis set description: 24 h after PK infusion	

Primary: Total annualized bleeding rate (TABR) - FAS

End point title	Total annualized bleeding rate (TABR) - FAS[1]

End point description:

The primary endpoint of this study is to determine the total annualised bleeding rate (TABR) during prophylactic treatment with IMP.
The TABR was calculated as the total number of spontaneous bleeds, traumatic bleeds, and other bleeds occurring in the time period between first prophylactic dose of wilate and the study completion visit, divided by the duration (in years) between first prophylactic dose of wilate and the study completion visit.

End point type	Primary

End point timeframe:

Time period between first prophylactic dose of wilate and the study completion visit

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	BEs (all BEs)	TABR -mean (all BEs)	BEs (treated BEs)	TABR - mean (treated BEs)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: number				
number (not applicable)	56	4.6	45	3.7

Statistical analyses

No statistical analyses for this end point

Primary: Total annualized bleeding rate (TABR) - PP

End point title	Total annualized bleeding rate (TABR) - PP[2]

End point description:

The primary endpoint of this study is to determine the total annualized bleeding rate (TABR) during prophylactic treatment with IMP.
The TABR was calculated as the total number of spontaneous bleeds, traumatic bleeds, and other bleeds occurring in the time period between first prophylactic dose of wilate and the study completion visit, divided by the duration (in years) between first prophylactic dose of wilate and the study completion visit.

End point type	Primary

End point timeframe:

time period between first prophylactic dose of wilate and the study completion visit

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	BEs (all BEs)	TABR - mean (all BEs)	BEs (treated BEs)	TABR - mean (treated BEs)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	8	8
Units: number				
number (not applicable)	24	3.0	17	2.1

Statistical analyses

No statistical analyses for this end point

Secondary: PK profile characteristics of wilate (PK-PP)

End point title	PK profile characteristics of wilate (PK-PP)

End point description:

For the PK assessment, a single dose of 80 (70–85) IU/kg BW wilate was to be adminis-tered. All PK assessments were performed according to schedule with respect to time points and dosage in the patients were included in the PK-PP set (N=10).

End point type	Secondary

End point timeframe:

Pre-dose (baseline), 15 min, 3, 9, 24, 48 and 72 h after dosing of 80 IU/kg BW wilate

End point values	VWF:RCo, N=10	FVIII OS, N=8		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	8		
Units: value				
arithmetic mean (standard deviation)				
AUC, h*IU/dL	1100 (± 532)	2410 (± 1122)		
AUCnorm, h*kg*IU/dL/IU	13.7 (± 6.7)	30.1 (± 14.2)		
CL, dL/h/kg	0.09 (± 0.04)	0.04 (± 0.03)		
Cmax, IU/dL	105.0 (± 19.7)	114.1 (± 27.1)		
MRT, h	15.6 (± 9.5)	22.5 (± 9.4)		
T1/2, h	11.7 (± 9.6)	15.0 (± 7.5)		
Tmax, h	0.27 (± 0.04)	0.26 (± 0.05)		
Vd, dL/kg	1.12 (± 0.24)	0.82 (± 0.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: IVR of wilate VWF:RCo over time

End point title	IVR of wilate VWF:RCo over time

End point description:

End point type	Secondary

End point timeframe:

In -Vivo Recovery for von Willebrand Factor Activity VWF:RCo Assay over time (at baseline and at 1, 2, 3, 6, 9, and 12 months of treatment)

End point values	VWF:RCo			
Subject group type	Subject analysis set			
Number of subjects analysed	12[3]			
Units: kg/dL				
arithmetic mean (confidence interval 95%)				
Baseline PK (n=12)	1.261 (1.00 to 1.53)			
1-Month (n=10)	1.705 (1.42 to 1.99)			
2-Months (n=10)	1.616 (1.33 to 1.90)			
3-Months (n=11)	1.627 (1.45 to 1.80)			
6-Months (n=11)	1.585 (1.45 to 1.72)			
9-Months (n=11)	1.647 (1.46 to 1.84)			
12-Months/Completion (n=11)	1.754 (1.58 to 1.92)			

Notes:

[3] - FAS (n=12)

Statistical analyses

No statistical analyses for this end point

Secondary: IVR of Wilate FVIII:C[OS]

End point title	IVR of Wilate FVIII:C[OS]

End point description:

End point type	Secondary

End point timeframe:

In -Vivo Recovery for von Willebrand Factor Factor VIII Activity One-Stage Assay over time (at baseline and at 1, 2, 3, 6, 9, and 12 months of treatment)

End point values	FVIII (OS)			
Subject group type	Subject analysis set			
Number of subjects analysed	12[4]			
Units: kg/dL				
arithmetic mean (confidence interval 95%)				
Baseline PK (n=9)	1.479 (1.23 to 1.73)			
1-Month (n=11)	1.671 (1.41 to 1.93)			
2-Months (n=9)	1.795 (1.40 to 2.19)			
3-Months (n=11)	1.677 (1.39 to 1.97)			
6-Months (n=10)	1.670 (1.50 to 1.85)			
9-Months (n=9)	1.789 (1.59 to 1.99)			
12-Months/Completion (n=8)	1.691 (1.33 to 2.05)			

Notes:

[4] - FAS (n=12)

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy of wilate in the treatment of BEs

End point title	Efficacy of wilate in the treatment of BEs

End point description:

Efficacy of wilate in the prevention and treatment of spontaneous and traumatic breakthrough BEs based on their rate and the proportion of spontaneous and traumatic BEs successfully treated with wilate was assessed by a 4-point ordinal haemostatic efficacy scale (excellent – good – moderate – none)

End point type	Secondary

End point timeframe:

Assessed for all treated BEs

End point values	FAS (N=12) [47 BEs]	PP (N=8) [18 BEs]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: BEs				
number (not applicable)				
Excellent	46	17		
Excellent %	97.9	94.4		
Good	1	1		
Good %	2.1	5.6		
Moderate	0	0		
None	0	0		
Success	47	18		
Success %	100	100		

Non-success	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy of wilate as surgical prophylaxis

End point title	Efficacy of wilate as surgical prophylaxis

End point description:

End point type	Secondary

End point timeframe:

Assessed for all treated BEs

End point values	Surgery Set (SURG)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: BEs				
number (not applicable)				
Excellent	1			
Good	0			
Moderate	0			
None	0			
Sucess %	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Time on prophylaxis (consumption of wilate for prophylaxis)

End point title	Time on prophylaxis (consumption of wilate for prophylaxis)

End point description:

End point type	Secondary

End point timeframe:

Up to 12 months of treatment

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: month				
arithmetic mean (standard deviation)	11.4 (± 3.5)	12.2 (± 0.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of EDs (consumption of wilate for prophylaxis)

End point title	Number of EDs (consumption of wilate for prophylaxis)
End point description: ED = exposure day	
End point type	Secondary
End point timeframe: Up to 12 months of treatment	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: ED				
arithmetic mean (standard deviation)	109.0 (± 36.1)	118.4 (± 15.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of injections (consumption of wilate for prophylaxis)

End point title	Number of injections (consumption of wilate for prophylaxis)
End point description:	
End point type	Secondary
End point timeframe: Up to 12 months of treatment	

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: number				
arithmetic mean (standard deviation)	109.0 (± 36.1)	118.4 (± 15.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dose (consumption of wilate for prophylaxis)

End point title	Dose (consumption of wilate for prophylaxis)

End point description:

End point type	Secondary

End point timeframe:

Up to 12 months of treatment

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: IU/kg				
arithmetic mean (standard deviation)				
Dose per injection	54.0 (± 27.5)	42.9 (± 7.0)		
Dose per week	120.1 (± 65.0)	95.8 (± 19.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of injections per BE (consumption of wilate for on demand treatment)

End point title	Number of injections per BE (consumption of wilate for on demand treatment)

End point description:

End point type	Secondary

End point timeframe:

Up to 12 months of treatment

End point values	FAS (N=10), 47 BEs	PP (N=7), 18 BEs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	7		
Units: number				
arithmetic mean (standard deviation)	1.1 (± 0.2)	1.1 (± 0.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of EDs per BE (consumption of wilate for on demand treatment)

End point title	Number of EDs per BE (consumption of wilate for on demand treatment)

End point description:

Number of EDs per BE (ED = exposure day)

End point type	Secondary

End point timeframe:

Up to 12 months of treatment

End point values	FAS (N=10), 47 BEs	PP (N=7), 18 BEs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	7		
Units: ED				
arithmetic mean (standard deviation)	1.0 (± 0.2)	1.1 (± 0.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dose (consumption of wilate for on demand treatment)

End point title	Dose (consumption of wilate for on demand treatment)

End point description:

End point type	Secondary

End point timeframe:

Up to 12 months of treatment

End point values	FAS (N=10), 47 BEs	PP (N=7), 18 BEs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	7		
Units: IU/kg				
arithmetic mean (standard deviation)				
Dose per BE	58.7 (± 27.6)	54.2 (± 30.1)		
Dose per injection	55.0 (± 22.3)	46.8 (± 12.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of injections (consumption of wilate during surgical procedures)

End point title	Number of injections (consumption of wilate during surgical procedures)

End point description:

End point type	Secondary

End point timeframe:

during surgical procedure

End point values	Surgery Set (SURG)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: number				
number (not applicable)				
Preoperative (Within 3 h before Start)	1			
Intraoperative	0			
Postoperative	4			
Perioperative	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of EDs (consumption of wilate during surgical procedures)

End point title	Number of EDs (consumption of wilate during surgical procedures)

End point description:

End point type	Secondary

End point timeframe:
during surgery

End point values	Surgery Set (SURG)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: number				
number (not applicable)				
Preoperative (Within 3 h before Start)	1			
Intraoperative	0			
Postoperative	4			
Perioperative	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Dose (consumption of wilate during surgical procedures)

End point title	Dose (consumption of wilate during surgical procedures)

End point description:

End point type	Secondary

End point timeframe:
during surgery

End point values	Dose per Inj. (IU/kg)	Dose per ED (IU/kg)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	1		
Units: IU/kg				
number (not applicable)				
Preoperative (Within 3 h before Start)	62.11	62.11		
Intraoperative	0	0		
Postoperative	31.06	31.06		
Perioperative	37.27	46.58		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Haemophilia Joint Health Score

End point title	Total Haemophilia Joint Health Score

End point description:

Joint health status determination with the HJHS, given that the patient’s age and constitutional development allow this assessment

End point type	Secondary

End point timeframe:

Change from baseline to 12-months

End point values	Full Analysis Set	Per Protocol Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[5]	7		
Units: number				
arithmetic mean (standard deviation)				
Baseline	1.55 (± 3.01)	2.43 (± 3.55)		
12-months	0.80 (± 1.93)	1.14 (± 2.27)		
Change from baseline	-0.90 (± 1.37)	-1.29 (± 1.50)		

Notes:

[5] - Baseline (N=11)
12-months (N=10)
Change from baseline (N=10)

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of VWF and FVIII inhibitors

End point title	Incidence of VWF and FVIII inhibitors

End point description:

End point type	Secondary

End point timeframe:

Baseline to 12-Months

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Reference range indicator				
number (not applicable)				
Factor VIII (FVIII) inhibitor positive	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of thromboembolic events

End point title	Incidence of thromboembolic events

End point description:

End point type	Secondary

End point timeframe:

(Baseline up to Study Completion Visit)

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: number				
number (not applicable)				
TEE	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Exploratory endpoint (percentage of Small, Intermediate and Large Multimers)

End point title	Exploratory endpoint (percentage of Small, Intermediate and Large Multimers)

End point description:

The exploratory endpoint of this study, which was solely investigated in the hereditary Type 3 VWD patient group with ≥14.5 kg BW, was a VWF multimer analysis from the PK samples taken at 15 min, and 24 h after wilate injection, by using multimer analysis using low- and high-resolution electrophoresis gels.

End point type	Secondary

End point timeframe:

after wilate Infusion at the PK Assessment

End point values	15 min after PK infusion	24 h after PK infusion		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3	3		
Units: proportion				
arithmetic mean (standard deviation)				
Small (1–5)	39.4 (± 6.3)	49.2 (± 9.8)		
Intermediate (6–10)	45.8 (± 2.3)	41.5 (± 7.3)		
Large (>10)	14.8 (± 4.1)	9.2 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs have been elicited at each visit (Baseline up to Study Completion Visit) , whether scheduled or unscheduled.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Safety Set (SAF)

Reporting group description:

The safety set (SAF) included all patients who received at least one dose of wilate.

Serious adverse events	Safety Set (SAF)		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			

subjects affected / exposed	1 / 12 (8.33%)		
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 Set (SAF)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 12 (83.33%)		
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Lip injury			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin laceration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	4		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	6		
Gastrointestinal disorders			

Dental caries subjects affected / exposed occurrences (all) Mouth swelling subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 1 / 12 (8.33%) 3 1 / 12 (8.33%) 6		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Psychiatric disorders Attention deficit hyperactivity disorder subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Ear infection subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Nasopharyngitis	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		

subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory tract infection viral			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Scarlet fever			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Soft tissue infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2021	CSP Version 02 (amended protocol): The original study protocol for this study set a minimum weight of 12.5 kg for all patients at the time of screening to meet the blood volume restriction requirements for paediatric patients (based on an allowable blood draw of 1 % of total blood volume per day and a maximum of 3% per month). Given the rare disease in the underlying study, the challenge of identifying patients, and in order to meet the established recruitment timelines, it was decided to lower the minimum weight criterion to 11.0 kg, which allowed inclusion of patients who miss the initial 12.5 kg criterion by the end of the recruitment period. This could only be accompanied by a saving in blood collection volumes, achieved by shifting the protocol-specified time for the retention sample for later possible virus testing to a later time before first treatment and by omitting one test in a specific pharmacokinetic sample for patients with a body weight below 12.5 kg.
05 December 2022	CSP Version 03 (amended protocol) Further sites have been identified and new countries submitted and so the expected end date of the clinical trial had to be pushed back and was be reset to Q2/2024.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported