Clinical trial results:
The effect of liraglutide on pancreatic hormones and its size

Summary

EudraCT number	2016-004768-20
Trial protocol	DK
Global end of trial date	04 April 2019

Results information

Result version number	v1 (current)
This version publication date	21 May 2020
First version publication date	21 May 2020

Trial information

Trial identification

Sponsor protocol code	LIRAP

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03520062
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Copenhagen
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark,
Public contact	Nicolai Jacob Wewer Albrechtsen and Jens Juul Holst, University of Copenhagen, +45 29649329, hgk795@ku.dk
Scientific contact	Nicolai Jacob Wewer Albrechtsen and Jens Juul Holst, University of Copenhagen, +45 29649329, hgk795@ku.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	01 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 April 2019
Global end of trial reached?	Yes
Global end of trial date	04 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate if liraglutide increases the volumen of the pancreas and as a consequence increases plasma levels of amylase and lipase

Protection of trial subjects:

No certain protection was included

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	17
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Obese men were recruited by advertisement at forsoegspersoner.dk and from department of endocrinology, hvidovre hospital. The recruitment was initiated in march 2017 and ended in march 2019

Pre-assignment

Screening details:

Participants were overweight but otherwise healthy men, who were recruited through advertisement. Inclusion criteria were men; age 18-65 years; body mass index (BMI) 26-50 kg/m2; and written informed consent. Key exclusion criteria were type 1 or 2 diabetes (HbA1c > 42 mmol/mol (6·0%)); severe diseases of the heart, lung, liver, kidney (estimated g

Period 1

Period 1 title	overall trial baseline
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Liraglutide

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Saxenda
Investigational medicinal product code	
Other name	Liraglutide
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Following the baseline examinations, treatment with liraglutide (Saxenda, Novo Nordisk, Søborg, Denmark) injections once daily was initiated at a dose of 0·6 mg daily for the first week. Doses of liraglutide were titrated by additional 0·6 mg per week if tolerated until the maximum dose of 3·0 mg was achieved. The titration of liraglutide was supervised by weekly telephone consultations with evaluation of any side effects. In case of intolerable side effects, the study medication dosage could be reduced until recovery from symptoms occurred; however, all subjects in the study did reach the maximum dose of 3·0 mg. Adherence to study medication was evaluated by collection of all injection pens and, in addition, blood was sampled for analysis of plasma concentrations of liraglutide. Visits were repeated 4 weeks and 6 weeks after initiation of treatment, and a follow-up visit was performed 3 weeks after discontinuation of liraglutide treatment (follow-up).

Number of subjects in period 1	Liraglutide
Started	17
Completed	16
Not completed	1
unable to fit the MR scanner	1

Period 2

Period 2 title	overall trial
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Liraglutide

Arm description:

This was an open-label clinical study with prospective evaluation of pancreatic enzymes and MRI determination of pancreatic volume before (‘Baseline’), during initiation and titration of liraglutide (‘Week 4’) towards maximum dose of 3·0 mg, after 2 weeks of steady state treatment with liraglutide (‘Week 6’), and at a follow-up visit 3 weeks after discontinuation of liraglutide treatment (‘Follow-up’),

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Number of subjects in period 2	Liraglutide
Started	16
Completed	14
Not completed	2
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	overall trial baseline

Reporting group description: -

Reporting group values	overall trial baseline	Total	
Number of subjects	17	17	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	17	17	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	39		
standard deviation	± 11	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	17	17	

End points

End points reporting groups

Reporting group title	Liraglutide
Reporting group description: -	
Reporting group title	Liraglutide
Reporting group description:	
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Subject analysis set title	primary outcome
Subject analysis set type	Per protocol
Subject analysis set description:	
Six week effect of liraglutide on pancreatic volume	
Subject analysis set title	Comparison between baseline and after intervention
Subject analysis set type	Per protocol
Subject analysis set description:	
Delta values between baseline and 6 week after intervention with liraglutide for pancreatic volume, amylase and lipase and 4 weeks for FLT-uptake	

Primary: Pancreatic Volume

End point title	Pancreatic Volume
End point description:	
End point type	Primary
End point timeframe:	
From baseline to 6 week after intervention	

End point values	Liraglutide	Comparison between baseline and after intervention		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	14	14		
Units: cm3				
number (not applicable)	0.2	0.2		

Statistical analyses

Statistical analysis title	Paired Analyses on Primary Endpoint
Comparison groups	Liraglutide v Comparison between baseline and after intervention

Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[1] - Paired Analyses

Secondary: FLT uptake in the Pancreas

End point title	FLT uptake in the Pancreas

End point description:

End point type	Secondary

End point timeframe:

From Baseline to Four weeks after Intervention

End point values	Liraglutide	Comparison between baseline and after intervention		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	14	14		
Units: g/mL				
number (not applicable)	0.09	0.09		

Statistical analyses

Statistical analysis title	Paired Analyses on Secondary Endpoint
Comparison groups	Liraglutide v Comparison between baseline and after intervention
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided

Secondary: Plasma Amylase

End point title	Plasma Amylase

End point description:

End point type	Secondary

End point timeframe:

From Baseline to Six week after intervention

End point values	Liraglutide	Comparison between baseline and after intervention		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	14	14		
Units: U/L				
number (not applicable)	7	7		

Statistical analyses

Statistical analysis title	Paired Analyses on Secondary Endpoint
Comparison groups	Liraglutide v Comparison between baseline and after intervention
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided

Secondary: Plasma Lipase

End point title	Plasma Lipase

End point description:

End point type	Secondary

End point timeframe:

From Baseline to Six week after intervention

End point values	Liraglutide	Comparison between baseline and after intervention		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	14	14		
Units: U/L				
number (not applicable)	19	19		

Statistical analyses

Statistical analysis title	Paired Analyses on Secondary Endpoint
Comparison groups	Liraglutide v Comparison between baseline and after intervention
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline to Followup

Adverse event reporting additional description:

All participants reported adverse events. Most of these were gastrointestinal, observed in 79% of completers (nausea in 57%, diarrhea in 21%, abdominal pain in 14%, and vomiting in 14% of participants). Nearly half of the adverse events were mild and transient, and all completers followed the planned titration regimen and reached the maximum dose o

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Adverse Event

Reporting group description: -

Serious adverse events	Adverse Event		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 17 (17.65%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Obstipation	Additional description: One day of hospitalization due to flatulence and abdominal pain caused by obstipation		
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
postoperative	Additional description: elective knee surgery and subsequent admission due to postoperative pain in the knee		
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Adverse Event		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 17 (76.47%)		
Gastrointestinal disorders			
nausea			
subjects affected / exposed	13 / 17 (76.47%)		
occurrences (all)	13		

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