# 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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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<br>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:<br>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:<br>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<br>arithmetic mean<br>standard deviation | ± | ± | |
| Brachial diastolic blood pressure | | | |
| The combined study population had a mean diastolic blood pressure of 85.5 mmHg. | | | |
| Units: mmHg<br>arithmetic mean<br>standard deviation | ± | ± | |
| Heart rate<br>Units: Beats per min<br>arithmetic mean<br>standard deviation | ± | ± | |
| HbA1c | | | |
| The combined study population had a mean baseline HbA1c of 7.5%. | | | |
| Units: Percentage %<br>arithmetic mean<br>standard deviation | ± | ± | |
| HbA1c | | | |
| The combined study population had a mean baseline HbA1c of 58.8 mmol/mol. | | | |
| Units: mmol/mol<br>arithmetic mean<br>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<br>arithmetic mean<br>standard deviation | ± | ± | |
| PEDSR Circumferential | | | |
| PEDSR = peak early diastolic strain rate<br>Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group. | | | |
| Units: s^-1<br>arithmetic mean<br>standard deviation | ± | ± | |
| PEDSR Longitudinal | | | |
| PEDSR = peak early diastolic strain rate<br>Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group. | | | |
| Units: s^-1<br>arithmetic mean<br>standard deviation | ± | ± | |
| LVEDMI | | | |
| LVEDMI = left ventricular end diastolic mass index<br>Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group. | | | |
| Units: g/m^2<br>arithmetic mean<br>standard deviation | ± | ± | |
| LVEDVI | | | |
| LVEDVI = left ventricular end-diastolic volume index<br>Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group. | | | |
| Units: mL/m^2<br>arithmetic mean<br>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<br>arithmetic mean<br>standard deviation | ± | ± | |
| LVEF | | | |
| LVEF = left ventricular ejection fraction<br>Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group. | | | |
| Units: Percentage %<br>arithmetic mean<br>standard deviation | ± | ± | |
| LVMV ratio | | | |
| LVMV = left ventricular mass volume | | | |
| Units: g/ml^3<br>arithmetic mean<br>standard deviation | ± | ± | |
| PSS (circ) | | | |
| PSS (circ) = peak systolic strain (circumferential) | | | |
| Units: s^-1<br>arithmetic mean<br>standard deviation | ± | ± | |
| Total cholesterol<br>Units: mmol/l<br>arithmetic mean<br>standard deviation | ± | ± | |
| LDL cholesterol | | | |
| Data was available for 36 participants in each arm. | | | |
| Units: mmol/l<br>arithmetic mean<br>standard deviation | ± | ± | |
| HDL cholesterol | | | |
| Data were available for 37 participants in the sitagliptin group. | | | |
| Units: mmol/l<br>arithmetic mean<br>standard deviation | ± | ± | |
| Triglyceride<br>Units: mmol/l<br>arithmetic mean<br>standard deviation | ± | ± | |
| Alanine Transaminase<br>Units: IU/l<br>arithmetic mean<br>standard deviation | ± | ± | |
| eGFR | | | |
| Estimated Glomerular Filtration Rate | | | |
| Units: ml/min<br>arithmetic mean<br>standard deviation | ± | ± | |
| LV GCS | | | |
| LV GCS = left ventricular global circumferential strain<br>Data were available for 34 people in the liraglutide group and 35 in the sitagliptin group. | | | |
| Units: Percentage %<br>arithmetic mean | | | |

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

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

## 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:<br>LV GLS = left ventriular global longitudinal strain | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>LVEF = left ventricular ejection fraction. | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>LVCO = left ventricular cardiac output. | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>LVM = left ventricular end-diastolic mass. | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>LA vol = left atrial volume. | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>LA vol = left atrial volume. | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>MBF = myocardial blood flow. | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>MBF = myocardial blood flow. | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>MPR = myocardial perfusion reserve. | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>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:<br>eGFR = estimated glomerular filtration rate. | |
| End point type | Secondary |
| End point timeframe:<br>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: