



Clinical trial results:

Safety, tolerability, and pharmacokinetics study of single and multiple subcutaneous doses of turoctocog alfa pegol in patients with haemophilia A

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2016-002396-99 |
| Trial protocol | AT DE BG FR GB |
| Global end of trial date | 15 October 2018 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 26 April 2019 |
| First version publication date | 26 April 2019 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | NN7170-4213 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|--|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02994407 |
| WHO universal trial number (UTN) | U1111-1183-5111 |
| Other trial identifiers | Japanese trial registration: JapicCTI-173683 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novo Nordisk |
| Sponsor organisation address | Novo Allé, Bagsvaerd, Denmark, 2880 |
| Public contact | Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk, clinicaltrials@novonordisk.com |
| Scientific contact | Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk, 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? | No |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 02 April 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 15 October 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 October 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of s.c. administration of turoctocog alfa pegol (SC N8-GP) in patients with severe haemophilia A

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and ICH Good Clinical Practice, including archiving of essential documents (2009) and 21 CFR 312.120.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

| | |
|---|-----------------|
| Actual start date of recruitment | 30 January 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 | Austria: 4 |
| Country: Number of subjects enrolled | Bulgaria: 2 |
| Country: Number of subjects enrolled | Germany: 5 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | Japan: 2 |
| Country: Number of subjects enrolled | Serbia: 5 |
| Country: Number of subjects enrolled | Turkey: 2 |
| Country: Number of subjects enrolled | United States: 7 |
| Worldwide total number of subjects | 36 |
| EEA total number of subjects | 20 |

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) | 3 |
| Adults (18-64 years) | 33 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 25 sites in 9 countries as follows: Austria: 2 sites; Bulgaria: 1 site; France: 1 site; Germany: 3 sites; Japan: 2 sites; Serbia: 5 sites; Turkey: 1 site; United Kingdom: 3 sites; United States: 7 sites.

Pre-assignment

Screening details:

The study consisted of two parts: one single dose, dose escalation part (part A) and one multiple dose part (part B) with daily administrations of SC N8-GP for a period of 3 months. Subjects having completed part A and who had wanted to continue to part B treated themselves with their regular FVIII product in the period between part A and B.

Period 1

| | |
|------------------------------|---------------------------------------|
| Period 1 title | Part A |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Monitor, Carer, Subject |

Blinding implementation details:

Double blinded

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|--------------------------------|
| Arm title | Part A - SC N8-GP (12.5 IU/kg) |
|------------------|--------------------------------|

Arm description:

Subjects received a single dose (12.5 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | SC turoctocog alfa pegol A 2000 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received a single dose of SC N8-GP 12.5 IU/kg and placebo as subcutaneous injection with a syringe. The two treatments (SC N8-GP and placebo) were administered immediately after one another (one in the abdomen above the umbilicus and one below the umbilicus) in a blinded randomised manner.

| | |
|------------------|------------------------------|
| Arm title | Part A - SC N8-GP (25 IU/kg) |
|------------------|------------------------------|

Arm description:

Subjects received a single dose (25 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | SC turoctocog alfa pegol A 2000 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received a single dose of SC N8-GP 25 IU/kg and placebo as subcutaneous injection with a syringe. The two treatments (SC N8-GP and placebo) were administered immediately after one another (one in the abdomen above the umbilicus and one below the umbilicus) in a blinded randomised manner.

| | |
|--|-----------------------------------|
| Arm title | Part A - SC N8-GP (50 IU/kg) |
| Arm description: Subjects received a single dose (50 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Arm type | Experimental |
| Investigational medicinal product name | SC turoctocog alfa pegol A 2000 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received a single dose of SC N8-GP 50 IU/kg and placebo as subcutaneous injection with a syringe. The two treatments (SC N8-GP and placebo) were administered immediately after one another (one in the abdomen above the umbilicus and one below the umbilicus) in a blinded randomised manner.

| | |
|---|-----------------------------------|
| Arm title | Part A - SC N8-GP (100 IU/kg) |
| Arm description: Subjects received a single dose (100 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Arm type | Experimental |
| Investigational medicinal product name | SC turoctocog alfa pegol A 2000 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received a single dose of SC N8-GP 100 IU/kg and placebo as subcutaneous injection with a syringe. The two treatments (SC N8-GP and placebo) were administered immediately after one another (one in the abdomen above the umbilicus and one below the umbilicus) in a blinded randomised manner.

| Number of subjects in period 1^[1] | Part A - SC N8-GP (12.5 IU/kg) | Part A - SC N8-GP (25 IU/kg) | Part A - SC N8-GP (50 IU/kg) |
|---|--------------------------------|------------------------------|------------------------------|
| Started | 6 | 6 | 6 |
| Completed | 6 | 6 | 6 |

| Number of subjects in period 1^[1] | Part A - SC N8-GP (100 IU/kg) |
|---|-------------------------------|
| Started | 6 |
| Completed | 6 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Only one period can be selected for baseline period. Therefore the baseline characteristics of the second period (part B) is explained by means of subject analysis set.

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Part B |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|----------|
| Arm title | SC N8-GP |
|------------------|----------|

Arm description:

Subjects received daily subcutaneous administrations of SC N8-GP for a period of 3 months (13 weeks). In addition to 12 new subjects, fourteen subjects having completed part A continued to part B and treated himself with his regular FVIII product in the period between part A and B.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | SC turoctocog alfa pegol A 2000 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received daily subcutaneous administrations of SC N8-GP for a period of 3 months (13 weeks). The starting dose for all patients depended on their individual body weight. Based on available safety data from part A, SC N8-GP doses of up to 100 IU/kg per day were considered safe also for repeated daily dosing.

| | |
|---|----------|
| Number of subjects in period 2^[2] | SC N8-GP |
| Started | 12 |
| Completed | 12 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The number of subjects mentioned here (12) are the new subjects enrolled in part B, in addition to the 14 subjects who continued from the previous period.

Baseline characteristics

Reporting groups

| | |
|--|--------------------------------|
| Reporting group title | Part A - SC N8-GP (12.5 IU/kg) |
| Reporting group description: Subjects received a single dose (12.5 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Reporting group title | Part A - SC N8-GP (25 IU/kg) |
| Reporting group description: Subjects received a single dose (25 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Reporting group title | Part A - SC N8-GP (50 IU/kg) |
| Reporting group description: Subjects received a single dose (50 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Reporting group title | Part A - SC N8-GP (100 IU/kg) |
| Reporting group description: Subjects received a single dose (100 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |

| Reporting group values | Part A - SC N8-GP (12.5 IU/kg) | Part A - SC N8-GP (25 IU/kg) | Part A - SC N8-GP (50 IU/kg) |
|--|-----------------------------------|---------------------------------|---------------------------------|
| Number of subjects | 6 | 6 | 6 |
| Age Categorical | | | |
| Number of subjects in each age category. | | | |
| Units: Subjects | | | |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 6 | 6 | 6 |
| From 65-84 years | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 36.0 | 37.8 | 34.7 |
| standard deviation | ± 10.5 | ± 15.8 | ± 16.7 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 6 | 6 | 6 |

| Reporting group values | Part A - SC N8-GP (100 IU/kg) | Total | |
|--|----------------------------------|-------|--|
| Number of subjects | 6 | 24 | |
| Age Categorical | | | |
| Number of subjects in each age category. | | | |
| Units: Subjects | | | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 6 | 24 | |
| From 65-84 years | 0 | 0 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 38.7 | | |
| standard deviation | ± 16.1 | - | |

| | | | |
|--------------------|---|----|--|
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 6 | 24 | |

Subject analysis sets

| | |
|----------------------------|-----------------|
| Subject analysis set title | Part B SC-N8-GP |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Subjects received daily subcutaneous administrations of SC N8-GP for a period of 3 months (13 weeks). In addition to 12 new subjects, fourteen subjects having completed part A continued to part B and treated themselves with their regular FVIII product in the period between part A and B. Thus the subject analysis set included 26 subjects.

| | | | |
|--|-----------------|--|--|
| Reporting group values | Part B SC-N8-GP | | |
| Number of subjects | 26 | | |
| Age Categorical | | | |
| Number of subjects in each age category. | | | |
| Units: Subjects | | | |
| Adolescents (12-17 years) | 3 | | |
| Adults (18-64 years) | 22 | | |
| From 65-84 years | 1 | | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 33.9 | | |
| standard deviation | ± 15.4 | | |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 0 | | |
| Male | 26 | | |

End points

End points reporting groups

| | |
|--|--------------------------------|
| Reporting group title | Part A - SC N8-GP (12.5 IU/kg) |
| Reporting group description: Subjects received a single dose (12.5 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Reporting group title | Part A - SC N8-GP (25 IU/kg) |
| Reporting group description: Subjects received a single dose (25 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Reporting group title | Part A - SC N8-GP (50 IU/kg) |
| Reporting group description: Subjects received a single dose (50 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Reporting group title | Part A - SC N8-GP (100 IU/kg) |
| Reporting group description: Subjects received a single dose (100 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo. | |
| Reporting group title | SC N8-GP |
| Reporting group description: Subjects received daily subcutaneous administrations of SC N8-GP for a period of 3 months (13 weeks). In addition to 12 new subjects, fourteen subjects having completed part A continued to part B and treated himself with his regular FVIII product in the period between part A and B. | |
| Subject analysis set title | Part B SC-N8-GP |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Subjects received daily subcutaneous administrations of SC N8-GP for a period of 3 months (13 weeks). In addition to 12 new subjects, fourteen subjects having completed part A continued to part B and treated themselves with their regular FVIII product in the period between part A and B. Thus the subject analysis set included 26 subjects. | |

Primary: Number of adverse events reported after exposure to SC N8-GP

| | |
|--|---|
| End point title | Number of adverse events reported after exposure to SC N8-GP ^[1] |
| End point description: Number of treatment emergent adverse events reported after exposure to SC N8-GP until 7 days after last exposure. The reporting period of adverse events was changed to until 7 days after last exposure due to the half-time of SC N8-GP. | |
| End point type | Primary |
| End point timeframe: Until 7 days after last exposure | |

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 primary endpoint investigates safety and is analysed using descriptive statistics, and thus no statistical analysis is performed.

| End point values | Part A - SC N8-GP (12.5 IU/kg) | Part A - SC N8-GP (25 IU/kg) | Part A - SC N8-GP (50 IU/kg) | Part A - SC N8-GP (100 IU/kg) |
|-----------------------------|--------------------------------|------------------------------|------------------------------|-------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 6 | 6 | 6 |
| Units: number of events | 7 | 4 | 1 | 3 |

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | Part B SC-N8-GP | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 26 | | | |
| Units: number of events | 40 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic parameter Cmax (up to 144 hours after dose)

| | |
|---|---|
| End point title | Pharmacokinetic parameter Cmax (up to 144 hours after dose) |
| End point description: The maximal FVIII activity measured after single dose administration. | |
| End point type | Secondary |
| End point timeframe: After single dose administration (part A) | |

| End point values | Part A - SC N8-GP (12.5 IU/kg) | Part A - SC N8-GP (25 IU/kg) | Part A - SC N8-GP (50 IU/kg) | Part A - SC N8-GP (100 IU/kg) |
|--------------------------------------|--------------------------------|------------------------------|------------------------------|-------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 6 | 6 | 6 |
| Units: IU/dL | | | | |
| arithmetic mean (standard deviation) | 1.3 (± 106.9) | 2.5 (± 62.8) | 4.6 (± 32.6) | 15.2 (± 75.6) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the first day of trial product administration until 7 days after last exposure i.e. total duration of visit 2 for part A and from visit 2 to 7 days after visit 8 in part B.

Adverse event reporting additional description:

Adverse events were reported for the safety analysis set which included all patients exposed to the trial product. The reporting period of adverse events was changed from 28 days to 'until 7 days after last exposure' due to the half-time of SC N8-GP.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 21 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Part A - SC N8-GP (12.5 IU/kg) |
|-----------------------|--------------------------------|

Reporting group description:

Subjects received a single dose (12.5 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo.

| | |
|-----------------------|------------------------------|
| Reporting group title | Part A - SC N8-GP (25 IU/kg) |
|-----------------------|------------------------------|

Reporting group description:

Subjects received a single dose (25 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo.

| | |
|-----------------------|------------------------------|
| Reporting group title | Part A - SC N8-GP (50 IU/kg) |
|-----------------------|------------------------------|

Reporting group description:

Subjects received a single dose (50 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Part A - SC N8-GP (100 IU/kg) |
|-----------------------|-------------------------------|

Reporting group description:

Subjects received a single dose (100 IU/kg) of SC N8-GP and a single subcutaneous injection of placebo.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Part B - SC-N8-GP (once daily) |
|-----------------------|--------------------------------|

Reporting group description:

Subjects received daily subcutaneous administrations of SC N8-GP for a period of 3 months (13 weeks). In addition to 12 new subjects, fourteen subjects having completed part A continued to part B and treated himself with his regular FVIII product in the period between part A and B. Thus the subject analysis set included 26 subjects

| Serious adverse events | Part A - SC N8-GP (12.5 IU/kg) | Part A - SC N8-GP (25 IU/kg) | Part A - SC N8-GP (50 IU/kg) |
|---|-----------------------------------|---------------------------------|---------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Factor VIII inhibition | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue | | | |

| | | | |
|---|---------------|---------------|---------------|
| disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Part A - SC N8-GP (100 IU/kg) | Part B - SC-N8-GP (once daily) | |
|---|----------------------------------|-----------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 26 (7.69%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Blood and lymphatic system disorders | | | |
| Factor VIII inhibition | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Part A - SC N8-GP (12.5 IU/kg) | Part A - SC N8-GP (25 IU/kg) | Part A - SC N8-GP (50 IU/kg) |
|---|-----------------------------------|---------------------------------|---------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | 2 / 6 (33.33%) | 1 / 6 (16.67%) |
| Injury, poisoning and procedural complications | | | |
| Scratch | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration | | | |

| | | | |
|--|----------------|----------------|----------------|
| site conditions | | | |
| Injection site bruising | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Injection site haematoma | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site bruise | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 6 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Renal and urinary disorders | | | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------------------------|-----------------------------------|--|
| Non-serious adverse events | Part A - SC N8-GP (100 IU/kg) | Part B - SC-N8-GP (once daily) | |
| Total subjects affected by non-serious | | | |

| | | | |
|--|----------------|-----------------|--|
| adverse events | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 7 / 26 (26.92%) | |
| Injury, poisoning and procedural complications | | | |
| Scratch | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 26 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 26 (11.54%) | |
| occurrences (all) | 0 | 6 | |
| General disorders and administration site conditions | | | |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 26 (3.85%) | |
| occurrences (all) | 0 | 1 | |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 26 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injection site haematoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 26 (3.85%) | |
| occurrences (all) | 0 | 2 | |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 26 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Injection site swelling | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 26 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vessel puncture site bruise | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 26 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 26 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 26 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|--|---------------------|----------------------|--|
| Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 26 (0.00%) 0 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 3 / 26 (11.54%) 3 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 31 October 2016 | Text regarding stopping rules and SUSAR reporting have been updated |
| 27 December 2017 | To specify the dose for part B and updates based on authority commitments prior to the start of part B. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported