# Clinical trial results:
# A Trial Investigating the Pharmacokinetic Properties of NN1250 in Children, Adolescents and Adults with Type 1 Diabetes

## Summary

| | |
|---|---|
| EudraCT number | 2008-008306-43 |
| Trial protocol | DE |
| Global end of trial date | 03 May 2010 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 27 March 2016 |
| First version publication date | 01 August 2015 |
| Version creation reason | • New data added to full data set<br>AE data to be added |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | NN1250-1995 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01030926 |
| WHO universal trial number (UTN) | U1111-1112-4715 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Novo Nordisk A/S |
| Sponsor organisation address | Novo Allé, Bagsvaerd, Denmark, 2880 |
| Public contact | Global Clinical Registry (GCR, 1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com |
| Scientific contact | Global Clinical Registry (GCR, 1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000456-PIP01-08, EMEA-000479-PIP01-08 |
| 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 | 22 December 2010 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 May 2010 |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 May 2010 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To investigate the pharmacokinetic total exposure of SIBA (NN1250, IDeg) in children, adolescents and adult subjects with type 1 diabetes

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (59th WMA General Assembly, Seoul 2008. Last amended with Note of Clarification on Paragraph 29 by the WMA General Assembly, Washington 2002, and Note of Clarification on Paragraph 30 by the WMA General assembly, Tokyo 2004) and International Conference on Harmonisation (ICH) Good Clinical Practice (June 1996).

Background therapy:

The following non-investigational medicinal products were used:
NPH insulin: Protaphane®, Novolin® N 100 IU/mL, in 3 mL FlexPen®)
Insulin aspart: NovoRapid®, NovoLog® 100 U/mL, in 3 mL FlexPen®and in 10 mL vials)

Evidence for comparator:

Not applicable

| | |
|---|---|
| Actual start date of recruitment | 08 December 2009 |
| 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 | Germany: 39 |
| Worldwide total number of subjects | 39 |
| EEA total number of subjects | 39 |

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) | 13 |
| Adolescents (12-17 years) | 13 |
| Adults (18-64 years) | 13 |

| | |
|---|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at one site in Germany.

### Pre-assignment

Screening details:

Not applicable

### Period 1

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

Blinding implementation details:

In order to maintain the blinding, a person not otherwise involved in the conduct of the trial prepared the doses according to the randomisation provided by Novo Nordisk A/S. It was ensured that the cartridge or syringe containing trial product was not revealed to the subject or to the Investigator.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | IDeg in Period 1 |

Arm description:

In Period 1, subjects were randomly assigned to receive a single dose of IDeg.

| | |
|---|---|
| Arm type | Cross-over assignment |
| Investigational medicinal product name | IDeg |
| Investigational medicinal product code | |
| Other name | SIBA, NN1250, insulin degludec |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of IDeg (0.4 U/kg body weight [BW]), administered as a subcutaneous (s.c.) injection into a lifted skin fold on the anterior surface of the thigh.

| | |
|---|---|
| **Arm title** | IGlar in Period 1 |

Arm description:

In Period 1, subjects were randomly assigned to receive a single dose of IGlar.

| | |
|---|---|
| Arm type | Cross-over assignment |
| Investigational medicinal product name | IGlar |
| Investigational medicinal product code | |
| Other name | Insulin glargine, Lantus |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of IGlar (0.4 U/kg BW), administered as a s.c. injection into a lifted skin fold on the anterior surface of the thigh.

| Number of subjects in period 1 | IDeg in Period 1 | IGlar in Period 1 |
|---|---|---|
| Started | 19 | 20 |
| Exposed | 18 | 20 |
| Completed | 18 | 20 |
| Not completed | 1 | 0 |
| Consent withdrawn by subject | 1 | - |

## Period 2

| | |
|---|---|
| Period 2 title | Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

In order to maintain the blinding, a person not otherwise involved in the conduct of the trial prepared the doses according to the randomisation provided by Novo Nordisk A/S. It was ensured that the cartridge or syringe containing trial product was not revealed to the subject or to the Investigator.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | IDeg in Period 2 |

Arm description:

Subjects, who received IGlar in Period 1, were assigned to receive a single dose of IDeg in Period 2. There was a wash-out period of 7-21 days in between Period 1 and Period 2.

| | |
|---|---|
| Arm type | Cross-over assignment |
| Investigational medicinal product name | IDeg |
| Investigational medicinal product code | |
| Other name | SIBA, NN1250, insulin degludec |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of IDeg (0.4 U/kg BW), administered as a subcutaneous (s.c.) injection into a lifted skin fold on the anterior surface of the thigh.

| | |
|---|---|
| **Arm title** | IGlar in Period 2 |

Arm description:

Subjects, who received IDeg in Period 1, were assigned to receive a single dose of IGlar in Period 2. There was a wash-out period of 7-21 days in between Period 1 and Period 2.

| | |
|---|---|
| Arm type | Cross-over assignment |
| Investigational medicinal product name | IGlar |
| Investigational medicinal product code | |
| Other name | Insulin glargine, Lantus |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of IGlar (0.4 U/kg BW), administered as a s.c. injection into a lifted skin fold on the anterior surface of the thigh.

| Number of subjects in period 2[1] | IDeg in Period 2 | IGlar in Period 2 |
|---|---|---|
| Started | 19 | 18 |
| Exposed | 19 | 18 |
| Completed | 19 | 18 |

Notes:

[1] - 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: One subject was withdrawn after Period 1 due to difficult venous conditions (difficulties of drawing blood).

## Period 3

| | |
|---|---|
| Period 3 title | Period 3 (completers) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

In order to maintain the blinding, a person not otherwise involved in the conduct of the trial prepared the doses according to the randomisation provided by Novo Nordisk A/S. It was ensured that the cartridge or syringe containing trial product was not revealed to the subject or to the Investigator.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | No |
| **Arm title** | IDeg: Children |

Arm description:

Subjects (children [6-11 years]) were randomly assigned to receive a single dose of IDeg.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IDeg |
| Investigational medicinal product code | |
| Other name | SIBA, NN1250, insulin degludec |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of IDeg (0.4 U/kg BW), administered as a subcutaneous (s.c.) injection into a lifted skin fold on the anterior surface of the thigh.

| | |
|---|---|
| **Arm title** | IDeg: Adolescents |

Arm description:

Subjects (adolescents [12-17 years]) were randomly assigned to receive a single dose of IDeg.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IDeg |
| Investigational medicinal product code | |
| Other name | SIBA, NN1250, insulin degludec |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of IDeg (0.4 U/kg BW), administered as a subcutaneous (s.c.) injection into a lifted skin

fold on the anterior surface of the thigh.

| **Arm title** | IDeg: Adults |
|---|---|
| Arm description: | |
| Subjects (adults [18-65 years]) were randomly assigned to receive a single dose of IDeg. | |
| Arm type | Experimental |
| Investigational medicinal product name | IDeg |
| Investigational medicinal product code | |
| Other name | SIBA, NN1250, insulin degludec |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| A single dose of IDeg (0.4 U/kg BW), administered as a subcutaneous (s.c.) injection into a lifted skin fold on the anterior surface of the thigh. | |
| **Arm title** | IGlar: Children |
| Arm description: | |
| Subjects (children [6-11 years]) were randomly assigned to receive a single dose of IGlar. | |
| Arm type | Experimental |
| Investigational medicinal product name | IGlar |
| Investigational medicinal product code | |
| Other name | Insulin glargine, Lantus |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| A single dose of IGlar (0.4 U/kg BW), administered as a s.c. injection into a lifted skin fold on the anterior surface of the thigh. | |
| **Arm title** | IGlar: Adolescents |
| Arm description: | |
| Subjects (adolescents [12-17 years]) were randomly assigned to receive a single dose of IDeg. | |
| Arm type | Experimental |
| Investigational medicinal product name | IGlar |
| Investigational medicinal product code | |
| Other name | Insulin glargine, Lantus |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| A single dose of IGlar (0.4 U/kg BW), administered as a s.c. injection into a lifted skin fold on the anterior surface of the thigh. | |
| **Arm title** | IGlar: Adults |
| Arm description: | |
| Subjects (adults [18-65 years]) were randomly assigned to receive a single dose of IGlar. | |
| Arm type | Experimental |
| Investigational medicinal product name | IGlar |
| Investigational medicinal product code | |
| Other name | Insulin glargine, Lantus |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of IGlar (0.4 U/kg BW), administered as a s.c. injection into a lifted skin fold on the anterior surface of the thigh.

| **Number of subjects in period 3** | IDeg: Children | IDeg: Adolescents | IDeg: Adults |
|---|---|---|---|
| Started | 12 | 13 | 12 |
| Exposed | 12 | 13 | 12 |
| Completed | 12 | 13 | 12 |

| **Number of subjects in period 3** | IGlar: Children | IGlar: Adolescents | IGlar: Adults |
|---|---|---|---|
| Started | 12 | 13 | 12 |
| Exposed | 12 | 13 | 12 |
| Completed | 12 | 13 | 12 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | IDeg in Period 1 |
| Reporting group description: | |
| In Period 1, subjects were randomly assigned to receive a single dose of IDeg. | |
| Reporting group title | IGlar in Period 1 |
| Reporting group description: | |
| In Period 1, subjects were randomly assigned to receive a single dose of IGlar. | |

| Reporting group values | IDeg in Period 1 | IGlar in Period 1 | Total |
|---|---|---|---|
| Number of subjects | 19 | 20 | 39 |
| Age categorical<br>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) | 5 | 8 | 13 |
| Adolescents (12-17 years) | 5 | 8 | 13 |
| Adults (18-64 years) | 9 | 4 | 13 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 10 | 8 | 18 |
| Male | 9 | 12 | 21 |

## End points

### End points reporting groups

| Reporting group title | IDeg in Period 1 |
|---|---|
| Reporting group description: | |
| In Period 1, subjects were randomly assigned to receive a single dose of IDeg. | |
| Reporting group title | IGlar in Period 1 |
| Reporting group description: | |
| In Period 1, subjects were randomly assigned to receive a single dose of IGlar. | |
| Reporting group title | IDeg in Period 2 |
| Reporting group description: | |
| Subjects, who received IGlar in Period 1, were assigned to receive a single dose of IDeg in Period 2. There was a wash-out period of 7-21 days in between Period 1 and Period 2. | |
| Reporting group title | IGlar in Period 2 |
| Reporting group description: | |
| Subjects, who received IDeg in Period 1, were assigned to receive a single dose of IGlar in Period 2. There was a wash-out period of 7-21 days in between Period 1 and Period 2. | |
| Reporting group title | IDeg: Children |
| Reporting group description: | |
| Subjects (children [6-11 years]) were randomly assigned to receive a single dose of IDeg. | |
| Reporting group title | IDeg: Adolescents |
| Reporting group description: | |
| Subjects (adolescents [12-17 years]) were randomly assigned to receive a single dose of IDeg. | |
| Reporting group title | IDeg: Adults |
| Reporting group description: | |
| Subjects (adults [18-65 years]) were randomly assigned to receive a single dose of IDeg. | |
| Reporting group title | IGlar: Children |
| Reporting group description: | |
| Subjects (children [6-11 years]) were randomly assigned to receive a single dose of IGlar. | |
| Reporting group title | IGlar: Adolescents |
| Reporting group description: | |
| Subjects (adolescents [12-17 years]) were randomly assigned to receive a single dose of IDeg. | |
| Reporting group title | IGlar: Adults |
| Reporting group description: | |
| Subjects (adults [18-65 years]) were randomly assigned to receive a single dose of IGlar. | |

### Primary: AUC_IDeg, 0-∞, SD, area under the serum IDeg concentration-time curve from 0 to infinity after single-dose

| End point title | AUC_IDeg, 0-∞, SD, area under the serum IDeg concentration-time curve from 0 to infinity after single-dose |
|---|---|
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| 0 to infinity | |

| End point values | IDeg: Children | IDeg: Adolescents | IDeg: Adults | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 13 | 12 | |
| Units: pmol*h/L | | | | |
| geometric mean (geometric coefficient of variation) | 145891 (± 73) | 130713 (± 30) | 98594 (± 21) | |

## Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Statistical analysis description: | |
| The endpoints were log-transformed and analysed using an ANOVA model with age group and period as fixed effects and with different error-terms for each age-group. | |
| Comparison groups | IDeg: Children v IDeg: Adults |
| Number of subjects included in analysis | 24 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean ratio |
| Point estimate | 1.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.98 |
| upper limit | 2.24 |

| Statistical analysis title | Statistical analysis 2 |
|---|---|
| Comparison groups | IDeg: Adolescents v IDeg: Adults |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean ratio |
| Point estimate | 1.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.08 |
| upper limit | 1.64 |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the start of first trial product administration to 7 to 21 days after last dosing visit.

Adverse event reporting additional description:

Safety Analysis Set included all subjects receiving at least one dose of the investigational product or its comparator. Subjects in the safety analysis set contributed to the evaluation 'as treated'.

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

### Dictionary used

| Dictionary name | MedDRA |
|---|---|
| Dictionary version | 13.1 |

### Reporting groups

| Reporting group title | IDeg: Children (6-11 years) |
|---|---|

Reporting group description:

Subjects (children [6-11 years]), who received at least one dose of IDeg.

| Reporting group title | IDeg: Adolescents (12-17 years) |
|---|---|

Reporting group description:

Subjects (adolescents [12-17 years]), who received at least one dose of IDeg.

| Reporting group title | IDeg: Adults (18-65 years) |
|---|---|

Reporting group description:

Subjects (adults [18-65 years]), who received at least one dose of IDeg.

| Reporting group title | IGlar: Children (6-11 years) |
|---|---|

Reporting group description:

Subjects (children [6-11 years]), who received at least one dose of IGlar.

| Reporting group title | IGlar: Adolescents (12-17 years) |
|---|---|

Reporting group description:

Subjects (adolescents [12-17 years]), who received at least one dose of IGlar.

| Reporting group title | IGlar: Adults (18-65 years) |
|---|---|

Reporting group description:

Subjects (adults [18-65 years]), who received at least one dose of IGlar.

| Serious adverse events | IDeg: Children (6-11 years) | IDeg: Adolescents (12-17 years) | IDeg: Adults (18-65 years) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | IGlar: Children (6-11 years) | IGlar: Adolescents (12-17 years) | IGlar: Adults (18-65 years) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (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 |

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

| Non-serious adverse events | IDeg: Children (6-11 years) | IDeg: Adolescents (12-17 years) | IDeg: Adults (18-65 years) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 3 / 13 (23.08%) | 1 / 12 (8.33%) |
| Injury, poisoning and procedural complications | | | |
| Injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wrong drug administered | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 13 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Catheter site phlebitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 13 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | IGlar: Children (6-11 years) | IGlar: Adolescents (12-17 years) | IGlar: Adults (18-65 years) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 3 / 13 (23.08%) | 1 / 12 (8.33%) |
| Injury, poisoning and procedural complications | | | |
| Injury | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wrong drug administered | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Catheter site phlebitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 13 (7.69%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 13 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 18 November 2009 | The Protocol was amended mainly due to the following reasons:<br>This trial was conducted with the purpose of investigating the pharmacokinetic properties of NN1250 (insulin degludec). To increase convenience for the children it was decided to allow the subjects and the investigator to decide on the injection site for insulin aspart. This had no influence on bioavailability and trial results.<br>To align time windows on blood glucose sampling times with the time windows on the blood sampling for determination of insulin 454 and insulin glargine.<br>For clarity on some of the question asked in relation to a hypoglycaemic episode.<br>The period for when a hypoglycaemic episode is deemed as treatment emergent, had incorrectly been stated as until 5 days after last trial product administration, this should be 7 days.<br>The period for when an adverse event is deemed as treatment emergent, had incorrectly been stated as until the follow up visit, this should be until 7 days after the last trial product administration. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| Not applicable |

Notes: