Clinical trial results:
A 32-week randomised, multinational, treat-to-target, open label, parallel group comparison of stepwise insulin intensification of biphasic insulin aspart (BIAsp) 30 and basal-bolus therapy with insulin glargine and insulin aspart in insulin naïve type 2 diabetic patients inadequately controlled on oral anti-diabetic therapy

Summary

EudraCT number	2014-003708-62
Trial protocol	BG HU
Global end of trial date	21 September 2016

Results information

Result version number	v1 (current)
This version publication date	14 October 2017
First version publication date	14 October 2017

Trial information

Trial identification

Sponsor protocol code	BIAsp-4157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02453685
WHO universal trial number (UTN)	U1111-1158-7280

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)	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	22 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 September 2016
Global end of trial reached?	Yes
Global end of trial date	21 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of intensification with BIAsp 30 versus intensification with basal bolus insulin analogues (insulin glargine [IGlar] and insulin aspart [IAsp]) on glycaemic control.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and ICH Good Clinical Practice (1996) and FDA 21 CFR 312.120.

Background therapy:

Pre-trial treatment with metformin and sulphonylurea (SU) were continued as background treatment throughout the entire trial.

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 September 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	United Arab Emirates: 31
Country: Number of subjects enrolled	Australia: 15
Country: Number of subjects enrolled	Bulgaria: 42
Country: Number of subjects enrolled	Hungary: 35
Country: Number of subjects enrolled	India: 66
Country: Number of subjects enrolled	Korea, Republic of: 31
Country: Number of subjects enrolled	Serbia: 52
Country: Number of subjects enrolled	Thailand: 23
Country: Number of subjects enrolled	Turkey: 40
Worldwide total number of subjects	335
EEA total number of subjects	77

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	257
From 65 to 84 years	78
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 41 sites in 9 countries, as follows: Australia: 4 sites; Bulgaria: 5 sites; Hungary: 3 sites; India: 7 sites; Korea, Republic of: 4 sites; Serbia: 5 sites; Thailand: 4 sites; Turkey: 5 sites; United Arab Emirates: 4 sites.

Pre-assignment

Screening details:

Not applicable

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	BIAsp 30

Arm description:

Subjects received subcutaneous (s.c.) injection of biphasic insulin aspart 30 (BIAsp 30 - a mixture of soluble IAsp 30% and protaminated IAsp 70%) during a 32-week treatment period (divided into 4 periods of 8 weeks each). Subjects started treatment with 1 daily injection of BIAsp 30 (starting dose 12 unit) with the largest meal.

Insulin titration: Subjects underwent a weekly insulin dose titration during the entire treatment period in order to achieve the pre-meal self-measured plasma glucose (SMPG) target of 4.4−6.1 mmol/L (80−110 mg/dL).

Insulin intensification: At the end of each 8-week period, insulin treatment was intensified in a stepwise manner by adding an additional injection of BIAsp 30 depending on whether subjects achieved the pre-defined glycaemic target (haemoglobin A1c [HbA1c]) <7.0%). Subjects had the possibility of receiving up to 3 daily injections of BIAsp 30.

Subjects continued pre-trial treatment with metformin and SU throughout the trial.

Arm type	Experimental
Investigational medicinal product name	Biphasic insulin aspart 30
Investigational medicinal product code	
Other name	NovoMix®30
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

BIAsp 30 was administered as s.c. injections according to the locally approved label. The chosen region of the body where the injections were administered should remain the same throughout the trial. However, the injection site within the chosen body region should rotate or change for each administration.

Arm title	Basal-bolus

Arm description:

Subjects received s.c. injections of IGlar during a 32-week treatment period (divided into 4 periods of 8 weeks each). Subjects started with 1 daily injection of IGlar (administrated at same point of time every day) with starting dose of 10 units.

Insulin titration: Subjects underwent a weekly insulin dose titration during the entire treatment period in order to achieve the pre-meal SMPG target of 4.4−6.1 mmol/L (80−110 mg/dL).

Insulin intensification: At the end of each 8-week period, insulin treatment was intensified in a stepwise manner by adding an additional injection of IAsp depending on whether subjects achieved the pre-defined glycaemic target (HbA1c <7.0%). Subjects had the possibility of receiving 1 daily injection of IGlar plus up to 3 daily injections of IAsp.

Subjects continued their pre-trial treatment with metformin and SU throughout the trial.

Arm type	Active comparator
Investigational medicinal product name	Insulin aspart
Investigational medicinal product code	
Other name	NovoRapid®
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

IAsp was administered as s.c. injections according to the locally approved label. The chosen region of the body where the injections were administered should remain the same throughout the trial. However, the injection site within the chosen body region should rotate or change for each administration.

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

Dosage and administration details:

IGlar was administered as s.c. injections according to the locally approved label. The chosen region of the body where the injections were administered should remain the same throughout the trial. However, the injection site within the chosen body region should rotate or change for each administration.

Number of subjects in period 1	BIAsp 30	Basal-bolus
Started	168	167
Exposed	166	166
Completed	149	155
Not completed	19	12
Consent withdrawn by subject	8	4
Adverse event, non-fatal	-	1
Unclassified	4	2
Lost to follow-up	-	1
Protocol deviation	7	4

Baseline characteristics

Reporting groups	
Reporting group title	BIAsp 30

Reporting group description:

Subjects received subcutaneous (s.c.) injection of biphasic insulin aspart 30 (BIAsp 30 - a mixture of soluble IAsp 30% and protaminated IAsp 70%) during a 32-week treatment period (divided into 4 periods of 8 weeks each). Subjects started treatment with 1 daily injection of BIAsp 30 (starting dose 12 unit) with the largest meal.

Insulin titration: Subjects underwent a weekly insulin dose titration during the entire treatment period in order to achieve the pre-meal self-measured plasma glucose (SMPG) target of 4.4−6.1 mmol/L (80−110 mg/dL).

Insulin intensification: At the end of each 8-week period, insulin treatment was intensified in a stepwise manner by adding an additional injection of BIAsp 30 depending on whether subjects achieved the pre-defined glycaemic target (haemoglobin A1c [HbA1c]) <7.0%). Subjects had the possibility of receiving up to 3 daily injections of BIAsp 30.

Subjects continued pre-trial treatment with metformin and SU throughout the trial.

Reporting group title	Basal-bolus

Reporting group description:

Subjects received s.c. injections of IGlar during a 32-week treatment period (divided into 4 periods of 8 weeks each). Subjects started with 1 daily injection of IGlar (administrated at same point of time every day) with starting dose of 10 units.

Insulin titration: Subjects underwent a weekly insulin dose titration during the entire treatment period in order to achieve the pre-meal SMPG target of 4.4−6.1 mmol/L (80−110 mg/dL).

Insulin intensification: At the end of each 8-week period, insulin treatment was intensified in a stepwise manner by adding an additional injection of IAsp depending on whether subjects achieved the pre-defined glycaemic target (HbA1c <7.0%). Subjects had the possibility of receiving 1 daily injection of IGlar plus up to 3 daily injections of IAsp.

Subjects continued their pre-trial treatment with metformin and SU throughout the trial.

Reporting group values	BIAsp 30	Basal-bolus	Total
Number of subjects	168	167	335
Age Categorical Units: Subjects			
Adults (18-64 years)	131	126	257
From 65-84 years	37	41	78
Age Continuous Units: years			
arithmetic mean	56.6	56.5	
standard deviation	± 10.4	± 10.1	-
Gender Categorical Units: Subjects			
Female	79	90	169
Male	89	77	166
HbA1c Units: Percentage of HbA1c			
arithmetic mean	8.31	8.23	
standard deviation	± 0.73	± 0.69	-

End points

End points reporting groups

Reporting group title	BIAsp 30

Reporting group description:

Subjects received subcutaneous (s.c.) injection of biphasic insulin aspart 30 (BIAsp 30 - a mixture of soluble IAsp 30% and protaminated IAsp 70%) during a 32-week treatment period (divided into 4 periods of 8 weeks each). Subjects started treatment with 1 daily injection of BIAsp 30 (starting dose 12 unit) with the largest meal.

Insulin titration: Subjects underwent a weekly insulin dose titration during the entire treatment period in order to achieve the pre-meal self-measured plasma glucose (SMPG) target of 4.4−6.1 mmol/L (80−110 mg/dL).

Insulin intensification: At the end of each 8-week period, insulin treatment was intensified in a stepwise manner by adding an additional injection of BIAsp 30 depending on whether subjects achieved the pre-defined glycaemic target (haemoglobin A1c [HbA1c]) <7.0%). Subjects had the possibility of receiving up to 3 daily injections of BIAsp 30.

Subjects continued pre-trial treatment with metformin and SU throughout the trial.

Reporting group title	Basal-bolus

Reporting group description:

Subjects received s.c. injections of IGlar during a 32-week treatment period (divided into 4 periods of 8 weeks each). Subjects started with 1 daily injection of IGlar (administrated at same point of time every day) with starting dose of 10 units.

Insulin titration: Subjects underwent a weekly insulin dose titration during the entire treatment period in order to achieve the pre-meal SMPG target of 4.4−6.1 mmol/L (80−110 mg/dL).

Insulin intensification: At the end of each 8-week period, insulin treatment was intensified in a stepwise manner by adding an additional injection of IAsp depending on whether subjects achieved the pre-defined glycaemic target (HbA1c <7.0%). Subjects had the possibility of receiving 1 daily injection of IGlar plus up to 3 daily injections of IAsp.

Subjects continued their pre-trial treatment with metformin and SU throughout the trial.

Primary: Change from baseline in HbA1c

End point title	Change from baseline in HbA1c

End point description:

Change in HbA1c from baseline (week 0) to week 32. Analysis was performed on the full analysis set.

End point type	Primary

End point timeframe:

After 32 weeks of treatment

End point values	BIAsp 30	Basal-bolus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164[1]	164[2]		
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-1.16 (± 0.98)	-1.3 (± 0.9)		

Notes:

[1] - Week 32 data after application of Last observation carried forward; 164 subjects contributed

[2] - Week 32 data after application of Last observation carried forward; 164 subjects contributed

Statistical analyses

Statistical analysis title	BIAsp 30 vs Basal-bolus

Statistical analysis description:

Analysis was performed using mixed model repeated measurements (MMRM) including treatment, region, and strata as fixed effects, HbA1c at baseline as covariate, interactions between all fixed effects and visit and using an unstructured residual covariance matrix. Below, 'treatment difference' refers to "BIAsp 30 minus Basal-bolus.

Comparison groups	BIAsp 30 v Basal-bolus
Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0435
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.36

Secondary: HbA1c < 7.0% without severe hypoglycaemic episodes (yes/no)

End point title	HbA1c < 7.0% without severe hypoglycaemic episodes (yes/no)

End point description:

Percentage of subjects with HbA1c below 7.0% after 32 weeks of randomised treatment without treatment emergent severe hypoglycaemic episodes during the last 12 weeks of treatment. Subjects withdrawn before 32 weeks were handled as non-responders. Severe hypoglycaemic episode was defined as an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions. Plasma glucose (PG) concentrations may not be available during an event, but neurological recovery following the return of PG to normal is considered sufficient evidence that the event was induced by a low PG concentration. Analysis was performed on the full analysis set.

End point type	Secondary

End point timeframe:

After 32 weeks of treatment

End point values	BIAsp 30	Basal-bolus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	167		
Units: Percentage of subjects				
number (not applicable)				
Yes	42.3	56.3		
No	57.7	43.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment emergent hypoglycaemic episodes classified according to the ADA and the Novo Nordisk definitions

End point title	Number of treatment emergent hypoglycaemic episodes classified according to the ADA and the Novo Nordisk definitions

End point description:

Hypoglycaemic episodes were classified as severe, Asymptomatic, Documented symptomatic, Pseudo, and Probable symptomatic as per ADA classification. As symptoms of hypoglycaemia occur below a PG level of 3.1 mmol/L, (56 mg/dL) Novo Nordisk classification included hypoglycaemia with plasma glucose (PG) levels below 3.1 mmol/L (56 mg/dL) in the definition of blood glucose confirmed hypoglycaemia. Hence, Novo Nordisk classification included following types of hypoglycaemia in addition to ADA classification: Severe hypoglycaemia, Symptomatic blood glucose confirmed hypoglycaemia, Asymptomatic blood glucose confirmed hypoglycaemia, Severe or blood glucose confirmed symptomatic hypoglycaemia, Blood glucose confirmed hypoglycaemia, and Severe or blood glucose confirmed hypoglycaemia. Reported data represents total of all hypoglycaemic episodes. Analysis was performed on the safety analysis set (all subjects receiving at least one dose of the investigational product or its comparator).

End point type	Secondary

End point timeframe:

During 32 weeks of treatment

End point values	BIAsp 30	Basal-bolus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	166		
Units: Hypoglycaemic episodes				
ADA classification	1650	1841		
Novo Nordisk classification	1650	1841		

Statistical analyses

No statistical analyses for this end point

Secondary: Total daily insulin dose

End point title	Total daily insulin dose

End point description:

Total daily insulin dose in the basal bolus treatment group and in BIAsp 30 treatment group at each week of each treatment. Analysis was performed on the safety analysis set.

End point type	Secondary

End point timeframe:

During 32 weeks of treatment

End point values	BIAsp 30	Basal-bolus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	166		
Units: U/kg				
arithmetic mean (standard deviation)				
Week 1 (n=164, 165)	0.157 (± 0.038)	0.127 (± 0.026)		
Week 2 (n=162, 165)	0.187 (± 0.053)	0.167 (± 0.042)		
Week 3 (n=163, 164)	0.214 (± 0.07)	0.197 (± 0.061)		
Week 4 (n=160, 161)	0.238 (± 0.088)	0.224 (± 0.076)		
Week 5 (n=158, 158)	0.259 (± 0.102)	0.244 (± 0.088)		
Week 6 (n=157, 161)	0.28 (± 0.114)	0.264 (± 0.1)		
Week 7 (n=155, 161)	0.296 (± 0.131)	0.281 (± 0.11)		
Week 8 (n=155, 161)	0.308 (± 0.145)	0.296 (± 0.119)		
Week 9 (n=154, 159)	0.369 (± 0.172)	0.339 (± 0.137)		
Week 10 (n=154, 159)	0.397 (± 0.199)	0.365 (± 0.16)		
Week 11 (n=154, 159)	0.421 (± 0.224)	0.391 (± 0.182)		
Week 12 (n=153, 160)	0.443 (± 0.245)	0.413 (± 0.202)		
Week 13 (n=150, 158)	0.456 (± 0.267)	0.425 (± 0.214)		
Week 14 (n=151, 158)	0.472 (± 0.277)	0.439 (± 0.228)		
Week 15 (n=151, 159)	0.487 (± 0.295)	0.455 (± 0.237)		
Week 16 (n=151, 159)	0.501 (± 0.308)	0.468 (± 0.248)		
Week 17 (n=149, 156)	0.528 (± 0.324)	0.496 (± 0.27)		
Week 18 (n=150, 157)	0.546 (± 0.334)	0.516 (± 0.294)		
Week 19 (n=149, 157)	0.557 (± 0.353)	0.532 (± 0.316)		
Week 20 (n=148, 155)	0.569 (± 0.367)	0.544 (± 0.32)		
Week 21 (n=149, 155)	0.588 (± 0.387)	0.563 (± 0.347)		
Week 22 (n=149, 156)	0.602 (± 0.401)	0.58 (± 0.359)		

Week 23 (n=148, 156)	0.607 (± 0.411)	0.59 (± 0.373)		
Week 24 (n=148, 156)	0.615 (± 0.426)	0.605 (± 0.386)		
Week 25 (n=147, 154)	0.628 (± 0.435)	0.618 (± 0.398)		
Week 26 (n=147, 156)	0.643 (± 0.454)	0.643 (± 0.434)		
Week 27 (n=149, 155)	0.661 (± 0.472)	0.653 (± 0.452)		
Week 28 (n=149, 155)	0.671 (± 0.487)	0.664 (± 0.466)		
Week 29 (n=149, 155)	0.688 (± 0.509)	0.674 (± 0.484)		
Week 30 (n=149, 155)	0.692 (± 0.511)	0.682 (± 0.497)		
Week 31 (n=149, 155)	0.703 (± 0.525)	0.693 (± 0.515)		
Week 32 (n=153, 155)	0.7 (± 0.542)	0.708 (± 0.537)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first randomised treatment (week 0) to last randomised treatment (week 32) + 7 days.

Adverse event reporting additional description:

Safety analysis set included all subjects receiving at least one dose of the investigational product or its comparator. All the adverse events mentioned here were treatment emergent (an event that has an 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).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	BIAsp 30

Reporting group description:

Subjects received s.c. injection of BIAsp 30 (a mixture of soluble IAsp 30% and protaminated IAsp 70%) during a 32-week treatment period (divided into 4 periods of 8 weeks each). Subjects started treatment with 1 daily injection of BIAsp 30 (starting dose 12 unit) with the largest meal.

Insulin titration: Subjects underwent a weekly insulin dose titration during the entire treatment period in order to achieve the pre-meal SMPG target of 4.4−6.1 mmol/L (80−110 mg/dL).

Insulin intensification: At the end of each 8-week period, insulin treatment was intensified in a stepwise manner by adding an additional injection of BIAsp 30 depending on whether subjects achieved the pre-defined glycaemic target (HbA1c <7.0%). Subjects had the possibility of receiving up to 3 daily injections of BIAsp 30.

Subjects continued their pre-trial treatment with metformin and SU throughout the trial.

Reporting group title	Basal-bolus

Reporting group description:

Subjects received s.c. injections of IGlar during a 32-week treatment period (divided into 4 periods of 8 weeks each). Subjects started with 1 daily injection of IGlar (administrated at same point of time every day) with starting dose of 10 units.

Insulin titration: Subjects underwent a weekly insulin dose titration during the entire treatment period in order to achieve the pre-meal SMPG target of 4.4−6.1 mmol/L (80−110 mg/dL).

Insulin intensification: At the end of each 8-week period, insulin treatment was intensified in a stepwise manner by adding an additional injection of IAsp depending on whether subjects achieved the pre-defined glycaemic target (HbA1c <7.0%). Subjects had the possibility of receiving 1 daily injection of IGlar plus up to 3 daily injections of IAsp.

Subjects continued their pre-trial treatment with metformin and SU throughout the trial.

Serious adverse events	BIAsp 30	Basal-bolus	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 166 (8.43%)	12 / 166 (7.23%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Invasive breast carcinoma			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (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			
Fall			
subjects affected / exposed	0 / 166 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 166 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 166 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	2 / 166 (1.20%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (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			
Cerebellar infarction			
subjects affected / exposed	0 / 166 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetic neuropathy			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			
subjects affected / exposed	0 / 166 (0.00%)	3 / 166 (1.81%)	
occurrences causally related to treatment / all	0 / 0	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic unconsciousness			
subjects affected / exposed	0 / 166 (0.00%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 166 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			

subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis erosive			
subjects affected / exposed	0 / 166 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (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 / 166 (0.60%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restrictive pulmonary disease			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 166 (0.60%)	0 / 166 (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 / 166 (0.00%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 166 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 166 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	2 / 166 (1.20%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	2 / 2	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	BIAsp 30	Basal-bolus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 166 (22.29%)	40 / 166 (24.10%)	
Nervous system disorders			

Headache			
subjects affected / exposed	12 / 166 (7.23%)	15 / 166 (9.04%)	
occurrences (all)	24	27	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 166 (6.02%)	11 / 166 (6.63%)	
occurrences (all)	19	12	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 166 (6.63%)	6 / 166 (3.61%)	
occurrences (all)	16	7	
Back pain			
subjects affected / exposed	11 / 166 (6.63%)	8 / 166 (4.82%)	
occurrences (all)	13	9	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	21 / 166 (12.65%)	18 / 166 (10.84%)	
occurrences (all)	31	27	
Upper respiratory tract infection			
subjects affected / exposed	11 / 166 (6.63%)	11 / 166 (6.63%)	
occurrences (all)	15	13	

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