



Clinical trial results:

A 26-week open label, randomised, 2-armed, parallel group, multi-centre trial investigating efficacy and safety of insulin detemir versus insulin Neutral Protamine Hagedorn in combination with the maximum tolerated dose of metformin and diet/exercise on glycaemic control in children and adolescents with type 2 diabetes insufficiently controlled on the maximum tolerated dose of metformin \pm other oral antidiabetic drug(s) \pm basal insulin

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2013-005500-33 |
| Trial protocol | HU IT DE HR GR ES PT |
| Global end of trial date | 14 June 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 29 December 2016 |
| First version publication date | 29 December 2016 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | NN304-4093 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02131272 |
| WHO universal trial number (UTN) | U1111-1151-4056 |

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) | 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 | 21 November 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 June 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 June 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of insulin detemir in combination with metformin and diet/exercise versus insulin neutral protamine hagedorn (NPH) in combination with the maximum tolerated dose (MTD) of metformin and diet/exercise in controlling glycaemia, after 26 weeks of treatment, in children and adolescents (aged 10–17 years) with type 2 diabetes, who are insufficiently treated with the MTD of metformin ± other OAD(s) ± basal insulin.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, ICH Good Clinical Practice and FDA 21 CFR 312.120.

Background therapy:

Subjects continued treatment with metformin on their pre-study dose(s) throughout the trial.

Evidence for comparator:

Not applicable

| | |
|---|--------------|
| Actual start date of recruitment | 11 June 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Brazil: 1 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | India: 4 |
| Country: Number of subjects enrolled | Israel: 1 |
| Country: Number of subjects enrolled | Malaysia: 4 |
| Country: Number of subjects enrolled | Mexico: 6 |
| Country: Number of subjects enrolled | Russian Federation: 1 |
| Country: Number of subjects enrolled | Korea, Republic of: 2 |
| Country: Number of subjects enrolled | Taiwan: 8 |
| Country: Number of subjects enrolled | Turkey: 3 |
| Country: Number of subjects enrolled | United States: 11 |
| Worldwide total number of subjects | 42 |
| EEA total number of subjects | 1 |

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) | 3 |
| Adolescents (12-17 years) | 39 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The following 12 countries screened subjects (no. of sites that randomised subjects within parentheses): Brazil (1), Germany (1), India (3), Israel (1), South Korea (1), Malaysia (3), Mexico (1), Russian Federation (1) Taiwan (3), Turkey (3), United States (6), Hungary (0). A total of 24 sites in 11 countries randomised subjects to treatment.

Pre-assignment

Screening details:

Subjects continued their treatment with metformin during the trial.

Period 1

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

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Insulin detemir + metformin + diet/exercise |

Arm description:

Subjects were treated with insulin detemir 100 U/mL administered subcutaneously in the thigh region once or twice daily for a period of 26 weeks. All subjects continued treatment with metformin on their pre-study dose(s) throughout the trial. The diet/exercise intervention was performed through changes in eating and activity behaviours.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Insulin detemir |
| Investigational medicinal product code | |
| Other name | Insulin detemir |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

For insulin naïve subjects, insulin detemir was initiated at a dose of 0.1–0.2 U/kg with a maximum dose of 10 U at the investigators discretion. Subjects who were already on basal insulin were switched to insulin detemir unit-to-unit once or twice daily, depending on previous injection frequency. Subjects were dosed according to individual requirements during the trial period.

| | |
|------------------|---|
| Arm title | Insulin NPH + metformin + diet/exercise |
|------------------|---|

Arm description:

Subjects were treated with insulin NPH 100 IU/mL administered subcutaneously in the thigh region once or twice daily for a period of 26 weeks. All subjects continued treatment with metformin on their pre-study dose(s) throughout the trial. The diet/exercise intervention was performed through changes in eating and activity behaviours.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Insulin neutral protamine hagedorn (NPH) |
| Investigational medicinal product code | |
| Other name | Insulin human |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

For insulin naïve subjects, insulin NPH was initiated at a dose of 0.1–0.2 U/kg with a maximum dose of 10 U at the investigators discretion. Subjects who were already on basal insulin were switched to insulin NPH unit-to-unit once or twice daily, depending on previous injection frequency. Subjects were dosed according to individual requirements during the trial period.

| Number of subjects in period 1 | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise |
|---------------------------------------|---|---|
| Started | 20 | 22 |
| Completed | 19 | 20 |
| Not completed | 1 | 2 |
| Withdrawal Criteria | 1 | - |
| Consent withdrawn by subject | - | 1 |
| Consent withdrawn by parent | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|---|
| Reporting group title | Insulin detemir + metformin + diet/exercise |
| Reporting group description: | |
| Subjects were treated with insulin detemir 100 U/mL administered subcutaneously in the thigh region once or twice daily for a period of 26 weeks. All subjects continued treatment with metformin on their pre-study dose(s) throughout the trial. The diet/exercise intervention was performed through changes in eating and activity behaviours. | |
| Reporting group title | Insulin NPH + metformin + diet/exercise |
| Reporting group description: | |
| Subjects were treated with insulin NPH 100 IU/mL administered subcutaneously in the thigh region once or twice daily for a period of 26 weeks. All subjects continued treatment with metformin on their pre-study dose(s) throughout the trial. The diet/exercise intervention was performed through changes in eating and activity behaviours. | |

| Reporting group values | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise | Total |
|---|---|---|-------|
| Number of subjects | 20 | 22 | 42 |
| Age Categorical | | | |
| Units: Subjects | | | |
| Adolescents (10-14 years) | 9 | 11 | 20 |
| Adults (15-17 years) | 11 | 11 | 22 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 15 | 15 | - |
| standard deviation | ± 2.1 | ± 2.2 | - |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 12 | 15 | 27 |
| Male | 8 | 7 | 15 |
| Glycosylated haemoglobin (HbA1c) | | | |
| Units: percentage of glycosylated HbA1c | | | |
| arithmetic mean | 8.72 | 8.95 | - |
| standard deviation | ± 0.86 | ± 1.05 | - |
| Body weight standard deviation score (SDS) | | | |
| The body weight SD scores were derived from the age and sex of the subjects and the body weight together with growth curves defined for the reference population (US population). | | | |
| Units: standard deviation score | | | |
| arithmetic mean | 1.532 | 1.26 | - |
| standard deviation | ± 0.685 | ± 0.835 | - |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Insulin detemir + metformin + diet/exercise |
| Reporting group description: Subjects were treated with insulin detemir 100 U/mL administered subcutaneously in the thigh region once or twice daily for a period of 26 weeks. All subjects continued treatment with metformin on their pre-study dose(s) throughout the trial. The diet/exercise intervention was performed through changes in eating and activity behaviours. | |
| Reporting group title | Insulin NPH + metformin + diet/exercise |
| Reporting group description: Subjects were treated with insulin NPH 100 IU/mL administered subcutaneously in the thigh region once or twice daily for a period of 26 weeks. All subjects continued treatment with metformin on their pre-study dose(s) throughout the trial. The diet/exercise intervention was performed through changes in eating and activity behaviours. | |

Primary: Change in HbA1c

| | |
|---|-----------------|
| End point title | Change in HbA1c |
| End point description: Estimated mean change in glycosylated haemoglobin from baseline to week 26. | |
| End point type | Primary |
| End point timeframe: From baseline to week 26 | |

| End point values | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 22 | | |
| Units: Percentage of glycosylated haemoglobin | | | | |
| least squares mean (standard error) | -0.64 (± 0.32) | -0.81 (± 0.31) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Mixed model for repeated measurements (MMRM) |
| Statistical analysis description: HbA1c measurements were analysed using MMRM with an unstructured covariance matrix. The model included treatment, visit, age group, prior antidiabetic therapy and interaction between prior antidiabetic therapy and age group as fixed factors and the HbA1c baseline value as covariate. Interactions between visit and all factors and covariates were also included in the model. | |
| Comparison groups | Insulin detemir + metformin + diet/exercise v Insulin NPH + metformin + diet/exercise |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 42 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| P-value | = 0.3075 ^[2] |
| Method | Mixed models analysis |
| Parameter estimate | Treatment contrast |
| Point estimate | 0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.74 |
| upper limit | 1.09 |

Notes:

[1] - Efficacy conclusions cannot be drawn from the analysis due to low number of subjects included in the trial.

[2] - P value is reported for one-sided test.

Secondary: Change in body weight standard deviation score (SDS)

| | |
|------------------------|--|
| End point title | Change in body weight standard deviation score (SDS) |
| End point description: | Change in body weight standard deviation score (SDS) from baseline to week 26. The SD scores were derived from the age and sex of the subjects and the body weight together with growth curves defined for the reference population (US population). |
| End point type | Secondary |
| End point timeframe: | From baseline to Week 26 |

| End point values | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 22 | | |
| Units: standard deviation score | | | | |
| arithmetic mean (standard deviation) | 0.006 (± 0.192) | 0.098 (± 0.139) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects achieving HbA1c <7.0%, who have not experienced any treatment emergent severe hypoglycaemic episodes within the last 14 weeks of treatment

| | |
|-----------------|---|
| End point title | Proportion of subjects achieving HbA1c <7.0%, who have not experienced any treatment emergent severe hypoglycaemic episodes within the last 14 weeks of treatment |
|-----------------|---|

End point description:

Percentage of subjects achieving HbA1c <7.0%, who have not experienced any treatment emergent severe hypoglycaemic episodes (an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions) within the last 14 weeks of treatment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At week 26 | |

| End point values | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 21 ^[3] | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 25 | 33.3 | | |

Notes:

[3] - Subjects who have been exposed for a minimum of 14 weeks are included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects achieving HbA1c <7.5%, who have not experienced any treatment emergent severe hypoglycaemic episodes within the last 14 weeks of treatment

| | |
|-----------------|---|
| End point title | Proportion of subjects achieving HbA1c <7.5%, who have not experienced any treatment emergent severe hypoglycaemic episodes within the last 14 weeks of treatment |
|-----------------|---|

End point description:

Percentage of subjects achieving HbA1c <7.5%, who have not experienced any treatment emergent severe hypoglycaemic episodes (an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions) within the last 14 weeks of treatment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Week 26 | |

| End point values | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 21 ^[4] | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 30 | 38.1 | | |

Notes:

[4] - Subjects who have been exposed for a minimum of 14 weeks contributed to the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Total number of treatment emergent nocturnal (23:00-06:59) severe or blood glucose (BG) confirmed symptomatic hypoglycaemic episodes

| | |
|---|--|
| End point title | Total number of treatment emergent nocturnal (23:00-06:59) severe or blood glucose (BG) confirmed symptomatic hypoglycaemic episodes |
| End point description: The total number of blood glucose confirmed symptomatic nocturnal (time of onset between 23:00 and 06:59 both inclusive) severe (an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions) or blood glucose confirmed symptomatic hypoglycaemic episodes (plasma glucose value <3.1 mmol/L [56 mg/dL] with symptoms consistent with hypoglycaemia) experienced by the subjects during the trial. | |
| End point type | Secondary |
| End point timeframe: During 26 weeks of treatment | |

| End point values | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise | | |
|-------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 22 | | |
| Units: Number of episodes | | | | |
| Severe | 0 | 0 | | |
| Blood glucose confirmed symptomatic | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Total number of treatment emergent severe or BG confirmed symptomatic hypoglycaemic episodes

| | |
|---|--|
| End point title | Total number of treatment emergent severe or BG confirmed symptomatic hypoglycaemic episodes |
| End point description: Total number of treatment emergent severe (an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions) or blood glucose confirmed symptomatic hypoglycaemic episodes (plasma glucose value <3.1 mmol/L [56 mg/dL] with symptoms consistent with hypoglycaemia) experienced by the subjects during the trial. | |
| End point type | Secondary |
| End point timeframe: During 26 weeks of treatment | |

| End point values | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 ^[5] | 22 ^[6] | | |
| Units: Number of episodes | | | | |
| Severe | 0 | 0 | | |
| BG confirmed symptomatic | 4 | 12 | | |

Notes:

[5] - One subject contributed to the events reported in this arm.

[6] - 5 subjects contributed to the events reported in this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of adverse events (AEs)

| | |
|-----------------|-----------------------------------|
| End point title | Incidence of adverse events (AEs) |
|-----------------|-----------------------------------|

End point description:

The total number of treatment emergent adverse events (the onset of the adverse event is on or after the first day of trial product administration, and no later than 7 days after the last day of trial product administration) reported during the 26 weeks of treatment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 26 weeks of treatment

| End point values | Insulin detemir + metformin + diet/exercise | Insulin NPH + metformin + diet/exercise | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 ^[7] | 22 ^[8] | | |
| Units: Number of events | 30 | 41 | | |

Notes:

[7] - AEs were reported by 8 subjects in this arm.

[8] - AEs were reported by 13 subjects in this arm.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events from the first trial-related activity (week -2) after the subject and/or his/her legally acceptable representative has signed the informed consent until the end of the trial (week 26).

Adverse event reporting additional description:

Safety analysis set included all subjects receiving at least one dose of randomised treatment. A treatment emergent adverse event was defined as an event that had the onset date on or after the first day of trial product administration, and no later than 7 days after the last day of trial product administration.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 19.0 |

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Insulin NPH + metformin + diet/exercise |
|-----------------------|---|

Reporting group description:

Subjects were treated with NPH 100 IU/mL administered subcutaneously in the thigh region once or twice daily for a period of 26 weeks. All subjects continued treatment with metformin on their pre-study dose(s) throughout the trial. The diet/exercise intervention was performed through changes in eating and activity behaviours.

| | |
|-----------------------|---|
| Reporting group title | Insulin detemir + metformin + diet/exercise |
|-----------------------|---|

Reporting group description:

Subjects were treated with insulin detemir 100 U/mL administered subcutaneously in the thigh region once or twice daily for a period of 26 weeks. All subjects continued treatment with metformin on their pre-study dose(s) throughout the trial. The diet/exercise intervention was performed through changes in eating and activity behaviours.

| Serious adverse events | Insulin NPH + metformin + diet/exercise | Insulin detemir + metformin + diet/exercise | |
|---|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 20 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 20 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Insulin NPH + metformin + diet/exercise | Insulin detemir + metformin + diet/exercise | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 22 (40.91%) | 8 / 20 (40.00%) | |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Soft tissue injury | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 3 / 20 (15.00%) | |
| occurrences (all) | 4 | 4 | |
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 2 / 20 (10.00%) | |
| occurrences (all) | 0 | 2 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 2 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 1 / 20 (5.00%) | |
| occurrences (all) | 1 | 1 | |
| Lip dry | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Toothache | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 20 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vomiting | | | |

| | | | |
|--|---------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 22 (0.00%) 0 | 2 / 20 (10.00%) 4 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 22 (13.64%) | 1 / 20 (5.00%) | |
| occurrences (all) | 3 | 1 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 4 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 2 / 20 (10.00%) | |
| occurrences (all) | 0 | 2 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Impetigo | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 20 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 20 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 1 / 20 (5.00%) | |
| occurrences (all) | 2 | 1 | |
| Viral infection | | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 29 April 2015 | <ul style="list-style-type: none">• Reduced the number of fasting visits, blood samples and assessments.• Clinic visit 3 had been changed to a phone contact.• The trial population was updated to include subjects who were treated with a maximum tolerated dose of metformin or who had documented complete metformin intolerance.• An additional exclusion criterion had been added.• Additional text regarding the informed consent process had been added. |

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.

| |
|---|
| The trial was terminated earlier than planned. Based on the low number of subjects, the conclusions should be interpreted with caution. |
|---|

Notes: