Clinical trial results:
A clinical trial comparing glycaemic control and safety of insulin degludec/liraglutide (IDegLira) versus insulin glargine (IGlar) as add-on therapy to SGLT2i in subjects with type 2 diabetes mellitus.

Summary

EudraCT number	2015-001596-48
Trial protocol	SI FI HU ES SK
Global end of trial date	23 October 2017

Results information

Result version number	v1 (current)
This version publication date	08 November 2018
First version publication date	08 November 2018

Trial information

Trial identification

Sponsor protocol code	nn9068-4229

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02773368
WHO universal trial number (UTN)	U1111-1168-9343

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, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 September 2017
Global end of trial reached?	Yes
Global end of trial date	23 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the effect of insulin degludec/liraglutide (IDegLira) in terms of glycaemic control in subjects with type 2 diabetes mellitus (T2DM) on previous treatment with sodium-glucose co-transporter 2 inhibitors (SGLT2i) ± oral anti-diabetic drug (OAD) therapy. This is done by comparing the difference in change from baseline in HbA1c after 26 weeks to a non-inferiority margin of 0.3% for IDegLira versus insulin glargine (IGlar), both in combination with SGLT2i ± OAD.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (64th WMA Assembly, October 2013) and ICH Good Clinical Practice, including archiving of essential documents (June 1996) and 21 CFR 312.120.

Background therapy:

Subjects on pre-trial OAD treatment with stable daily dose of SGLT2i either as monotherapy or in combination with metformin ± dipeptidyl peptidase-4 inhibitors (DPP4i) ± pioglitazone according to locally approved label for at least 90 days prior to screening. Subjects on DPP4i before the trial had to be discontinued at randomisation.

Evidence for comparator:

Not applicable

Actual start date of recruitment	23 May 2016
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	Argentina: 45
Country: Number of subjects enrolled	Canada: 30
Country: Number of subjects enrolled	Finland: 25
Country: Number of subjects enrolled	Hungary: 37
Country: Number of subjects enrolled	India: 58
Country: Number of subjects enrolled	Russian Federation: 49
Country: Number of subjects enrolled	Slovakia: 38
Country: Number of subjects enrolled	Slovenia: 24
Country: Number of subjects enrolled	Spain: 47
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	United States: 59
Worldwide total number of subjects	420
EEA total number of subjects	171

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)	322
From 65 to 84 years	98
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 74 sites in 11 countries as follows: Argentina (3), Canada (5), Finland (6), Hungary (5), India (8), Russian Federation (7), Slovakia (5), Slovenia (4), Spain (6), Switzerland (5) and United States (20).

Pre-assignment

Screening details:

Eligible subjects with type 2 diabetes mellitus on OAD therapy with stable daily dose of SGLT2i either as monotherapy or in combination with metformin ± DPP4i ± pioglitazone as per locally approved label for at least 90 days prior to screening. Subjects on DPP4i before the trial had to discontinue at randomisation.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	IDegLira

Arm description:

Subjects were administered with insulin degludec/liraglutide (IDegLira: 100 U/3.6 mg per mL) once daily for a duration of 26 weeks. IDegLira treatment was initiated at starting dose of 10 dose steps. The dose of IDeglira was adjusted individually twice weekly according to a predefined titration algorithm with a maximum daily dose of 50 dose steps. Pre-trial OAD treatments were continued according to current local label. The randomised subjects would be on either SGLT2i monotherapy or SGLT2i ± metformin ± pioglitazone excluding DPP4i. This treatment was to be unchanged throughout the trial, unless there was a safety concern.

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

Dosage and administration details:

IDegLira was supplied in a 3 mL prefilled PDS290 pen-injector with a fixed IDeg/liraglutide ratio of 100 units/3.6 mg per mL solution subcutaneously in the thigh, upper arm (deltoid) or abdomen approximately at the same time every day throughout the trial. IDegLira treatment was initiated at 10 dose steps (containing 10 units IDeg /0.36 mg liraglutide). Dose was adjusted individually twice weekly on fixed days based on the mean of three pre-breakfast self-measured plasma glucose (SMPG) values measured on the days of the titration and the two days prior to the titration (target SMPG: 4.0-5.0 mmol/L [72- 90 mg/dL]). The maximum daily dose for IDegLira was 50 dose steps.

Arm title	IGlar

Arm description:

Subjects were administered with insulin glargine (IGlar: 100 U/mL) once daily for a duration of 26 weeks. IGlar treatment was initiated with the starting dose of 10 U and adjusted individually twice weekly according to a predefined titration algorithm. Pre-trial OAD treatments were continued according to current local label. The randomised subjects would be on either SGLT2i monotherapy or SGLT2i ± metformin ± pioglitazone excluding DPP4i. This treatment was to be unchanged throughout the trial, unless there was a safety concern.

Arm type	Active comparator

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

Dosage and administration details:

IGlar was supplied in a 3 mL pre-filled Solostar® pen at 100 U/mL solution and administered subcutaneously according to the local labelling. Dose adjustment was based on the mean of three pre-breakfast self-measured plasma glucose (SMPG) values measured individually on the days of the titration and two days prior to the titration (target SMPG: 4.0-5.0 mmol/L [72 - 90 mg/dL]). There was no maximum dose specified for IGlar.

Number of subjects in period 1	IDegLira	IGlar
Started	210	210
Exposed	209	210
Completed	200	206
Not completed	10	4
Consent withdrawn by subject	5	1
Unclassified	1	1
Lost to follow-up	4	1
Missing	-	1

Baseline characteristics

Reporting groups	
Reporting group title	IDegLira
Reporting group description:	
Subjects were administered with insulin degludec/liraglutide (IDegLira: 100 U/3.6 mg per mL) once daily for a duration of 26 weeks. IDegLira treatment was initiated at starting dose of 10 dose steps. The dose of IDeglira was adjusted individually twice weekly according to a predefined titration algorithm with a maximum daily dose of 50 dose steps. Pre-trial OAD treatments were continued according to current local label. The randomised subjects would be on either SGLT2i monotherapy or SGLT2i ± metformin ± pioglitazone excluding DPP4i. This treatment was to be unchanged throughout the trial, unless there was a safety concern.	
Reporting group title	IGlar
Reporting group description:	
Subjects were administered with insulin glargine (IGlar: 100 U/mL) once daily for a duration of 26 weeks. IGlar treatment was initiated with the starting dose of 10 U and adjusted individually twice weekly according to a predefined titration algorithm. Pre-trial OAD treatments were continued according to current local label. The randomised subjects would be on either SGLT2i monotherapy or SGLT2i ± metformin ± pioglitazone excluding DPP4i. This treatment was to be unchanged throughout the trial, unless there was a safety concern.	

Reporting group values	IDegLira	IGlar	Total
Number of subjects	210	210	420
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)	160	162	322
From 65-84 years	50	48	98
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	56.1	57.2	
standard deviation	± 10.4	± 10.2	-
Gender Categorical Units: Subjects			
Female	89	84	173
Male	121	126	247
Glycosylated haemoglobin (HbA1c) Units: percentage of glycosylated haemoglobin			
arithmetic mean	8.20	8.36	
standard deviation	± 0.93	± 1.08	-
Body Weight Units: kg			
arithmetic mean	89.3	87.2	
standard deviation	± 17.6	± 17.2	-

Fasting plasma glucose (FPG) Units: mmol/L			
arithmetic mean	9.51	9.57	
standard deviation	± 2.69	± 2.40	-

End points

End points reporting groups

Reporting group title	IDegLira

Reporting group description:

Subjects were administered with insulin degludec/liraglutide (IDegLira: 100 U/3.6 mg per mL) once daily for a duration of 26 weeks. IDegLira treatment was initiated at starting dose of 10 dose steps. The dose of IDeglira was adjusted individually twice weekly according to a predefined titration algorithm with a maximum daily dose of 50 dose steps. Pre-trial OAD treatments were continued according to current local label. The randomised subjects would be on either SGLT2i monotherapy or SGLT2i ± metformin ± pioglitazone excluding DPP4i. This treatment was to be unchanged throughout the trial, unless there was a safety concern.

Reporting group title	IGlar

Reporting group description:

Subjects were administered with insulin glargine (IGlar: 100 U/mL) once daily for a duration of 26 weeks. IGlar treatment was initiated with the starting dose of 10 U and adjusted individually twice weekly according to a predefined titration algorithm. Pre-trial OAD treatments were continued according to current local label. The randomised subjects would be on either SGLT2i monotherapy or SGLT2i ± metformin ± pioglitazone excluding DPP4i. This treatment was to be unchanged throughout the trial, unless there was a safety concern.

Primary: Change from baseline in HbA1c

End point title	Change from baseline in HbA1c

End point description:

The mean change from baseline (week 0) in HbA1c values evaluated after 26 weeks of randomised treatment. The full analysis set (FAS) included all randomised subjects. The statistical evaluation of the FAS followed the intent-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". Number analysed = Number of subjects contributed to the analysis at week 26. The results presented included retrieved data at week 26 for subjects who prematurely discontinued the trial product.

End point type	Primary

End point timeframe:

After 26 weeks

End point values	IDegLira	IGlar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	202		
Units: Percentage of glycosylated haemoglobin				
arithmetic mean (standard deviation)				
HbA1c (%) change from baseline to week 26	-1.94 (± 0.95)	-1.68 (± 1.05)		

Statistical analyses

Statistical analysis title	Analysis 1: Non-inferiority Analysis

Statistical analysis description:

Analysis was based on ANCOVA model with treatment, pre-trial OAD, region as factors and baseline

HbA1c as covariate. Missing data were imputed using unconditional reference based multiple imputation including data obtained after premature treatment discontinuation. The non-inferiority margin of 0.3 % was added to the end-of-treatment value for prematurely discontinued and withdrawn from trial IDegLira subjects. Number of subjects contributed to the analysis included all randomised subjects (420)

Comparison groups	IDegLira v IGlar
Number of subjects included in analysis	399
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	ANCOVA
Parameter estimate	Treatment Contrast
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	-0.2

Notes:

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

Statistical analysis title	Analysis 2: Superiority analysis

Statistical analysis description:

This endpoint was analysed using an ANCOVA model with treatment, pre-trial OAD and region as factors and corresponding baseline value as covariate. Data obtained after premature treatment discontinuation were included in the analysis. Missing data were imputed using unconditional reference based multiple imputation including data obtained after premature treatment discontinuation. Number of subjects contributed to the analysis included all randomised subjects (420).

Comparison groups	IDegLira v IGlar
Number of subjects included in analysis	399
Analysis specification	Pre-specified
Analysis type	superiority[2]
Method	ANCOVA
Parameter estimate	Treatment Contrast
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.21

Notes:

[2] - Superiority of IDegLira was considered confirmed if the test procedure was not stopped (i.e. non-inferiority of IDegLira was confirmed for change from baseline in HbA1c; and superiority of IDegLira was confirmed for weight change and the number of treatment-emergent severe or BG confirmed symptomatic hypoglycaemic episodes) and if the upper limit of the two-sided 95% CI for the mean treatment difference (IDegLira minus IGlar) in change from baseline in HbA1c was strictly below 0%.

Secondary: Change from baseline in body weight

End point title	Change from baseline in body weight

End point description:

The mean change from baseline (week 0) in body weight evaluated after 26 weeks of randomised treatment. The FAS included all randomised subjects. The statistical evaluation of the FAS followed the intent-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". Number analysed = Number of subjects contributed to the analysis at week 26. The results presented included retrieved data at week 26 for subjects who prematurely discontinued the trial product.

End point type	Secondary

End point timeframe:

After 26 weeks

End point values	IDegLira	IGlar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	204		
Units: kg				
arithmetic mean (standard deviation)				
Body weight (kg) change from baseline to week 26	-0.0 (± 3.8)	2.0 (± 3.9)		

Statistical analyses

Statistical analysis title	Analysis 1: Superiority analysis

Statistical analysis description:

This endpoint was analysed using an ANCOVA model with treatment, pre-trial OAD and region as factors and corresponding baseline weight as covariate. Data obtained after premature treatment discontinuation were included in the analysis. Missing data were imputed using unconditional reference based multiple imputation including data obtained after premature treatment discontinuation. Number of subjects contributed to the analysis included all randomised subjects (420).

Comparison groups	IDegLira v IGlar
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority[3]
Method	ANCOVA
Parameter estimate	Treatment Contrast
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.64
upper limit	-1.19

Notes:

[3] - Superiority of IDegLira was considered confirmed if the test procedure was not stopped (i.e. non-inferiority of IDegLira was confirmed for change from baseline in HbA1c) and if the upper limit of the two-sided 95% CI for the mean treatment difference (IDegLira minus IGlar) in change from baseline in body weight was strictly below 0 kg.

Secondary: Number of treatment-emergent severe or BG confirmed symptomatic hypoglycaemic episodes

End point title	Number of treatment-emergent severe or BG confirmed symptomatic hypoglycaemic episodes

End point description:

Severe or BG confirmed symptomatic hypoglycaemic episodes were defined as episodes that were severe (subjects who were not able to self-treat) and/or BG confirmed by a plasma glucose values <3.1 mmol/L (56 mg/dL) with accompanied symptoms consistent with hypoglycaemia. The safety analysis set (SAS) included all subjects who received at least one dose of the investigational product or comparator.

End point type	Secondary

End point timeframe:

During 26 weeks

End point values	IDegLira	IGlar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	210		
Units: Number of episodes	38	95		

Statistical analyses

Statistical analysis title	Analysis 1: Superiority analysis

Statistical analysis description:

This endpoint was analysed using a negative binomial regression model with a log link and the logarithm of the exposure time as offset. The model included treatment and pre-trial OAD as fixed factors. Missing data were imputed using multiple imputations (conditioning on expected event rate before premature treatment discontinuation or withdrawal from trial as if treated with IGlar).

Comparison groups	IDegLira v IGlar
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	superiority[4]
Method	Negative binomial regression model
Parameter estimate	Treatment Ratio
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.75

Notes:

[4] - Superiority of IDegLira was considered confirmed if the test procedure was not stopped (i.e. non-inferiority of IDegLira was confirmed for change from baseline in HbA1c and superiority of IDegLira was confirmed for change from baseline in body weight) and if the upper limit of the two-sided 95% CI for the rate ratio (IDegLira over IGlar) of rate of treatment-emergent severe or BG confirmed symptomatic hypoglycaemic episodes was strictly below 1.

Secondary: Insulin dose, total daily dose (U)

End point title	Insulin dose, total daily dose (U)

End point description:

Actual daily total insulin dose (Units) was evaluated after 26 weeks of randomised treatment. The results presented included retrieved data at week 26 for subjects who prematurely discontinued the trial product. The FAS included all randomised subjects. The statistical evaluation of the FAS followed the intent-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". Number analysed = Number of subjects contributed to the analysis at week 26.

End point type	Secondary

End point timeframe:

After 26 weeks

End point values	IDegLira	IGlar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	201		
Units: Units (U)				
arithmetic mean (standard deviation)	36.2 (± 13.4)	53.5 (± 26.1)		

Statistical analyses

Statistical analysis title	Analysis 1: Superiority analysis

Statistical analysis description:

The endpoint was analysed using an ANCOVA model with treatment, pre-trial OAD and region as factors and corresponding baseline HbA1c as covariate. Missing data were imputed using unconditional reference based multiple imputation including data obtained after premature treatment discontinuation. Number of subjects contributed to the analysis included all randomised subjects receiving at least one dose of the investigational product or comparator (419).

Comparison groups	IDegLira v IGlar
Number of subjects included in analysis	397
Analysis specification	Pre-specified
Analysis type	superiority[5]
Method	ANCOVA
Parameter estimate	Treatment Contrast
Point estimate	-15.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.6
upper limit	-11.13

Notes:

[5] - Superiority of IDegLira was considered confirmed if the test procedure was not stopped (i.e. non-inferiority of IDegLira was confirmed for change from baseline in HbA1c; and superiority of IDegLira was confirmed for weight change, number of treatment-emergent severe or BG confirmed symptomatic hypoglycaemic episodes and change in HbA1c) and if the upper limit of the two-sided 95% CI for the mean treatment difference (IDegLira minus IGlar) in insulin dose after 26 weeks was strictly below 0 U.

Secondary: Responder (Yes/No) for HbA1c < 7.0%

End point title	Responder (Yes/No) for HbA1c < 7.0%

End point description:

The proportion of subjects achieving pre-defined HbA1c targets <7.0% after 26 weeks of randomised treatment. The FAS included all randomised subjects. The statistical evaluation of the FAS followed the intent-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". Number analysed = Number of subjects contributed to the analysis at week 26. The results presented included retrieved data at week 26 for subjects who prematurely discontinued the trial product.

End point type	Secondary

End point timeframe:

After 26 weeks

End point values	IDegLira	IGlar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	202		
Units: Number of participants				
Yes	167	144		
No	30	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in fasting plasma glucose (FPG)

End point title	Change from baseline in fasting plasma glucose (FPG)

End point description:

Change from baseline (week 0) in FPG was evaluated after 26 weeks of randomised treatment. The FAS included all randomised subjects. The statistical evaluation of the FAS followed the intent-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". Number analysed = Number of subjects contributed to the analysis at week 26.

End point type	Secondary

End point timeframe:

After 26 weeks

End point values	IDegLira	IGlar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	195		
Units: mmol/L				
arithmetic mean (standard deviation)				
FPG (mmol/L) change from baseline to week 26	-3.72 (± 2.89)	-3.50 (± 2.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-emergent adverse events

End point title	Number of treatment-emergent adverse events

End point description:

Treatment emergent adverse events (TEAEs) were recorded from week 0-week 26. A TEAE was defined as an event that had onset date on or after the first day of exposure to randomised treatment and no later than 7 days after the last day of randomised treatment. If the event had onset date before the first day of exposure on randomised treatment and increased in severity during the treatment period and until 7 days after the last drug date, then this event should also be considered as a TEAE. Major cardiovascular events (MACEs) were considered treatment-emergent until 30 calendar days after the last day of randomised treatment. The safety analysis set included all subjects who received at least one dose of the investigational product or comparator.

End point type	Secondary

End point timeframe:
During 26 weeks

End point values	IDegLira	IGlar		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	210		
Units: Number of events	450	386		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first day of exposure until the end of treatment (week 0 to week 26) plus 7 days after last dose of trial product or 30 days for major cardiovascular events.

Adverse event reporting additional description:

TEAE: An event that had onset date on or after the first day of exposure to randomised treatment and no later than 7 days (30 days for MACEs) after the last day of randomised treatment (or an event that increased in severity during this period but had an onset date before first day of exposure).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	IDegLira

Reporting group description:

Subjects were administered with insulin degludec/liraglutide (IDegLira: 100 U/3.6 mg per mL) once daily for a duration of 26 weeks. IDegLira treatment was initiated at starting dose of 10 dose steps. The dose of IDeglira was adjusted individually twice weekly according to a predefined titration algorithm with a maximum daily dose of 50 dose steps. Pre-trial OAD treatments were continued according to current local label. The randomised subjects would be on either SGLT2i monotherapy or SGLT2i ± metformin ± pioglitazone excluding DPP4i. This treatment was to be unchanged throughout the trial, unless there was a safety concern.

Reporting group title	IGlar

Reporting group description:

Subjects were administered with insulin glargine (IGlar: 100 U/mL) once daily for a duration of 26 weeks. IGlar treatment was initiated with the starting dose of 10 U and adjusted individually twice weekly according to a predefined titration algorithm. Pre-trial OAD treatments were continued according to current local label. The randomised subjects would be on either SGLT2i monotherapy or SGLT2i ± metformin ± pioglitazone excluding DPP4i. This treatment was to be unchanged throughout the trial, unless there was a safety concern.

Serious adverse events	IDegLira	IGlar	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 209 (2.87%)	7 / 210 (3.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood potassium increased			
subjects affected / exposed	1 / 209 (0.48%)	0 / 210 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular evaluation			

subjects affected / exposed	1 / 209 (0.48%)	0 / 210 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 209 (0.00%)	1 / 210 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	0 / 209 (0.00%)	1 / 210 (0.48%)	
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	0 / 209 (0.00%)	1 / 210 (0.48%)	
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	1 / 209 (0.48%)	0 / 210 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Haemorrhagic stroke			
subjects affected / exposed	1 / 209 (0.48%)	0 / 210 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 209 (0.00%)	1 / 210 (0.48%)	
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 / 209 (0.00%)	1 / 210 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 209 (0.00%)	1 / 210 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device failure			
subjects affected / exposed	1 / 209 (0.48%)	0 / 210 (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			
Infected skin ulcer			
subjects affected / exposed	0 / 209 (0.00%)	1 / 210 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 209 (0.96%)	1 / 210 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 209 (0.00%)	1 / 210 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	IDegLira	IGlar	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 209 (23.44%)	45 / 210 (21.43%)	
Investigations			
Lipase increased			
subjects affected / exposed	12 / 209 (5.74%)	3 / 210 (1.43%)	
occurrences (all)	15	3	

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 18 / 209 (8.61%) 35	 19 / 210 (9.05%) 27	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 12 / 209 (5.74%) 22	 1 / 210 (0.48%) 2	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 11 / 209 (5.26%) 12	 9 / 210 (4.29%) 15	
Infections and infestations Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	 16 / 209 (7.66%) 22	 22 / 210 (10.48%) 24	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 January 2017	Update of section 18 with 'Acute Gallstone disease' in accordance with IDegLira minimum mandatory safety text. Update of procedures and minor administrative corrections and typographical errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported