Clinical trial results:
Effect of liraglutide on vascular inflammation in type-2 diabetes: A randomized, placebo-controlled, double-blind, parallel clinical PET/CT trial

Summary

EudraCT number	2016-001523-31
Trial protocol	DK
Global end of trial date	16 August 2019

Results information

Result version number	v1 (current)
This version publication date	25 October 2020
First version publication date	25 October 2020

Trial information

Trial identification

Sponsor protocol code	U1111-1181-4107

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03449654
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Steno Diabetes Center Copenhagen
Sponsor organisation address	Niels Steensens vej 2, Gentofte, Denmark,
Public contact	Peter Rossing, Steno Diabetes Center Copenhagen, +45 30913383, peter.rossing@regionh.dk
Scientific contact	Peter Rossing, Steno Diabetes Center Copenhagen, +45 30913383, peter.rossing@regionh.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 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 August 2019
Global end of trial reached?	Yes
Global end of trial date	16 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial is to determine whether 6 months Liraglutide treatment is associated with improvement in atherosclerotic phenotype through anti-inflammatory effects compared to placebo.

Protection of trial subjects:

Regular blood suger measuring when starting liraglutide/placebo.

Background therapy:

Standard of care.

Evidence for comparator: -

Actual start date of recruitment	26 October 2016
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: 102
Worldwide total number of subjects	102
EEA total number of subjects	102

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)	44
From 65 to 84 years	57
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from the outpatient clinic at the Steno Diabetes Center Copenhagen in Denmark and through newspaper advertisements.

Pre-assignment

Screening details:

Patients were eligible if they met the inclusion criteria: type 2 diabetes (WHO criteria); age > 50 years; HbA1c ≥ 48 mmol/mol (6·5%); eGFR ≥ 30 mL/min/1·73 m2 (estimated by CKD-EPI formula); stable glucose- and cholesterol-lowering treatment for a minimum of 4 weeks prior to the baseline PET/CT. 147 were screened. 102 were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Dosage and administration as for liraglutide.

Arm title	Liraglutide

Arm description: -

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

Dosage and administration details:

Liraglutide will be introduced at a dose of 0.6 mg/day escalated to 1.2 mg/day after one week and after another week to 1.8 mg/day. Dose escalation can be postponed based on the subject's tolerance to the trial medication. Further, the liraglutide dose can be reduced at any time during the trial if required by the subject's tolerance to the product. If the dose of 1.8 mg/day is not tolerated by the patient, the patient will be allowed to continue in the study with a dose of 0.6 or 1.2 mg/day (maximal tolerated dose).
Injection can be given at any time during the day. It is however recommended that the time of injection is consistent from day to day.

Number of subjects in period 1	Placebo	Liraglutide
Started	51	51
Completed	49	50
Not completed	2	1
Adverse event, serious fatal	2	-
Adverse event, non-fatal	-	1

Baseline characteristics

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

Reporting group values	Placebo	Liraglutide	Total
Number of subjects	51	51	102
Age categorical			
age			
Units: Subjects			
Adults (18-64 years)	24	20	44
From 65-84 years	27	30	57
85 years and over	0	1	1
Age continuous			
Units: years			
arithmetic mean	65.9	66.9	
standard deviation	± 8.6	± 7.8	-
Gender categorical			
Units: Subjects			
Female	6	10	16
Male	45	41	86

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Liraglutide
Reporting group description: -	

Primary: Arterial vascular inflammation	
End point title	Arterial vascular inflammation
End point description: Change in vascular inflammation over 26 weeks	
End point type	Primary
End point timeframe: Arterial vascular inflammation assessed at baseline and after 26 weeks liraglutide / placebo treatment.	

End point values	Placebo	Liraglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: ratio				
arithmetic mean (confidence interval 95%)	-0.04 (-0.17 to 0.08)	-0.09 (-0.19 to 0.01)		

Statistical analyses

Statistical analysis title	un-paired t-test
Comparison groups	Placebo v Liraglutide
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	t-test, 2-sided
Confidence interval	
sides	2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: screening until end-of-treatment at week 26.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	placebo
Reporting group description: -	
Reporting group title	liraglutide
Reporting group description: -	

Serious adverse events	placebo	liraglutide	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 51 (7.84%)	4 / 51 (7.84%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	2 / 51 (3.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyp			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Coronary artery surgery			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
mesenteric adenitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
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: 5 %

Non-serious adverse events	placebo	liraglutide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 51 (68.63%)	48 / 51 (94.12%)	
Investigations			
Investigations			
subjects affected / exposed	0 / 51 (0.00%)	7 / 51 (13.73%)	
occurrences (all)	0	7	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Cardiac disorders			

Dizziness			
subjects affected / exposed	4 / 51 (7.84%)	3 / 51 (5.88%)	
occurrences (all)	4	3	
cardiac disorders			
subjects affected / exposed	7 / 51 (13.73%)	5 / 51 (9.80%)	
occurrences (all)	7	5	
Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	3 / 51 (5.88%)	2 / 51 (3.92%)	
occurrences (all)	3	2	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 51 (1.96%)	5 / 51 (9.80%)	
occurrences (all)	1	5	
General disorders and administration site conditions			
tiredness			
subjects affected / exposed	5 / 51 (9.80%)	5 / 51 (9.80%)	
occurrences (all)	5	5	
Ear and labyrinth disorders			
Ear and labyrinth disorders			
subjects affected / exposed	1 / 51 (1.96%)	4 / 51 (7.84%)	
occurrences (all)	1	4	
Eye disorders			
Eye disorders			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
gastrointestinal symptoms			
subjects affected / exposed	18 / 51 (35.29%)	41 / 51 (80.39%)	
occurrences (all)	18	41	
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	2 / 51 (3.92%)	4 / 51 (7.84%)	
occurrences (all)	2	4	
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			

subjects affected / exposed occurrences (all)	6 / 51 (11.76%) 6	1 / 51 (1.96%) 1	
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	9 / 51 (17.65%) 9	5 / 51 (9.80%) 5	

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