Clinical trial results:
Efficacy and Safety of Once Weekly Insulin Icodec Compared to Once Daily Insulin Degludec 100 Units/mL, Both in Combination With Insulin Aspart, in Adults With Type 1 Diabetes. A 26-week, Randomised, Multicentre, Open-label, Active-controlled, Parallel Group, Two Armed, Treat-to-target Trial Investigating the Effect on Glycaemic Control and Safety of Treatment With Once Weekly Insulin Icodec Compared to Once Daily Insulin Degludec, Both in Combination With Insulin Aspart in Adults With Type 1 Diabetes, With a 26-week Extension Investigating Long Term Safety

Summary

EudraCT number	2020-002374-27
Trial protocol	DE NL AT IT
Global end of trial date	02 December 2022

Results information

Result version number	v1 (current)
This version publication date	17 December 2023
First version publication date	17 December 2023

Trial information

Trial identification

Sponsor protocol code	NN1436-4625

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04848480
WHO universal trial number (UTN)	U1111-1251-7315
Other trial identifiers	Japanese trial registration number: jRCT2031210031

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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

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

Global end of trial reached?	Yes
Global end of trial date	02 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the effect on glycaemic control of once weekly insulin icodec in combination with insulin aspart, in subjects with T1D. This includes comparing the difference in change from baseline in HbA1c between once weekly insulin icodec and once daily insulin degludec both in combination with insulin aspart after 26 weeks of treatment to a non-inferiority limit of 0.3%.

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 of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, including archiving of essential documents (Current Step 4 version, Nov 2016), and 21 US Code of Federal Regulations (CFR) 312.120.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	30 April 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	Austria: 15
Country: Number of subjects enrolled	Canada: 29
Country: Number of subjects enrolled	Germany: 46
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	United Kingdom: 45
Country: Number of subjects enrolled	India: 36
Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Japan: 80
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Russian Federation: 67
Country: Number of subjects enrolled	Turkey: 31
Country: Number of subjects enrolled	United States: 162

Worldwide total number of subjects	582
EEA total number of subjects	132

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)	538
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 97 sites in 12 countries as follows (number of sites that screened subjects/ number of sites that randomised subject): Austria-(6/6), Canada-(5/5), Germany-(8/8), India-(6/6), Italy-(5/5), Japan-(7/7), Netherlands-(3/3), Russia-(10/10), Spain-(4/4), Turkey-(7/7), United Kingdom-(8/8), United States-(29/28).

Pre-assignment

Screening details:

This was a 52-week trial. The first 26 weeks of the trial constituted the main phase which was followed by a 26-week extension phase with focus on evaluating long term safety and provide long-term exposure data.

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 + insulin aspart

Arm description:

Subjects received insulin icodec with insulin aspart for 52 weeks subcutaneously. Subjects received once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 7 times the pre-trial total daily basal insulin dose + 50% or 100% of their 7 times total daily basal insulin dose depending on insulin regime and HbA1c level. Following weekly dose was 7 times the total daily dose of 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 2 previous days and the day of 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. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Arm type	Experimental
Investigational medicinal product name	Insulin aspart
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin aspart was administered s.c. for 52 weeks. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Investigational medicinal product name	Insulin icodec
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Once weekly s.c. injection of insulin icodec was administered using PDS290 prefilled pen-injector for 52 weeks.

Arm title	Insulin degludec + insulin aspart

Arm description:

Subjects received insulin degludec along with insulin aspart for 52 weeks subcutaneously. Subjects received once daily s.c. injection of insulin degludec 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 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. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime SMPG measured weekly.

Arm type	Experimental
Investigational medicinal product name	Insulin aspart
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin aspart was administered s.c. for 52 weeks. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Investigational medicinal product name	Insulin degludec
Investigational medicinal product code	
Other name	Tresiba 100 units/mL solution for injection in pre-filled pen
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Once daily s.c. injection of insulin degludec was administered using PDS290 prefilled pen-injector for 52 weeks.

Number of subjects in period 1	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart
Started	290	292
Completed	274	281
Not completed	16	11
Physician decision	1	-
Consent withdrawn by subject	13	9
Death	1	-
Lost to follow-up	1	2

Baseline characteristics

Reporting groups

Reporting group title	Insulin icodec + insulin aspart

Reporting group description:

Subjects received insulin icodec with insulin aspart for 52 weeks subcutaneously. Subjects received once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 7 times the pre-trial total daily basal insulin dose + 50% or 100% of their 7 times total daily basal insulin dose depending on insulin regime and HbA1c level. Following weekly dose was 7 times the total daily dose of 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 2 previous days and the day of 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. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Reporting group title	Insulin degludec + insulin aspart

Reporting group description:

Subjects received insulin degludec along with insulin aspart for 52 weeks subcutaneously. Subjects received once daily s.c. injection of insulin degludec 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 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. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime SMPG measured weekly.

Reporting group values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart	Total
Number of subjects	290	292	582
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	267	271	538
From 65-84 years	23	21	44
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	44.08	44.28	
standard deviation	± 14.07	± 14.07	-
Gender Categorical Units: Subjects			
Female	125	120	245
Male	165	172	337

End points

End points reporting groups

Reporting group title	Insulin icodec + insulin aspart

Reporting group description:

Subjects received insulin icodec with insulin aspart for 52 weeks subcutaneously. Subjects received once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 7 times the pre-trial total daily basal insulin dose + 50% or 100% of their 7 times total daily basal insulin dose depending on insulin regime and HbA1c level. Following weekly dose was 7 times the total daily dose of 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 2 previous days and the day of 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. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Reporting group title	Insulin degludec + insulin aspart

Reporting group description:

Subjects received insulin degludec along with insulin aspart for 52 weeks subcutaneously. Subjects received once daily s.c. injection of insulin degludec 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 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. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime SMPG measured weekly.

Primary: Change in Glycosylated Haemoglobin (HbA1c) at Week 26

End point title	Change in Glycosylated Haemoglobin (HbA1c) at Week 26

End point description:

Change in HbA1c from baseline to week 26 is presented. Data is reported for 'in-trial' 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); death for subjects who died before any of the above. Full analysis set included all randomised subjects.

End point type	Primary

End point timeframe:

From baseline (week 0) to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Percentage of HbA1c				
least squares mean (standard error)	-0.47 (± 0.07)	-0.51 (± 0.06)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Change from baseline in HbA1c after 26 weeks was analysed using ANCOVA model with treatment, region, HbA1c group at screening and pre-trial basal
insulin treatment as fixed factors, and baseline response as covariate. Non-inferiority was considered confirmed if the estimated treatment difference was below 0.3%.

Comparison groups	Insulin icodec + insulin aspart v Insulin degludec + insulin aspart
Number of subjects included in analysis	582
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0065
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.23

Secondary: Change in Glycosylated Haemoglobin (HbA1c) at Week 52

End point title	Change in Glycosylated Haemoglobin (HbA1c) at Week 52

End point description:

Change in HbA1c from baseline to week 52 is presented. Data is reported for 'in-trial' 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); 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) to week 52

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Percentage of HbA1c				
least squares mean (standard error)	-0.37 (± 0.05)	-0.54 (± 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Diabetes Treatment Satisfaction Questionnaire (DTSQs) in Total Treatment Satisfaction

End point title	Change in Diabetes Treatment Satisfaction Questionnaire (DTSQs) in Total Treatment Satisfaction

End point description:

Change in DTSQs in total treatment satisfaction from baseline to week 26 is presented. The sum score for DTSQ in total treatment satisfaction was calculated by adding the six item scores of items 1, 4, 5, 6, 7 and 8. The sum score for DTSQ can range from 0 to 36, with 0 being the lowest and 36 being the highest score in total treatment satisfaction. Higher scores on the DTSQ total score indicate higher treatment satisfaction. Data is reported for 'in-trial' 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); death for subjects who died before any of the above. Full analysis set included all randomised subjects. Number of Subjects Analyzed = Subjects with sufficient available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	291		
Units: Score on a scale				
least squares mean (standard error)	1.97 (± 0.27)	3.06 (± 0.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Time in Range 3.9–10.0 mmol/L (70-180 Milligrams Per Deciliter [mg/dL]) Using Continuous Glucose Monitoring (CGM) System

End point title	Percentage of Time in Range 3.9–10.0 mmol/L (70-180 Milligrams Per Deciliter [mg/dL]) Using Continuous Glucose Monitoring (CGM) System

End point description:

Percentage of time in range 3.9–10.0 mmol/L (70-180 mg/dL) using CGM system from week 22 to week 26 is presented. Time in range is defined as 100 times the number of recorded measurements in glycaemic range 3.9-10.0 mmol/L (70-180 mg/dL), both inclusive, divided by the total number of recorded measurements. Data is reported for 'in-trial' 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); death for subjects who died before any of the above. Full analysis set included all randomised subjects. Number of Subjects Analyzed = Subjects with sufficient available data.

End point type	Secondary

End point timeframe:

From week 22 to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	272		
Units: Percentage of time				
arithmetic mean (standard deviation)	59.10 (± 15.66)	60.85 (± 15.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Fasting Plasma Glucose (FPG)

End point title	Change in Fasting Plasma Glucose (FPG)

End point description:

Change in FPG from baseline to week 26 is presented. Data is reported for 'in-trial' period. In-trial observation period started at randomisation and ended at the date of: the last direct subjects-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); death for subjects who died before any of the above. Full analysis set included all randomised subjects. Number of Subjects Analyzed = Subjects with sufficient available data.

End point type	Secondary

End point timeframe:

From baseline (week 0) to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	287		
Units: millimoles per liter (mmol/l)				
least squares mean (standard error)	-0.84 (± 0.20)	-1.87 (± 0.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 26

End point title	Number of Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 26

End point description:

Number of severe hypoglycaemic episodes (level 3) from baseline to week 26 are presented. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Data is reported for 'main-on-treatment' period. The main-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 date of the on-treatment period; week 26. On-treatment: Onset date on or after the first dose of trial product and no later than

the first date of either the follow-up visit, the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for the in-trial 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) to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Episodes				
number (not applicable)	47	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 57

End point title	Number of Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 57

End point description:

Number of severe hypoglycaemic episodes (level 3) from baseline to week 57 are presented. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Data is reported for 'on-treatment' period. The on-treatment period: Onset date on or after the first dose of trial product and no later than the first date of either the follow-up visit (FU2), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for the in-trial 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) to week 57

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Episodes				
number (not applicable)	56	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL) Confirmed by Blood Glucose [BG] Meter): From Baseline (Week 0) to Week 26

End point title	Number of Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL) Confirmed by Blood Glucose [BG] Meter): From Baseline (Week 0) to Week 26

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) from baseline to week 26 are 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. Data is reported for 'main-on-treatment' period. The main-on-treatment period started at the date of first dose of trial product as recorded on the eCRF, and ended at the first date of any of the following: the end date of the on-treatment period; week 26. The on-treatment period: Onset date on or after the first dose of trial product and no later than the first date of either the follow-up visit (FU2), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for the in-trial 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) to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Episodes				
number (not applicable)	2789	1478		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL), Confirmed by BG Meter) or Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 26

End point title	Number of Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL), Confirmed by BG Meter) or Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 26

End point description:

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. Data is reported for 'main-on-treatment' period, started at date of 1st dose of trial product as recorded on eCRF, and ended at first date of any of following: end date of on-treatment period; week 26. On-treatment period: Onset date on or after first dose of trial product and no later than first date of either follow-up visit (FU2), last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or end-date for in-trial 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) to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Episodes				
number (not applicable)	2836	1495		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL) Confirmed by BG Meter): From Baseline (Week 0) to Week 57

End point title	Number of Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL) Confirmed by BG Meter): From Baseline (Week 0) to Week 57

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) from baseline to week 57 are 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. Data is reported for 'on-treatment' period. The on-treatment period: Onset date on or after the first dose of trial product and no later than the first date of either the follow-up visit (FU2), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for the in-trial 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) to week 57

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Episodes				
number (not applicable)	5047	2811		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Nocturnal Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL), Confirmed by BG Meter) or Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 26

End point title	Number of Nocturnal Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL), Confirmed by BG Meter) or Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 26

End point description:

Nocturnal: The period between 00:01 and 05:59 (both included). Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Data is reported for 'main-on-treatment' period. The main-on-treatment period started at the date of first dose of trial product as recorded on the eCRF, and ended at the first date of any of the following: the end date of the on-treatment period; week 26. On-treatment period: Onset date on or after first dose of trial product and no later than first date of either follow-up visit, last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for in-trial 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) to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Episodes				
number (not applicable)	481	227		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL), Confirmed by BG Meter) or Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 57

End point title	Number of Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL), Confirmed by BG Meter) or Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 57

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) or severe hypoglycaemic episodes (level 3) from baseline to week 57 are 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. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Data is reported for 'on-treatment' period. The on-treatment period: Onset date on or after the first dose of trial product and no later than the first date of either the follow-up visit (FU2), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for the in-trial 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) to week 57

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Episodes				
number (not applicable)	5103	2836		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Time spent Less Than (<) 3.0 mmol/L (54 mg/dL) Using Continuous Glucose Monitoring (CGM) System

End point title	Percentage of Time spent Less Than (<) 3.0 mmol/L (54 mg/dL) Using Continuous Glucose Monitoring (CGM) System

End point description:

Percentage of time spent < 3.0 mmol/L using CGM system from week 22 to week 26 is presented. Time spent below threshold (< 3.0 mmol/L [54 mg/dL]) was defined as 100 times the number of recorded measurements below the threshold, divided by the total number of recorded measurements. Data is reported for 'in-trial' period. In-trial observation period started at randomisation and ended at the date of: the last direct participant-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); death for participants who died before any of the above. Full analysis set included all randomised subjects. Number of Subjects Analyzed = Subjects with sufficient available data.

End point type	Secondary

End point timeframe:

From week 22 to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	272		
Units: Percentage of time				
arithmetic mean (standard deviation)	1.02 (± 1.64)	0.68 (± 1.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Nocturnal Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL), Confirmed by BG Meter) or Severe

Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 57

End point title	Number of Nocturnal Clinically Significant Hypoglycaemic Episodes (Level 2) (Less Than 3.0 mmol/L (54 mg/dL), Confirmed by BG Meter) or Severe Hypoglycaemic Episodes (Level 3): From Baseline (Week 0) to Week 57

End point description:

Number of nocturnal clinically significant hypoglycaemic episodes (level 2) or severe hypoglycaemic episodes (level 3) from baseline to week 57 are presented. Nocturnal: The period between 00:01 and 05:59 (both included). Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Data is reported for 'on-treatment' period. The on-treatment period: Onset date on or after the first dose of trial product and no later than the first date of either the follow-up visit (FU2), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for the in-trial 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) to week 57

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: Episodes				
number (not applicable)	870	462		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Time spent Greater Than (>) 10 mmol/L (180 mg/dL) Using Continuous Glucose Monitoring (CGM) System

End point title	Percentage of Time spent Greater Than (>) 10 mmol/L (180 mg/dL) Using Continuous Glucose Monitoring (CGM) System

End point description:

Percentage of time spent > 10 mmol/L using CGM system from week 22 to week 26 is presented. Time spent above threshold (> 10 mmol/L [180 mg/dL]) was defined as 100 times the number of recorded measurements above the threshold, divided by the total number of recorded measurements. Data is reported for 'in-trial' 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); death for participants who died before any of the above. Full analysis set included all randomised subjects. Number of Subjects Analyzed = Subjects with sufficient available data.

End point type	Secondary

End point timeframe:

From week 22 to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	272		
Units: Percentage of time				
arithmetic mean (standard deviation)	37.03 (± 16.21)	36.25 (± 15.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Total Weekly Insulin Dose: From Week 24 to Week 26

End point title	Mean Total Weekly Insulin Dose: From Week 24 to Week 26

End point description:

Mean total weekly insulin dose from week 24 to week 26 is presented. Data is reported for 'main-on-treatment' period. The main-on-treatment period started at the date of first dose of trial product as recorded on the eCRF, and ended at the first date of any of the following: the end date of the on-treatment period; week 26. The on-treatment period: Onset date on or after the first dose of trial product and no later than the first date of either the follow-up visit (FU2), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for the in-trial period. Full analysis set included all randomised subjects. Number of Subjects Analyzed = Subjects with sufficient available data.

End point type	Secondary

End point timeframe:

From week 24 to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	271		
Units: Units of insulin				
least squares mean (confidence interval 95%)	310.52 (295.70 to 326.08)	322.68 (307.46 to 338.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Total Weekly Insulin Dose: From Week 50 to Week 52

End point title	Mean Total Weekly Insulin Dose: From Week 50 to Week 52

End point description:

Mean total weekly insulin dose from week 50 to week 52 is presented. Data is reported for 'on-treatment' period. The on-treatment period: Onset date on or after the first dose of trial product and no later than the first date of either the follow-up visit (FU2), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin or the end-date for the in-trial period. Full

analysis set included all randomised subjects. Number of Subjects Analyzed = Subjects with sufficient available data.

End point type	Secondary

End point timeframe:

From week 50 to week 52

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273	269		
Units: Units of insulin				
least squares mean (confidence interval 95%)	310.14 (294.85 to 326.22)	328.90 (312.86 to 345.75)		

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 to week 26 is presented. Data is reported for 'in-trial' 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); 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) to week 26

End point values	Insulin icodec + insulin aspart	Insulin degludec + insulin aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	292		
Units: kilograms				
least squares mean (standard error)	1.29 (± 0.23)	1.01 (± 0.23)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Week 1 to week 57

Adverse event reporting additional description:

Treatment emergent adverse events that had onset date during on-treatment period: started 1st dose date of trial product as recorded on eCRF & ended at 1st date of any of: end of trial V56, last date on trial product+5 weeks for once daily insulin &+6 weeks for once weekly insulin, end-date for in-trial observation period. Safety analysis set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Insulin degludec + insulin aspart

Reporting group description:

Subjects received insulin degludec along with insulin aspart for 52 weeks subcutaneously. Subjects received once daily s.c. injection of insulin degludec 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 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. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime SMPG measured weekly.

Reporting group title	Insulin icodec + insulin aspart

Reporting group description:

Subjects received insulin icodec with insulin aspart for 52 weeks subcutaneously. Subjects received once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 7 times the pre-trial total daily basal insulin dose + 50% or 100% of their 7 times total daily basal insulin dose depending on insulin regime and HbA1c level. Following weekly dose was 7 times the total daily dose of 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 2 previous days and the day of 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. Dose titration of insulin aspart was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Serious adverse events	Insulin degludec + insulin aspart	Insulin icodec + insulin aspart	
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 292 (6.85%)	24 / 290 (8.28%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Brachiocephalic artery stenosis			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cardiac ablation			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site dermatitis			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose fluctuation			

subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product administration error			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	2 / 292 (0.68%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myocardial ischaemia			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypoglycaemic unconsciousness			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			
subjects affected / exposed	1 / 292 (0.34%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Proctitis ulcerative			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar hernia			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cystitis escherichia			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (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 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	1 / 292 (0.34%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (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	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 292 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			

subjects affected / exposed	1 / 292 (0.34%)	8 / 290 (2.76%)	
occurrences causally related to treatment / all	1 / 1	12 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	1 / 292 (0.34%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	1 / 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 aspart	Insulin icodec + insulin aspart	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	162 / 292 (55.48%)	145 / 290 (50.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 292 (5.48%)	17 / 290 (5.86%)	
occurrences (all)	22	27	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	20 / 292 (6.85%)	16 / 290 (5.52%)	
occurrences (all)	25	22	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	26 / 292 (8.90%)	24 / 290 (8.28%)	
occurrences (all)	29	28	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	15 / 292 (5.14%)	12 / 290 (4.14%)	
occurrences (all)	16	13	
Back pain			
subjects affected / exposed	17 / 292 (5.82%)	5 / 290 (1.72%)	
occurrences (all)	31	5	
Infections and infestations			
COVID-19			

subjects affected / exposed	83 / 292 (28.42%)	74 / 290 (25.52%)	
occurrences (all)	88	80	
Upper respiratory tract infection			
subjects affected / exposed	11 / 292 (3.77%)	15 / 290 (5.17%)	
occurrences (all)	13	18	
Nasopharyngitis			
subjects affected / exposed	61 / 292 (20.89%)	48 / 290 (16.55%)	
occurrences (all)	84	75	

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