

# Pioglitazone Influence of triglyceRide Accumulation in the Myocardium In Diabetes

**Submission date**

20/12/2005

**Recruitment status**

No longer recruiting

☐ Prospectively registered

☐ Protocol

**Registration date**

20/12/2005

**Overall study status**

Completed

☐ Statistical analysis plan

☒ Results

**Last Edited**

31/01/2012

**Condition category**

Nutritional, Metabolic, Endocrine

☐ Individual participant data

**Plain English summary of protocol**

Not provided at time of registration

## Contact information

**Type(s)**

Scientific

**Contact name**

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**Contact details**

Diabetes Centre/Department of Endocrinology

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De Boelelaan 1117

Amsterdam

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1081 HV

## Additional identifiers

**Protocol serial number**

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- $\alpha$  (PPAR $\alpha$ ) 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  $\alpha$  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

**Primary study design**

Interventional

**Study design**

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

**Study type(s)**

Treatment

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

Diabetes Mellitus type two (DM2), heart disease

**Interventions**

80 subjects on monotherapy sulfonylurea 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(s)**

Changes in cardiac function and metabolism following treatment with PPAR $\alpha$  agonist versus current state of the art therapy, metformin.

**Key secondary outcome(s)**

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)

**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<sup>2</sup>

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<sup>2</sup>
4. Normal glucose tolerance as assessed by 75 g oral glucose tolerance test

**Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

Male

**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, hypersensitivity 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)

**ROR**

<https://ror.org/00q6h8f30>

**Funder(s)****Funder type**

Industry

**Funder Name**

Eli Lilly Nederland B.V. (Netherlands)

**Results and Publications****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? |
|---------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a> | results | 21/04/2009   |            | Yes            | No              |
| <a href="#">Results article</a> | results | 01/07/2010   |            | Yes            | No              |
| <a href="#">Results article</a> | results | 19/07/2011   |            | Yes            | No              |