Clinical trial results:
Does the GLP-1 receptor agonist (Victoza®) improve the metabolic response to physical training in patients with type 2 diabetes?

Summary

EudraCT number	2011-002739-24
Trial protocol	DK
Global end of trial date	31 December 2013

Results information

Result version number	v1 (current)
This version publication date	02 June 2022
First version publication date	02 June 2022

Trial information

Trial identification

Sponsor protocol code	60

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1122-0819

Notes:

Sponsors

Sponsor organisation name	Gentofte Hospital
Sponsor organisation address	Gentofte Hospitalsvej 1, 2900 Hellerup, Denmark,
Public contact	Department of Internal Medicine F, Dr. med. Tina Vilsbøll, +45 3977 2297, t.vilsboll@dadlnet.dk
Scientific contact	Department of Internal Medicine F, Dr. med. Tina Vilsbøll, +45 3977 2297, t.vilsboll@dadlnet.dk

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	04 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to investigate the effects of physical training in patients with type 2 diabetes during treatment with the GLP-1 receptor agonist liraglutide (Victoza®) in a 16-weeks double-blinded, randomized placebo-controlled clinical trial

Protection of trial subjects:

Treated in rutine care

Background therapy:

Medical treatment was similar in the groups and remained unchanged during the study. Besides metformin, patients received no medication known to interfere with glucose metabolism

Evidence for comparator: -

Actual start date of recruitment	01 October 2011
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	Denmark: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

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)	23
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the Diabetes Outpatient Clinic at Gentofte Hospital, Denmark, and through advertisement. Oral and written informed consent were obtained before inclusion.

Pre-assignment

Screening details:

Inclusion criteria were: age >18 years; type 2 diabetes treated with diet and/or metformin; HbA1c between 7% and 11% (53-97 mmol/mol), body mass index (BMI) > 25 kg/m2 ; and sedentary lifestyle (self-reported physical activity <150 min/wk). Exclusion criteria were clinically relevant cardiovascular disease, impaired liver function, anaemia a

Period 1

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

Blinding implementation details:

An employee otherwise not involved in the study carried out the randomization at a 1:1 ratio from a prespecified randomization list.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treated

Arm description:

Exercise+Liraglutide

Arm type	Experimental
Investigational medicinal product name	liraglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection , Subcutaneous use

Dosage and administration details:

Liraglutide was injected subcutaneous (s.c.) once-daily of 0.1 mL (0.6 mg) in the evening for 1 week, 0.2 mL (1.2 mg) the following week and thereafter 0.3 mL (1.8 mg) for the remaining study period.

Arm title	Placebo

Arm description:

Exercise+placebo

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

Dosage and administration details:

Saline (placebo) was injected subcutaneous (s.c.) once-daily of 0.1 mL (0.6 mg) in the evening for 1 week, 0.2 mL (1.2 mg) the following week and thereafter 0.3 mL (1.8 mg) for the remaining study period.

Number of subjects in period 1	Treated	Placebo
Started	19	17
Completed	17	16
Not completed	2	1
Withdrawn consent, patient decision	2	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Treated
Reporting group description:	
Exercise+Liraglutide	
Reporting group title	Placebo
Reporting group description:	
Exercise+placebo	

Reporting group values	Treated	Placebo	Total
Number of subjects	19	17	36
Age categorical			
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)	12	11	23
From 65-84 years	7	6	13
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	56.5	55.6	
standard deviation	± 9	± 12	-
Gender categorical			
Units: Subjects			
Female	4	6	10
Male	15	11	26

Subject analysis sets	
Subject analysis set title	HbA1c
Subject analysis set type	Per protocol

Subject analysis set description:

Per-protocol analyses were performed. Data are reported as +/-mean standard deviation; in case of non-normal distribution, data were log-transformed and back-transformed. Estimates are reported as geometric means with 95% confidence interval (CI). Differences between mean values in the two groups were analysed using Student’s t-test. Analyses of between-group differences were performed by analysis of covariance (ANCOVA) with the end-of-study value as the dependent variable

Reporting group values	HbA1c		
Number of subjects	33		
Age categorical			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over	 23 13 		
Age continuous Units: years arithmetic mean standard deviation	 ±		
Gender categorical Units: Subjects			
Female Male	10 23		

End points

End points reporting groups

Reporting group title	Treated
Reporting group description: Exercise+Liraglutide	
Reporting group title	Placebo
Reporting group description: Exercise+placebo	
Subject analysis set title	HbA1c
Subject analysis set type	Per protocol
Subject analysis set description: Per-protocol analyses were performed. Data are reported as +/-mean standard deviation; in case of non-normal distribution, data were log-transformed and back-transformed. Estimates are reported as geometric means with 95% confidence interval (CI). Differences between mean values in the two groups were analysed using Student's t-test. Analyses of between-group differences were performed by analysis of covariance (ANCOVA) with the end-of-study value as the dependent variable	

Primary: HbA1c

End point title	HbA1c
End point description:	
End point type	Primary
End point timeframe: 16 weeks	

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: mmol/mol				
arithmetic mean (standard deviation)	44.0 (± 8.0)	61.0 (± 17.0)		

Statistical analyses

Statistical analysis title	HbA1c
Comparison groups	Treated v Placebo
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	ANCOVA

Secondary: Fasting plasma glucose

End point title	Fasting plasma glucose

End point description:

End point type	Secondary

End point timeframe:

16 weeks

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: mmol				
arithmetic mean (standard deviation)	7.0 (± 1.6)	9.8 (± 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Glucagon

End point title	Glucagon

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: pmol				
arithmetic mean (standard deviation)	9.4 (± 3.2)	8.2 (± 2.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: GLP-1

End point title	GLP-1

End point description:

End point type	Secondary

End point timeframe:
Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: pmol				
arithmetic mean (standard deviation)	19.3 (± 5.6)	18.1 (± 5.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: GIP

End point title	GIP

End point description:

End point type	Secondary

End point timeframe:
Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: pmol				
arithmetic mean (standard deviation)	16.3 (± 5.2)	17.0 (± 8.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Body weight

End point title	Body weight

End point description:

End point type	Secondary

End point timeframe:
Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: kg				
arithmetic mean (standard deviation)	97.6 (± 14.9)	95.2 (± 17.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Body mass index

End point title	Body mass index

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: kg/m2				
arithmetic mean (standard deviation)	31.3 (± 3.4)	31.8 (± 5.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fat percent

End point title	Fat percent

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: percent				
arithmetic mean (standard deviation)	31.8 (± 6.8)	34.8 (± 7.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Gynoid fat

End point title	Gynoid fat

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: percent				
arithmetic mean (standard deviation)	32.5 (± 9.6)	36.3 (± 8.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Android fat

End point title	Android fat

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: percent				
arithmetic mean (standard deviation)	41.4 (± 5.2)	42.8 (± 7.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lean body mass

End point title	Lean body mass

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: kg				
arithmetic mean (standard deviation)	63.4 (± 12.8)	58.7 (± 12.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Systolic blood pressure

End point title	Systolic blood pressure

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: mmHg				
arithmetic mean (standard deviation)	130.8 (± 8.8)	135.8 (± 11.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Diastolic blood pressure

End point title	Diastolic blood pressure

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: mmHg				
arithmetic mean (standard deviation)	81.5 (± 7.2)	81.8 (± 8.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Resting heart rate

End point title	Resting heart rate

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: beats per minutes				
arithmetic mean (standard deviation)	71.3 (± 9.4)	68.1 (± 12.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: VO2max

End point title	VO2max

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: L/O2/min				
arithmetic mean (standard deviation)	3.4 (± 1.1)	2.9 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total cholesterol

End point title	Total cholesterol

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	6		
Units: mmol				
arithmetic mean (standard deviation)	4.4 (± 1.3)	4.3 (± 0.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: HDL cholesterol

End point title	HDL cholesterol

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: mmol				
arithmetic mean (standard deviation)	1.2 (± 0.4)	1.3 (± 0.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: LDL cholesterol

End point title	LDL cholesterol

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: mmol				
arithmetic mean (standard deviation)	2.4 (± 1.2)	2.3 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: VLDL cholesterol

End point title	VLDL cholesterol

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: mmol				
arithmetic mean (standard deviation)	0.7 (± 0.4)	0.7 (± 0.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin

End point title	Insulin

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: pM				
geometric mean (confidence interval 95%)	111 (91 to 135)	93 (63 to 138)		

Statistical analyses

No statistical analyses for this end point

Secondary: C-peptide

End point title	C-peptide

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: pM				
geometric mean (confidence interval 95%)	913 (814 to 1023)	799 (634 to 1008)		

Statistical analyses

No statistical analyses for this end point

Secondary: HOMA2-IR, insulin

End point title	HOMA2-IR, insulin

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: AU				
geometric mean (confidence interval 95%)	2.2 (1.8 to 2.7)	2.0 (1.4 to 3.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: HOMA2-IR c-peptide

End point title	HOMA2-IR c-peptide

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: AU				
geometric mean (confidence interval 95%)	2.2 (2.0 to 2.5)	2.4 (1.9 to 3.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: HOMA2-beta, insulin

End point title	HOMA2-beta, insulin

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: AU				
geometric mean (confidence interval 95%)	86.5 (70.1 to 106.7)	45.7 (30.3 to 69.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: HOMA2-beta, c-peptide

End point title	HOMA2-beta, c-peptide

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: AU				
geometric mean (confidence interval 95%)	86.7 (70.7 to 106.3)	51.6 (36.8 to 72.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Triglycerides

End point title	Triglycerides

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: mM				
geometric mean (confidence interval 95%)	1.5 (1.0 to 2.1)	1.4 (1.1 to 1.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Alanine aminotransferase

End point title	Alanine aminotransferase

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: U/L				
geometric mean (confidence interval 95%)	32.9 (23.2 to 46.5)	28.4 (22.7 to 35.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Aspartate aminotransferase

End point title	Aspartate aminotransferase

End point description:

End point type	Secondary

End point timeframe:

Changes between baseline and end of study

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: U/L				
geometric mean (confidence interval 95%)	33.2 (27.5 to 40.1)	27.6 (23.7 to 32.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events and serious adverse events were recorded throughout the study in the time period December 2011 to March 2013

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	Liraglutide
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Liraglutide	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Liraglutide	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events were reported

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28188972

http://www.ncbi.nlm.nih.gov/pubmed/27717126