Clinical trial results:
The efficacy and safety of liraglutide adjunct to insulin treatment in type 1 diabetes. A 26 week randomised, insulin capped, placebo-controlled, double-blind, parallel group, multinational, multi-centre trial

Summary

EudraCT number	2012-005778-74
Trial protocol	AT FI BG SE IT ES BE NL DK FR
Global end of trial date	27 April 2015

Results information

Result version number	v1 (current)
This version publication date	12 May 2016
First version publication date	12 May 2016

Trial information

Trial identification

Sponsor protocol code	NN9211-4083

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02098395
WHO universal trial number (UTN)	U1111-1138-0619

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	10 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2015
Global end of trial reached?	Yes
Global end of trial date	27 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm superiority of liraglutide compared to placebo, both adjunct to insulin treatment, on glycaemic control, after 26 weeks of treatment in subjects with established type 1 diabetes in inadequate glycaemic control.

Protection of trial subjects:

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

Background therapy:

Subjects continued their pre-trial insulin treatment (either basal bolus insulin treatment or continuous subcutaneous insulin infusion [CSII] treatment) throughout the trial. The type and brand of basal or bolus insulin was not to be changed (unless for safety of the subject) throughout the trial, as differences in insulin action and profiles could have the potential to interfere with the endpoints of the trial.

Evidence for comparator:

Not applicable

Actual start date of recruitment	08 May 2014
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	Netherlands: 27
Country: Number of subjects enrolled	Spain: 63
Country: Number of subjects enrolled	Sweden: 33
Country: Number of subjects enrolled	Austria: 40
Country: Number of subjects enrolled	Belgium: 64
Country: Number of subjects enrolled	Bulgaria: 54
Country: Number of subjects enrolled	Denmark: 32
Country: Number of subjects enrolled	Finland: 41
Country: Number of subjects enrolled	France: 41
Country: Number of subjects enrolled	Italy: 69
Country: Number of subjects enrolled	Canada: 57
Country: Number of subjects enrolled	United States: 267
Country: Number of subjects enrolled	South Africa: 47
Worldwide total number of subjects	835
EEA total number of subjects	464

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)	783
From 65 to 84 years	51
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Subjects were randomised at 113 sites in 13 countries: Austria 2 sites, Belgium 9 sites, Bulgaria 5 sites, Canada 9 sites, Denmark 4 sites, Finland 6 sites, France 9 sites, Italy 7 sites, Netherlands 5 sites, South Africa 2 sites, Spain 5 sites, Sweden 5 sites, United States 45 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	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Subjects were randomised to either liraglutide (0.6 mg, 1.2 mg or 1.8 mg) or placebo in a double-blinded manner; to preserve blinding, the dose volume (0.1 ml, 0.2 ml, 0.3 ml) in the liraglutide placebo groups were matched to the relevant active group (0.6 mg, 1.2 mg and 1.8 mg).

Arms

Are arms mutually exclusive?	Yes
Arm title	Liraglutide 0.6 mg

Arm description:

Subjects randomised to 0.6 mg liraglutide treatment as an add-on to their pre-trial insulin treatment and remained on this dose throughout the trial (26 weeks).

Arm type	Experimental
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	Victoza
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Liraglutide 0.6 mg, administered subcutaneously (s.c., under the skin) once daily.

Arm title	Liraglutide 1.2 mg

Arm description:

Subjects randomised to 1.2 mg liraglutide treatment as an add-on to their pre-trial insulin treatment received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	Victoza
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 24 weeks. Administered subcutaneously (s.c., under the skin) once daily.

Arm title	Liraglutide 1.8 mg

Arm description:

Subjects randomised to 1.8 mg liraglutide treatment as an add-on to their pre-trial insulin treatment

received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 2 weeks. After 4 weeks of treatment subjects received 1.8 mg liraglutide for 22 weeks.

Arm type	Experimental
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	Victoza
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 2 weeks. After 4 weeks of treatment subjects received 1.8 mg liraglutide for 22 weeks. Administered subcutaneously (s.c., under the skin) once daily.

Arm title	Liraglutide placebo

Arm description:

Subjects randomised to 3 different placebo arms as an add-on to their pre-trial insulin treatment. Administered subcutaneously (s.c., under the skin) once daily. All the 3 arms were pooled together for data analysis.
a. Placebo 0.1 mL arm: Subjects received 0.1 mL placebo throughout the trial.
b. Placebo 0.2 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 24 weeks.
c. Placebo 0.3 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 2 weeks and 0.3 mL for next 22 weeks of the trial period.

Arm type	Placebo
Investigational medicinal product name	Liraglutide placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

a. Placebo 0.1 mL arm: Subjects received 0.1 mL placebo throughout the trial.
b. Placebo 0.2 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 24 weeks.
c. Placebo 0.3 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 2 weeks and 0.3 mL for next 22 weeks of the trial period.

Number of subjects in period 1	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg
Started	212	209	207
Exposed	211	209	206
Completed	186	177	165
Not completed	26	32	42
Adverse event, non-fatal	12	19	34
Unclassified	-	-	3
Lost to follow-up	2	1	-
Protocol deviation	2	2	-
Withdrawal by subject	10	10	5

Number of subjects in period 1	Liraglutide placebo
Started	207
Exposed	206

Completed	180
Not completed	27
Adverse event, non-fatal	2
Unclassified	2
Lost to follow-up	3
Protocol deviation	7
Withdrawal by subject	13

Baseline characteristics

Reporting groups	
Reporting group title	Liraglutide 0.6 mg
Reporting group description:	
Subjects randomised to 0.6 mg liraglutide treatment as an add-on to their pre-trial insulin treatment and remained on this dose throughout the trial (26 weeks).	

Reporting group title	Liraglutide 1.2 mg
Reporting group description:	
Subjects randomised to 1.2 mg liraglutide treatment as an add-on to their pre-trial insulin treatment received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 24 weeks.	
Reporting group title	Liraglutide 1.8 mg
Reporting group description:	
Subjects randomised to 1.8 mg liraglutide treatment as an add-on to their pre-trial insulin treatment received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 2 weeks. After 4 weeks of treatment subjects received 1.8 mg liraglutide for 22 weeks.	
Reporting group title	Liraglutide placebo
Reporting group description:	
Subjects randomised to 3 different placebo arms as an add-on to their pre-trial insulin treatment. Administered subcutaneously (s.c., under the skin) once daily. All the 3 arms were pooled together for data analysis. a. Placebo 0.1 mL arm: Subjects received 0.1 mL placebo throughout the trial. b. Placebo 0.2 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 24 weeks. c. Placebo 0.3 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 2 weeks and 0.3 mL for next 22 weeks of the trial period.	

Reporting group values	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg
Number of subjects	212	209	207
Age categorical Units: Subjects			

Age continuous			
Baseline age values were collected for full analysis set (FAS = 831 subjects). In FAS, number of subjects in liraglutide 0.6 mg arm was 211; number of subjects in liraglutide 1.2 mg arm was 209; number of subjects in liraglutide 1.8 mg arm was 205; number of subjects in liraglutide placebo arm was 206. Out of 835 randomised subjects, 4 were excluded from FAS: 1 subject each in the liraglutide 1.8 mg, 0.6 mg and placebo arm were not exposed to trial treatment and 1 subject in the liraglutide 1.8 mg arm had no post-baseline measurements.			
Units: years			
arithmetic mean	43.9	42.8	43.2
standard deviation	± 12.88	± 13.31	± 12.9
Gender categorical			
Baseline gender data were collected for full analysis set (FAS = 831 subjects). In FAS, number of subjects in liraglutide 0.6 mg arm was 211; number of subjects in liraglutide 1.2 mg arm was 209; number of subjects in liraglutide 1.8 mg arm was 205; number of subjects in liraglutide placebo arm was 206. Out of 835 randomised subjects, 4 were excluded from FAS: 1 subject each in the liraglutide 1.8 mg, 0.6 mg and placebo arm were not exposed to trial treatment and 1 subject in the liraglutide 1.8 mg arm had no post-baseline measurements.			
Units: Subjects			
Female	118	106	113
Male	93	103	92
Not recorded	1	0	2

Glycosylated haemoglobin (HbA1c)			
Baseline HbA1c values were collected for full analysis set (FAS = 831 subjects). In FAS, number of subjects in liraglutide 0.6 mg arm was 211; number of subjects in liraglutide 1.2 mg arm was 209; number of subjects in liraglutide 1.8 mg arm was 205; number of subjects in liraglutide placebo arm was 206. Out of 835 randomised subjects, 4 were excluded from FAS: 1 subject each in the liraglutide 1.8 mg, 0.6 mg and placebo arm were not exposed to trial treatment and 1 subject in the liraglutide 1.8 mg arm had no post-baseline measurements.			
Units: Percent (%) glycosylated haemoglobin			
arithmetic mean	8.09	8.07	8.04
standard deviation	± 0.743	± 0.731	± 0.736
Body weight			
Baseline body weight values were collected for full analysis set (FAS = 831 subjects). In FAS, number of subjects in liraglutide 0.6 mg arm was 211; number of subjects in liraglutide 1.2 mg arm was 209; number of subjects in liraglutide 1.8 mg arm was 205; number of subjects in liraglutide placebo arm was 206. Out of 835 randomised subjects, 4 were excluded from FAS: 1 subject each in the liraglutide 1.8 mg, 0.6 mg and placebo arm were not exposed to trial treatment and 1 subject in the liraglutide 1.8 mg arm had no post-baseline measurements.			
Units: kilogram(s)			
arithmetic mean	83.1	84.69	83.64
standard deviation	± 16.137	± 18.155	± 17.62

Reporting group values	Liraglutide placebo	Total	
Number of subjects	207	835	
Age categorical			
Units: Subjects			

Age continuous			
Baseline age values were collected for full analysis set (FAS = 831 subjects). In FAS, number of subjects in liraglutide 0.6 mg arm was 211; number of subjects in liraglutide 1.2 mg arm was 209; number of subjects in liraglutide 1.8 mg arm was 205; number of subjects in liraglutide placebo arm was 206. Out of 835 randomised subjects, 4 were excluded from FAS: 1 subject each in the liraglutide 1.8 mg, 0.6 mg and placebo arm were not exposed to trial treatment and 1 subject in the liraglutide 1.8 mg arm had no post-baseline measurements.			
Units: years			
arithmetic mean	42.7		
standard deviation	± 12.97	-	
Gender categorical			
Baseline gender data were collected for full analysis set (FAS = 831 subjects). In FAS, number of subjects in liraglutide 0.6 mg arm was 211; number of subjects in liraglutide 1.2 mg arm was 209; number of subjects in liraglutide 1.8 mg arm was 205; number of subjects in liraglutide placebo arm was 206. Out of 835 randomised subjects, 4 were excluded from FAS: 1 subject each in the liraglutide 1.8 mg, 0.6 mg and placebo arm were not exposed to trial treatment and 1 subject in the liraglutide 1.8 mg arm had no post-baseline measurements.			
Units: Subjects			
Female	112	449	
Male	94	382	
Not recorded	1	4	
Glycosylated haemoglobin (HbA1c)			
Baseline HbA1c values were collected for full analysis set (FAS = 831 subjects). In FAS, number of subjects in liraglutide 0.6 mg arm was 211; number of subjects in liraglutide 1.2 mg arm was 209; number of subjects in liraglutide 1.8 mg arm was 205; number of subjects in liraglutide placebo arm was 206. Out of 835 randomised subjects, 4 were excluded from FAS: 1 subject each in the liraglutide 1.8 mg, 0.6 mg and placebo arm were not exposed to trial treatment and 1 subject in the liraglutide 1.8 mg arm had no post-baseline measurements.			
Units: Percent (%) glycosylated haemoglobin			
arithmetic mean	8.12		
standard deviation	± 0.723	-	

Body weight			
Baseline body weight values were collected for full analysis set (FAS = 831 subjects). In FAS, number of subjects in liraglutide 0.6 mg arm was 211; number of subjects in liraglutide 1.2 mg arm was 209; number of subjects in liraglutide 1.8 mg arm was 205; number of subjects in liraglutide placebo arm was 206. Out of 835 randomised subjects, 4 were excluded from FAS: 1 subject each in the liraglutide 1.8 mg, 0.6 mg and placebo arm were not exposed to trial treatment and 1 subject in the liraglutide 1.8 mg arm had no post-baseline measurements.			
Units: kilogram(s)			
arithmetic mean	84.2		
standard deviation	± 16.539	-	

End points

End points reporting groups

Reporting group title	Liraglutide 0.6 mg

Reporting group description:

Subjects randomised to 0.6 mg liraglutide treatment as an add-on to their pre-trial insulin treatment and remained on this dose throughout the trial (26 weeks).

Reporting group title	Liraglutide 1.2 mg

Reporting group description:

Subjects randomised to 1.2 mg liraglutide treatment as an add-on to their pre-trial insulin treatment received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 24 weeks.

Reporting group title	Liraglutide 1.8 mg

Reporting group description:

Subjects randomised to 1.8 mg liraglutide treatment as an add-on to their pre-trial insulin treatment received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 2 weeks. After 4 weeks of treatment subjects received 1.8 mg liraglutide for 22 weeks.

Reporting group title	Liraglutide placebo

Reporting group description:

Subjects randomised to 3 different placebo arms as an add-on to their pre-trial insulin treatment. Administered subcutaneously (s.c., under the skin) once daily. All the 3 arms were pooled together for data analysis.
a. Placebo 0.1 mL arm: Subjects received 0.1 mL placebo throughout the trial.
b. Placebo 0.2 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 24 weeks.
c. Placebo 0.3 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 2 weeks and 0.3 mL for next 22 weeks of the trial period.

Primary: Change from baseline in glycosylated haemoglobin (HbA1c)

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

End point description:

Change from baseline in glycosylated haemoglobin (HbA1c), after 26 weeks of treatment. Missing data imputed from a mixed model for repeated measurements with treatment, stratification and country as fixed factors and baseline value as a fixed covariate, all nested within visit. Full analysis set (FAS) included all randomised subjects who had received at least one dose and had any post-randomisation data (FAS = 831 subjects). Number subject analysed were subjects from FAS with available HbA1c data for week 26. Out of the 831 subjects in FAS, 22 subjects in lira 0.6 mg arm, 33 subjects in lira 1.2 mg arm, 35 subjects in lira 1.8 mg arm and 16 in placebo arm did not contribute to this analysis.

End point type	Primary

End point timeframe:

After 26 weeks of treatment

End point values	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg	Liraglutide placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	189	176	170	190
Units: Percent (%) glycosylated haemoglobin				
arithmetic mean (standard deviation)	-0.23 (± 0.744)	-0.23 (± 0.731)	-0.32 (± 0.73)	0.01 (± 0.674)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Liraglutide 1.8 mg v Liraglutide placebo
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.2

Notes:

[1] - Superiority of liraglutide 1.8 mg versus placebo was planned to be concluded if and only if the upper limit of the two-sided 95% confidence interval for the estimated difference in HbA1c was less than zero.

Statistical analysis title	Statistical analysis 2
Comparison groups	Liraglutide 1.2 mg v Liraglutide placebo
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0021
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	-0.08

Notes:

[2] - Superiority of liraglutide 1.2 mg was planned to be evaluated only if superiority for liraglutide 1.8 mg was concluded.

Statistical analysis title	Statistical analysis 3
Comparison groups	Liraglutide 0.6 mg v Liraglutide placebo

Number of subjects included in analysis	379
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0011
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	-0.1

Notes:

[3] - Superiority of liraglutide 0.6 mg versus placebo was planned to be evaluated only if superiority of liraglutide 1.2 mg was concluded.

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. Missing data imputed from a mixed model for repeated measurements with treatment, stratification and country as fixed factors and baseline value as a fixed covariate, all nested within visit. Full analysis set (FAS) included all randomised subjects who had received at least one dose and had any post-randomisation data (FAS = 831 subjects). Number subject analysed were subjects from FAS with available body weight data for week 26. Out of the 831 subjects in FAS, 27 subjects in lira 0.6 mg arm, 38 subjects in lira 1.2 mg arm, 35 subjects in lira 1.8 mg arm and 26 in placebo arm did not contribute to the analysis.

End point type	Secondary

End point timeframe:

After 26 weeks of treatment

End point values	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg	Liraglutide placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	184	171	170	180
Units: kilogram(s)				
arithmetic mean (standard deviation)	-2.37 (± 3.015)	-4.03 (± 3.677)	-5.1 (± 3.787)	-0.26 (± 2.782)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-emergent symptomatic hypoglycaemic episodes

End point title	Number of treatment-emergent symptomatic hypoglycaemic episodes

End point description:

Number of treatment-emergent symptomatic hypoglycaemic episodes during 26 weeks of treatment. Symptomatic hypoglycaemic episodes were defined as episodes that were severe according to the American Diabetes Association (ADA) classification or a self measured plasma glucose (SMPG) value of <3.1 mmol/L (56 mg/dL), with symptoms consistent with hypoglycaemia. Safety analysis set (SAS)

included all subjects exposed to at least one dose of randomised liraglutide or placebo (SAS = 832 subjects). Severe hypoglycaemia as per ADA classification is defined as an episode that required assistance of another person to actively administer carbohydrate, glucagon or take other corrective actions. Plasma glucose (PG) concentration may not have been available during an event, but neurological recovery following the return of PG to normal was considered sufficient evidence that the event was induced by a low PG concentration.

End point type	Secondary

End point timeframe:

During 26 weeks of treatment

End point values	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg	Liraglutide placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	211[4]	209[5]	206[6]	206[7]
Units: Number of episodes	1437	1943	1490	1567

Notes:

[4] - 1437 episodes of symptomatic hypoglycaemia were reported by 166 subjects.

[5] - 1943 episodes of symptomatic hypoglycaemia were reported by 175 subjects.

[6] - 1490 episodes of symptomatic hypoglycaemia were reported by 160 subjects.

[7] - 1567 episodes of symptomatic hypoglycaemia were reported by 162 subjects.

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 (week 0) to randomised treatment to 7 days after the last day of randomised treatment (week 26).

Adverse event reporting additional description:

Safety analysis set (SAS) included all subjects exposed to at least one dose of randomised liraglutide or placebo.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Liraglutide 0.6 mg

Reporting group description:

Subjects randomised to 0.6 mg liraglutide treatment as an add-on to their pre-trial insulin treatment and remained on this dose throughout the trial (26 weeks).

Reporting group title	Liraglutide 1.2 mg

Reporting group description:

Subjects randomised to 1.2 mg liraglutide treatment as an add-on to their pre-trial insulin treatment received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 24 weeks.

Reporting group title	Liraglutide 1.8 mg

Reporting group description:

Subjects randomised to 1.8 mg liraglutide treatment as an add-on to their pre-trial insulin treatment received 0.6 mg liraglutide for 2 weeks followed by 1.2 mg liraglutide for 2 weeks. After 4 weeks of treatment subjects received 1.8 mg liraglutide for 22 weeks.

Reporting group title	Liraglutide placebo

Reporting group description:

Subjects randomised to 3 different placebo arms as an add-on to their pre-trial insulin treatment. Administered subcutaneously (s.c., under the skin) once daily. All the 3 arms were pooled together for data analysis.
a. Placebo 0.1 mL arm: Subjects received 0.1 mL placebo throughout the trial.
b. Placebo 0.2 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 24 weeks.
c. Placebo 0.3 mL arm: Subjects received 0.1 mL placebo for 2 weeks followed by 0.2 mL for 2 weeks and 0.3 mL for next 22 weeks of the trial period.

Serious adverse events	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 211 (9.48%)	21 / 209 (10.05%)	14 / 206 (6.80%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Uterine leiomyoma			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Wrist surgery			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Respiratory distress			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed mood			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc injury			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Joint dislocation			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 211 (0.47%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic fracture			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemic coma			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemic unconsciousness			
subjects affected / exposed	3 / 211 (1.42%)	6 / 209 (2.87%)	2 / 206 (0.97%)
occurrences causally related to treatment / all	1 / 5	5 / 7	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIth nerve paralysis			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 211 (0.00%)	2 / 209 (0.96%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 211 (0.00%)	2 / 209 (0.96%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic nephropathy			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 211 (0.47%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 211 (0.47%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 211 (0.00%)	0 / 209 (0.00%)	2 / 206 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 211 (0.00%)	1 / 209 (0.48%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	5 / 211 (2.37%)	2 / 209 (0.96%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	4 / 6	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Liraglutide placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 206 (6.80%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Wrist surgery			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			

Ovarian cyst ruptured				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Respiratory distress				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Anxiety disorder				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed mood				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Animal bite				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Forearm fracture				

subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc injury				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament sprain				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic fracture				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina unstable				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				

subjects affected / exposed	2 / 206 (0.97%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Carpal tunnel syndrome				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemic coma				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemic unconsciousness				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radiculopathy				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VIth nerve paralysis			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Volvulus			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Bile duct stone			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic nephropathy			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			

subjects affected / exposed	1 / 206 (0.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	1 / 206 (0.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Diabetic ketoacidosis				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	2 / 206 (0.97%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	0 / 206 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				

subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Liraglutide 0.6 mg	Liraglutide 1.2 mg	Liraglutide 1.8 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	137 / 211 (64.93%)	164 / 209 (78.47%)	162 / 206 (78.64%)
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 211 (7.58%)	26 / 209 (12.44%)	30 / 206 (14.56%)
occurrences (all)	27	33	43
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 211 (6.16%)	17 / 209 (8.13%)	22 / 206 (10.68%)
occurrences (all)	13	18	25
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 211 (1.42%)	14 / 209 (6.70%)	7 / 206 (3.40%)
occurrences (all)	4	18	7
Abdominal pain upper			
subjects affected / exposed	8 / 211 (3.79%)	8 / 209 (3.83%)	14 / 206 (6.80%)
occurrences (all)	8	13	17
Constipation			
subjects affected / exposed	6 / 211 (2.84%)	23 / 209 (11.00%)	14 / 206 (6.80%)
occurrences (all)	6	29	15
Diarrhoea			
subjects affected / exposed	14 / 211 (6.64%)	25 / 209 (11.96%)	30 / 206 (14.56%)
occurrences (all)	17	30	43
Dyspepsia			
subjects affected / exposed	8 / 211 (3.79%)	19 / 209 (9.09%)	24 / 206 (11.65%)
occurrences (all)	9	23	35
Nausea			
subjects affected / exposed	68 / 211 (32.23%)	97 / 209 (46.41%)	102 / 206 (49.51%)
occurrences (all)	81	122	170

Vomiting			
subjects affected / exposed	19 / 211 (9.00%)	29 / 209 (13.88%)	35 / 206 (16.99%)
occurrences (all)	25	40	65
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	10 / 211 (4.74%)	4 / 209 (1.91%)	14 / 206 (6.80%)
occurrences (all)	12	4	19
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 211 (1.42%)	5 / 209 (2.39%)	8 / 206 (3.88%)
occurrences (all)	4	6	10
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	6 / 211 (2.84%)	11 / 209 (5.26%)	8 / 206 (3.88%)
occurrences (all)	7	11	9
Influenza			
subjects affected / exposed	15 / 211 (7.11%)	18 / 209 (8.61%)	18 / 206 (8.74%)
occurrences (all)	15	23	19
Nasopharyngitis			
subjects affected / exposed	44 / 211 (20.85%)	40 / 209 (19.14%)	47 / 206 (22.82%)
occurrences (all)	59	52	67
Sinusitis			
subjects affected / exposed	7 / 211 (3.32%)	11 / 209 (5.26%)	3 / 206 (1.46%)
occurrences (all)	7	12	3
Upper respiratory tract infection			
subjects affected / exposed	14 / 211 (6.64%)	11 / 209 (5.26%)	11 / 206 (5.34%)
occurrences (all)	20	13	14
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	21 / 211 (9.95%)	40 / 209 (19.14%)	50 / 206 (24.27%)
occurrences (all)	21	42	55
Hyperglycaemia			
subjects affected / exposed	10 / 211 (4.74%)	13 / 209 (6.22%)	12 / 206 (5.83%)
occurrences (all)	14	17	16

Non-serious adverse events	Liraglutide placebo		
Total subjects affected by non-serious			

adverse events subjects affected / exposed	125 / 206 (60.68%)		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	30 / 206 (14.56%) 40		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	3 / 206 (1.46%) 5		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	6 / 206 (2.91%) 7 5 / 206 (2.43%) 5 9 / 206 (4.37%) 12 17 / 206 (8.25%) 22 1 / 206 (0.49%) 1 34 / 206 (16.50%) 40 7 / 206 (3.40%) 8		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	6 / 206 (2.91%) 10		
Musculoskeletal and connective tissue			

disorders Back pain subjects affected / exposed occurrences (all)	 14 / 206 (6.80%) 15		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 6 / 206 (2.91%) 6 17 / 206 (8.25%) 20 46 / 206 (22.33%) 56 4 / 206 (1.94%) 4 25 / 206 (12.14%) 31		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all)	 9 / 206 (4.37%) 10 4 / 206 (1.94%) 4		

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