Clinical trial results:
Liraglutide in Polycystic Ovary Syndrome

A randomised, double-blind, placebo-controlled study of the effect of Liraglutide in Polycystic ovary syndrome on risk markers of vascular Thrombosis

Summary

EudraCT number	2013-003862-15
Trial protocol	DK
Global end of trial date	21 December 2015

Results information

Result version number	v1 (current)
This version publication date	28 June 2021
First version publication date	28 June 2021
Summary attachment (see zip file)	Manuscript on primary end point - LIPT (89.full.pdf)

Trial information

Trial identification

Sponsor protocol code	2013-601

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02073929
WHO universal trial number (UTN)	U1111-1134-6841

Notes:

Sponsors

Sponsor organisation name	Herlev Hospital
Sponsor organisation address	Herlev ringvej 75, Copenhagen, Denmark, DK-2730
Public contact	Dept. of Medicine O, Jens Faber, 0045 38689016, jens.faber@regionh.dk
Scientific contact	Dept. of Medicine O, Jens Faber, 0045 38689016, jens.faber@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	16 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2015
Global end of trial reached?	Yes
Global end of trial date	21 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of liraglutide 1.8 mg once daily compared to placebo on changes in thrombin generation (TGT), measured as plasma levels of endogenous thrombin potential (ETP).

Protection of trial subjects:

Patients were treated according to the Helsinki Declaration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2014
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: 72
Worldwide total number of subjects	72
EEA total number of subjects	72

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)	72
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

As described in Nylander et al., Endocr Connect. 2017 Feb;6(2):89-99. doi: 10.1530/EC-16-0113.

Pre-assignment

Screening details:

As described in CONSORT-flow in Nylander et al., Endocr Connect. 2017 Feb;6(2):89-99. doi: 10.1530/EC-16-0113.

Period 1

Period 1 title	basaeline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

treatment with Liraglutide 1,8 mg/day

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:

daily s.c. injection of Liraglutide 1.8 mg

Arm title	Placebo

Arm description:

Injection with saline

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	En pen containing saline instead of active drug
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Daily s.c. injection with pen containing saline

Number of subjects in period 1	Active	Placebo
Started	48	24
Completed	48	24

Period 2	
Period 2 title	overall trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms	
Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:
treatment with liraglutide 1.8 mg/day for 6 month

Arm type	Active comparator
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
daily s.c. injection of Liraglutide 1.8 mg

Arm title	placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	En pen containing saline instead of active drug
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
Daily s.c. injection with pen containing saline

Number of subjects in period 2	Active	placebo
Started	48	24
Completed	48	24

Baseline characteristics

End points

End points reporting groups

Reporting group title	Active
Reporting group description: treatment with Liraglutide 1,8 mg/day	
Reporting group title	Placebo
Reporting group description: Injection with saline	
Reporting group title	Active
Reporting group description: treatment with liraglutide 1.8 mg/day for 6 month	
Reporting group title	placebo
Reporting group description: -	

Primary: Endogenous thrombin potential (ETP)

End point title	Endogenous thrombin potential (ETP)
End point description: Change in ETP after 6 month of Liraglutide/placebo treatment	
End point type	Primary
End point timeframe: Measured before and at the end of six months of treatment with liraglutide 1.8 mg/day or placebo	

End point values	Active	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	24		
Units: nmol/L x min				
median (confidence interval 95%)	-57.6 (-132.3 to 17.2)	-8.2 (-98.7 to 82.3)		

Statistical analyses

Statistical analysis title	Analysis of EPT
Statistical analysis description: A sample size calculation based on an estimated standard deviation of 130 units obtained from in-house data, declared 63 subjects, randomized 2:1, needed for 80% power to find a difference in effect size of 100nmol/min of ETP. This effect size was supported by a previous study finding a similar reduction in ETP with a 5% reduction in BMI (22). To allow for drop-outs, 72 women were randomized.	
Comparison groups	Active v placebo

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 5
Method	t-test, 2-sided
Parameter estimate	mixed model with maximum likelihood

Notes:

[1] - In the initial protocol, we planned on calculating the between-group difference using an unpaired t-test on the intention-to-treat population. As a mixed model with maximum likelihood is a more optimal way of analyzing repeated measurements, we have chosen this statistic approach, and between-group differences in treatment effect are assessed using a repeated measurements mixed model (with maximum likelihood) with study drug as between-subjects effect and visit (time) as within

Adverse events

Adverse events information	
Timeframe for reporting adverse events: March 2014- December 2015.	
Assessment type	Systematic
Dictionary used	
Dictionary name	GCP
Dictionary version	1
Reporting groups	
Reporting group title	Active group
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Serious adverse events	Active group	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 47 (0.00%)	0 / 23 (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: 2 %

Non-serious adverse events	Active group	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 47 (63.83%)	11 / 23 (47.83%)	
General disorders and administration site conditions			
Nausea	Additional description: Nausea Vomiting Diarrhea Constipation Gallstone pain Cholecysectomy Dizziness upper resp tract infektion urinary tract infektion rash		
subjects affected / exposed	30 / 47 (63.83%)	11 / 23 (47.83%)	
occurrences (all)	30	11	

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