



Clinical trial results:

DUAL™VII - Insulin degludec/liraglutide (IDegLira) vs. basal-bolus therapy: A clinical trial comparing efficacy and safety of insulin degludec/liraglutide (IDegLira) versus basal-bolus therapy in subjects with type 2 diabetes mellitus

Summary

EudraCT number	2014-003621-18
Trial protocol	HU SK GR ES CZ FR
Global end of trial date	05 October 2016

Results information

Result version number	v1 (current)
This version publication date	19 October 2017
First version publication date	19 October 2017

Trial information

Trial identification

Sponsor protocol code	NN9068-4185
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02420262
WHO universal trial number (UTN)	U1111-1160-6923

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Global Clinical Registry (GCR, 1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Global Clinical Registry (GCR, 1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	
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	30 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 October 2016
Global end of trial reached?	Yes
Global end of trial date	05 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the efficacy of insulin degludec/liraglutide (IDegLira) in terms of glycaemic control in subjects with type 2 diabetes mellitus on previous treatment with insulin glargine (IGlar) and metformin. This was done by comparing the difference in change in HbA1c from baseline after 26 weeks of treatment to a non-inferiority limit of 0.30% for once daily IDegLira versus basal-bolus therapy with once daily IGlar plus prandial insulin aspart (IAsp), both arms in combination with metformin.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (64th WMA Assembly) and ICH Good Clinical Practice (May 1996) and 21 CFR 312.120.

Background therapy:

All subjects were to continue with metformin at the stable pre-trial dose level, unless there was a safety concern.

Evidence for comparator:

Not applicable

Actual start date of recruitment	26 July 2015
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	Czech Republic: 37
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Greece: 44
Country: Number of subjects enrolled	Hungary: 37
Country: Number of subjects enrolled	Israel: 30
Country: Number of subjects enrolled	Mexico: 46
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	Slovakia: 36
Country: Number of subjects enrolled	Spain: 45
Country: Number of subjects enrolled	Turkey: 40
Country: Number of subjects enrolled	United States: 80
Worldwide total number of subjects	506
EEA total number of subjects	215

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)	382
From 65 to 84 years	123
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 89 sites in 12 countries: Argentina (3 sites), Czech Republic (5 sites), France (3 sites), Greece (6 sites), Hungary (3 sites), Israel (6 sites), Mexico (3 sites), Russia (7 sites), Slovakia (5 sites), Spain (6 sites), Turkey (5 sites) and United States (37 sites).

Pre-assignment

Screening details:

Subjects with type 2 diabetes mellitus were on treatment with stable daily dose of insulin glargine (IGlar) between 20 units and 50 units (both inclusive) for at least 56 days prior to screening in combination with a stable daily dose of metformin (≥ 1500 mg or maximum tolerated dose) for at least 90 days prior to screening.

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:

Insulin Degludec/Liraglutide (IDegLira) was administered once daily (OD) for a duration of 26 weeks. IDegLira treatment was initiated at starting dose 16 dose steps and was titrated according to a predefined titration algorithm. The maximum daily dose was 50 dose steps. All subjects continued with metformin at pre-trial doses (≥ 1500 mg or the maximum tolerated dose), 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 pre-filled PDS290 pen-injector with a fixed IDeg/liraglutide ratio of 100 units/3.6 mg per mL solution. IDegLira treatment was initiated at 16 dose steps (containing 16 units IDeg /0.6 mg liraglutide) and adjusted twice weekly 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 was 50 dose steps (50U IDeg /1.8 mg Lira).

Arm title	IGlar + IAsp
------------------	--------------

Arm description:

Subjects received insulin glargine plus prandial insulin aspart (IGlar + IAsp) for a duration of 26 weeks. A stable pre-trial OD dose of IGlar was continued with metformin therapy (≥ 1500 mg or the maximum tolerated dose). IAsp was added to the IGlar therapy with a start dose of 4U as prandial insulin treatment before each main meal and was titrated in a treat-to-target fashion in accordance with a predefined titration algorithm. There was no maximum dose specified for IGlar or IAsp.

Arm type	Active comparator
----------	-------------------

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

Dosage and administration details:

A stable pre- trial OD dose of IGlar (20-50 units, in a 3 mL pre-filled Solostar®. The dose of IGlar was adjusted twice weekly based on the mean of three pre-breakfast 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]).

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

Dosage and administration details:

IAsp was added to the IGlar therapy with a start dose of 4U using a 3 mL pre-filled FlexPen®, as prandial insulin treatment before each main meal. The dose of IAsp was titrated twice weekly based on pre-prandial and bedtime SMPGs, obtained on the three previous days (target SMPG: 4.0 – 6.0 mmol/L).

Number of subjects in period 1	IDegLira	IGlar + IAsp
Started	252	254
Exposed	252	253
Completed	250	249
Not completed	2	5
Consent withdrawn by subject	1	4
Adverse event, non-fatal	1	-
Unclassified	-	1

Baseline characteristics

Reporting groups

Reporting group title	IDegLira
-----------------------	----------

Reporting group description:

Insulin Degludec/Liraglutide (IDegLira) was administered once daily (OD) for a duration of 26 weeks. IDegLira treatment was initiated at starting dose 16 dose steps and was titrated according to a predefined titration algorithm. The maximum daily dose was 50 dose steps. All subjects continued with metformin at pre-trial doses (≥ 1500 mg or the maximum tolerated dose), unless there was a safety concern.

Reporting group title	IGlar + IAsp
-----------------------	--------------

Reporting group description:

Subjects received insulin glargine plus prandial insulin aspart (IGlar + IAsp) for a duration of 26 weeks. A stable pre-trial OD dose of IGlar was continued with metformin therapy (≥ 1500 mg or the maximum tolerated dose). IAsp was added to the IGlar therapy with a start dose of 4U as prandial insulin treatment before each main meal and was titrated in a treat-to-target fashion in accordance with a predefined titration algorithm. There was no maximum dose specified for IGlar or IAsp.

Reporting group values	IDegLira	IGlar + IAsp	Total
Number of subjects	252	254	506
Age categorical Units: Subjects			
Adults (18-64 years)	182	200	382
From 65-84 years	70	53	123
85 years and over	0	1	1
Age Continuous Units: years			
arithmetic mean	58.6	58.0	-
standard deviation	± 9.0	± 8.6	-
Gender, Male/Female Units: Subjects			
Female	142	137	279
Male	110	117	227
Study Specific Characteristic Glycosylated haemoglobin (HbA1c) Units: percentage of glycosylated haemoglobin			
arithmetic mean	8.21	8.24	-
standard deviation	± 0.76	± 0.81	-
Study Specific Characteristic Body Weight Units: kg			
arithmetic mean	87.2	88.2	-
standard deviation	± 16.0	± 17.2	-

End points

End points reporting groups

Reporting group title	IDegLira
-----------------------	----------

Reporting group description:

Insulin Degludec/Liraglutide (IDegLira) was administered once daily (OD) for a duration of 26 weeks. IDegLira treatment was initiated at starting dose 16 dose steps and was titrated according to a predefined titration algorithm. The maximum daily dose was 50 dose steps. All subjects continued with metformin at pre-trial doses (≥ 1500 mg or the maximum tolerated dose), unless there was a safety concern.

Reporting group title	IGlar + IAsp
-----------------------	--------------

Reporting group description:

Subjects received insulin glargine plus prandial insulin aspart (IGlar + IAsp) for a duration of 26 weeks. A stable pre-trial OD dose of IGlar was continued with metformin therapy (≥ 1500 mg or the maximum tolerated dose). IAsp was added to the IGlar therapy with a start dose of 4U as prandial insulin treatment before each main meal and was titrated in a treat-to-target fashion in accordance with a predefined titration algorithm. There was no maximum dose specified for IGlar or IAsp.

Primary: Change from baseline in HbA1c (glycosylated haemoglobin)

End point title	Change from baseline in HbA1c (glycosylated haemoglobin)
-----------------	--

End point description:

Change from baseline in HbA1c values after 26 weeks of treatment. The analysis of this efficacy endpoint was based on the full analysis set (FAS). The FAS included all randomised subjects. The statistical evaluation of the FAS followed the intention-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". 14 subjects in IDegLira and 21 subjects in IGlar + IAsp arm did not contribute to the analysis for this endpoint.

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

End point timeframe:

After 26 weeks of treatment

End point values	IDegLira	IGlar + IAsp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	245		
Units: Percentage of glycosylated haemoglobin				
least squares mean (standard error)	-1.48 (± 0.05)	-1.46 (± 0.05)		

Statistical analyses

Statistical analysis title	Primary statistical analysis
----------------------------	------------------------------

Statistical analysis description:

Change from baseline in HbA1c was analysed using a mixed model for repeated measurements with an unstructured covariance matrix. The model included treatment, visit and region as fixed factors and baseline HbA1c as covariate. Interactions between visit and all factors and the covariate were also included in the model.

Comparison groups	IGlar + IAsp v IDegLira
-------------------	-------------------------

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment contrast
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.12

Notes:

[1] - Non-inferiority for IDegLira vs basal-bolus (IGlar + IAsp) was considered confirmed if the upper boundary of the two-sided 95% confidence interval was strictly below 0.30% or equivalent for non-inferiority using one-sided test for null hypothesis (H0): $D \geq 0.30\%$ against alternative hypothesis (HA): $D < 0.30\%$ was less than or equal to 2.5%, where D is the mean treatment difference (IDegLira minus basal-bolus).

Secondary: Number of treatment emergent severe or blood glucose confirmed symptomatic hypoglycaemic episodes

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

End point description:

Severe or blood glucose (BG) confirmed symptomatic hypoglycaemic episodes were defined as episodes that were severe and/or BG confirmed by a plasma glucose value of <56 mg/dL (3.1 mmol/L), with symptoms consistent with hypoglycaemia. The safety analysis set (SAS) included all subjects receiving at least one dose of the investigational product or comparator. Subjects in the safety set contributed to the evaluation "as treated". One subject in IGlar + IAsp arm did not contribute to the analysis for this endpoint.

End point type	Secondary
End point timeframe:	
During 26 weeks of treatment	

End point values	IDegLira	IGlar + IAsp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	252	253		
Units: Number of episodes	129	975		

Statistical analyses

Statistical analysis title	Confirmatory secondary statistical analysis
Statistical analysis description:	
Hypoglycaemic episodes were analysed using a negative binomial regression. The model included treatment and region as fixed factors and logarithm of the time period in which a hypoglycaemic episode considered treatment emergent as offset.	
Comparison groups	IDegLira v IGlar + IAsp

Number of subjects included in analysis	505
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	< 0.0001
Method	Negative binomial regression model
Parameter estimate	Treatment ratio
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	0.17

Notes:

[2] - Superiority for IDegLira vs basal-bolus was considered confirmed if the 95% confidence interval for the treatment rate ratio was entirely below 1.0. The test for superiority of the confirmatory secondary endpoints was carried out only if non-inferiority of IDegLira vs basal-bolus for primary endpoint was confirmed.

Secondary: Change from baseline in body weight

End point title	Change from baseline in body weight
End point description:	
Change from baseline in body weight after 26 weeks of treatment. The analysis of this efficacy endpoint was based on the full analysis set (FAS). The FAS included all randomised subjects. The statistical evaluation of the FAS followed the intention-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". 08 subjects in both IDegLira and IGlara + IAsp arm did not contribute to the analysis for this endpoint.	
End point type	Secondary
End point timeframe:	
After 26 weeks of treatment	

End point values	IDegLira	IGlar + IAsp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	246		
Units: kg				
least squares mean (standard error)	-0.93 (± 0.22)	2.64 (± 0.22)		

Statistical analyses

Statistical analysis title	Confirmatory secondary statistical analysis
Statistical analysis description:	
Body weight measurements were analysed using a linear mixed model with an unstructured covariance matrix. The model included treatment, visit and region as fixed factors and baseline bodyweight as covariate. Interactions between visit and all factors and the covariate were also included in the model.	
Comparison groups	IDegLira v IGlara + IAsp

Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	-3.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.19
upper limit	-2.95

Notes:

[3] - Superiority for IDegLira vs basal-bolus was considered confirmed if the 95% confidence interval for the treatment difference was below 0 or equal to 0.

Secondary: Responder for HbA1c below 7.0%

End point title	Responder for HbA1c below 7.0%
End point description:	
Number of subjects with HbA1c below 7% after 26 weeks of treatment. The analysis of this efficacy endpoint was based on the full analysis set (FAS). The FAS included all randomised subjects. The statistical evaluation of the FAS followed the intention-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". 14 subjects in IDegLira and 21 subjects in IGlar + IAsp arm did not contribute to the analysis for this endpoint.	
End point type	Secondary
End point timeframe:	
After 26 weeks of treatment	

End point values	IDegLira	IGlar + IAsp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	233		
Units: Participants				
Yes	157	156		
No	81	77		

Statistical analyses

No statistical analyses for this end point

Secondary: Responder for HbA1c below or equal to 6.5 %

End point title	Responder for HbA1c below or equal to 6.5 %
End point description:	
Number of subjects with HbA1c below 7% after 26 weeks of treatment. The analysis of this efficacy endpoint was based on the full analysis set (FAS). The FAS included all randomised subjects. The statistical evaluation of the FAS followed the intention-to-treat (ITT) principle and subjects contributed to the evaluation "as randomised". 14 subjects in IDegLira and 21 subjects in IGlar + IAsp arm did not contribute to the analysis for this endpoint.	
End point type	Secondary

End point timeframe:
After 26 weeks of treatment

End point values	IDegLira	IGlar + IAsp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	233		
Units: Participants				
Yes	118	104		
No	120	129		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Until 26 weeks+ follow-up contact (comprising of 7 days) after end of randomised treatment.

Adverse event reporting additional description:

A treatment emergent adverse event was defined as an event that had onset time after the first day of exposure to randomised treatment and no later than seven days after the last day of randomised treatment (26 weeks + 7 days of follow-up). Analysis was performed using SAS, included all subjects receiving at least one dose of trial product.

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

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	19
--------------------	----

Reporting groups

Reporting group title	IDegLira
-----------------------	----------

Reporting group description:

Insulin Degludec/Liraglutide (IDegLira) was administered once daily (OD) for a duration of 26 weeks. IDegLira treatment was initiated at starting dose 16 dose steps and was titrated according to a predefined titration algorithm. The maximum daily dose was 50 dose steps. All subjects continued with metformin at pre-trial doses (≥ 1500 mg or the maximum tolerated dose), unless there was a safety concern.

Reporting group title	IGlar + IAsp
-----------------------	--------------

Reporting group description:

Subjects received insulin glargine plus prandial insulin aspart (IGlar + IAsp) for a duration of 26 weeks. A stable pre-trial OD dose of IGlar was continued with metformin therapy (≥ 1500 mg or the maximum tolerated dose). IAsp was added to the IGlar therapy with a start dose of 4U as prandial insulin treatment before each main meal and was titrated in a treat-to-target fashion in accordance with a predefined titration algorithm. There was no maximum dose specified for IGlar or IAsp.

Serious adverse events	IDegLira	IGlar + IAsp	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 252 (4.76%)	10 / 253 (3.95%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Embolism arterial			

subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (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	1 / 252 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Silent myocardial infarction			

subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (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 fistula			
subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic cyst			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (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			
Diabetic foot			
subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Stag horn calculus			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (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			
Musculoskeletal chest pain			

subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diabetic foot infection			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 252 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 252 (0.40%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 252 (0.40%)	0 / 253 (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	IDegLira	IGlar + IAsp	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 252 (33.33%)	79 / 253 (31.23%)	
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 252 (5.56%)	18 / 253 (7.11%)	
occurrences (all)	17	23	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	9 / 252 (3.57%)	14 / 253 (5.53%)	
occurrences (all)	9	15	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	16 / 252 (6.35%)	10 / 253 (3.95%)	
occurrences (all)	24	17	
Nausea			
subjects affected / exposed	28 / 252 (11.11%)	4 / 253 (1.58%)	
occurrences (all)	37	4	
Infections and infestations			
Influenza			
subjects affected / exposed	18 / 252 (7.14%)	12 / 253 (4.74%)	
occurrences (all)	21	13	
Nasopharyngitis			
subjects affected / exposed	12 / 252 (4.76%)	30 / 253 (11.86%)	
occurrences (all)	12	35	
Upper respiratory tract infection			
subjects affected / exposed	15 / 252 (5.95%)	17 / 253 (6.72%)	
occurrences (all)	15	19	

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