# Clinical trial results:
# A 26-week trial comparing the effect and safety of once weekly insulin icodec and once daily insulin degludec, both with or without non-insulin anti-diabetic drugs, in subjects with type 2 diabetes treated with basal insulin

## Summary

| | |
|---|---|
| EudraCT number | 2020-000454-10 |
| Trial protocol | DE PT BG |
| Global end of trial date | 01 March 2022 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 17 March 2023 |
| First version publication date | 17 March 2023 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | NN1436-4478 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04770532 |
| WHO universal trial number (UTN) | U1111-1247-4945 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Novo Nordisk A/S |
| Sponsor organisation address | Novo Allé, 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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 21 April 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 01 March 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to demonstrate the effect on glycaemic control of once weekly insulin icodec, with or without non-insulin anti-diabetic drugs, in subjects with type 2 diabetes (T2D) treated with basal insulin.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (64th World Medical Association (WMA) general Assembly; Oct 2013) and International Council for Harmonisation (ICH) Good Clinical Practice, including archiving of essential documents (Current Step 4 version, Nov 2016), and 21 Code of Federal Regulations (CFR) 312.120.

Background therapy:

After randomisation subjects continued their pre-trial non-insulin anti-diabetic background medication throughout the entire trial except from sulfonylureas and glinides, which had to be discontinued at randomisation.

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 05 March 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Bulgaria: 33 |
| Country: Number of subjects enrolled | Germany: 45 |
| Country: Number of subjects enrolled | Japan: 100 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 70 |
| Country: Number of subjects enrolled | Poland: 30 |
| Country: Number of subjects enrolled | Portugal: 29 |
| Country: Number of subjects enrolled | South Africa: 50 |
| Country: Number of subjects enrolled | Ukraine: 30 |
| Country: Number of subjects enrolled | United States: 139 |
| Worldwide total number of subjects | 526 |
| EEA total number of subjects | 137 |

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) | 0 |
| Adults (18-64 years) | 294 |
| From 65 to 84 years | 232 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at 71 sites in 9 countries as follows: United States of America (USA) (26), Ukraine (4), Portugal (6), Poland (3), Republic of Korea (7), Japan (9), Germany (6), Bulgaria (4), South Africa (6).

### Pre-assignment

Screening details:

After randomisation subjects continued their pre-trial non-insulin anti-diabetic background medication throughout the entire trial except from sulfonylureas and glinides, which had to be discontinued at randomisation.

### 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 Icodec |

Arm description:

Subjects were to receive once weekly subcutaneous (s.c.) injection of Insulin icodec for 26 weeks, using PDS290 prefilled pen-injector at a starting dose of 7 times the pre-trial total daily basal insulin dose + 50% of their 7 times total daily basal insulin dose. The following weekly dose was 7 times the total daily dose of the respective subjects ('unit to unit switch' approach: current daily dose x 7). Subjects were to perform once daily pre-breakfast self-monitoring plasma glucose (SMPG). The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 millimoles per liter (mmol/L): dose reduced by 3 units (U); 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 3 U.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Insulin icodec 700 U/mL PDS290 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Insulin icodec was administered once-weekly subcutaneously at a dose strength of 700 units/ milliliter (mL).

| | |
|---|---|
| **Arm title** | Insulin degludec |

Arm description:

Subjects were to receive once daily s.c. injection of Insulin degludec for 26 weeks, using PDS290 prefilled pen-injector at a dose in accordance with local label. Subjects were to perform once daily SMPG. The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 20 U.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tresiba 100 units/mL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Insulin degludec was administered once daily subcutaneously at a dose strength of 100 units/mL.

| **Number of subjects in period 1** | Insulin Icodec | Insulin degludec |
|---|---|---|
| Started | 263 | 263 |
| Full analysis set (FAS) | 263 | 263 |
| Safety analysis set (SAS) | 262 | 263 |
| Completed | 260 | 258 |
| Not completed | 3 | 5 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | - | 3 |
| Death | 2 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Insulin Icodec |
| Reporting group description: | |
| Subjects were to receive once weekly subcutaneous (s.c.) injection of Insulin icodec for 26 weeks, using PDS290 prefilled pen-injector at a starting dose of 7 times the pre-trial total daily basal insulin dose + 50% of their 7 times total daily basal insulin dose. The following weekly dose was 7 times the total daily dose of the respective subjects ('unit to unit switch' approach: current daily dose x 7). Subjects were to perform once daily pre-breakfast self-monitoring plasma glucose (SMPG). The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 millimoles per liter (mmol/L): dose reduced by 3 units (U); 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 3 U. | |
| Reporting group title | Insulin degludec |
| Reporting group description: | |
| Subjects were to receive once daily s.c. injection of Insulin degludec for 26 weeks, using PDS290 prefilled pen-injector at a dose in accordance with local label. Subjects were to perform once daily SMPG. The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 20 U. | |

| Reporting group values | Insulin Icodec | Insulin degludec | Total |
|---|---|---|---|
| Number of subjects | 263 | 263 | 526 |
| 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) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 145 | 149 | 294 |
| From 65-84 years | 118 | 114 | 232 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 62.35 | 62.60 | |
| standard deviation | ± 9.79 | ± 8.42 | - |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 101 | 123 | 224 |
| Male | 162 | 140 | 302 |

## End points

### End points reporting groups

| Reporting group title | Insulin Icodec |
|---|---|

Reporting group description:

Subjects were to receive once weekly subcutaneous (s.c.) injection of Insulin icodec for 26 weeks, using PDS290 prefilled pen-injector at a starting dose of 7 times the pre-trial total daily basal insulin dose + 50% of their 7 times total daily basal insulin dose. The following weekly dose was 7 times the total daily dose of the respective subjects ('unit to unit switch' approach: current daily dose x 7). Subjects were to perform once daily pre-breakfast self-monitoring plasma glucose (SMPG). The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 millimoles per liter (mmol/L): dose reduced by 3 units (U); 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 3 U.

| Reporting group title | Insulin degludec |
|---|---|

Reporting group description:

Subjects were to receive once daily s.c. injection of Insulin degludec for 26 weeks, using PDS290 prefilled pen-injector at a dose in accordance with local label. Subjects were to perform once daily SMPG. The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 20 U.

### Primary: Change in glycated haemoglobin (HbA1c)

| End point title | Change in glycated haemoglobin (HbA1c) |
|---|---|

End point description:

Change in HbA1c from baseline week 0 (V2) to week 26 (V28) was presented. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. Full analysis set (FAS) included all randomised subjects.

| End point type | Primary |
|---|---|

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

| **End point values** | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 263 | | |
| Units: Percentage (%) of HbA1c | | | | |
| least squares mean (standard error) | -0.93 (± 0.05) | -0.71 (± 0.06) | | |

### Statistical analyses

| **Statistical analysis title** | Statistical Analysis Set 1 |
|---|---|

Statistical analysis description:

The response and change from baseline in response after 26 weeks were analysed using an analysis of covariance (ANCOVA) model with treatment, region and personal continuous glucose monitoring (CGM) device use as fixed factors, and baseline response as covariate.

| | |
|---|---|
| Comparison groups | Insulin Icodec v Insulin degludec |
| Number of subjects included in analysis | 526 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[1] |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Treatment difference |
| Point estimate | -0.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.37 |
| upper limit | -0.08 |

Notes:

[1] - Non-inferiority of insulin icodec was considered confirmed if the upper limit of the two-sided 95% confidence interval (CI) for mean treatment difference (insulin icodec minus insulin degludec) was strictly below 0.3%.

## Secondary: Change in fasting plasma glucose (FPG)

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|---|---|
| End point title | Change in fasting plasma glucose (FPG) |

End point description:

Change in FPG from baseline week 0 (V2) to week 26 (V28) is presented. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

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

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

| End point values | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 260 | 257 | | |
| Units: millimoles per liter (mmol/L) | | | | |
| least squares mean (standard error) | -1.58 (± 0.12) | -1.62 (± 0.12) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time in target-range 3.9–10.0 mmol/L (70-180 milligrams per deciliter [mg/dL]) using continuous glucose monitoring (CGM) system, Dexcom G6

| | |
|---|---|
| End point title | Time in target-range 3.9–10.0 mmol/L (70-180 milligrams per deciliter [mg/dL]) using continuous glucose monitoring (CGM) system, Dexcom G6 |

End point description:

Percentage of time in target-range 3.9–10.0 mmol/L (70-180 milligrams per deciliter [mg/dL]) using

continuous glucose monitoring (CGM) system, Dexcom G6 is presented. Time in target range is defined as 100 times the number of recorded measurements in glycaemic target range 3.9-10.0 mmol/L (70-180 mg/dL), both inclusive, divided by the total number of recorded measurements. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

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

End point timeframe:

From week 22 (V24) to week 26 (V28)

| **End point values** | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 238 | 239 | | |
| Units: Percentage (%) of time | | | | |
| arithmetic mean (standard deviation) | 63.13 (± 17.40) | 59.50 (± 18.92) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change in DTSQs (Diabetes Treatment Satisfaction Questionnaire) in total treatment satisfaction

| End point title | Change in DTSQs (Diabetes Treatment Satisfaction Questionnaire) in total treatment satisfaction |
|---|---|

End point description:

Change in DTSQs in total treatment satisfaction is presented. The DTSQ domain score was calculated by adding six item scores of items 1 and 4-8. Higher scores indicate higher levels of treatment satisfaction for items 1, 4 -8. For items 2 and 3, a higher score indicates a subject perceived experience of hyperglycaemia and hypoglycaemia. Lower scores indicate that blood glucose levels were unacceptably high (item 2) or low (item 3). The score has a minimum of 0 and a maximum of 36. The endpoint data was evaluated based on in-trial observation period. The period started at randomisation and ended at the date of: Last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, Last subject-investigator contact as defined by investigator for subjects who were lost to follow-up and death for subjects who died before any of the above. FAS included all randomised subjects. Number of subjects analysed=subjects with available data for this endpoint.

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

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

| End point values | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 252 | 244 | | |
| Units: Score on a scale | | | | |
| least squares mean (standard error) | 4.22 (± 0.30) | 2.96 (± 0.31) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of severe hypoglycaemic episodes (level 3)

| End point title | Number of severe hypoglycaemic episodes (level 3) |
|---|---|

End point description:

Number of severe hypoglycaemic episodes (level 3) is presented. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. The endpoint data was evaluated based on the on-treatment observation period. The on-treatment period started at the date of first dose of trial product as recorded on the electronic case report form (eCRF), and ended at the first date of any of the following: The end of trial visit (V30), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin (corresponding to 5 weeks after the end of the dosing interval for both treatment arms) and the end-date for the in-trial observation period. The on-treatment period represented the time period in which a subject was considered exposed to trial product. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

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

End point timeframe:

From baseline week 0 (V2) to week 31 (V30)

| End point values | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 262 | 263 | | |
| Units: Episodes | | | | |
| number (not applicable) | 0 | 1 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L [54 mg/dL], confirmed by blood glucose [BG] meter)

| End point title | Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L [54 mg/dL], confirmed by blood glucose [BG] meter) |
|---|---|

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 millimoles per liter [mmol/L] (54 mg/dL), confirmed by BG meter) is presented. Clinically significant hypoglycaemia (level 2) is defined as plasma glucose value of less than (<) 3.0 mmol/L (54 mg/dL) confirmed by BG meter. The endpoint

data was evaluated based on on-treatment observation period. On-treatment period started at the date of first dose of trial product and ended at the first date of any of the following: End of trial visit (V30), Last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin (corresponding to 5 weeks after the end of dosing interval for both treatment arms) and the end-date for in-trial observation period. The on-treatment period represented the time period in which a subject was considered exposed to trial product. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

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

End point timeframe:

From baseline week 0 (V2) to week 31 (V30)

| **End point values** | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 262 | 263 | | |
| Units: Episodes | | | | |
| number (not applicable) | 113 | 41 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3)

| End point title | Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) |
|---|---|

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) is presented. Clinically significant hypoglycaemia (level 2) is defined as plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. The endpoint data was evaluated based on on-treatment observation period. On-treatment period started at the date of first dose of trial product and ended at the first date of any of the following: The end of trial visit (V30), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin and the end-date for in-trial observation period. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

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

End point timeframe:

From baseline week 0 (V2) to week 31 (V30)

| End point values | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 262 | 263 | | |
| Units: Episodes | | | | |
| number (not applicable) | 113 | 42 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time spent < 3.0 mmol/L (54 mg/dL) using continuous glucose monitoring (CGM) system, Dexcom G6

| End point title | Time spent < 3.0 mmol/L (54 mg/dL) using continuous glucose monitoring (CGM) system, Dexcom G6 |
|---|---|

End point description:

Percentage of time spent less than (<) 3.0 mmol/L (54 mg/dL) using CGM system, Dexcom G6 is presented. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. Full analysis set included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

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

End point timeframe:

From week 22 (V24) to week 26 (V28)

| End point values | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 238 | 239 | | |
| Units: Percentage of time | | | | |
| arithmetic mean (standard deviation) | 0.34 (± 0.88) | 0.22 (± 0.45) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time spent > 10 mmol/L (180 mg/dL) using CGM system, Dexcom G6

| End point title | Time spent > 10 mmol/L (180 mg/dL) using CGM system, Dexcom G6 |
|---|---|

End point description:

Percentage of time spent > 10 mmol/L (180 mg/dL) using CGM system, Dexcom G6 is presented. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. Full analysis set included all randomised subjects. Number of subjects

analyzed = subjects with available data for this endpoint.

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

End point timeframe:

From week 22 (V24) to week 26 (V28)

| **End point values** | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 238 | 239 | | |
| Units: Percentage of time | | | | |
| arithmetic mean (standard deviation) | 35.52 (± 17.95) | 39.71 (± 19.34) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean weekly insulin dose

| End point title | Mean weekly insulin dose |
|---|---|

End point description:

Mean weekly insulin dose is presented. The endpoint data was evaluated based on the on-treatment observation period. The on-treatment period started at the date of first dose of trial product as recorded on the electronic case report form (eCRF), and ended at the first date of any of the following: The end of trial visit (V30), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin (corresponding to 5 weeks after the end of the dosing interval for both treatment arms) and the end-date for the in-trial observation period. The on-treatment period represented the time period in which a subject was considered exposed to trial product. FAS included all randomised subjects.

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

End point timeframe:

From week 24 (V26) to week 26 (V28)

| **End point values** | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 263 | | |
| Units: Units of Insulin | | | | |
| least squares mean (confidence interval 95%) | 267.96 (252.19 to 284.70) | 244.22 (229.99 to 259.33) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in body weight

| End point title | Change in body weight |
|---|---|

End point description:

Change in body weight from baseline week 0 (V2) to week 26 (V28) is presented. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. Full analysis set included all randomised subjects.

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

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

| **End point values** | Insulin Icodec | Insulin degludec | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 263 | | |
| Units: Kilograms (kg) | | | | |
| least squares mean (standard error) | 1.40 (± 0.32) | -0.30 (± 0.36) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From baseline (Week 0) to Week 31

Adverse event reporting additional description:

Safety analysis set included all randomised subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product. A treatment-emergent AE (TEAE) was defined as an AE that initiated or worsened on or after the date of first dose of study drug up to the end of trial (week 31). All presented AEs are treatment emergent.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Insulin Degludec |

Reporting group description:

Subjects were to receive once daily s.c. injection of Insulin degludec for 26 weeks, using PDS290 prefilled pen-injector at a dose in accordance with local label. Subjects were to perform once daily SMPG. The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 20 U.

| | |
|---|---|
| Reporting group title | Insulin Icodec |

Reporting group description:

Subjects were to receive once weekly subcutaneous (s.c.) injection of Insulin icodec for 26 weeks, using PDS290 prefilled pen-injector at a starting dose of 7 times the pre-trial total daily basal insulin dose + 50% of their 7 times total daily basal insulin dose. The following weekly dose was 7 times the total daily dose of the respective subjects ('unit to unit switch' approach: current daily dose x 7). Subjects were to perform once daily pre-breakfast self-monitoring plasma glucose (SMPG). The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 millimoles per liter (mmol/L): dose reduced by 3 units (U); 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 3 U.

| Serious adverse events | Insulin Degludec | Insulin Icodec | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 263 (6.08%) | 22 / 262 (8.40%) | |
| number of deaths (all causes) | 2 | 2 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer stage II | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic myeloid leukaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric cancer | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic carcinoma metastatic | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Toe amputation | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Hand fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombotic stroke | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Thalamic infarction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal vein occlusion | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastric dysplasia | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic pseudocyst | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Renal and urinary disorders | | | |
| Urethral stenosis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenocortical insufficiency acute | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 2 / 263 (0.76%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polymyalgia rheumatica | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| COVID-19 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 263 (0.00%) | 2 / 262 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 2 / 262 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraspinal abscess | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 2 / 262 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 262 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 262 (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 Degludec | Insulin Icodec | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 39 / 263 (14.83%) | 50 / 262 (19.08%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 9 / 263 (3.42%) | 14 / 262 (5.34%) | |
| occurrences (all) | 10 | 20 | |
| Eye disorders | | | |
| Diabetic retinopathy | | | |
| subjects affected / exposed | 16 / 263 (6.08%) | 10 / 262 (3.82%) | |
| occurrences (all) | 17 | 11 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 263 (3.42%) | 14 / 262 (5.34%) | |
| occurrences (all) | 9 | 17 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 10 / 263 (3.80%) | 22 / 262 (8.40%) | |
| occurrences (all) | 14 | 28 | |

## 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