Clinical trial results:
Effect of liraglutide on body weight and microvascular function in non-diabetic overweight women with coronary microvascular dysfunction

Summary

EudraCT number	2015-002153-35
Trial protocol	DK
Global end of trial date	18 April 2017

Results information

Result version number	v1 (current)
This version publication date	13 May 2021
First version publication date	13 May 2021

Trial information

Trial identification

Sponsor protocol code	GAP

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bispebjerg Universitetshospital
Sponsor organisation address	Bispebjerg Bakke 23, København NV, Denmark, 2400
Public contact	Eva Prescott, Bispebjerg University Hospital, 0045 22572614, eva.irene.bossano.prescott@regionh.dk
Scientific contact	Eva Prescott, Bispebjerg University Hospital, 0045 22572614, eva.irene.bossano.prescott@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	28 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 April 2017
Global end of trial reached?	Yes
Global end of trial date	18 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of treatment with Liraglutide on the coronary microvasculature and angina symptoms in overweight patients with microvascular dysfunction and angina pectoris but no coronary artery stenosis

Protection of trial subjects:

Side-effects were evaluated regularly at up-titration visits by interview and blood samples, and study participants had access to a medical doctor at all times in case of any discomfort or doubts.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2015
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: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	12
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We included 33 women between November 19th 2015 and December 13th 2016 and 29 completed the study. We recruited women with angina like symptoms and no obstructive CAD defined as <50% coronary artery stenosis assessed by invasive CAG in eastern Denmark.

Pre-assignment

Screening details:

Participants from the iPOWER (ImProve diagnOsis and treatment of Women with angina pEctoris and micRovessel disease) study cohort. Of 938, 52 fullfilled inclusion criteria. 19 were excluded after baseline/screening visit and 33 were included.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	control

Arm description:

No treatment

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	intervention

Arm description:

Liraglutide 3 mg daily for 12 weeks

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

Dosage and administration details:

3 mg administered subcutaineously once daily

Number of subjects in period 1	control	intervention
Started	33	30
Completed	30	29
Not completed	3	1
Adverse event, non-fatal	-	1
unrelated to the study	3	-

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	33	33	
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)	12	12	
From 65-84 years	21	21	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	33	33	
Male	0	0	

End points

End points reporting groups	
Reporting group title	control
Reporting group description: No treatment	
Reporting group title	intervention
Reporting group description: Liraglutide 3 mg daily for 12 weeks	

Primary: Change in CFVR	
End point title	Change in CFVR
End point description:	
End point type	Primary
End point timeframe: Change after 5 weeks in the control period and 12 weeks in the experimental period	

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: ratio				
arithmetic mean (confidence interval 95%)	0.11 (-0.02 to 0.25)	0.07 (-0.07 to 0.21)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	intervention v control
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Primary: Seattle angina questionnaire 1	
End point title	Seattle angina questionnaire 1
End point description: Physical limitation score	

End point type	Primary

End point timeframe:

Control period of approximately 5 weeks and experimental period of approximately 12 weeks

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: score				
arithmetic mean (confidence interval 95%)	-2.26 (-6.34 to 1.83)	7.78 (3.41 to 12.12)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	control v intervention
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Primary: Seattle Angina Questionnaire 2

End point title	Seattle Angina Questionnaire 2

End point description:

Angina stability score

End point type	Primary

End point timeframe:

Change in the control period after approximately 5 weeks and after the experimental period of approximately 12 weeks

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: score				
arithmetic mean (confidence interval 95%)	-9.29 (-20.61 to 2.03)	26.60 (14.85 to 38.35)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	control v intervention
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Primary: Seattle Angina Questionnaire 3

End point title	Seattle Angina Questionnaire 3
End point description: Angina frequency score	
End point type	Primary
End point timeframe: control period of 5 weeks and experimental period of 12 weeks	

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: score				
arithmetic mean (confidence interval 95%)	-1.38 (-6.10 to 3.33)	8.48 (3.52 to 13.44)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	control v intervention
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Primary: Seattle Angina Questionnaire 4

End point title	Seattle Angina Questionnaire 4
End point description: Treatment satisfaction score	

End point type	Primary

End point timeframe:

control period of 5 weeks and experimental period of 12 weeks

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: score				
arithmetic mean (confidence interval 95%)	2.68 (-5.12 to 10.47)	9.18 (1.08 to 17.28)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	control v intervention
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Primary: Seattle Angina Questionnaire 5

End point title	Seattle Angina Questionnaire 5

End point description:

Disease perception score

End point type	Primary

End point timeframe:

control period of 5 weeks and experimental period of 12 weeks

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: score				
arithmetic mean (confidence interval 95%)	8.11 (3.16 to 13.06)	1.82 (-3.33 to 6.97)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	control v intervention
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Secondary: Changes in endothelial function assessed by flow mediated dilation (FMD) of the brachial artery by ultrasound

End point title	Changes in endothelial function assessed by flow mediated dilation (FMD) of the brachial artery by ultrasound

End point description:

End point type	Secondary

End point timeframe:

Intervention period compared with control period

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: ratio				
arithmetic mean (confidence interval 95%)	0.60 (-2.09 to 3.28)	0.48 (-2.39 to 3.35)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	intervention v control
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Median difference (final values)

Secondary: Changes in cardiac function assessed by speckle tracking echocardiography

End point title	Changes in cardiac function assessed by speckle tracking echocardiography

End point description:

End point type	Secondary

End point timeframe:

control period of 5 weeks and experimental period of 12 weeks

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: percent				
arithmetic mean (confidence interval 95%)	-0.45 (-1.18 to 0.28)	0.14 (-0.61 to 0.90)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	control v intervention
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Secondary: Change in body weight

End point title	Change in body weight

End point description:

End point type	Secondary

End point timeframe:

control period of 5 weeks and experimental period of 12 weeks

End point values	control	intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: kilogram(s)				
arithmetic mean (confidence interval 95%)	0.55 (-0.23 to 1.32)	-6.03 (-6.84 to -5.22)		

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	control v intervention
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

adverse event were reported during the inverventional period from day one on liraglutide until one week after last dosage.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Adverse events

Reporting group description: -

Serious adverse events	Adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)		
General disorders and administration site conditions			
Headache			
subjects affected / exposed	11 / 30 (36.67%)		
occurrences (all)	11		
Discomfort			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Injection related reaction			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Fatigue			

subjects affected / exposed occurrences (all)	18 / 30 (60.00%) 18		
Gastrointestinal disorders Appetite disorder subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Gastrointestinal pain subjects affected / exposed occurrences (all)	 29 / 30 (96.67%) 29 6 / 30 (20.00%) 6 27 / 30 (90.00%) 27		

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/30773266