Clinical trial results:
A double-blinded, randomised, placebo-controlled trial of liraglutide 3.0 mg in patients with poor weight-loss and a suboptimal glucagon-like peptide-1 response following bariatric surgery.

Summary

EudraCT number	2017-002407-10
Trial protocol	GB
Global end of trial date	24 September 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	17/0238

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03341429
WHO universal trial number (UTN)	U1111-1185-8283
Other trial identifiers	UCL Data Protection Registration Number: Z6364106/2017/12/103

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	1st floor Maple House, 149 Tottenham Court Road, London, United Kingdom, W1T 7NF
Public contact	Alisia Carnemolla, UCL, a.carnemolla@ucl.ac.uk
Scientific contact	Alisia Carnemolla, UCL/UCLH Joint Research Office, randd@nhs.net

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	24 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 May 2021
Global end of trial reached?	Yes
Global end of trial date	24 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to compare the efficacy of 24 weeks of subcutaneous liraglutide 3.0 mg versus placebo administration, as an adjunct to diet and exercise, on %WL in participants with poor weight-loss and a sub-optimal active GLP-1 response following primary RYGB or SG at the end of the 24-week treatment period.

Protection of trial subjects:

Patients were exposed to ionising radiation during the DXA scans: this is not a painful procedure. However, to
minimise risks inherent to the procedure, only a trained DXA operator will undertake the procedure.
Blood sampling involved a venepuncture in the forearm which is a commonly performed routine procedure and
does not involve any pain or discomfort other than a little scratch at needle insertion. A trained healthcare professional performed the venepuncture.
Side effects of the study drug included nausea, vomiting or diarrhoea related: participant were provided with details of persons to contact should they have any problem while on the treatment. In addition, participants were monitored closely throughout the study period. In the case of a severe adverse event where it is
necessary for the authorised investigator and treating health care professional to know which treatment the
participant is receiving before providing appropriate treatment arrangements for the trial code to be broken to reveal group allocation were in place.
Participants were expected to experience time and financial constraints to attend a total of 7 study visits. Any
reasonable travel expenses incurred by participants in attending the study visits were reimbursed.

Background therapy:

Counselling on lifestyle modification (500-kcal deficient diet and 150 minute of physical activity/week).

Evidence for comparator:

A placebo, which does not contain any active ingredients, but similar in appearance was used as comparator.

Actual start date of recruitment	31 July 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 70
Worldwide total number of subjects	70
EEA total number of subjects	0

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)	70
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place between 1st April 2018 and 28th November 2019. Participants were recruited from UCLH Trust and Homerton University Hospital Foundation Trust.

Pre-assignment

Screening details:

Interested subjects were asked to sign a first consent form in order to undergo screening for the trial, as the assessment included a meal test that is considered research procedure. Written informed consent was sought within one week with a minimum of 24 hours after being approached and given the Participants Information Sheet.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

The pharmacist and the Trial Co-ordinator were the solely holders of the code list, other than Sealed Envelope, the company providing the randomisation system.

Arms

Are arms mutually exclusive?	Yes
Arm title	Liraglutide

Arm description:

3.0 mg liraglutide, once daily via subcutaneous injection

Arm type	Experimental
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	ACT: A10BJ02
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosage: 3.0 mg liraglutide/placebo, daily subcutaneous injection for 20 weeks following a dose escalation period of 4 weeks.

Dose escalation (4 weeks)=
Week 1: 0.6 mg,
Week 2: 1.2 mg,
Week 3: 1.8 mg,
Week 4 2.4 mg.
Week 5 – 24: Maintenance dose 3.0 mg

Arm title	Placebo

Arm description:

Control, no active ingredient, but same appearance

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

Once daily subcutaneous injection

Number of subjects in period 1	Liraglutide	Placebo
Started	35	35
Completed	31	26
Not completed	4	9
no BIA weight at V7	4	9

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	70	70	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	70	70	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	47.55		
standard deviation	± 10.7	-	
Gender categorical Units: Subjects			
Female	52	52	
Male	18	18	
Type 2 Diabetes Units: Subjects			
T2D Status - Diabetic	9	9	
T2D Status - Non Diabetic	61	61	
Surgical procedure Units: Subjects			
RYGB	5	5	
SG	65	65	
Ethnicity			
White British, White Irish, and White Other combined to form White group. African, Caribbean and Black other combined to form Black group Indian, Pakistani, Bangladeshi and other Asian background combined to form Asian group			
Units: Subjects			
White	44	44	
Black	14	14	
Asian	5	5	
Other mixed background	3	3	
White & Asian	1	1	
White & Black Caribbean	3	3	
Family history of obesity			

Units: Subjects			
Yes	52	52	
No	18	18	
Education level Units: Subjects			
None	4	4	
GCSE/O level or equivalent	18	18	
A level or equivalent	19	19	
Degree	21	21	
Postgraduate	8	8	
IPAQ			
The IPAQ questionnaire was used to categorise the levels of activities of the participants			
Units: Subjects			
Low	26	26	
Moderate	23	23	
High	20	20	
Not recorded	1	1	
Weight Units: kg			
arithmetic mean	119.78		
standard deviation	± 24.3	-	
Fat mass			
Fat mass measured using DXA, it was measured in grams, for the analysis, the unit was converted to kilograms. 2 patients in the placebo were missing baseline fat mass measurement.			
Units: kg			
arithmetic mean	51.9		
standard deviation	± 13.5	-	
Lean mass			
Lean mass measured using DXA, it was measured in grams, for the analysis, the unit was converted to kilograms. 2 patients in the placebo were missing baseline lean mass measurement.			
Units: kg			
arithmetic mean	65.5		
standard deviation	± 12.2	-	
Bone density			
Bone density measured using DXA. 2 patients in the placebo were missing baseline bone density measurement.			
Units: g/cm2			
arithmetic mean	1.2		
standard deviation	± 0.1	-	
Glucose Units: mmol/L			
arithmetic mean	5.2		
standard deviation	± 1.4	-	
HbA1c Units: percentage			
arithmetic mean	5.9		
standard deviation	± 0.8	-	
Heart rate			
The heart rate is the pre six minute walk test heart rate			

Units: Beats per minute			
arithmetic mean	75.7		
standard deviation	± 12.6	-	
Systolic blood pressure			
Units: mmHg			
arithmetic mean	131.3		
standard deviation	± 14.7	-	
Diastolic blood pressure			
Units: mmHg			
arithmetic mean	76.0		
standard deviation	± 10.7	-	
BDI			
Units: Subjects			
arithmetic mean	15.0		
standard deviation	± 11.9	-	
IWQOL			
IWQOL total score			
Units: Subjects			
arithmetic mean	56.1		
standard deviation	± 23.3	-	
6 Minute Walk Test			
Units: meter			
arithmetic mean	455.1		
standard deviation	± 92.5	-	
5 Sit Stand Test			
Units: second			
arithmetic mean	12.7		
standard deviation	± 4.4	-	
Hand Grip Test			
Units: kg			
arithmetic mean	33.6		
standard deviation	± 11.9	-	
Insulin - 0 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm).			
Units: iu/L			
arithmetic mean	10.7		
standard deviation	± 7.4	-	
Insulin - 15 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	94.5		
standard deviation	± 62.3	-	
Insulin - 30 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	100.7		
standard deviation	± 65.0	-	
Insulin - 60 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	111.6		
standard deviation	± 78.9	-	

Insulin - 120 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	30.2		
standard deviation	± 20.5	-	
Insulin - 180 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	11.9		
standard deviation	± 10.5	-	
IWQOL-lite physical function			
Units: Subjects			
arithmetic mean	55.6		
standard deviation	± 25.1	-	
IWQOL-lite self-esteem			
Units: Subjects			
arithmetic mean	42.5		
standard deviation	± 29.0	-	
IWQOL-lite sex life			
2 sex-life scores missing (1 each arm)			
Units: Subjects			
arithmetic mean	62.7		
standard deviation	± 32.3	-	
IWQOL-lite public distress			
Units: Subjects			
arithmetic mean	59.2		
standard deviation	± 29.3	-	
IWQOL-lite work			
1 missing work score in liraglutide arm			
Units: Subjects			
arithmetic mean	72.2		
standard deviation	± 28.9	-	

Subject analysis sets	
Subject analysis set title	Liraglutide
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants that received the study drug, liraglutide 3.0 mg/ml	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants that received placebo.	

Reporting group values	Liraglutide	Placebo	
Number of subjects	35	35	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	35	35	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	46.7	48.4	
standard deviation	± 10.8	± 10.6	
Gender categorical			
Units: Subjects			
Female	26	26	
Male	9	9	
Type 2 Diabetes			
Units: Subjects			
T2D Status - Diabetic	5	4	
T2D Status - Non Diabetic	30	31	
Surgical procedure			
Units: Subjects			
RYGB	2	3	
SG	33	32	
Ethnicity			
White British, White Irish, and White Other combined to form White group. African, Caribbean and Black other combined to form Black group Indian, Pakistani, Bangladeshi and other Asian background combined to form Asian group			
Units: Subjects			
White	22	22	
Black	5	9	
Asian	4	1	
Other mixed background	1	2	
White & Asian	1	0	
White & Black Caribbean	2	1	
Family history of obesity			
Units: Subjects			
Yes	23	29	
No	12	6	
Education level			
Units: Subjects			
None	2	2	
GCSE/O level or equivalent	11	7	
A level or equivalent	5	14	
Degree	12	9	
Postgraduate	5	3	
IPAQ			
The IPAQ questionnaire was used to categorise the levels of activities of the participants			
Units: Subjects			
Low	11	15	
Moderate	15	8	
High	8	12	

Not recorded	1	0	

Weight			
Units: kg			
arithmetic mean	116.1	123.5	
standard deviation	± 23.6	± 24.8	
Fat mass			
Fat mass measured using DXA, it was measured in grams, for the analysis, the unit was converted to kilograms. 2 patients in the placebo were missing baseline fat mass measurement.			
Units: kg			
arithmetic mean	49.4	54.2	
standard deviation	± 11.3	± 15.1	
Lean mass			
Lean mass measured using DXA, it was measured in grams, for the analysis, the unit was converted to kilograms. 2 patients in the placebo were missing baseline lean mass measurement.			
Units: kg			
arithmetic mean	63.7	67.1	
standard deviation	± 11.0	± 13.1	
Bone density			
Bone density measured using DXA. 2 patients in the placebo were missing baseline bone density measurement.			
Units: g/cm2			
arithmetic mean	1.2	1.2	
standard deviation	± 0.1	± 0.1	
Glucose			
Units: mmol/L			
arithmetic mean	5.0	5.3	
standard deviation	± 1.3	± 1.5	
HbA1c			
Units: percentage			
arithmetic mean	5.8	6.0	
standard deviation	± 0.7	± 0.9	
Heart rate			
The heart rate is the pre six minute walk test heart rate			
Units: Beats per minute			
arithmetic mean	74.0	77.3	
standard deviation	± 13.6	± 11.5	
Systolic blood pressure			
Units: mmHg			
arithmetic mean	131.3	131.3	
standard deviation	± 15.0	± 14.5	
Diastolic blood pressure			
Units: mmHg			
arithmetic mean	75.9	76.2	
standard deviation	± 10.4	± 11.2	
BDI			
Units: Subjects			
arithmetic mean	16.3	13.8	

standard deviation	± 10.0	± 13.6	
IWQOL			
IWQOL total score			
Units: Subjects			
arithmetic mean	56.3	55.8	
standard deviation	± 23.8	± 23.1	
6 Minute Walk Test			
Units: meter			
arithmetic mean	464.5	445.6	
standard deviation	± 89.7	± 95.7	
5 Sit Stand Test			
Units: second			
arithmetic mean	13.3	12.2	
standard deviation	± 5.4	± 3.3	
Hand Grip Test			
Units: kg			
arithmetic mean	31.6	35.6	
standard deviation	± 9.9	± 13.5	
Insulin - 0 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm).			
Units: iu/L			
arithmetic mean	10.0	11.4	
standard deviation	± 7.0	± 8.1	
Insulin - 15 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	98.8	89.2	
standard deviation	± 64.7	± 60.7	
Insulin - 30 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	119.3	100.2	
standard deviation	± 78.0	± 44.4	
Insulin - 60 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	110.4	113.1	
standard deviation	± 78.2	± 82.1	
Insulin - 120 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	31.0	29.1	
standard deviation	± 21.2	± 20.2	
Insulin - 180 minute			
30 insulin measurements missing (17 in placebo arm and 13 in liraglutide arm)			
Units: iu/L			
arithmetic mean	12.9	10.8	
standard deviation	± 12.5	± 7.6	
IWQOL-lite physical function			
Units: Subjects			
arithmetic mean	55.0	56.1	
standard deviation	± 25.2	± 25.4	

IWQOL-lite self-esteem Units: Subjects arithmetic mean standard deviation	 43.3 ± 29.4	 41.7 ± 29.0	
IWQOL-lite sex life			
2 sex-life scores missing (1 each arm)			
Units: Subjects arithmetic mean standard deviation	 61.8 ± 30.9	 63.6 ± 34.0	
IWQOL-lite public distress Units: Subjects arithmetic mean standard deviation	 63.3 ± 27.8	 55.1 ± 30.6	
IWQOL-lite work			
1 missing work score in liraglutide arm			
Units: Subjects arithmetic mean standard deviation	 71.1 ± 31.3	 73.2 ± 26.7	

End points

End points reporting groups

Reporting group title	Liraglutide
Reporting group description: 3.0 mg liraglutide, once daily via subcutaneous injection	
Reporting group title	Placebo
Reporting group description: Control, no active ingredient, but same appearance	
Subject analysis set title	Liraglutide
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants that received the study drug, liraglutide 3.0 mg/ml	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants that received placebo.	

Primary: Primary outcome - % weight loss

End point title	Primary outcome - % weight loss
End point description: The primary outcome of this trial is %WL from the baseline visit to the end of treatment visit at 24 weeks. Percentage weight loss will be calculated using the following formula: %WL = [(weight at the baseline visit–weight at the end of the 24-week treatment period)/ weight at the baseline visit] x 100, measured at the end of trial.	
End point type	Primary
End point timeframe: From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	26		
Units: percent				
arithmetic mean (standard deviation)	-8.8 (± 4.9)	-0.5 (± 3.3)		

Statistical analyses

Statistical analysis title	Primary Outcome Analysis
Comparison groups	Liraglutide v Placebo

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.4
upper limit	-5.7

Notes:

[1] - Specifically, the following linear regression model will be fitted:
%WL_i=β_0+β_1 TRT_i+β_2 Baseline_weight_i + β_3 Type_i+β_4 T2D_i+_i
where:
%WL_i is the weight loss at 24 weeks for the ith patient
TRT_i is an indicator for the allocated treatment for the ith patient (0 = placebo, 1 = liraglutide)
Baseline_weight_i is the weight at baseline for the ith patient
Type_i is an indicator for the type of surgical treatment the ith patient receives (0 = SG , 1 = RYGB) and i

Statistical analysis title	Sensitivity analysis for influential points

Statistical analysis description:

A sensitivity analysis for influential points was carried out, observations with leverage greater than or equal to 0.1, 13 observations (5 in placebo and 8 in liraglutide arm), were removed and the primary outcome model was re-fitted.

Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.4
upper limit	-6.1

Statistical analysis title	Sensitivity analysis for normality

Statistical analysis description:

A quantile regression model for median was fitted as a sensitivity analysis for the violation of the normality assumption of residuals in the primary analysis.

Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
Method	Quantile regression for median
Parameter estimate	Median difference (final values)
Point estimate	-8.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	-5.3

Statistical analysis title	Sensitivity analysis for homoscedasticity
Comparison groups	Placebo v Liraglutide
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
Method	Linear regression with robust SE
Parameter estimate	Mean difference (final values)
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.3
upper limit	-5.7

Primary: % WL self reported weight	
End point title	% WL self reported weight
End point description:	
BIA measurement could not be completed for 1 patient in placebo arm because they had unstable feet, but their weight was measured in at the clinic. 7 patients in placebo arm that could not attend the 24-week visit due to covid-19 restrictions provided self-reported weights. 1 patient in liraglitide arm could not attend 24-week visit due to tooth infection also provided self-reported weight. As a secondary analysis, the self-reported weights were used in addition to the original data available	
End point type	Primary
End point timeframe:	
From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: percent				
arithmetic mean (standard deviation)	-8.6 (± 5.0)	-0.1 (± 3.3)		

Statistical analyses

Statistical analysis title	% WL - self reported weight
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.4
upper limit	-6.2

Primary: % WL over time (week 2)	
End point title	% WL over time (week 2)
End point description:	
The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.	
End point type	Primary
End point timeframe:	
From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: percent				
arithmetic mean (standard deviation)	-1.8 (± 1.0)	-0.3 (± 1.0)		

Statistical analyses

Statistical analysis title	% WL over time (week 2)
Comparison groups	Placebo v Liraglutide
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	-0.3

Primary: % WL over time (week 4)

End point title	% WL over time (week 4)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately

End point type	Primary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: percent				
arithmetic mean (standard deviation)	-3.4 (± 1.4)	-0.4 (± 1.3)		

Statistical analyses

Statistical analysis title	% WL over time (week 4)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	-1.7

Primary: % WL over time (week 8)

End point title	% WL over time (week 8)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.

End point type	Primary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: percent				
arithmetic mean (standard deviation)	-5.0 (± 2.1)	-0.4 (± 1.9)		

Statistical analyses

Statistical analysis title	% WL over time (week 8)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	-3.2

Primary: % WL over time (17 weeks)

End point title	% WL over time (17 weeks)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.

End point type	Primary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	30		
Units: percent				
arithmetic mean (standard deviation)	7.8 (± 3.9)	-0.7 (± 2.7)		

Statistical analyses

Statistical analysis title	% WL over time (week 17)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.2
upper limit	-5.6

Primary: % WL over time (24 weeks)

End point title	% WL over time (24 weeks)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.

End point type	Primary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: percent				
arithmetic mean (standard deviation)	-8.6 (± 5.0)	-0.1 (± 3.3)		

Statistical analyses

Statistical analysis title	% WL over time (week 24)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	-7.2

Secondary: Actual weight loss

End point title	Actual weight loss
End point description:	
End point type	Secondary
End point timeframe:	
Weight was measured at baseline, 2 weeks, 4 weeks, 8 weeks, 17 weeks and 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: kg				
arithmetic mean (standard deviation)	-9.5 (± 5.1)	-0.4 (± 3.9)		

Statistical analyses

Statistical analysis title	Actual weight loss at 24 weeks
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	-6.9

Secondary: Change in fat mass between baseline and 24 weeks	
End point title	Change in fat mass between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe:	
Baseline and 24-week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: kg				
arithmetic mean (standard deviation)	-4.1 (± 4.2)	0.7 (± 3.9)		

Statistical analyses

Statistical analysis title	Change in fatmass from baseline to 24-week
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	-2.5

Secondary: Change in lean mass between baseline and 24 weeks	
End point title	Change in lean mass between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe:	
Baseline, 24-week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: kg				
arithmetic mean (standard deviation)	-4.2 (± 3.0)	-1.1 (± 3.3)		

Statistical analyses

Statistical analysis title	Change in lean mass between baseline and 24 weeks
Comparison groups	Placebo v Liraglutide
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	-1.6

Secondary: Change in bone density between baseline and 24 weeks

End point title	Change in bone density between baseline and 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Bone density was measured at baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: g/cm2				
arithmetic mean (standard deviation)	-0.01 (± 0.02)	0.0005 (± 0.04)		

Statistical analyses

Statistical analysis title	Change in bone density
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.02

Secondary: Change in glucose between baseline and 24 weeks	
End point title	Change in glucose between baseline and 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and 24 week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	27		
Units: mmol/L				
arithmetic mean (standard deviation)	-0.43 (± 0.81)	-0.02 (± 0.88)		

Statistical analyses

Statistical analysis title	Change in glucose
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.17

Secondary: Change in HbA1c between baseline and 24 weeks

End point title	Change in HbA1c between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe:	
Baseline and 24 week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: Percentage				
arithmetic mean (standard deviation)	-0.27 (± 0.37)	-0.03 (± 0.22)		

Statistical analyses

Statistical analysis title	Change in HbAic
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	-0.16

Secondary: Change in heart rate between baseline and 24 weeks

End point title	Change in heart rate between baseline and 24 weeks
End point description:	

End point type	Secondary

End point timeframe:
Baseline and 24 week

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	31		
Units: beats/ minute				
arithmetic mean (standard deviation)	4.6 (± 12.4)	2.4 (± 11.6)		

Statistical analyses

Statistical analysis title	Change in heartrate
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	6.2

Secondary: Change in systolic blood pressure between baseline and 24 weeks

End point title	Change in systolic blood pressure between baseline and 24 weeks

End point description:

End point type	Secondary

End point timeframe:
Baseline, 2 week, 4 week, 8 week, 17 week and 24 week

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: mmHg				
arithmetic mean (standard deviation)	-6.3 (± 16.4)	2.3 (± 18.9)		

Statistical analyses

Statistical analysis title	Change in systolic blood pressure
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.2
upper limit	-1.9

Statistical analysis title	Change in systolic blood pressure over time
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.3
upper limit	-6.1

Secondary: Change in diastolic blood pressure between baseline and 24 weeks	
End point title	Change in diastolic blood pressure between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe:	
Baseline, 2 week, 4 week, 8 week, 17 week and 24 week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: mmG				
arithmetic mean (standard deviation)	-0.4 (± 13.2)	-0.3 (± 13.2)		

Statistical analyses

Statistical analysis title	Change in diastolic blood pressure
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	5.1

Statistical analysis title	Change in diastolic blood pressure over time
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	0.5

Secondary: Change in insulin between baseline and 24 weeks

End point title	Change in insulin between baseline and 24 weeks

End point description:

Repeated measures of Insulin at 0, 15, 30, 60, 120 and 180 minutes after meal.

End point type	Secondary
End point timeframe: Baseline, 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	18		
Units: mmol				
arithmetic mean (standard deviation)	-0.7 (± 5.3)	-2.0 (± 4.5)		

Statistical analyses

Statistical analysis title	Change in insulin
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2
upper limit	19.2

Secondary: Change in BDI scores between baseline and 24 weeks

End point title	Change in BDI scores between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe: Baseline, 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	33		
Units: Subjects				
arithmetic mean (standard deviation)	-5.7 (± 8.6)	-1.9 (± 9.4)		

Statistical analyses

Statistical analysis title	Change in BDI score
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	0.5

Secondary: Change in IWQOL scores between baseline and 24 weeks	
End point title	Change in IWQOL scores between baseline and 24 weeks
End point description:	
End point type	Secondary
End point timeframe: Baseline, 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	33		
Units: Subjects				
arithmetic mean (standard deviation)	5.0 (± 15.1)	-0.9 (± 10.7)		

Statistical analyses

Statistical analysis title	Change in IWQOL-Lite total score
Comparison groups	Liraglutide v Placebo

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	13.7

Secondary: Change in 6 Minute Walk Test between baseline and 24 weeks

End point title	Change in 6 Minute Walk Test between baseline and 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Baseline, 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	24		
Units: meter				
arithmetic mean (standard deviation)	21.3 (± 48.6)	15.5 (± 51.3)		

Statistical analyses

Statistical analysis title	Change in 6 minute walk test
Comparison groups	Placebo v Liraglutide
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.1
upper limit	39.4

Secondary: Change in 5 Sit Stand Test between baseline and 24 weeks	
End point title	Change in 5 Sit Stand Test between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe:	
Baseline, 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: second				
arithmetic mean (standard deviation)	-1.8 (± 3.7)	0.4 (± 3.3)		

Statistical analyses

Statistical analysis title	Change in 5 Sit Stand Test
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	-0.03

Secondary: Change in Hand Grip Test between baseline and 24 weeks	
End point title	Change in Hand Grip Test between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe:	
Baseline, 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	28		
Units: kg				
arithmetic mean (standard deviation)	-2.1 (± 5.0)	-3.7 (± 10.2)		

Statistical analyses

Statistical analysis title	Change in Hand Grip Test
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	3.7

Secondary: Change in CRP between baseline and 24 weeks

End point title	Change in CRP between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe:	
Baseline and 24 week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: mg/L				
arithmetic mean (standard deviation)	-1.2 (± 2.6)	-0.5 (± 2.8)		

Statistical analyses

Statistical analysis title	Change in CRP
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Median difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.3

Secondary: Change in cholesterol between baseline and 24 weeks	
End point title	Change in cholesterol between baseline and 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Baseline, 24 week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	31		
Units: mmol/L				
arithmetic mean (standard deviation)	-0.5 (± 0.6)	0.1 (± 0.5)		

Statistical analyses

Statistical analysis title	Change in cholesterol
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.2

Secondary: Change in LDL between baseline and 24 weeks

End point title	Change in LDL between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe:	
Baseline, 24 week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	30		
Units: mmol/L				
arithmetic mean (standard deviation)	-0.26 (± 0.58)	-0.03 (± 0.32)		

Statistical analyses

Statistical analysis title	Change in LDL
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.2

Secondary: Change in HDL between baseline and 24 weeks

End point title	Change in HDL between baseline and 24 weeks
End point description:	

End point type	Secondary

End point timeframe: Baseline, 24 week

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	31		
Units: mmol/L				
arithmetic mean (standard deviation)	-0.10 (± 0.18)	0.02 (± 0.21)		

Statistical analyses

Statistical analysis title	Change in HDL
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	-0.01

Secondary: Change in triglyceride between baseline and 24 weeks

End point title	Change in triglyceride between baseline and 24 weeks
End point description:	

End point type	Secondary
End point timeframe: Baseline, 24 week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	31		
Units: mmol/L				
arithmetic mean (standard deviation)	-0.2 (± 0.7)	0.2 (± 1.5)		

Statistical analyses

Statistical analysis title	Change in triglyceride
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.2

Secondary: IPAQ at 24 weeks	
End point title	IPAQ at 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Baseline, 24 week	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	30		
Units: Subjects				
Low	13	8		
Moderate	7	11		
High	13	11		

Statistical analyses

Statistical analysis title	Analysis of IPAQ questinnaire
Comparison groups	Liraglutide v Placebo

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
Method	Proportional odds model
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	2.9

Secondary: Weight loss over time (2 weeks)

End point title	Weight loss over time (2 weeks)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.

End point type	Secondary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: kg				
arithmetic mean (standard deviation)	-2.0 (± 1.1)	-0.3 (± 1.2)		

Statistical analyses

Statistical analysis title	Weight loss over time (2 weeks)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	-0.6

Secondary: Weight loss over time (4 weeks)

End point title	Weight loss over time (4 weeks)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.

End point type	Secondary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: kg				
arithmetic mean (standard deviation)	-3.9 (± 1.7)	-0.5 (± 1.6)		

Statistical analyses

Statistical analysis title	Weight loss over time (4 weeks)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	-2.2

Secondary: Weight loss over time (8 weeks)

End point title	Weight loss over time (8 weeks)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.

End point type	Secondary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: kg				
arithmetic mean (standard deviation)	-5.6 (± 2.4)	-0.6 (± 2.2)		

Statistical analyses

Statistical analysis title	Weight loss over time (8 weeks)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	-3.7

Secondary: Weight loss over time (17 weeks)

End point title	Weight loss over time (17 weeks)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.

End point type	Secondary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	30		
Units: kg				
arithmetic mean (standard deviation)	-8.6 (± 4.1)	-1.0 (± 3.2)		

Statistical analyses

Statistical analysis title	Weight loss over time (17 weeks)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	-6.2

Secondary: Weight loss over time (24 weeks)

End point title	Weight loss over time (24 weeks)

End point description:

The time-treatment interaction is significant, hence the treatment effect estimate for each week is entered separately.

End point type	Secondary

End point timeframe:

From baseline to end of treatment (i.e., 24-week treatment): measured at baseline and at 2, 4, 8, 17 and 24 weeks post randomisation.

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: kg				
arithmetic mean (standard deviation)	-9.5 (± 5.1)	-0.4 (± 3.9)		

Statistical analyses

Statistical analysis title	Weight loss over time (24 weeks)
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	-7.8

Secondary: Difference in GP visits at the surgery or health centre between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in GP visits at the surgery or health centre between liraglutide and placebo from baseline to 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Number of visits				
arithmetic mean (standard deviation)	2.4 (± 2.5)	2.5 (± 2.5)		

Statistical analyses

Statistical analysis title	Difference in GP visits at the surgery or centre
Comparison groups	Liraglutide v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.3

Secondary: Difference in GP visits at home between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in GP visits at home between liraglutide and placebo from baseline to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Number of visits				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in Telephone calls with GP between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Telephone calls with GP between liraglutide and placebo from baseline to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Number of calls				
arithmetic mean (standard deviation)	1.5 (± 2.9)	1.3 (± 2.2)		

Statistical analyses

Statistical analysis title	Difference in Telephone calls with GP
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.6

Secondary: Difference in Nurse visits at home between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Nurse visits at home between liraglutide and placebo from baseline to 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Number of visits				
arithmetic mean (standard deviation)	0 (± 0.2)	0 (± 0.2)		

Statistical analyses

Statistical analysis title	Difference in Nurse visits at home
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Secondary: Difference in Nurse visits at the surgery or health centre between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Nurse visits at the surgery or health centre between liraglutide and placebo from baseline to 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Number of visits				
arithmetic mean (standard deviation)	0.7 (± 0.8)	0.7 (± 1)		

Statistical analyses

Statistical analysis title	Difference in Nurse visits at the surgery or centr
Comparison groups	Liraglutide v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.5

Secondary: Difference in Telephone calls with nurse between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Telephone calls with nurse between liraglutide and placebo from baseline to 24 weeks
End point description:	
End point type	Secondary
End point timeframe: Baseline and 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Number of calls				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0.2)		

Statistical analyses

Statistical analysis title	Difference in Telephone calls with nurse
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0

Secondary: Difference in Visits with an NHS dietitian between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Visits with an NHS dietitian between liraglutide and placebo from baseline to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Number of visits				
arithmetic mean (standard deviation)	0.4 (± 0.7)	0.4 (± 1.1)		

Statistical analyses

Statistical analysis title	Difference in Visits with an NHS dietitian
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.5

Secondary: Difference in Visits with an NHS physiotherapist between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Visits with an NHS physiotherapist between liraglutide and placebo from baseline to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Number of visits				
arithmetic mean (standard deviation)	0 (± 0.2)	1.2 (± 3.1)		

Statistical analyses

Statistical analysis title	Difference in Visits with an NHS physiotherapist
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.1

Secondary: Difference in Inpatient stays between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Inpatient stays between liraglutide and placebo from baseline to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: Number of stays				
arithmetic mean (standard deviation)	0.1 (± 0.3)	0 (± 0)		

Statistical analyses

Statistical analysis title	Difference in Inpatient stays
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.2

Secondary: Difference in Outpatient visits between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Outpatient visits between liraglutide and placebo from baseline to 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and 24 weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: Number of visits				
arithmetic mean (standard deviation)	0.6 (± 0.9)	1 (± 1.9)		

Statistical analyses

Statistical analysis title	Difference in Outpatient visits
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.3

Secondary: Difference in Emergency Department visits between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Emergency Department visits between liraglutide and placebo from baseline to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: Number of visits				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in Number of concomitant NHS medications between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Number of concomitant NHS medications between liraglutide and placebo from baseline to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	35		
Units: Number of medications				
arithmetic mean (standard deviation)	6.6 (± 2.8)	5.3 (± 3)		

Statistical analyses

Statistical analysis title	Difference in Number of concomitant NHS medication
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	2.7

Secondary: Difference in Number of doses of liraglutide between liraglutide and placebo from baseline to 24 weeks

End point title	Difference in Number of doses of liraglutide between liraglutide and placebo from baseline to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	35		
Units: Number of doses				
arithmetic mean (standard deviation)	29.8 (± 0.9)	0 (± 0)		

Statistical analyses

Statistical analysis title	Difference in Number of doses of liraglutide
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	29.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	29.5
upper limit	30.1

Secondary: Difference in EQ-5D-3L utility score between liraglutide and placebo at 24 weeks

End point title	Difference in EQ-5D-3L utility score between liraglutide and placebo at 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	32		
Units: Utility score on a scale of 0 to 1				
arithmetic mean (standard deviation)	0.583 (± 0.392)	0.735 (± 0.289)		

Statistical analyses

Statistical analysis title	Difference in EQ-5D-3L utility score
Comparison groups	Liraglutide v Placebo

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.152
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.019
upper limit	0.324

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs were collected and are reported on from randomisation to end of study.	
Assessment type	Systematic
Dictionary used	
Dictionary name	Trial specific
Dictionary version	1
Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 70 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 70 (100.00%)		
Cardiac disorders			
Palpitations			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
General disorders and administration site conditions			
Dizziness			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	5		
Dry mouth			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	5		
Fatigue			

subjects affected / exposed	7 / 70 (10.00%)		
occurrences (all)	7		
Headache			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal bloating			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	11 / 70 (15.71%)		
occurrences (all)	11		
Decreased appetite			
subjects affected / exposed	14 / 70 (20.00%)		
occurrences (all)	14		
Diarrhoea			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Dyspepsia			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	25 / 70 (35.71%)		
occurrences (all)	25		
Vomiting			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			

Influenza subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 70 (7.14%) 5 7 / 70 (10.00%) 7		
Skin and subcutaneous tissue disorders Injection related reaction subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 5 / 70 (7.14%) 6 1 / 70 (1.43%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 4 / 70 (5.71%) 4 1 / 70 (1.43%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2018	Changes to the protocol requested by MHRA during their initial review of the study. To seek approval for the use of a 'Patient Booklet', to be distributed to participants, detailing the use of the injection pens for the administration of the study treatment. To change the PI at the PIC.
02 July 2019	To request approval for the addition of a new recruiting site. To report changes to study personnel.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

COVID-19 lockdown measures affected the collection of end of treatment data - not all participants were able to provide these.

Notes: