Clinical trial results:
Impact of liraglutide on cardiac function and structure in young adults with type 2 diabetes: an open label, randomised active-comparator trial.

Summary

EudraCT number	2012-002422-78
Trial protocol	GB
Global end of trial date	29 September 2017

Results information

Result version number	v1 (current)
This version publication date	18 January 2020
First version publication date	18 January 2020

Trial information

Trial identification

Sponsor protocol code	UNOLE 0398

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02043054
WHO universal trial number (UTN)	U1111-1131-8802

Notes:

Sponsors

Sponsor organisation name	University of Leicester
Sponsor organisation address	Research & Enterprise Division, University of Leicester, Leicester General Hospital, Leicester , United Kingdom, LE5 4PW
Public contact	Professor Melanie Davies, University of Leicester, +44 01162586481, melanie.davies@uhl-tr.nhs.uk
Scientific contact	Professor Melanie Davies, University of Leicester, +44 01162586481, melanie.davies@uhl-tr.nhs.uk

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	13 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 September 2017
Global end of trial reached?	Yes
Global end of trial date	29 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal question is whether Lirgalutide improves cardiac function (as measured by left-ventricular function) to a greater extent than Sitagliptin in younger adults with type 2 diabetes who are likely to present with abnormalities.

Protection of trial subjects:

All study participants were required to read a patient Information Sheet (PIS) about the trial (including trial treatments and any known side-effects) and sign an Informed Consent Form (ICF). Patients were monitored regularly throughout the trial duration.

Background therapy:

None. Liraglutide was the Investigational Medicinal Product and Sitagliptin was the comparator product. There were no other products used in this CTIMP.

Evidence for comparator:

At the time of writing the trial protocol, there were recent advances in therapies for the treatment of T2DM which included the GLP1 analogues and the DPP IV inhibitors. Both of these therapies target the incretin system using different methods to elevate/maintain circulating levels of GLP1 to subsequently achieve improved blood sugar control. Interestingly, GLP1 analogues were reported not only to improve blood sugar control but to additionally induce weight-loss and emerging experimental evidence at that time indicated that it may have beneficial effects on the heart's structure and function. Due to the profile of this condition being a lot worse and younger patients having greater CVD risk, a therapy offering multiple positive effects, in particular the potential cardiometabolic effects, made this line of therapy attractive in this patient population. Further, at that time, there were signals from secondary outcomes from other cardiovascular trials that Saxagliptin may have an adverse effect on Cardiovascular function measures. Consequently, the study Investigators chose to use Sitagliptin as the active comparator in this trial. The aim of this research was to investigate the cardiometabolic effects of Liraglutide (GLP1 analogue) compared to that of its clinically relevant comparator Sitagliptin (DPP IV inhibitor).

Actual start date of recruitment	08 July 2013
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: 76
Worldwide total number of subjects	76
EEA total number of subjects	76

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)	76
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Sponsor Greenlight was issued on 28/01/2014. First Patient First Visit date was 18/02/2014 and Last Patient Last Visit date was 13/09/2017.

Pre-assignment

Screening details:

76 people (41 women and 35 men) who had obesity (average body mass index (BMI) 35 kg·m-2) and had been diagnosed with type 2 diabetes for an average of 4.4 years were enrolled into the study. Sixty-four people completed the study (31 in the liraglutide group and 33 in the sitagliptin group).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Liraglutide

Arm description:

Participants received 1.8mg/daily Liraglutide. Liraglutide was administered using labelled 3ml prefilled pens (Victoza® 6mgml-1) supplied by the manufacturer.

Arm type	Investigational Medicinal Product
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	Victoza
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Liraglutide doses were self-administrated by the participant through daily subcutaneous injections, using labelled 3ml prefilled pens (Victoza® 6mgml-1) supplied by the manufacturer. Liraglutide doses were initiated at 0.6 mg and then increased to 1.2 mg in week two and 1.8mg in week three. The dose was then maintained at 1.8 mg. Where 1.8 mg doses were not tolerated by the patient, the dose was lowered to the maximum tolerated dose at the investigators discretion.

Arm title	Sitagliptin

Arm description:

Sitagliptin 100mg/daily.

Arm type	Active comparator
Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	Januvia
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin doses were self-administered by the participant orally at 100mg/day throughout the 26 week period of the study.

Number of subjects in period 1	Liraglutide	Sitagliptin
Started	38	38
Completed	24	28
Not completed	14	10
Withdrawn	3	3
Lost to follow-up	11	7

Baseline characteristics

Reporting groups	
Reporting group title	Liraglutide
Reporting group description:	
Participants received 1.8mg/daily Liraglutide. Liraglutide was administered using labelled 3ml prefilled pens (Victoza® 6mgml-1) supplied by the manufacturer.	
Reporting group title	Sitagliptin
Reporting group description:	
Sitagliptin 100mg/daily.	

Reporting group values	Liraglutide	Sitagliptin	Total
Number of subjects	38	38	76
Age categorical			
76 people (41 women and 35 men) with Type 2 Diabetes were enrolled. They had an average age of 44 years.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	38	38	76
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
76 people (41 women and 35 men) with type 2 Diabetes were enrolled into the study. Participants had an average age of 44 years.			
Units: years			
arithmetic mean	43.4	44.8	
standard deviation	± 7.0	± 5.9	-
Gender categorical			
We recruited 76 people (41 women and 35 men) with type 2 diabetes. 18 women were randomized to the IMP arm and 23 women to the active comparator arm. 20 men were randomized to the IMP arm and 15 men to the active comparator arm.			
Units: Subjects			
Female	18	23	41
Male	20	15	35
Smoking status			
There were 11 current smokers in the liraglutide group and 8 in the sitagliptin group.			
Units: Subjects			
Current smoker	11	8	19
Never Smoked	19	18	37
Ex smoker	8	12	20
Duration of diabetes			
The combined study population had a median T2DM duration of 3 years.			
Units: years			
arithmetic mean	4.5	4.4	

standard deviation	± 4.5	± 4.4	-
Body weight			
The combined study population had a mean body weight of 100.7kg.			
Units: kg			
arithmetic mean	100.8	100.7	
standard deviation	± 18.8	± 21.1	-
BMI			
The combined study population had a mean BMI of 35.3 kg/m^2.			
Units: kg/m^2			
arithmetic mean	35.7	34.9	
standard deviation	± 7	± 5.3	-
Brachial systolic blood pressure			
The combined study population had an average systolic blood pressure of 125.8 mmHg.			
Units: mmHg			
arithmetic mean	129	128	
standard deviation	± 11.9	± 15.6	-
Brachial diastolic blood pressure			
The combined study population had a mean diastolic blood pressure of 85.5 mmHg.			
Units: mmHg			
arithmetic mean	86	85	
standard deviation	± 9.0	± 9.8	-
Heart rate			
Units: Beats per min			
arithmetic mean	81.0	76.5	
standard deviation	± 11.1	± 11.9	-
HbA1c			
The combined study population had a mean baseline HbA1c of 7.5%.			
Units: Percentage %			
arithmetic mean	7.5	7.6	
standard deviation	± 0.8	± 0.8	-
HbA1c			
The combined study population had a mean baseline HbA1c of 58.8 mmol/mol.			
Units: mmol/mol			
arithmetic mean	58.4	59.1	
standard deviation	± 9.3	± 9.1	-
VO2 max			
Data were available for 32 people in the liraglutide group and 30 in the sitagliptin group.			
Units: ml per kg per min			
arithmetic mean	23.7	23.5	
standard deviation	± 6.1	± 5.0	-
PEDSR Circumferential			
PEDSR = peak early diastolic strain rate Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: s^-1			
arithmetic mean	1.1	1.0	
standard deviation	± 0.3	± 0.3	-
PEDSR Longitudinal			
PEDSR = peak early diastolic strain rate Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: s^-1			
arithmetic mean	0.9	0.9	
standard deviation	± 0.2	± 0.2	-

LVEDMI			
LVEDMI = left ventricular end diastolic mass index Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: g/m^2			
arithmetic mean	55.3	54.5	
standard deviation	± 10.3	± 8.7	-
LVEDVI			
LVEDVI = left ventricular end-diastolic volume index Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL/m^2			
arithmetic mean	69.9	70.8	
standard deviation	± 15.0	± 13.9	-
LVESVI			
LVESVI = left ventricular end-systolic volume index Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL/m^2			
arithmetic mean	25.8	24.8	
standard deviation	± 13.3	± 8.8	-
LVEF			
LVEF = left ventricular ejection fraction Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: Percentage %			
arithmetic mean	64.5	65.6	
standard deviation	± 10.4	± 6.2	-
LVMV ratio			
LVMV = left ventricular mass volume			
Units: g/ml^3			
arithmetic mean	0.68	0.66	
standard deviation	± 0.10	± 0.12	-
PSS (circ)			
PSS (circ) = peak systolic strain (circumferential)			
Units: s^-1			
arithmetic mean	-22.98	-23.20	
standard deviation	± 3.45	± 2.99	-
Total cholesterol			
Units: mmol/l			
arithmetic mean	4.7	4.6	
standard deviation	± 1.2	± 0.9	-
LDL cholesterol			
Data was available for 36 participants in each arm.			
Units: mmol/l			
arithmetic mean	2.3	2.4	
standard deviation	± 0.8	± 0.6	-
HDL cholesterol			
Data were available for 37 participants in the sitagliptin group.			
Units: mmol/l			
arithmetic mean	1.1	1.2	
standard deviation	± 0.2	± 0.3	-
Triglyceride			
Units: mmol/l			
arithmetic mean	2.6	2.4	
standard deviation	± 1.5	± 1.7	-
Alanine Transaminase			

Units: IU/l			
arithmetic mean	39.6	33.1	
standard deviation	± 21.8	± 14.7	-
eGFR			
Estimated Glomerular Filtration Rate			
Units: ml/min			
arithmetic mean	87.6	89.1	
standard deviation	± 4.6	± 3.3	-
LV GCS			
LV GCS = left ventricular global circumferential strain Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: Percentage %			
arithmetic mean	-19.0	-19.4	
standard deviation	± 3.3	± 2.8	-
LV GLS			
LV GLS = left ventricular global longitudinal strain Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: Percentage %			
arithmetic mean	-15.8	-16.4	
standard deviation	± 2.8	± 2.3	-
LV EDV			
LV EDV = left ventricular end-diastolic volume Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL			
arithmetic mean	152.7	153.9	
standard deviation	± 41.3	± 43.8	-
LV ESV			
LV ESV = left ventricular end-systolic volume Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL			
arithmetic mean	56.6	54.5	
standard deviation	± 32.1	± 24.1	-
LVSV			
Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL			
arithmetic mean	96.1	99.5	
standard deviation	± 22.4	± 23.5	-
LVCO			
LVCO = left ventricular cardiac output Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: L/min			
arithmetic mean	7.4	7.2	
standard deviation	± 1.4	± 1.6	-
LVM			
LVM = left ventricular end diastolic mass Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: grams			
arithmetic mean	120.6	118	
standard deviation	± 28.7	± 27.8	-
LV peak filling rate			
Data were available for 34 people in the liraglutide group and 34 in the sitagliptin group.			
Units: mL/s			
arithmetic mean	555.9	547.7	
standard deviation	± 109.4	± 108	-

LMV/V			
Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: g/mL			
arithmetic mean	0.80	0.79	
standard deviation	± 0.13	± 0.14	-
Min LA vol			
LA vol = left atrial volume Data were available for 32 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL			
arithmetic mean	30.6	32.5	
standard deviation	± 14.3	± 10.5	-
Max LA vol			
Data were available for 32 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL			
arithmetic mean	68.3	73.7	
standard deviation	± 21.0	± 20.1	-
LAEF			
LAEF = left atrial ejection fraction Data were available for 32 people in the liraglutide group and 35 in the sitagliptin group.			
Units: Percentage %			
arithmetic mean	56.0	55.8	
standard deviation	± 9.0	± 6.9	-
Global stress MBF			
MBF = myocardial blood flow Data were available for 30 people in the liraglutide group and 34 in the sitagliptin group.			
Units: mL/min/g			
arithmetic mean	3.7	3.6	
standard deviation	± 1.2	± 0.9	-
Global rest MBF			
Data were available for 30 people in the liraglutide group and 33 in the sitagliptin group.			
Units: mL/min/g			
arithmetic mean	1.4	1.4	
standard deviation	± 0.5	± 0.5	-
MPR			
MPR = myocardial perfusion reserve Data were available for 30 people in the liraglutide group and 33 in the sitagliptin group.			
Units: None			
arithmetic mean	3.0	2.9	
standard deviation	± 1.2	± 1.0	-

Subject analysis sets

Subject analysis set title	Liraglutide (imputed)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Patients allocated to liraglutide with missing outcome data imputed.	
Subject analysis set title	Sitagliptin (imputed)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Patients allocated to sitagliptin with missing outcome data imputed.	

Reporting group values	Liraglutide (imputed)	Sitagliptin (imputed)	
Number of subjects	31	33	
Age categorical			
76 people (41 women and 35 men) with Type 2 Diabetes were enrolled. They had an average age of 44 years.			
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)	31	33	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
76 people (41 women and 35 men) with type 2 Diabetes were enrolled into the study. Participants had an average age of 44 years.			
Units: years			
arithmetic mean			
standard deviation	±	±	
Gender categorical			
We recruited 76 people (41 women and 35 men) with type 2 diabetes. 18 women were randomized to the IMP arm and 23 women to the active comparator arm. 20 men were randomized to the IMP arm and 15 men to the active comparator arm.			
Units: Subjects			
Female			
Male			
Smoking status			
There were 11 current smokers in the liraglutide group and 8 in the sitagliptin group.			
Units: Subjects			
Current smoker			
Never Smoked			
Ex smoker			
Duration of diabetes			
The combined study population had a median T2DM duration of 3 years.			
Units: years			
arithmetic mean			
standard deviation	±	±	
Body weight			
The combined study population had a mean body weight of 100.7kg.			
Units: kg			
arithmetic mean			
standard deviation	±	±	
BMI			
The combined study population had a mean BMI of 35.3 kg/m^2.			
Units: kg/m^2			
arithmetic mean			
standard deviation	±	±	
Brachial systolic blood pressure			
The combined study population had an average systolic blood pressure of 125.8 mmHg.			

Units: mmHg arithmetic mean standard deviation	±	±	
Brachial diastolic blood pressure			
The combined study population had a mean diastolic blood pressure of 85.5 mmHg.			
Units: mmHg arithmetic mean standard deviation	±	±	
Heart rate Units: Beats per min arithmetic mean standard deviation	±	±	
HbA1c			
The combined study population had a mean baseline HbA1c of 7.5%.			
Units: Percentage % arithmetic mean standard deviation	±	±	
HbA1c			
The combined study population had a mean baseline HbA1c of 58.8 mmol/mol.			
Units: mmol/mol arithmetic mean standard deviation	±	±	
VO2 max			
Data were available for 32 people in the liraglutide group and 30 in the sitagliptin group.			
Units: ml per kg per min arithmetic mean standard deviation	±	±	
PEDSR Circumferential			
PEDSR = peak early diastolic strain rate Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: s^-1 arithmetic mean standard deviation	±	±	
PEDSR Longitudinal			
PEDSR = peak early diastolic strain rate Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: s^-1 arithmetic mean standard deviation	±	±	
LVEDMI			
LVEDMI = left ventricular end diastolic mass index Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: g/m^2 arithmetic mean standard deviation	±	±	
LVEDVI			
LVEDVI = left ventricular end-diastolic volume index Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL/m^2 arithmetic mean standard deviation	±	±	
LVESVI			
LVESVI = left ventricular end-systolic volume index			

Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL/m^2 arithmetic mean standard deviation	±	±	
LVEF			
LVEF = left ventricular ejection fraction Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: Percentage % arithmetic mean standard deviation	±	±	
LVMV ratio			
LVMV = left ventricular mass volume			
Units: g/ml^3 arithmetic mean standard deviation	±	±	
PSS (circ)			
PSS (circ) = peak systolic strain (circumferential)			
Units: s^-1 arithmetic mean standard deviation	±	±	
Total cholesterol Units: mmol/l arithmetic mean standard deviation	±	±	
LDL cholesterol			
Data was available for 36 participants in each arm.			
Units: mmol/l arithmetic mean standard deviation	±	±	
HDL cholesterol			
Data were available for 37 participants in the sitagliptin group.			
Units: mmol/l arithmetic mean standard deviation	±	±	
Triglyceride Units: mmol/l arithmetic mean standard deviation	±	±	
Alanine Transaminase Units: IU/l arithmetic mean standard deviation	±	±	
eGFR			
Estimated Glomerular Filtration Rate			
Units: ml/min arithmetic mean standard deviation	±	±	
LV GCS			
LV GCS = left ventricular global circumferential strain Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: Percentage % arithmetic mean			

standard deviation	±	±	
LV GLS			
LV GLS = left ventricular global longitudinal strain Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: Percentage % arithmetic mean standard deviation	±	±	
LV EDV			
LV EDV = left ventricular end-diastolic volume Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL arithmetic mean standard deviation	±	±	
LV ESV			
LV ESV = left ventricular end-systolic volume Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL arithmetic mean standard deviation	±	±	
LVSV			
Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL arithmetic mean standard deviation	±	±	
LVCO			
LVCO = left ventricular cardiac output Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: L/min arithmetic mean standard deviation	±	±	
LVM			
LVM = left ventricular end diastolic mass Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: grams arithmetic mean standard deviation	±	±	
LV peak filling rate			
Data were available for 34 people in the liraglutide group and 34 in the sitagliptin group.			
Units: mL/s arithmetic mean standard deviation	±	±	
LMV/V			
Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group.			
Units: g/mL arithmetic mean standard deviation	±	±	
Min LA vol			
LA vol = left atrial volume Data were available for 32 people in the liraglutide group and 35 in the sitagliptin group.			
Units: mL arithmetic mean standard deviation	±	±	
Max LA vol			
Data were available for 32 people in the liraglutide group and 35 in the sitagliptin group.			

Units: mL arithmetic mean standard deviation	± 	± 	
LAEF			
LAEF = left atrial ejection fraction Data were available for 32 people in the liraglutide group and 35 in the sitagliptin group.			
Units: Percentage % arithmetic mean standard deviation	± 	± 	
Global stress MBF			
MBF = myocardial blood flow Data were available for 30 people in the liraglutide group and 34 in the sitagliptin group.			
Units: mL/min/g arithmetic mean standard deviation	± 	± 	
Global rest MBF			
Data were available for 30 people in the liraglutide group and 33 in the sitagliptin group.			
Units: mL/min/g arithmetic mean standard deviation	± 	± 	
MPR			
MPR = myocardial perfusion reserve Data were available for 30 people in the liraglutide group and 33 in the sitagliptin group.			
Units: None arithmetic mean standard deviation	± 	± 	

End points

End points reporting groups	
Reporting group title	Liraglutide
Reporting group description:	
Participants received 1.8mg/daily Liraglutide. Liraglutide was administered using labelled 3ml prefilled pens (Victoza® 6mgml-1) supplied by the manufacturer.	
Reporting group title	Sitagliptin
Reporting group description:	
Sitagliptin 100mg/daily.	
Subject analysis set title	Liraglutide (imputed)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Patients allocated to liraglutide with missing outcome data imputed.	
Subject analysis set title	Sitagliptin (imputed)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Patients allocated to sitagliptin with missing outcome data imputed.	

Primary: PEDSR (circ.)	
End point title	PEDSR (circ.)
End point description:	
Peak early diastolic strain rate (circumferential), measured by cardiac MRI at baseline and 26-weeks.	
End point type	Primary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin	Liraglutide (imputed)	Sitagliptin (imputed)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	28	33	31	33
Units: s^-1				
least squares mean (confidence interval 95%)	-0.06 (-0.10 to -0.01)	-0.05 (-0.10 to -0.01)	-0.07 (-0.12 to -0.02)	-0.06 (-0.10 to -0.01)

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Statistical analysis description:	
Linear regression was used to compare treatment effects adjusted for baseline values (age, sex, HbA1c, weight) with results presented as mean between group differences (Liraglutide minus Sitagliptin) and 95% confidence intervals. The primary analysis was conducted on a complete case ITT basis.	
Comparison groups	Liraglutide v Sitagliptin

Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.874
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	0.61

Statistical analysis title	Liraglutide vs Sitagliptin (imputed)
Statistical analysis description:	
Same as ITT analysis above, but given not all participants had outcome data available multiple imputation was used to perform a full intention to treat analysis for the primary outcome only.	
Comparison groups	Liraglutide (imputed) v Sitagliptin (imputed)
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.707
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.05

Secondary: LV GCS	
End point title	LV GCS
End point description:	
LV GCS = left ventricular global circumferential strain	
End point type	Secondary
End point timeframe:	
Baseline to completion of study (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: Percentage %				
least squares mean (confidence interval 95%)	0.66 (0.15 to 1.17)	0.27 (-0.20 to 0.73)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.274
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.09

Secondary: PEDSR (long.)

End point title	PEDSR (long.)
End point description: PEDSR (long.) = peak early diastolic strain rate (longitudinal)	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: s^-1				
least squares mean (confidence interval 95%)	-0.08 (-0.13 to -0.03)	-0.04 (-0.08 to -0.01)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.254
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.03

Secondary: LV GLS	
End point title	LV GLS
End point description: LV GLS = left ventriular global longitudinal strain	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: Percentage %				
least squares mean (confidence interval 95%)	0.33 (-0.35 to 1.01)	0.43 (-0.19 to 1.05)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.841
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.85

Secondary: LV EDV

End point title	LV EDV
End point description:	
LV EDV = left ventricular end-diastolic volume.	
End point type	Secondary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: mL				
least squares mean (confidence interval 95%)	-3.74 (-8.75 to 1.26)	-3.46 (-7.95 to 1.03)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.936
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.14
upper limit	6.58

Secondary: LV EDVi

End point title	LV EDVi

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: mL/m^2				
least squares mean (confidence interval 95%)	-0.23 (-2.90 to 2.44)	-1.50 (-3.93 to 0.92)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.497
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	4.94

Secondary: LV ESV

End point title	LV ESV

End point description:

LV ESV = left ventricular end-systolic volume

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: mL				
least squares mean (confidence interval 95%)	-1.20 (-4.76 to 2.35)	-3.67 (-6.86 to -0.47)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Sitagliptin v Liraglutide
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.322
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.41
upper limit	7.33

Secondary: LV ESVi

End point title	LV ESVi
End point description:	
LV ESVi = left ventricular end-systolic volume index.	
End point type	Secondary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: mL/m^2				
least squares mean (confidence interval 95%)	0.01 (-1.69 to 1.69)	-1.55 (-3.09 to -0.01)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Sitagliptin v Liraglutide
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	3.88

Secondary: LVEF	
End point title	LVEF
End point description: LVEF = left ventricular ejection fraction.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: Percentage %				
least squares mean (confidence interval 95%)	-0.60 (-2.72 to 1.53)	1.39 (-0.52 to 3.30)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.183
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-1.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	0.94

Secondary: LVSV

End point title	LVSV

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: mL				
least squares mean (confidence interval 95%)	-2.59 (-7.53 to 2.34)	0.22 (-4.19 to 4.63)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.421
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-2.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.66
upper limit	4.03

Secondary: LVCO

End point title	LVCO

End point description: LVCO = left ventricular cardiac output.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: L/min				
least squares mean (confidence interval 95%)	-0.10 (-0.49 to 0.29)	0.12 (-0.23 to 0.48)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.421
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.32

Secondary: LVM	
End point title	LVM
End point description: LVM = left ventricular end-diastolic mass.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: grams				
least squares mean (confidence interval 95%)	0.72 (-3.94 to 5.37)	-0.43 (-4.59 to 3.75)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.726
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.23
upper limit	7.5

Secondary: LVMi

End point title	LVMi
End point description:	
LVMi = left ventricular end-diastolic mass index.	
End point type	Secondary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: g/m^2				
least squares mean (confidence interval 95%)	1.27 (-0.88 to 3.42)	-0.26 (-2.22 to 1.69)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.308
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.41
upper limit	4.49

Secondary: LV peak filling rate	
End point title	LV peak filling rate
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: mL/s				
least squares mean (confidence interval 95%)	10.87 (-18.0 to 39.7)	-18.72 (-44.90 to 7.46)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.145
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	29.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.15
upper limit	69.32

Secondary: LMV/V

End point title	LMV/V

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	32		
Units: g/mL				
least squares mean (confidence interval 95%)	0.03 (-0.11 to 0.07)	0.01 (-0.03 to 0.05)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.07

Secondary: Min LA vol

End point title	Min LA vol

End point description: LA vol = left atrial volume.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	32		
Units: mL				
least squares mean (confidence interval 95%)	-0.81 (-3.52 to 1.89)	1.89 (-0.61 to 4.38)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.161
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.47
upper limit	1.07

Secondary: Max LA vol	
End point title	Max LA vol
End point description: LA vol = left atrial volume.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	32		
Units: mL				
least squares mean (confidence interval 95%)	-3.82 (-8.88 to 1.23)	-0.81 (-5.49 to 3.85)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.406
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-3.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	4.09

Secondary: LAEF

End point title	LAEF
End point description:	
LAEF = left atrial ejection fraction.	
End point type	Secondary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	32		
Units: Percentage %				
least squares mean (confidence interval 95%)	-1.65 (-3.46 to 0.17)	-2.80 (-4.48 to -1.12)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.37
upper limit	3.67

Secondary: Global stress MBF	
End point title	Global stress MBF
End point description: MBF = myocardial blood flow.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	30		
Units: mL/min/g				
least squares mean (confidence interval 95%)	-0.21 (-0.49 to 0.06)	-0.15 (-0.40 to 0.97)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Sitagliptin v Liraglutide
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.748
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	0.32

Secondary: Global rest MBF

End point title	Global rest MBF
End point description: MBF = myocardial blood flow.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	30		
Units: mL/min/g				
least squares mean (confidence interval 95%)	-0.14 (-0.26 to -0.02)	-0.21 (-0.32 to -0.10)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.412
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.23

Secondary: MPR

End point title	MPR

End point description: MPR = myocardial perfusion reserve.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	30		
Units: None				
least squares mean (confidence interval 95%)	-0.09 (-0.46 to 0.28)	0.19 (-0.15 to 0.53)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.291
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.24

Secondary: HbA1c (%)	
End point title	HbA1c (%)
End point description:	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: Percentage %				
least squares mean (confidence interval 95%)	-0.89 (-1.18 to -0.60)	-0.48 (-0.76 to -0.18)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	-0.01

Secondary: HbA1c (mmol/mol)

End point title	HbA1c (mmol/mol)

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: mmol/mol				
least squares mean (confidence interval 95%)	-9.90 (-13.12 to -6.67)	-5.32 (-8.46 to -2.19)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-4.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	-0.37

Secondary: Weight

End point title	Weight
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: kg				
least squares mean (confidence interval 95%)	-4.51 (-5.84 to -3.19)	-0.63 (-1.92 to 0.66)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-3.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.74
upper limit	-2.01

Secondary: BMI

End point title	BMI

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: kg/m^2				
least squares mean (confidence interval 95%)	-1.60 (-2.10 to -1.10)	-0.28 (-0.77 to 0.20)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	-0.62

Secondary: Systolic blood pressure

End point title	Systolic blood pressure

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: mmHg				
least squares mean (confidence interval 95%)	-8.90 (-12.02 to -5.78)	-8.73 (-11.77 to -5.69)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.939
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.56
upper limit	4.22

Secondary: Diastolic blood pressure

End point title	Diastolic blood pressure

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: mmHg				
least squares mean (confidence interval 95%)	-5.15 (-7.61 to -2.70)	-3.88 (-6.27 to -1.50)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.473
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.07
upper limit	2.09

Secondary: Heart rate

End point title	Heart rate

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: Beats per min				
least squares mean (confidence interval 95%)	13.49 (9.57 to 17.41)	7.96 (4.15 to 11.78)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.052
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	5.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	11.12

Secondary: Total cholesterol

End point title	Total cholesterol
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: mmol/l				
least squares mean (confidence interval 95%)	0.11 (-0.11 to 0.34)	-0.23 (-0.45 to -0.01)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	0.35

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.67

Secondary: LDL cholesterol

End point title	LDL cholesterol

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	31		
Units: mmol/l				
least squares mean (confidence interval 95%)	0.21 (0.02 to 0.40)	-0.09 (-0.27 to 0.09)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Sitagliptin v Liraglutide
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.57

Secondary: HDL cholesterol

End point title	HDL cholesterol

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: mmol/l				
least squares mean (confidence interval 95%)	0.03 (-0.02 to 0.08)	0.01 (-0.04 to 0.07)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.62
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.1

Secondary: Triglycerides

End point title	Triglycerides

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: mmol/l				
least squares mean (confidence interval 95%)	-0.32 (-0.57 to -0.06)	-0.35 (-0.60 to -0.10)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.833
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.39

Secondary: Alanine Transaminase

End point title	Alanine Transaminase

End point description:

End point type	Secondary

End point timeframe:

Baseline to study completion (26 weeks).

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: IU/l				
least squares mean (confidence interval 95%)	-4.92 (-11.22 to 1.37)	6.35 (-0.23 to 12.46)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	-11.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.17
upper limit	-2.37

Secondary: eGFR	
End point title	eGFR
End point description: eGFR = estimated glomerular filtration rate.	
End point type	Secondary
End point timeframe: Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: ml/min				
least squares mean (confidence interval 95%)	-0.58 (-2.47 to 1.31)	-3.02 (-4.85 to -1.18)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.08
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	2.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	5.16

Secondary: VO2 max

End point title	VO2 max
End point description:	
VO2 max = maximal oxygen consumption.	
End point type	Secondary
End point timeframe:	
Baseline to study completion (26 weeks).	

End point values	Liraglutide	Sitagliptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: ml/kg/min				
least squares mean (confidence interval 95%)	0.46 (-0.40 to 1.33)	-0.47 (-1.30 to 0.35)		

Statistical analyses

Statistical analysis title	Liraglutide vs Sitagliptin (ITT)
Comparison groups	Liraglutide v Sitagliptin
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.135
Method	Regression, Linear
Parameter estimate	LS Mean difference
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	2.17

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Consent to last dose of drug.

Adverse event reporting additional description:

At each visit, the investigator documented adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of relation to study treatment. All SAEs and non-serious AEs classified as severe or possibly/probably related were followed up until resolution.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Liraglutide

Reporting group description:

Liraglutide was administered using labelled 3ml prefilled pens (Victoza® 6mgml-1) supplied by the manufacturer. Starting at a dose of 0.6mg daily, a weekly 0.6mg incremental dose escalation protocol was followed at the investigator's discretion towards a maintenance dose of 1.8mg weekly.

Reporting group title	Sitagliptin

Reporting group description:

Sitagliptin was obtained from the manufacturer and prescribed at a dose of 100mg daily from the point of treatment initiation.

Serious adverse events	Liraglutide	Sitagliptin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	4 / 38 (10.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal Injury	Additional description: Participant stepped off the pavement and twisted her ankle and hyperextended her knee causing serious knee injury.		

subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Chest infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Liraglutide	Sitagliptin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 38 (92.11%)	38 / 38 (100.00%)	
Vascular disorders			
Haemorrhoids			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Hypertension	Additional description: Worsening of blood pressure		
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Dental problem			
subjects affected / exposed	2 / 38 (5.26%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
General disorders and administration site conditions			
Tiredness			
subjects affected / exposed	1 / 38 (2.63%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Hot flush			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Lethargy			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Swelling of feet			

subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	2	
Immune system disorders			
Hay fever			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	6 / 38 (15.79%)	8 / 38 (21.05%)	
occurrences (all)	6	8	
Cough			
subjects affected / exposed	1 / 38 (2.63%)	7 / 38 (18.42%)	
occurrences (all)	1	7	
Asthma attack			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Sinus pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Sore throat			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
low mood			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Stress			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Investigations			
Cardiac murmur			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Cholesterol levels raised			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	

Abnormal ECG	Additional description: Abnormal ECG result (exercise)		
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Injection site reaction			
subjects affected / exposed	3 / 38 (7.89%)	0 / 38 (0.00%)	
occurrences (all)	3	0	
Wasp sting			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 38 (2.63%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Chest pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 38 (21.05%)	9 / 38 (23.68%)	
occurrences (all)	8	9	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Neuropathic pain	Additional description: Worsening of neuropathic pain		
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Faint	Additional description: Fainted during VO2 exercise test		
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	4 / 38 (10.53%)	5 / 38 (13.16%)	
occurrences (all)	5	5	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	19 / 38 (50.00%)	9 / 38 (23.68%)	
occurrences (all)	23	9	
Vomiting			
subjects affected / exposed	6 / 38 (15.79%)	2 / 38 (5.26%)	
occurrences (all)	7	3	
Abdominal pain			
subjects affected / exposed	4 / 38 (10.53%)	5 / 38 (13.16%)	
occurrences (all)	4	5	
Diarrhoea			
subjects affected / exposed	15 / 38 (39.47%)	8 / 38 (21.05%)	
occurrences (all)	17	8	
Constipation			
subjects affected / exposed	5 / 38 (13.16%)	2 / 38 (5.26%)	
occurrences (all)	5	2	
Flatulence			
subjects affected / exposed	6 / 38 (15.79%)	2 / 38 (5.26%)	
occurrences (all)	6	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 38 (13.16%)	1 / 38 (2.63%)	
occurrences (all)	6	1	
Taste disorder	Additional description: Strange taste		
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dry skin	Additional description: Dry skin on knees		
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Excess Sweating			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Hard skin	Additional description: Hard skin on right foot		

subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
itchy skin			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal injury			
subjects affected / exposed	6 / 38 (15.79%)	8 / 38 (21.05%)	
occurrences (all)	6	8	
Swelling of knees			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Thrush			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemic event			
subjects affected / exposed	2 / 38 (5.26%)	4 / 38 (10.53%)	
occurrences (all)	3	5	
Excessive Thirst			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	

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

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

Unfortunately, despite the best efforts of the research team, this study did not recruit to target. After a challenging recruitment period, the study team managed to recruit 76 participants of an overall recruitment target of 90 participants.

Notes: