ISRCTN53177482 https://doi.org/10.1186/ISRCTN53177482

Pioglitazone Influence of triglyceRide Accumulation in the Myocardium In Diabetes

Submission date	Recruitment status	[_] Prospectively registered
20/12/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
20/12/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
31/01/2012	Nutritional, Metabolic, Endocrine	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr L J Rijzewijk

Contact details
Diabetes Centre/Department of Endocrinology
VU medisch centrum
De Boelelaan 1117
Amsterdam
Netherlands
1081 HV

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NTR180

Study information

Scientific Title

Acronym
The PIRAMID study

Study objectives
Patients with type two Diabetes Mellitus (DM2) have a considerably higher risk to develop cardiac disease with a poorer outcome. Ectopic Triglyceride (TG) accumulation underlies diabetic cardiomyopathy. These cardiac abnormalities can be reversed by lowering myocardial TG using a Peroxisome Proliferator-Activated Receptor-g (PPARg) agonist. Metformin, the present gold standard treatment for type two diabetes, might also have cardioprotective properties due to its recently proposed mechanism of action.

Hypothesis:
Lipotoxicity-related cardiac abnormalities can be reversed by PPAR g agonist therapy in type two diabetes patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Multicentre, randomised, double blinded, active controlled, parallel group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

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
Diabetes Mellitus type two (DM2), heart disease

Interventions
80 subjects on monotherapy sulfanylurea for at least ten weeks will be enrolled. Following this, participants will be randomised to metformin or pioglitazone for 24 weeks. Ten healthy subject will only undergo baseline measurements

Please note that the anticipated end date of this trial has been extended to the 15th January 2007.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure
Changes in cardiac function and metabolism following treatment with PPARg agonist versus current state of the art therapy, metformin.

Secondary outcome measures
1. Glucose and Free Fatty Acid (FFA) uptake by adipose tissue and skeletal muscle
2. Cardiac High-Energy-Phosphate (HEP) metabolism
3. Haemodynamic and vascular parameters body composition (Body Mass Index [BMI], waist, adipose tissue distribution, including liver fat content, body fat percentage and fluid retention)
4. Plasma parameters of glycemic control and lipoprotein metabolism
5. Circulating levels of markers of inflammation, coagulation activation, fibrinolysis and endothelial functions
6. Whole-body insulin sensitivity (by clamp)

Overall study start date
01/09/2004

Completion date
01/09/2006

Eligibility

Key inclusion criteria
Type two diabetes patients:
1. Type two diabetes diagnosed male patients aged 45 to 65 years (diagnosed according to World Health Organisation [WHO] criteria)
2. Treated by monotherapy of sulfanylurea (i.e. unchanged during more than 30 days prior to inclusion)
3. At least three months stable HbA1c (less than 8.5%) under this therapy
4. Sitting blood pressure less than 150/85 mmHg with or without anti-hypertensive drugs
5. Body Mass Index (BMI) less than 32 kg/m^2

Healthy volunteers:
1. Healthy male subjects, 45 to 65 years
2. Normal sitting blood pressure less than 150/85 mmHg
3. BMI less than 32 kg/m^2
4. Normal glucose tolerance as assessed by 75 g oral glucose tolerance test

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Male

Target number of participants
90

Key exclusion criteria
Type two diabetes patients:
1. Coronary Artery Disease (CAD)
2. Active malignant disease
3. Impaired renal function (serum creatinine more than 176 mmol/l)
4. Weight greater than or equal to 45 kg (because of 11C-palmitate tracer)
5. Anti-coagulant therapy
6. Severe obstructive lung disease
7. Hereditary lipoprotein disease
8. Impaired hepatic function (defined as Alanine aminotransferase [ALT] more than three Upper Limit of Normal [ULN]) or a history of liver disease
9. Inability to understand study information
10. Inability/unwillingness to sign informed consent
11. Substance abuse
12. Familial polyposis coli
13. Less than three months after participation in other clinical trials or other research projects, whereby radiation is used
14. Haemoglobin less than 8 mmol/l
15. Metal implants and claustrophobia
16. Incompatible with Cardiovascular Magnetic Resonance (CMR)
17. Congestive heart failure (New York Heart Association [NYHA] functional score more than one)
18. Atrial fibrillation or history of sustained ventricular tachycardia
19. Stroke within six months prior to enrolment
20. Microvascular complications including:
a. diabetic nephropathy
b. proliferative retinopathy
c. symptomatic macrovascular complications, and/or
d. (autonomic) neuropathy, except for background diabetic retinopathy, leg ulcers, gangrene, hypersensibility to study medication, current use of Thiazolidinediones (TZD)/fibrates

Healthy volunteers:
1. History or current cardiovascular disease
2. Dyslipidemia, requiring pharmacological treatment according to the Dutch Cholesterol Consensus 1998

Date of first enrolment
01/09/2004

Date of final enrolment
01/09/2006

Locations

Countries of recruitment
Netherlands

Study participating centre
Diabetes Centre/Department of Endocrinology
Amsterdam
Netherlands
1081 HV

Sponsor information

Organisation
VU University Medical Centre (Netherlands)

Sponsor details
Van der Boechorststraat 7
Amsterdam
Netherlands
1081 BT

Sponsor type
University/education

Website
http://www.vumc.nl/english/

ROR
https://ror.org/00q6h8f30

Funder(s)

Funder type
Industry

Funder Name
Eli Lilly Nederland B.V. (Netherlands)

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	21/04/2009		Yes	No
Results article	results	01/07/2010		Yes	No
Results article	results	19/07/2011		Yes	No