

# A comparison of the effects of rosiglitazone on endothelial function and arterial stiffness in insulin resistant individuals and normal controls

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|----------------------------------------|-------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| <b>Submission date</b><br>12/09/2003   | <b>Recruitment status</b><br>Stopped            | <input type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol                       |
| <b>Registration date</b><br>12/09/2003 | <b>Overall study status</b><br>Stopped          | <input type="checkbox"/> Statistical analysis plan<br><input type="checkbox"/> Results                       |
| <b>Last Edited</b><br>27/09/2011       | <b>Condition category</b><br>Circulatory System | <input type="checkbox"/> Individual participant data<br><input type="checkbox"/> Record updated in last year |

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Protocol serial number

N0544093589

## Study information

## Scientific Title

### Study objectives

Rosiglitazone: endothelial function and arterial stiffness.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Not provided at time of registration

### Study design

Randomised controlled trial

### Primary study design

Interventional

### Study type(s)

Not Specified

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

Cardiovascular: Endothelial function and arterial stiffness

### Interventions

Rosiglitazone has been noted to have effects on the vasculature. We hypothesise that it may improve endothelial function and reduce arterial stiffness. We believe that the effects may be greater in people who are overweight as they tend to have insulin resistance and the actions of rosiglitazone may occur via its insulin-sensitizing effects. The effects may also be partially mediated via nitric oxide dependent mechanisms. We propose to study 12 obese and 12 non-obese subjects. They will be required to attend for three visits, the first of which will last for 30 min and the second and third for around 3 h each. The first visit will be a screening visit during which informed consent will be obtained and inclusion and exclusion criteria checked. Physical examination and medical history will be performed to ensure that it is safe for inclusion in the study. On the second and third visits, measurements of blood pressure, bio-impedance, forearm blood flow and arterial stiffness will be made (all non-invasive). Subjects will then be given a single oral dose of either rosiglitazone 8 mg or placebo. Two hours later, measurements of endothelial function will be made. A 27 gauge needle will be inserted into the left brachial artery under local anaesthesia (1% lignocaine). Saline or drugs will be infused at a constant rate of 1.0 ml/min by means of a constant rate infusion pump throughout the duration of the study. Basal blood flow will be recorded after 18 min of 0.9% saline infusion. Acetylcholine will then be co-infused with saline at a dose of 7.5 and 15 ug/min, each dose at 1.0 ml/min for 6 min. There will then be a 18 min washout period during which saline infusion will be given. Sodium nitroprusside will then be co-infused with saline at a dose of 3 and 10 ug/min, each dose at 1.0 ml/min for 6 min. There will then be a further 18 min washout period with saline. L-NG-monomethyl-arginine (L-NMMA) will then be co-infused with saline at a dose of 4 then 8 umol/min, each dose at 1.0 ml/min for 6 min. Further measurements of forearm blood flow will be made during the last 2 min of each infusion period by venous occlusion plethysmography over 1 min. Blood flow will be measured every alternate 3 min for a 3 min period by intermittent inflation of a blood pressure cuff around the upper arm to 40 mmHg. A second cuff will be inflated around the wrist to a pressure of 200 mmHg during measurements of blood flow (maximum duration 3 min) in order

to exclude the hand from the circulation during measurements. At the first visit subjects will also undergo measurement of Minimum Forearm Vascular Resistance (MFVR). In order to measure MFVR, a cuff will be inflated around the upper arm to a pressure of 300 mmHg to occlude arterial flow to the forearm for 13 min and then deflated and a measurement of forearm blood flow made by venous occlusion plethysmography. Arterial stiffness will be measured non-invasively using Pulse Wave Analysis (SphygmoCor, PWV Medical, Australia). This involves holding a small pressure sensitive probe against the skin overlying the radial, carotid and femoral arteries in turn. Following the assessment of endothelial function on the second and third visits, subjects will have baseline measurements of arterial stiffness repeated. They will then receive 400 micrograms of salbutamol by inhalation and after values have returned to baseline 500 micrograms of glyceryl trinitrate (GTN) sublingually, with repeat measurements of arterial stiffness immediately after each drug is given. This will allow endothelial function in the large arteries to be assessed. The study will be conducted according to International Conference on Harmonisation (ICH)-Good Clinical Practice (GCP) guidelines.

This trial has stopped due to lack of funding

### **Intervention Type**

Drug

### **Phase**

Not Specified

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

Rosiglitazone

### **Primary outcome(s)**

Not provided at time of registration

### **Key secondary outcome(s)**

Not provided at time of registration

### **Completion date**

30/09/2003

### **Reason abandoned (if study stopped)**

Lack of funding

## **Eligibility**

### **Key inclusion criteria**

Not provided at time of registration

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Not Specified

**Sex**

Not Specified

**Key exclusion criteria**

Not provided at time of registration

**Date of first enrolment**

26/01/2001

**Date of final enrolment**

30/09/2003

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Clinical Pharmacology Unit**

Cambridge

United Kingdom

CB2 2QQ

## **Sponsor information**

**Organisation**

Department of Health (UK)

## **Funder(s)**

**Funder type**

Government

**Funder Name**

Cambridge Consortium - Addenbrooke's (UK)

# Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration