Clinical trial results:
A 78-week trial comparing the effect and safety of once weekly insulin icodec and once daily insulin glargine 100 units/mL, both in combination with non-insulin anti-diabetic treatment, in insulin naïve subjects with type 2 diabetes

Summary

EudraCT number	2020-000442-34
Trial protocol	GB SK PL HR IT
Global end of trial date	01 December 2022

Results information

Result version number	v1 (current)
This version publication date	16 December 2023
First version publication date	16 December 2023

Trial information

Trial identification

Sponsor protocol code	NN1436-4477

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04460885
WHO universal trial number (UTN)	U1111-1247-3878

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Alle, 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 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the effect on glycaemic control of once weekly insulin icodec, in combination with non-insulin anti-diabetic drugs, in insulin naive subjects with type 2 diabetes (T2D). This included comparing the difference in change from baseline in glycosylated haemoglobin (HbA1c) between insulin icodec and insulin glargine after 52 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 Conference on Harmonization (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:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	25 November 2020
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	Spain: 36
Country: Number of subjects enrolled	United Kingdom: 48
Country: Number of subjects enrolled	Croatia: 36
Country: Number of subjects enrolled	India: 88
Country: Number of subjects enrolled	Israel: 37
Country: Number of subjects enrolled	Italy: 46
Country: Number of subjects enrolled	Japan: 164
Country: Number of subjects enrolled	Mexico: 41
Country: Number of subjects enrolled	Poland: 88
Country: Number of subjects enrolled	Russian Federation: 117
Country: Number of subjects enrolled	Slovakia: 63
Country: Number of subjects enrolled	United States: 220
Worldwide total number of subjects	984
EEA total number of subjects	269

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)	665
From 65 to 84 years	319
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted in 12 countries. The total number of sites which screened subjects/total number of sites which randomised subjects is as follows: Croatia (4/4), India (9/9), Israel (5/5), Italy (5/5), Japan (14/14), Mexico (3/3), Poland (8/8), Russia (14/14), Slovakia (7/7), Spain (5/5), United Kingdom (11/11) and United States (56/52).

Pre-assignment

Screening details:

A total of 984 subjects were randomised and exposed to the trial product in 1:1 ratio and 949 subjects completed the trial.

Period 1

Period 1 title	Overall (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 received once-weekly subcutaneous injection of insulin icodec at a starting dose of 70 U for 52 weeks using PDS 290 pre-filled injector in combination with non-insulin anti-diabetic drugs. The dose adjustment was based on the three pre-breakfast self-monitored plasma glucose (SMPG) values measured on two days prior to titration and on the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 millimoles per liter (mmol/L): dose reduced by 20 units (U); 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 20 units.

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 into the thigh, upper arm or abdomen using the PDS290 pen injector.

Arm title	Insulin glargine

Arm description:

Subjects received once daily subcutaneous injection of insulin glargine at a starting dose of 10 U using SoloSTAR pre-filled pen injector in combination with non-insulin anti-diabetic drugs. The dose adjustment was based on the three pre-breakfast self-monitored plasma glucose (SMPG) values measured on two days prior to titration and on the day of the contact. If atleast one pre-breakfast SMPG value was: < 4.4 mmol/L: the dose was reduced by 3 U; 4.4-7.2: no dose adjustment required and >7.2 mmol/L: dose was increased by 3 U

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

Dosage and administration details:

Insulin glargine was administered once daily subcutaneously into the thigh, upper arm or abdomen using the 3 mL SoloSTAR pre-filled pen injector.

Number of subjects in period 1	Insulin icodec	Insulin glargine
Started	492	492
Completed	474	475
Not completed	18	17
Physician decision	2	1
Consent withdrawn by subject	6	8
Death	5	4
Lost to follow-up	4	4
Site closure	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Insulin icodec
Reporting group description:	
Subjects received once-weekly subcutaneous injection of insulin icodec at a starting dose of 70 U for 52 weeks using PDS 290 pre-filled injector in combination with non-insulin anti-diabetic drugs. The dose adjustment was based on the three pre-breakfast self-monitored plasma glucose (SMPG) values measured on two days prior to titration and on the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 millimoles per liter (mmol/L): dose reduced by 20 units (U); 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 20 units.	
Reporting group title	Insulin glargine
Reporting group description:	
Subjects received once daily subcutaneous injection of insulin glargine at a starting dose of 10 U using SoloSTAR pre-filled pen injector in combination with non-insulin anti-diabetic drugs. The dose adjustment was based on the three pre-breakfast self-monitored plasma glucose (SMPG) values measured on two days prior to titration and on the day of the contact. If atleast one pre-breakfast SMPG value was: < 4.4 mmol/L: the dose was reduced by 3 U; 4.4-7.2: no dose adjustment required and >7.2 mmol/L: dose was increased by 3 U	

Reporting group values	Insulin icodec	Insulin glargine	Total
Number of subjects	492	492	984
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)	333	332	665
From 65-84 years	159	160	319
85 years and over	0	0	0
Age Continuous Units: years			
median	60.00	60.00	
full range (min-max)	27.00 to 84.00	28.00 to 80.00	-
Gender Categorical Units: Subjects			
Female	197	229	426
Male	295	263	558

End points

End points reporting groups

Reporting group title	Insulin icodec

Reporting group description:

Subjects received once-weekly subcutaneous injection of insulin icodec at a starting dose of 70 U for 52 weeks using PDS 290 pre-filled injector in combination with non-insulin anti-diabetic drugs. The dose adjustment was based on the three pre-breakfast self-monitored plasma glucose (SMPG) values measured on two days prior to titration and on the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 millimoles per liter (mmol/L): dose reduced by 20 units (U); 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 20 units.

Reporting group title	Insulin glargine

Reporting group description:

Subjects received once daily subcutaneous injection of insulin glargine at a starting dose of 10 U using SoloSTAR pre-filled pen injector in combination with non-insulin anti-diabetic drugs. The dose adjustment was based on the three pre-breakfast self-monitored plasma glucose (SMPG) values measured on two days prior to titration and on the day of the contact. If atleast one pre-breakfast SMPG value was: < 4.4 mmol/L: the dose was reduced by 3 U; 4.4-7.2: no dose adjustment required and >7.2 mmol/L: dose was increased by 3 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 52 (V46) was presented. The endpoint data was evaluated based on the in-trial observation period. The in-trial period started at randomization 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 randomized subjects.

End point type	Primary

End point timeframe:

From baseline week 0 (V2) to week 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	492		
Units: Percentage (%) of HbA1c				
least squares mean (standard error)	-1.55 (± 0.06)	-1.35 (± 0.05)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The response and change from baseline in response after 52 weeks are analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate.

Comparison groups	Insulin icodec v Insulin glargine

Number of subjects included in analysis	984
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	-0.03

Secondary: Change in fasting plasma glucose (FPG)

End point title	Change in fasting plasma glucose (FPG)

End point description:

Change in FPG from baseline (week 0) to week 52 is presented. The outcome data was evaluated based on the in-trial observation period. The in-trial period started at randomization 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 randomized subjects. Number of subjects analysed = Subjects with available data for the endpoint.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	474		
Units: millimoles per liter (mmol/L)				
least squares mean (standard error)	-3.35 (± 0.09)	-3.33 (± 0.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time in target range 3.9-10.0 mmol/L (70-180 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 mg/dL) using continuous glucose monitoring (CGM) system, Dexcom G6

End point description:

Time in target range 3.9-10.0 millimoles per liter (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 in-trial period started at randomization 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 randomized subjects. Number of subjects analysed=Subjects with available data for the endpoint.

End point type	Secondary

End point timeframe:

From week 48 (V42) to week 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	439	440		
Units: Percentage of time				
arithmetic mean (standard deviation)	71.94 (± 18.23)	66.90 (± 18.19)		

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 hypoglycaemic episode is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. The outcome data was evaluated based on main-on-treatment period. Main-on-treatment period started with onset date on or after the first dose of trial product and no later than the first date of either the end-date of the on-treatment period or week 52. On-treatment period started with 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 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 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	492		
Units: Episodes				
number (not applicable)	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (below 3.0 mmol/L (54 mg/dL) confirmed by BG meter)

End point title	Number of clinically significant hypoglycaemic episodes (level 2) (below 3.0 mmol/L (54 mg/dL) confirmed by BG meter)

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL) confirmed by BG meter) is presented. Clinically significant hypoglycaemia is defined as plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. The outcome data was evaluated based on main-on-treatment period. Main-on-treatment period started with onset date on or after the first dose of trial product and no later than the first date of either the end-date of the on-treatment period or week 52. On-treatment period started with 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 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 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	492		
Units: Episodes				
number (not applicable)	143	75		

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 is defined as plasma glucose value of < 3.0 mmol/L (54 mg/dL). Severe hypoglycaemic episode is defined as hypoglycaemia with severe cognitive impairment requiring external assistance. Outcome data was evaluated based on main-on-treatment period which started with onset date on or after the first dose of trial product and the first date of the end-date of the on-treatment period or week 52. On-treatment period started with onset date on or after first dose of trial product and 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 in-trial period. Safety analysis set included subjects 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 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	492		
Units: Episodes				
number (not applicable)	144	78		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of severe hypoglycaemic episodes (level 3) (From baseline week 0 (V2) to week 83 (V63))

End point title	Number of severe hypoglycaemic episodes (level 3) (From baseline week 0 (V2) to week 83 (V63))

End point description:

Number of severe hypoglycaemic episodes (level 3) is presented. Severe hypoglycaemic episode is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. The outcome data was evaluated based on on-treatment period. The 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 of trial visit (V63), 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 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 83 (V63)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	492		
Units: Episodes				
number (not applicable)	1	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (below 3.0 mmol/L (54 mg/dL) confirmed by BG meter) (From baseline week 0 (V2) to week 83 (V63))

End point title	Number of clinically significant hypoglycaemic episodes (level

	2) (below 3.0 mmol/L (54 mg/dL) confirmed by BG meter) (From baseline week 0 (V2) to week 83 (V63))

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL) confirmed by BG meter) is presented. Clinically significant hypoglycaemia is defined as plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. The outcome data was evaluated based on on-treatment period. The 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 of trial visit (V63), 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 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 83 (V63)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	492		
Units: Episodes				
number (not applicable)	226	114		

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 from week 50 (V44) to week 52 (V46) is presented. The outcome data was evaluated based on main on treatment period. Main-on-treatment period started with onset date on or after the first dose of trial product and no later than the first date of either the end-date of the on-treatment period or week 52. On-treatment period started with 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 randomly assigned to trial treatment and who took at least 1 dose of trial product. Number of subjects analysed = Subjects with available data for the endpoint.

End point type	Secondary

End point timeframe:

From week 50 (V44) to week 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	472	477		
Units: Unit (U) of insulin				
geometric mean (geometric coefficient of variation)	215.59 (± 77.39)	220.85 (± 76.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (below 3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) (From baseline week 0 (V2) to week 83 (V63))

End point title	Number of clinically significant hypoglycaemic episodes (level 2) (below 3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) (From baseline week 0 (V2) to week 83 (V63))

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (below 3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) is presented. Clinically significant hypoglycaemia is defined as plasma glucose value of below 3.0 mmol/L (54 mg/dL). Severe hypoglycaemic episode is defined as hypoglycaemia with severe cognitive impairment requiring external assistance. Outcome data was evaluated based on on-treatment period. On-treatment period started at date of first dose of trial product as recorded on eCRF and ended at the first date of any of the following: End of trial visit (V63), 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 dosing interval for both treatment arms) and the end-date for in-trial observation period. Safety analysis set included all subjects 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 83 (V63)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	492		
Units: Episodes				
number (not applicable)	227	121		

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 52 (V46) is presented. The outcome data was

evaluated based on the in-trial observation period. The in-trial period started at randomization 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 randomized subjects.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	492	492		
Units: kilograms (kg)				
least squares mean (standard error)	2.29 (± 0.21)	1.83 (± 0.21)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Time spent below 3.0 mmol/L (54 mg/dL) using continuous glucose monitoring (CGM) system, Dexcom G6 from week 48 (V42) to week 52 (V46) was presented. Time spent below threshold is defined as 100 times the number of recorded measurements below the threshold, divided by the total number of recorded measurements. The outcome data was evaluated based on the in-trial observation period. The in-trial period started at randomization 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 (that is, possibly an unscheduled phone visit), death for subjects who died before any of the above. Full analysis set included all randomized subjects. Number of subjects analysed=Subjects with available data for the endpoint.

End point type	Secondary

End point timeframe:

From week 48 (V42) to week 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	439	440		
Units: Percentage of time				
arithmetic mean (standard deviation)	0.27 (± 0.57)	0.21 (± 0.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time spent greater than 10 mmol/L (180 mg/dL) using continuous glucose monitoring (CGM) system, Dexcom G6

End point title	Time spent greater than 10 mmol/L (180 mg/dL) using continuous glucose monitoring (CGM) system, Dexcom G6

End point description:

Time spent greater than 10 mmol/L (180 mg/dL) using continuous glucose monitoring (CGM) system, Dexcom G6 from week 48 (V42) to week 52 (V46) is presented. Time spent above threshold is defined as 100 times the number of recorded measurements above the threshold, divided by the total number of recorded measurements. The outcome data was evaluated based on the in-trial observation period. The in-trial period started at randomization and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last participant-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 randomized subjects. Number of subjects analysed=Subjects with available data for the endpoint.

End point type	Secondary

End point timeframe:

From week 48 (V42) to week 52 (V46)

End point values	Insulin icodec	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	439	440		
Units: Percentage of time				
arithmetic mean (standard deviation)	26.86 (± 18.74)	32.27 (± 18.66)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline (week 0) to end of trial (week 83)

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 83). All presented AEs are treatment emergent.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Insulin glargine

Reporting group description:

Subjects received once daily subcutaneous injection of insulin glargine at a starting dose of 10 U using SoloSTAR pre-filled pen injector in combination with non-insulin anti-diabetic drugs. The dose adjustment was based on the three pre-breakfast self-monitored plasma glucose (SMPG) values measured on two days prior to titration and on the day of the contact. If atleast one pre-breakfast SMPG value was: < 4.4 mmol/L: the dose was reduced by 3 U; 4.4-7.2: no dose adjustment required and >7.2 mmol/L: dose was increased by 3 U.

Reporting group title	Insulin icodec

Reporting group description:

Subjects received once-weekly subcutaneous injection of insulin icodec at a starting dose of 70 U for 52 weeks using PDS 290 pre-filled injector in combination with non-insulin anti-diabetic drugs. The dose adjustment was based on the three pre-breakfast self-monitored plasma glucose (SMPG) values measured on two days prior to titration and on the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 millimoles per liter (mmol/L): dose reduced by 20 units (U); 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 20 units.

Serious adverse events	Insulin glargine	Insulin icodec	
Total subjects affected by serious adverse events			
subjects affected / exposed	72 / 492 (14.63%)	64 / 492 (13.01%)	
number of deaths (all causes)	4	5	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			

subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung adenocarcinoma			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic renal cell carcinoma			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to liver			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant melanoma in situ			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer metastatic			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			

subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neoplasm			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate cancer			
subjects affected / exposed	1 / 492 (0.20%)	2 / 492 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brachiocephalic arteriosclerosis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery stenosis			

subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	2 / 492 (0.41%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (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			
Removal of foreign body			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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			
Immunisation reaction			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 492 (0.00%)	2 / 492 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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 pulmonary oedema			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Cardiac stress test abnormal			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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			
Deafness traumatic			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endotracheal intubation complication			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	2 / 492 (0.41%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprocedural myocardial infarction			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural stroke			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			

subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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			
Hydrocele			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myocardial infarction			
subjects affected / exposed	5 / 492 (1.02%)	4 / 492 (0.81%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Angina unstable			
subjects affected / exposed	1 / 492 (0.20%)	4 / 492 (0.81%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 492 (0.41%)	5 / 492 (1.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	2 / 492 (0.41%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 492 (0.00%)	2 / 492 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic coronary syndrome			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	2 / 492 (0.41%)	4 / 492 (0.81%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 492 (0.00%)	2 / 492 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	3 / 492 (0.61%)	3 / 492 (0.61%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
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	1 / 492 (0.20%)	0 / 492 (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			
Carotid artery stenosis			

subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (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	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic stroke			

subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood loss anaemia			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Presbyacusis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinal oedema			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open angle glaucoma			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Large intestine polyp			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			

subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Myxoid cyst			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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			
Acute kidney injury			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ketonuria			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 492 (0.20%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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			
Back pain			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
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 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	3 / 492 (0.61%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plantar fasciitis			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Spinal pain			
subjects affected / exposed	2 / 492 (0.41%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	2 / 492 (0.41%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 492 (0.41%)	4 / 492 (0.81%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	3 / 492 (0.61%)	4 / 492 (0.81%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchitis			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 492 (0.41%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic hepatitis C			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			

subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal sepsis			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Laryngitis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			

subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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	3 / 492 (0.61%)	2 / 492 (0.41%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 492 (0.41%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Adult failure to thrive			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Electrolyte depletion			

subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 492 (0.00%)	1 / 492 (0.20%)	
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 / 492 (0.20%)	0 / 492 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 492 (0.20%)	0 / 492 (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 glargine	Insulin icodec	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	216 / 492 (43.90%)	221 / 492 (44.92%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	23 / 492 (4.67%)	27 / 492 (5.49%)	
occurrences (all)	27	30	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	32 / 492 (6.50%)	36 / 492 (7.32%)	
occurrences (all)	38	41	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	26 / 492 (5.28%)	39 / 492 (7.93%)	
occurrences (all)	29	54	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	22 / 492 (4.47%)	30 / 492 (6.10%)	
occurrences (all)	28	36	
Back pain			
subjects affected / exposed	32 / 492 (6.50%)	40 / 492 (8.13%)	
occurrences (all)	34	42	
Infections and infestations			
COVID-19			
subjects affected / exposed	101 / 492 (20.53%)	87 / 492 (17.68%)	
occurrences (all)	108	91	
Upper respiratory tract infection			
subjects affected / exposed	22 / 492 (4.47%)	28 / 492 (5.69%)	
occurrences (all)	24	40	
Nasopharyngitis			
subjects affected / exposed	47 / 492 (9.55%)	38 / 492 (7.72%)	
occurrences (all)	56	50	

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