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A study to investigate the effect of pioglitazone on whole body and myocardial glucose uptake and myocardial blood flow/coronary vasodilator reserve in patients with familial combined hyperlipidaemia

Submission date	Recruitment status
09/09/2005	No longer recruiting
Registration date	**Overall study status**
27/10/2005	Completed
Last Edited	**Condition category**
07/12/2007	Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Paolo Camici

Contact details
MRC Clinical Sciences Centre
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0NN

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
AD-4833 / EC414

Study information

Scientific Title

Study objectives
The disturbance of fat metabolism (utilisation) known as combined hyperlipidaemia (CHL) is very common and affects up to 2% of the population. Patients who suffer from this disorder have a 20% higher risk to develop obstructive disease of the blood vessels of the heart and heart attack.

The patients with CHL have abnormalities of blood lipids (fat) similar to those observed in patients who suffer from another condition known as the 'metabolic syndrome' who are also at higher risk of developing heart disease, stroke and diabetes. One of the features of this metabolic syndrome is a reduced response to the hormone insulin. This hormone helps the tissues of the body (in particular the muscles and the heart) to use sugar. Sugar is very important for the heart since it contributes to generate the energy which is used to sustain its function.

In patients with the metabolic syndrome insulin is less effective and the heart tissue has difficulties in using sugar and develops a condition known as 'insulin resistance'. Previous studies have shown that this condition of insulin resitance can contribute to the higher incidence of heart disease in patients with the metabolic syndrome.

Pioglitazone is a drug licenced in the UK which acts by sensitising the liver and peripheral tissues (including the heart) to the effect of insulin, which results in improved insulin-mediated sugar disposal. Previous studies have demonstrated that pioglitazone lowers sugar and insulin levels in the blood and improves lipid (fat) metabolism (utilisation) in patients with diabetes. We expect similar beneficial effects in patients with familial CHL treated with pioglitazone.

We therefore hypothesise that patients with CHL will have insulin resistance at the heart muscle level as well as an abnormal function of the vessels supplying blood to the heart and that treatment with pioglitazone will improve these

To prove our hypothesis we will use a special scan called Positron Emission Tomography (PET) which permits to measure the utilisation of sugar by the heart in a totally non-invasive fashion. PET is also capable of providing information on the function of the vessels supplying blood to the heart. Patients with familial CHL will be studied by means of PET before and after 4 months of treatment with pioglitazone. In addition, we will assess the effect of the drug on blood lipids (fat).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Hammersmith & Queen Charlotte's and Chelsea Hospitals Research Ethics Committee (ref: 2002/6373).

Study design

Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Familial Combined Hyperlipidaemia

Interventions
Treatment with pioglitazone versus placebo

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure
1. Whole body glucose uptake
2. Myocardial glucose uptake
3. Basal myocardial blood flow
4. Coronary vasodilator reserve

Secondary outcome measures
Parameters of lipid and carbohydrate metabolism.

Overall study start date
01/05/2004

Completion date
19/12/2006

Eligibility

Key inclusion criteria

Patients must be/have:
1. Male or female aged between 30 and 70 years
2. Familial Combined Hyperlipidaemia (CHL) that fits the diagnostic criteria
3. Inadequately controlled with conventional lipid lowering medication, with at least one of the following:
3.1. Total cholesterol more than 5.0 mmol/l
3.2. Triglyceride more than 1.7 mmol/l
3.3. High Density Lipoprotein (HDL) cholesterol less than 1.0 mmol/l
3.4. Total cholesterol: HDL-cholesterol ratio more than 5.0
4. On stable lipid lowering medication (dose and drug) for the previous two months
5. A Body Mass Index (BMI) of less than or equal to 35 kg/m^2
6. Willing and able to comply with the conditions and requirements of the study
7. Signed and dated an informed consent form and be able to comply with the study procedures

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
26

Key exclusion criteria
Patients must not be/have:
1. Had a myocardial infarction, stroke or transient ischaemic attack in the previous six months
2. Had malignant disease in the previous five years (except basal cell carcinoma)
3. Undergoing haemodialysis
4. Any of the following conditions:
4.1. Type one or type two diabetes mellitus
4.2. Chronic uncontrolled asthma
4.3. An inability to tolerate PET scanning
4.4. New York Heart Association (NYHA) class II, III or IV congestive heart failure
4.5. Alcohol or drug abuse
4.6. Significant renal impairment (defined as creatinine more than 135 µmol/l)
4.7. Abnormal liver tests (defined as alanine aminotransferase [ALT] more than 2.5 times the upper limit of the reference range)
4.8. Known Human Immunodeficiency Virus (HIV) infection or viral hepatitis
5. Had treatment with corticosteroids in the previous four weeks (use of topical or inhaled corticosteroids is allowed)
6. Taken another investigational study drug or product within the previous three months
7. Donated and/or received any blood or blood products within the previous three months
8. Female patients who are any of the following:
8.1. Pregnant, planning pregnancy during the study or breast feeding
8.2. Of child-bearing potential and not planning to use a reliable method of contraception

throughout the study (e.g. intrauterine device [IUD] or oral contraception)
9. Any other condition or circumstance that in the opinion of the investigator may compromise the patients ability to comply with the study protocol

Date of first enrolment
01/05/2004

Date of final enrolment
19/12/2006

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
MRC Clinical Sciences Centre
London
United Kingdom
W12 0NN

Sponsor information

Organisation
Takeda Europe R and D Centre (UK)

Sponsor details
Savannah House
11-12 Charles II Street
London
United Kingdom
SW1Y 4QU

Sponsor type
Industry

Website
http://www.tgrd.com

ROR
https://ror.org/05c0v3585

Funder(s)

Funder type
Industry

Funder Name
Takeda Europe R and D Centre (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	20/11/2007		Yes	No