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A 6 Month Randomised, Double-Blind, Placebo-Controlled, Magnetic Resonance Spectroscopy (MRS) and Imaging Study to Evaluate the Effect of Rosiglitazone on the Intrahepatic and Intramyocellular Lipid content in Subjects with Type 2 Diabetes Mellitus and Non-Alcoholic Fatty Liver Disease

Submission date
18/08/2005

Recruitment status
No longer recruiting

Registration date
01/09/2005

Overall study status
Completed

Last Edited
18/01/2011

Condition category
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

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title

Acronym
RAFL

Study objectives
1. Changes in fat deposition in the liver are reflected by metabolite abnormalities that can be detected non-invasively by in vivo hepatic 1H MRS
2. Multinuclear in vivo MRS may determine differences in the type of fat deposited in the liver with differing aetiology and allow the progression of steatosis to fibrosis to be followed non-invasively
3. Non-Alcoholic Steatohepatitis (NASH) in Type 2 Diabetic Patients may improve with treatment with Rosiglitazone
4. Dyslipidaemia in non-alcoholic steatohepatitis may be reversed by Rosiglitazone

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised, Double-Blind, Placebo-Controlled

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
Type 2 Diabetic Patients with Non-Alcoholic Fatty Liver Disease

Interventions
Rosiglitazone (4-8 mg/day) vs placebo

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure
The primary aim is to evaluate, using magnetic resonance imaging and spectroscopy (MRI and MRS), the effect of 26 weeks oral treatment with rosiglitazone in comparison to placebo on the change from baseline of intra-abdominal and sub-cutaneous adipose tissue volume, in patients with type 2 diabetes mellitus and non-alcoholic fatty liver disease or steatohepatitis and liver fat content as assessed by MRS.

Secondary outcome measures
Secondary objectives are to evaluate the effects of rosiglitazone on the following: glycaemic control, lipids and lipoproteins; insulin sensitivity and secretion using homeostatic model assessment (HOMA); circulating lipoprotein lipase, hepatic lipase, cholesterol ester transferase (CETP) and lecithin cholesterol acyl transferase activity (LCAT) activities; the composition of circulating high density lipoprotein (HDL) and its apolipoprotein A-I (apoA-1) isoforms; biomarkers of systemic inflammation and plaque stability; very low density apolipoprotein B100 (VLDL apoB100) and HDL apoA-I kinetics.

Overall study start date
12/08/2003

Completion date
31/08/2004

Eligibility

Key inclusion criteria
1. Patients with type 2 diabetes
2. Male or female patient who is 30 to 75 years of age, inclusive, at screening
3. Patients who have initiated statin and fibrate therapy at least 6 months prior to screening, and have been receiving a stable dose for at least 3 months prior to screening. Patients not receiving statin or fibrate therapy may enter the study providing that this method of treatment is not required as active treatment for their medical condition at the time of screening. If any of these patients develop the need for statin or fibrate therapy during the course of the study, therapy will be started without the need to withdraw the patient from the study.

4. Female patients must be post-menopausal (i.e. >6 months without menstrual period) or using contraceptive measures
5. Patients with an HbAlc value <10% at screening visit
6. Patients have an elevated alanine aminotransferase activity (ALT) or aspartate aminotransferase activity (AST) or ultrasound appearances of fatty liver

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
20

Key exclusion criteria
1. Patients who have taken >2 concomitant oral anti-hyperglycaemic agents (i.e. oral combination) within the 3 months prior to the screening visit (visit 1)
2. Patients who have required the chronic use of insulin for glycaemic control
3. Use of any investigational drug or previous exposure to a thiazolidinedione (TZD) or other PPAR-gamma; agonist (e.g. rosiglitazone, troglitazone, pioglitazone, GI262570) within 30 days or 5 half-lives (whichever is longer) preceding the first dose of medication at the start of the study
4. Systolic blood pressure >170 mmHg or diastolic blood pressure >100 mmHg
5. Patients with unstable or severe angina or congestive heart failure. Presence of clinically significant hepatic disease (i.e. patients with ALT, AST, total bilirubin, or alkaline phosphatase >2.5 times the upper limit of the normal laboratory range).
6. Any pre-existing condition or clinically significant abnormality identified on the Screening (visit 1) physical examination, electrocardiogram, ultrasound examination or laboratory tests which, in the judgement of the investigator, would preclude safe completion of the study
7. Clinically significant anaemia defined by haemoglobin concentration <11 g/dl for males or <10 g/dl for females
8. Patients with creatinine >150 umol/l
9. Women who are lactating, pregnant or planning to become pregnant during the course of the study
10. Alcohol or drug abuse within the last 6 months
11. Patients with chronic liver disease such as viral or autoimmune hepatitis and haemochromatosis
12. Patients with a history of claustrophobia (inability to tolerate MR procedure)
13. Pacemakers, cerebral aneurysm clips, claustrophobia or any implantable ferro-magnetic device incompatible with magnetic resonance imaging

Date of first enrolment
12/08/2003

Date of final enrolment
31/08/2004

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Metabolic Medicine Department
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Sponsor information

Organisation
Imperial College London (UK)

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Sponsor type
University/education

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ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research council

Funder Name
MRC Career Establishment Grant DMEHEPRO2929 (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	27/07/2009		Yes	No