Clinical trial results:
A multi-centre, open-label trial evaluating efficacy, safety and pharmacokinetics of nonacog beta pegol when used for treatment and prophylaxis of bleeding episodes in Chinese patients with haemophilia B.

Summary

EudraCT number	2021-004947-25
Trial protocol	Outside EU/EEA
Global end of trial date	11 May 2024

Results information

Result version number	v1 (current)
This version publication date	27 November 2024
First version publication date	27 November 2024

Trial information

Trial identification

Sponsor protocol code	NN7999-4670

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05365217
WHO universal trial number (UTN)	U1111-1260-0438

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical efficacy of nonacog beta pegol in haemostasis (treatment of bleeding episodes during on-demand and prophylaxis [PPX]) in Chinese patients aged 12-70 years with moderate to severe haemophilia B.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (Oct 2013) and International Council for Humanization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, including archiving of essential documents (May 1996) and EN International Organisation for Standardisation (ISO) 14155 Part 1 and 2 and Food and Drug Administration (FDA) 21 US Code of Federal Regulations (CFR) 312.120.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	18 May 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 30
Worldwide total number of subjects	30
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	5
Adults (18-64 years)	25

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This trial was conducted at 15 sites that enrolled subjects in 1 country (China mainland).

Pre-assignment

Screening details:

A total of 30 subjects were exposed to trial products, of which 15 subjects were in Arm A (on demand/Prophylaxis) treatment group and 15 in Arm B (Prophylaxis) treatment group.

Period 1

Period 1 title	Treatment Period 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Nonacog beta pegol (On-demand)

Arm description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 exposure days (EDs) to nonacog beta pegol in the entire trial were fulfilled.

Arm type	Experimental
Investigational medicinal product name	N9-GP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were administered nonacog beta pegol 40 IU/kg for mild or moderate bleeds and 80 IU/kg for severe bleeds.

Arm title	Arm B: Nonacog beta pegol (Prophylaxis)

Arm description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

Arm type	Experimental
Investigational medicinal product name	N9-GP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly.

Number of subjects in period 1	Arm A: Nonacog beta pegol (On-demand)	Arm B: Nonacog beta pegol (Prophylaxis)
Started	15	15
Completed	14	15
Not completed	1	0
Consent withdrawn by subject	1	-

Period 2

Period 2 title	Treatment Period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Nonacog beta pegol (Prophylaxis)

Arm description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 EDs to nonacog beta pegol in the entire trial were fulfilled.

Arm type	Experimental
Investigational medicinal product name	N9-GP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received nonacog beta pegol weekly intravenous dose of 40 IU/kg to prevent bleeding episodes.

Arm title	Arm B: Nonacog beta pegol (Prophylaxis)

Arm description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

Arm type	Experimental
Investigational medicinal product name	N9-GP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly.

Number of subjects in period 2	Arm A: Nonacog beta pegol (Prophylaxis)	Arm B: Nonacog beta pegol (Prophylaxis)
Started	14	15
Completed	14	15

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: Nonacog beta pegol (On-demand)
Reporting group description:	
Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 exposure days (EDs) to nonacog beta pegol in the entire trial were fulfilled.	
Reporting group title	Arm B: Nonacog beta pegol (Prophylaxis)
Reporting group description:	
Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.	

Reporting group values	Arm A: Nonacog beta pegol (On-demand)	Arm B: Nonacog beta pegol (Prophylaxis)	Total
Number of subjects	15	15	30
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	1	4	5
Adults (18-64 years)	14	11	25
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	29.9	26.9	
standard deviation	± 7.7	± 9.7	-
Gender Categorical Units: Subjects			
Female	0	0	0
Male	15	15	30

End points

End points reporting groups

Reporting group title	Arm A: Nonacog beta pegol (On-demand)

Reporting group description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 exposure days (EDs) to nonacog beta pegol in the entire trial were fulfilled.

Reporting group title	Arm B: Nonacog beta pegol (Prophylaxis)

Reporting group description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

Reporting group title	Arm A: Nonacog beta pegol (Prophylaxis)

Reporting group description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 EDs to nonacog beta pegol in the entire trial were fulfilled.

Reporting group title	Arm B: Nonacog beta pegol (Prophylaxis)

Reporting group description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

Subject analysis set title	Arm B: Nonacog beta pegol (Prophylaxis)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

Primary: Haemostatic Effect of Nonacog beta pegol when used for Treatment of Bleeding Episodes During on Demand and Prophylaxis (PPX)

End point title	Haemostatic Effect of Nonacog beta pegol when used for Treatment of Bleeding Episodes During on Demand and Prophylaxis (PPX)[1][2]

End point description:

Haemostatic effect of N8-GP for treatment of bleeding episodes was assessed by 4-point response scale: none, moderate, good or excellent. Evaluation during trial was done by subject and/or parent(s)/caregiver within approximately 8 hours after a single injection as follows: Excellent: Abrupt pain relief and/or clear improvement in objective signs of bleeding within approximately 8 hrs after a single injection; Good: Definite pain relief and/or improvement in signs of bleeding within approximately 8 hrs after a single injection, but possibly requiring more than one injection for complete resolution; Moderate: Probable or slight beneficial effect within approximately 8 hours after the first injection, but usually requiring more than one injection; None: No improvement, or worsening of symptoms. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

End point type	Primary

End point timeframe:

From start of treatment (week 0) until end of treatment (up to week 50)

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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.
[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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Arm A: Nonacog beta pegol (On-demand)	Arm A: Nonacog beta pegol (Prophylaxis)	Arm B: Nonacog beta pegol (Prophylaxis)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	14	15	
Units: Bleeding Episodes				
Excellent	195	11	26	
Good	8	1	16	
Moderate	3	0	1	
None	1	0	0	
Missing	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Treated Bleeding Episodes During Prophylaxis (PPX) Treatment (Arm B only)

End point title	Number of Treated Bleeding Episodes During Prophylaxis (PPX) Treatment (Arm B only)

End point description:

Number of bleeding episodes per year data is reported. Annualised bleeding rate (ABR) is the number of bleeding episodes per year. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

End point values	Arm B: Nonacog beta pegol (Prophylaxis)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: Bleeds per subject per year				
median (inter-quartile range (Q1-Q3))	3.12 (0.00 to 4.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Inhibitory Antibodies Against FIX Defined as Titre ≥0.6 Bethesda Units (BU)

End point title	Number of Subjects with Inhibitory Antibodies Against FIX Defined as Titre ≥0.6 Bethesda Units (BU)[3]

End point description:

Percentage of subjects who developed inhibitory antibodies (IA) against FVIII was presented. A subject was said to have FVIII-inhibitors if two consecutive tests, preferably within 2 weeks, were positive (greater than or equal to (≥) 0.6 bethesda unit (BU)). For the calculation of the inhibitor rate the numerator was included for all subjects with neutralising antibodies while the denominator was included for all subjects with a minimum of 50 exposures plus any subjects with less than 50 exposures but with neutralising inhibitor. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Arm A: Nonacog beta pegol (On-demand)	Arm A: Nonacog beta pegol (Prophylaxis)	Arm B: Nonacog beta pegol (Prophylaxis)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	14	15	
Units: Number of subjects with IA	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of Nonacog beta pegol for Treatment of Bleeding Episodes

End point title	Consumption of Nonacog beta pegol for Treatment of Bleeding Episodes[4]

End point description:

The mean number of injections of N9-GP used for treatment of a bleed from start to stop of a bleed was reported and it was measured in international units per kilogram per bleed (IU/kg/bleed). Results were based on the FAS which included all subjects exposed to N8-GP in this trial. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Arm A: Nonacog beta pegol (On-demand)	Arm A: Nonacog beta pegol (Prophylaxis)	Arm B: Nonacog beta pegol (Prophylaxis)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	14	15	
Units: IU/kg per bleed				
arithmetic mean (standard deviation)	42.5 (± 1.0)	41.4 (± 1.1)	41.6 (± 0.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of Nonacog beta pegol for Prophylaxis (PPX) Treatment (Arm B only)

End point title	Consumption of Nonacog beta pegol for Prophylaxis (PPX) Treatment (Arm B only)

End point description:

The mean consumption of N9-GP for prophylaxis per year per subject was reported and it was measured in international units per kilogram per year (IU/kg/year). Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

End point values	Arm B: Nonacog beta pegol (Prophylaxis)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: IU/kg per year				
arithmetic mean (standard deviation)	2212.3 (± 26.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: FIX Trough Levels During Prophylaxis (PPX) Treatment (Arm B only)

End point title	FIX Trough Levels During Prophylaxis (PPX) Treatment (Arm B only)

End point description:

Trough levels of FVIII was reported for all participnats who received prophylaxis treatment. Chromogenic assay was performed with N8-GP product specific standard (PSS) as a calibrator. The analysis is based on a mixed model on the log transformed plasma FVIII activity with age group as fixed effect and subject as a random effect. The mean trough is presented back-transformed to the natural scale. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

End point values	Arm B: Nonacog beta pegol (Prophylaxis)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: International unit per milliliter(IU/mL)				
arithmetic mean (confidence interval 95%)	0.298 (0.260 to 0.341)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-life (t½) (Arm B only)

End point title	Terminal Half-life (t½) (Arm B only)

End point description:

Terminal half life was calculated as ln(2)/λz; where λz is the terminal elimination rate constant. The terminal elimination rate constant was estimated using linear regression on the terminal part of the log (activity) versus time profile. The PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 0-168 hours post injection at week 0, Steady-state: 0-168 hours post injection at week 12

End point values	Arm B: Nonacog beta pegol (Prophylaxis)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: hour				
geometric mean (geometric coefficient of variation)				
Week 0 (n= 13) Week 12 (n=15)	90.868 (± 13.535) 90.738 (± 21.581)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Serious Adverse events (SAEs)

End point title	Number of Serious Adverse events (SAEs)[5]

End point description:

A serious adverse event (SAE) is defined as any untoward medical occurrence that at any dose results in death, or is life-threatening, or requires inpatient hospitalization or causes prolongation of existing hospitalization results in persistent or significant disability/incapacity, or may have caused a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage. All presented SAEs are treatment-emergent (any serious adverse events which occurred after trial product administration). Results were based on the SAS which included all subjects exposed to N9-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Arm A: Nonacog beta pegol (On-demand)	Arm A: Nonacog beta pegol (Prophylaxis)	Arm B: Nonacog beta pegol (Prophylaxis)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	14	15	
Units: Events	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Incremental Recovery (IR) (Arm B only)

End point title	Incremental Recovery (IR) (Arm B only)

End point description:

The incremental recovery was calculated by subtracting the FVIII activity (IU/mL) measured in plasma at time 0 from that measured at time 30 min after dosing and dividing this difference by the dose injected at time 0 expressed as IU/kg body weight. FVIII activity was measured with a chromogenic assay. The PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 30±10 minutes post injection at week 0, Steady-state: 30±10 minutes post injection at week 12

End point values	Arm B: Nonacog beta pegol (Prophylaxis)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: (IU/mL)/(IU/kg)				
geometric mean (geometric coefficient of variation)				
Week 0 (n=14) Week 12 (n=15)	0.0182 (± 18.9550) 0.0192 (± 17.2668)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Adverse Events (AEs)

End point title	Number of Adverse Events (AEs)[6]

End point description:

An adverse event (AE) was defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a product, whether or not considered related to the product. All presented AEs are treatment-emergent. A treatment-emergent adverse event was defined as an event with onset after first N8-GP administration. Results were based on the SAS which included all subjects exposed to N9-GP in this trial.

End point type	Secondary

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

End point values	Arm A: Nonacog beta pegol (On-demand)	Arm A: Nonacog beta pegol (Prophylaxis)	Arm B: Nonacog beta pegol (Prophylaxis)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	14	15	
Units: Events	16	19	29	

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) (Arm B only)

End point title	Clearance (CL) (Arm B only)

End point description:

Clearance (CL) of drug after intravenous administration was reported. Clearance was calculated using the formula CL= Dose / AUC(0-inf) for single dose and CL= Dose / AUC(0-96) h for steady state. The PK

analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 0-168 hours post injection at week 0, Steady-state: 0-168 hours post injection at week 12

End point values	Arm B: Nonacog beta pegol (Prophylaxis)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: mL/h/kg				
geometric mean (geometric coefficient of variation)				
Week 0 (n=13) Week 12 (n=15)	0.536 (± 22.143) 0.487 (± 26.552)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve (AUC) (Arm B only)

End point title	Area Under the Curve (AUC) (Arm B only)

End point description:

Area under the plasma activity versus time profile from time zero to 168 hours (AUC0-168h) was measured The PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for specific timepoints.

End point type	Secondary

End point timeframe:

Single-dose: 0-168 hours post injection at week 0, Steady-state: 0-168 hours post injection at week 12

End point values	Arm B: Nonacog beta pegol (Prophylaxis)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: h·IU/mL				
geometric mean (geometric coefficient of variation)				
Week 0 (n=14) Week 12 (n=15)	51.856 (± 30.134) 92.914 (± 21.725)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of treatment (Week 0) until end of trial (Week 54)

Adverse event reporting additional description:

All presented AEs are treatment-emergent adverse events. A TEAE was defined as an event with onset after first N8-GP administration. Results were based on the SAS which included all subjects exposed to N9-GP in this trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Arm A: Nonacog beta pegol (On-demand)

Reporting group description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 EDs to nonacog beta pegol in the entire trial were fulfilled.

Reporting group title	Arm B: Nonacog beta pegol (Prophylaxis)

Reporting group description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

Reporting group title	Arm A: Nonacog beta pegol (Prophylaxis)

Reporting group description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 IU/kg for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 EDs to nonacog beta pegol in the entire trial were fulfilled.

Serious adverse events	Arm A: Nonacog beta pegol (On-demand)	Arm B: Nonacog beta pegol (Prophylaxis)	Arm A: Nonacog beta pegol (Prophylaxis)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Haematoma infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (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

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

Non-serious adverse events	Arm A: Nonacog beta pegol (On-demand)	Arm B: Nonacog beta pegol (Prophylaxis)	Arm A: Nonacog beta pegol (Prophylaxis)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 15 (80.00%)	14 / 15 (93.33%)	4 / 14 (28.57%)
Vascular disorders			
Phlebitis superficial			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Influenza like illness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Pulmonary mass			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood fibrinogen decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Fibrin D dimer increased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blood fibrinogen increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Fibrinogen degradation products increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Procalcitonin increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrioventricular block			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1

Neuritis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Lymphadenitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Trichiasis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Haemophilic arthropathy			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Synovitis			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 15 (6.67%)	6 / 15 (40.00%)	0 / 14 (0.00%)
occurrences (all)	1	6	0
Coronavirus infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Periodontitis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	4 / 15 (26.67%)	0 / 14 (0.00%)
occurrences (all)	1	5	0
Metabolism and nutrition disorders			
Hypoproteinaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 14 (0.00%)
occurrences (all)	0	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported