# Do women with polycystic ovary syndrome have increased cardiovascular risk compared to normal controls and could this risk be reduced by liraglutide?

<b>Submission date</b> 08/05/2012	<b>Recruitment status</b> No longer recruiting	<ul><li>Prospectively registered</li></ul>
		☐ Protocol
Registration date 22/05/2012	Overall study status Completed	Statistical analysis plan
		[X] Results
<b>Last Edited</b> 02/10/2015	Condition category Nutritional, Metabolic, Endocrine	[] Individual participant data

#### Plain English summary of protocol

Background and study aims:

Polycystic ovary syndrome (PCOS) is a common condition in women of reproductive age. PCOS is associated with cardiovascular risk through increased insulin resistance. This in turn may lead to increased risk of non-alcoholic fatty liver disease (NAFLD). Both conditions are made worse by obesity. Liraglutide has been shown to reduce weight, but it is unknown if liraglutide improves cardiovascular risk factors in women with PCOS with or without NALFD.

#### Who can participate?

Two groups of women: 20 with PCOS; 20 age and weight matched normal control subjects.

#### What does the study involve?

Participants are treated with liraglutide 1.8mg once a day for 6 months followed by metformin 500mg three times a day for 3 months. Study participants will be seen every 3 months. At each visit blood will be taken to measure for insulin resistance, and for clotting and inflammations markers. Artery wall thickness will be measured at baseline and after 6 months treatment with liraglutide.

What are the possible benefits and risks of participating?

There will be no immediate direct benefit to those taking part but the study will improve our understanding of PCOS and the treatment of people with PCOS and fatty liver disease. Most common side effects with metformin and liraglutide use are nausea and diarrhoea. These side effects usually disappear after a few days. There might be some discomfort in blood testing and endothelial function measurement.

Where is the study run from? Diabetes Research Centre at Hull Royal Infirmary (UK).

When is the study starting and how long is it expected to run for? May 2010 to December 2012.

Who is funding the study? Diabetes Research fund, University of Hull (UK).

Who is the main contact? Professor Stephen L Atkin Stephen.atkin@hyms.ac.uk

## Contact information

## Type(s)

Scientific

#### Contact name

Prof Stephen Atkin

#### Contact details

Head of Diabetes, Endocrinology and Metabolism University of Hull Brocklehurst building Hull Royal Infirmary Hull United Kingdom HU3 2RW

Stephen.Atkin@hyms.ac.uk

## Additional identifiers

**EudraCT/CTIS** number

**IRAS** number

ClinicalTrials.gov number

Secondary identifying numbers

Protocol version 7

# Study information

#### Scientific Title

Are early and late cardiovascular risk markers in women with polycystic ovary syndrome increased with concomitant non-alcoholic steatohepatitis and can this be modified with liraglutide?

## Study objectives

Intervention with liraglutide significantly improves insulin resistance, carotid intima-media wall thickness (cIMT), platelet and endothelial function in women with PCOS and Non-alcoholic fatty liver disease (NAFLD).

#### Ethics approval required

Old ethics approval format

## Ethics approval(s)

Leeds East Research Ethics Committee, 08/02/2010

#### Study design

Open parallel single-centre trial

#### Primary study design

Interventional

## Secondary study design

Randomised controlled trial

#### Study setting(s)

Hospital

#### Study type(s)

**Treatment** 

## Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

## Health condition(s) or problem(s) studied

Polycystic Ovary Syndrome

#### **Interventions**

Women with PCOS were diagnosed according to the Rotterdam criteria. Other endocrine disorders with similar presentation were excluded. Normal control women underwent similar tests to rule out any unknown medical problem.

Participants (PCOS and nomal controls) are treated with liraglutide 1.8mg once a day for 6 months followed by metformin 500mg three times a day for 3 months. Study participants will be seen every 3 months during the study.

## Intervention Type

Drug

#### Phase

Not Applicable

## Drug/device/biological/vaccine name(s)

Liraglutide, metformin

#### Primary outcome measure

Improvement in cIMT and platelet function measured at baseline and after 6 months treatment with Liraglutide

#### Secondary outcome measures

- 1. Improvement in endothelial function will be measured using EndoPat 2000 at baseline, 3, 6 and 9 months of treatment
- 2. Liver fibrosis markers were measured at baseline, 3, 6 and 9months of treatment
- 3. Depression [Centre for Epidemiologic Studies Depression Scale (CES-D)] at baseline and after 6 months of treatment with liraglutide
- 4. Quality of life will be measured using WHO QoL questionaire at baseline and after 6 months of treatment with liraglutide

## Overall study start date

24/05/2010

#### Completion date

31/12/2012

# **Eligibility**

#### Key inclusion criteria

For PCOS:

Polycystic ovary syndrome (defined by the Rotterdam criteria) as 2 out of 3 of:

- 1. Oligo / anovulation
- 2. Clinical or biochemical evidence of hirsuitism, and/or
- 3. Polycystic ovaries on ultrasound and the exclusion of other disorders
- 4. Age 18-45 years

#### For normal controls:

- 1. Female, aged 18 45
- 2. Body madd index (BMI) 30 45
- 3. No current medical problems

#### Participant type(s)

**Patient** 

#### Age group

Adult

#### Lower age limit

18 Years

#### Upper age limit

45 Years

#### Sex

Female

## Target number of participants

#### 40 participants

#### Key exclusion criteria

- 1. Ketoacidosis
- 2. Severe gastrointestinal disease
- 3. Hypothyroidism
- 4. Subjects taking regular medications associated with high risk of hepatotoxicity like isoniazid and methotrexate
- 5. Not using a reliable method of contraception
- 6. Patients not allowing disclosure to their GP's
- 7. History of pancreatitis
- 8. Heart Failure
- 9. Chronic renal failure (creatinine clearance less than 60 ml/min or plasma creatinine >150 umol /L)
- 10. Pregnancy or breastfeeding women
- 11. Liver function tests >300% reference range normal (eg ALT>90 u/mL)
- 12. Type 2 diabetes mellitus
- 13. Acute conditions with the potential to alter renal function such as: dehydration / severe infection / shock / intravascular administration of iodinated contrast

#### Date of first enrolment

24/05/2010

#### Date of final enrolment

31/12/2012

## Locations

#### Countries of recruitment

England

United Kingdom

# Study participating centre University of Hull

Hull United Kingdom HU3 2RW

## Sponsor information

#### Organisation

Hull and East Yorkshire Hospitals NHS Trust (UK)

#### Sponsor details

c/o James Illingworth
Research and Development
Daisy Building
Castle Hill Hospital
Castle Road
Cottingham
Hull
England
United Kingdom
HU16 5JQ

\_

James.Illingworth@hey.nhs.uk

#### Sponsor type

Hospital/treatment centre

#### Website

http://www.hey.nhs.uk/

#### **ROR**

https://ror.org/01b11x021

# Funder(s)

## Funder type

University/education

#### **Funder Name**

University of Hull - Diabetes Research Fund (UK)

## **Results and Publications**

## Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type Details Date created Date added Peer reviewed? Patient-facing?

Results article results 02/04/2015 Yes

No