Clinical trial results:
A randomised, cross-over, open-label, multi-centre trial comparing the effect of insulin degludec and insulin glargine 100 Units per milliliter (U/mL), with or without OADs in subjects with type 2 diabetes using flash glucose monitoring

Summary

EudraCT number	2017-004047-20
Trial protocol	PL SK
Global end of trial date	27 December 2019

Results information

Result version number	v1 (current)
This version publication date	01 January 2021
First version publication date	01 January 2021

Trial information

Trial identification

Sponsor protocol code	NN1250-4419

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03687827
WHO universal trial number (UTN)	U1111-1203-0580

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, +1 866 8677178, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, +1 866 8677178, 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	04 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2019
Global end of trial reached?	Yes
Global end of trial date	27 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Percentage of time spent in glycaemic target range 70-180 milligrams per deciliter (mg/dL) (3.9–10.0 (millimoles per litre) mmol/L) both inclusive, using flash glucose monitoring (FGM).

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, adopted by the 18th World Medical Association (WMA) General Assembly, Helsinki, Finland, June 1964, and subsequent amendments and International Council for Harmonisation (ICH) Good Clinical Practice (GCP) European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use CHMP)/ICH/135/1995), including archiving of essential documents and the European Union Clinical Trial Directive (CTD)2001/20/EC.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	02 October 2018
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	Canada: 80
Country: Number of subjects enrolled	Poland: 66
Country: Number of subjects enrolled	Slovakia: 58
Country: Number of subjects enrolled	United States: 253
Country: Number of subjects enrolled	South Africa: 41
Worldwide total number of subjects	498
EEA total number of subjects	124

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)	257
From 65 to 84 years	236
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

The trial was conducted in 5 countries as follows:
Canada: 10 sites, Poland: 5 sites, Slovakia: 10 sites, South Africa: 7 sites, United States of America: 34 sites

Pre-assignment

Screening details:

This was a cross-over trial. The trial included a 2-week run-in period (which was after the screening visit) for eligibility assessment in regard to adherence to FGM requirements. The subjects were randomised into one of two treatment sequences.

Period 1

Period 1 title	Treatment Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence A: Insulin degludec then Insulin glargine

Arm description:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin degludec 100 Units per milliliter (U/mL) once daily (in treatment period 1), followed by a s.c. injection of Insulin glargine 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

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

Dosage and administration details:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin degludec 100U/mL once daily (in treatment period 1 and 2), for 36 weeks with or without oral anti-diabetic drugs using flash glucose monitoring.

Arm title	Sequence B: Insulin glargine then Insulin degludec

Arm description:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin glargine 100U/mL once daily (in treatment period 1), followed by a s.c. injection of Insulin degludec 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Arm type	Active comparator
Investigational medicinal product name	Insulin glargine
Investigational medicinal product code	
Other name	Lantus®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin glargine 100U/mL once daily (in treatment period 1 and 2), for 36 weeks with or without oral anti-diabetic drugs using flash glucose monitoring.

Number of subjects in period 1	Sequence A: Insulin degludec then Insulin glargine	Sequence B: Insulin glargine then Insulin degludec
Started	249	249
Completed	235	241
Not completed	14	8
Adverse event, serious fatal	-	1
Consent withdrawn by subject	7	3
Physician decision	5	2
Lost to follow-up	2	2

Period 2

Period 2 title	Treatment Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence A: Insulin degludec then Insulin glargine

Arm description:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin degludec 100U/mL once daily (in treatment period 1), followed by a s.c. injection of Insulin glargine 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

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

Dosage and administration details:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin degludec 100U/mL once daily (in treatment period 1 and 2), for 36 weeks with or without oral anti-diabetic drugs using flash glucose monitoring.

Arm title	Sequence B: Insulin glargine then Insulin degludec

Arm description:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin glargine 100U/mL once daily (in treatment period 1), followed by a s.c. injection of Insulin degludec 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Arm type	Active comparator

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

Dosage and administration details:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin glargine 100U/mL once daily (in treatment period 1 and 2), for 36 weeks with or without oral anti-diabetic drugs using flash glucose monitoring.

Number of subjects in period 2	Sequence A: Insulin degludec then Insulin glargine	Sequence B: Insulin glargine then Insulin degludec
Started	235	241
Completed	230	238
Not completed	5	3
Consent withdrawn by subject	1	2
Physician decision	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period 1
Reporting group description:	
Subjects were to receive either a subcutaneous (s.c.) injection of Insulin degludec 100U/mL once daily or a s.c. injection of Insulin glargine 100U/mL once daily (during treatment period 1 followed by treatment period 2); with or without oral anti-diabetic drugs using flash glucose monitoring.	

Reporting group values	Treatment Period 1	Total	
Number of subjects	498	498	
Age Categorical Units: Subjects			
Adults (18-64 years)	257	257	
From 65-84 years	236	236	
85 years and over	5	5	
Age Continuous Units: years			
arithmetic mean	62.8		
standard deviation	± 9.8	-	
Gender Categorical Units: Subjects			
Female	259	259	
Male	239	239	

End points

End points reporting groups

Reporting group title	Sequence A: Insulin degludec then Insulin glargine

Reporting group description:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin degludec 100 Units per milliliter (U/mL) once daily (in treatment period 1), followed by a s.c. injection of Insulin glargine 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Reporting group title	Sequence B: Insulin glargine then Insulin degludec

Reporting group description:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin glargine 100U/mL once daily (in treatment period 1), followed by a s.c. injection of Insulin degludec 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Reporting group title	Sequence A: Insulin degludec then Insulin glargine

Reporting group description:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin degludec 100U/mL once daily (in treatment period 1), followed by a s.c. injection of Insulin glargine 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Reporting group title	Sequence B: Insulin glargine then Insulin degludec

Reporting group description:

Subjects were to receive a subcutaneous (s.c.) injection of Insulin glargine 100U/mL once daily (in treatment period 1), followed by a s.c. injection of Insulin degludec 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Subject analysis set title	Insulin degludec 100U/mL
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects were to receive a subcutaneous (s.c.) injection of insulin degludec 100U/mL, once daily, in any of the treatment period, with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Subject analysis set title	Insulin glargine 100U/mL
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects were to receive a subcutaneous (s.c.) injection of insulin glargine 100U/mL, once daily, in any of the treatment period, with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Primary: Percentage of time spent in glycaemic target range 70-180 mg/dL (3.9–10.0 mmol/L) both inclusive, using Flash Glucose Monitoring.

End point title	Percentage of time spent in glycaemic target range 70-180 mg/dL (3.9–10.0 mmol/L) both inclusive, using Flash Glucose Monitoring.

End point description:

The percentage of time spent in glycaemic target range was calculated as the number of recorded measurements in glycaemic target range (70-180 mg/dL (3.9-10.0 mmol/L), both inclusive) divided by the total number of recorded measurements. The endpoint is based on data recorded by FGM system. It was required that at least 70% of the planned FGM measurements during weeks 16-17 and weeks 34-35 were available for endpoint data to be included in the analysis.

End point type	Primary

End point timeframe:

During the 2-week maintenance periods (week 16-17 in treatment period-1 and week 34-35 in treatment period-2).

End point values	Insulin degludec 100U/mL	Insulin glargine 100U/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	448	448		
Units: Percentage of time				
least squares mean (standard error)	72.11 (± 0.74)	70.68 (± 0.74)		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Due to cross-over design of the study, the following "number of subjects included in analysis" is being erroneously displayed as 896. The actual "number of subjects included in analysis" is 448.	
Comparison groups	Insulin degludec 100U/mL v Insulin glargine 100U/mL
Number of subjects included in analysis	896
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0321
Method	t-test, 2-sided
Parameter estimate	Estimated treatment difference
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	2.74

Notes:

[1] - Superiority is confirmed if non-inferiority is confirmed and the lower limit of the two-sided 95% confidence interval is entirely above zero

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Due to cross-over design of the study, the following "number of subjects included in analysis" is being erroneously displayed as 896. The actual "number of subjects included in analysis" is 448.	
Comparison groups	Insulin degludec 100U/mL v Insulin glargine 100U/mL
Number of subjects included in analysis	896
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	t-test, 2-sided
Parameter estimate	Estimated treatment difference
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	2.74

Notes:

[2] - A non-inferiority margin of -0.83% has been applied, corresponding to 0.2 hours/24 hours

Secondary: Time spent in tight glycaemic target range 70-140 mg/dL (3.9-7.8 mmol/L) both inclusive, using Flash Glucose Monitoring

End point title	Time spent in tight glycaemic target range 70-140 mg/dL (3.9-7.8 mmol/L) both inclusive, using Flash Glucose Monitoring

End point description:

The percentage of time spent in tight glycaemic target range 70-140 mg/dL (3.9–7.8 mmol/L) both inclusive, during the 2-week maintenance periods using FGM (visit 9-21 (week 16-17) and visit 37-39 (week 34-35))

End point type	Secondary

End point timeframe:

During the 2-week maintenance period: weeks 16-17 (period-1) and weeks 34-35 (period-2)

End point values	Insulin degludec 100U/mL	Insulin glargine 100U/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	448	448		
Units: Percentage of Time				
least squares mean (standard error)	52.97 (± 0.82)	51.45 (± 0.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time spent in nocturnal glycaemic target range 70-140 mg/dL (3.9-7.8 mmol/L) both inclusive, in the nocturnal period (00:01 am - 05:59 am both inclusive) using Flash Glucose Monitoring

End point title	Time spent in nocturnal glycaemic target range 70-140 mg/dL (3.9-7.8 mmol/L) both inclusive, in the nocturnal period (00:01 am - 05:59 am both inclusive) using Flash Glucose Monitoring

End point description:

Percentage of time spent in nocturnal glycaemic target range 70-140 mg/dL (3.9-7.8 mmol/L) both inclusive, in the nocturnal period (00:01 am – 05:59 am both inclusive) during the 2-week maintenance periods using FGM (visit 19-21 (week 16-17) and visit 37-39 (week 34-35)).

End point type	Secondary

End point timeframe:

During the 2-week maintenance period: weeks 16-17 (period-1) and weeks 34-35 (period-2).

End point values	Insulin degludec 100U/mL	Insulin glargine 100U/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	448	448		
Units: Percentage of Time				
least squares mean (standard error)	15.15 (± 0.26)	14.91 (± 0.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Level of glycated haemoglobin (HbA1c) - Percentage

End point title	Level of glycated haemoglobin (HbA1c) - Percentage

End point description:

Level of HbA1c after two weeks of maintenance periods (Visit 19-21 (week 16-17) and Visit 37-39 (week 34-35)).

End point type	Secondary

End point timeframe:

After the 2-week maintenance period: weeks 16-17 (period-1) and weeks 34-35 (period-2).

End point values	Insulin degludec 100U/mL	Insulin glargine 100U/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	448	448		
Units: Percentage of glycated haemoglobin				
least squares mean (standard error)	7.10 (± 0.04)	7.16 (± 0.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Level of glycated haemoglobin (HbA1c) - mmol/mol

End point title	Level of glycated haemoglobin (HbA1c) - mmol/mol

End point description:

Level of HbA1c after two weeks of maintenance periods (Visit 19-21 (week 16-17) and Visit 37-39 (week 34-35)).

End point type	Secondary

End point timeframe:

After the 2-week maintenance period: weeks 16-17 (period-1) and weeks 34-35 (period-2).

End point values	Insulin degludec 100U/mL	Insulin glargine 100U/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	448	448		
Units: millimoles per mole (mmol/mol)				
least squares mean (standard error)	54.10 (± 0.42)	54.78 (± 0.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean glucose levels using flash glucose monitoring (FGM) - mmol/L

End point title	Mean glucose levels using flash glucose monitoring (FGM) - mmol/L

End point description:

Mean glucose levels (mmol/L) during the 2-week maintenance periods using FGM (visit 19-21 (week 16-17) and visit 37-39 (week 34-35)).

End point type	Secondary

End point timeframe:

During the 2-week maintenance period: weeks 16-17 (period-1) and weeks 34-35 (period-2).

End point values	Insulin degludec 100U/mL	Insulin glargine 100U/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	448	448		
Units: mmol/L				
least squares mean (standard error)	7.57 (± 0.08)	7.61 (± 0.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean glucose levels using flash glucose monitoring (FGM) - mg/dL

End point title	Mean glucose levels using flash glucose monitoring (FGM) - mg/dL

End point description:

Mean glucose levels (mmol/L) during the 2-week maintenance periods using FGM (visit 19-21 (week 16-17) and visit 37-39 (week 34-35)).

End point type	Secondary

End point timeframe:

During the 2-week maintenance period: weeks 16-17 (period-1) and weeks 34-35 (period-2).

End point values	Insulin degludec 100U/mL	Insulin glargine 100U/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[3]	0[4]		
Units: mg/dL				
least squares mean (standard error)	()	()		

Notes:

[3] - Mean glucose levels (mg/dL) are not reported in the clinical trial report. Hence not reported here.

[4] - Mean glucose levels (mg/dL) are not reported in the clinical trial report. Hence not reported here.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From the randomization (week 0) up to end of treatment (week 36) and follow up (week 37).

Adverse event reporting additional description:

Safety Analysis Set was defined as all subjects that were randomized and treated with at least one dose of trial drug after randomization

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Insulin Glargine 100U/mL

Reporting group description:

Participants were to receive a subcutaneous (s.c.) injection of Insulin glargine 100U/mL once daily (in treatment period 1), followed by a s.c. injection of Insulin degludec 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Reporting group title	Insulin Degludec 100U/mL

Reporting group description:

Participants were to receive a subcutaneous (s.c.) injection of Insulin degludec 100U/mL once daily (in treatment period 1), followed by a s.c. injection of Insulin glargine 100U/mL once daily (in treatment period 2) with or without oral anti-diabetic drugs using flash glucose monitoring. Each treatment period consisted of a 16-week titration period followed by a 2-week maintenance period.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No values to display for non-serious AE with 5% threshold

Serious adverse events	Insulin Glargine 100U/mL	Insulin Degludec 100U/mL	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 484 (4.75%)	26 / 490 (5.31%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			

Haematoma			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Coronary arterial stent insertion			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (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			
Breast mass			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			

subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Scan myocardial perfusion abnormal			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
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			
Contusion			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Arteriovenous malformation			

subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (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 coronary syndrome			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 484 (0.21%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 484 (0.21%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			

subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
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 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic unconsciousness			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal neuralgia			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			

subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (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			
Iron deficiency anaemia			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diabetic gastroparesis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
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 / 484 (0.00%)	2 / 490 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 484 (0.21%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
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			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vertebral foraminal stenosis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (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	2 / 484 (0.41%)	3 / 490 (0.61%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	0 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			

subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (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	1 / 484 (0.21%)	0 / 490 (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 / 484 (0.00%)	1 / 490 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 484 (0.21%)	0 / 490 (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 Glargine 100U/mL	Insulin Degludec 100U/mL	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 484 (0.00%)	0 / 490 (0.00%)	

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