

# **PANTHEON-II: The peripheral effects of prednisolone on glucose metabolism, metabolic hormones, insulin sensitivity and insulin secretion in healthy young males and males with metabolic syndrome: a randomised, placebo controlled, double blind, dose-response, parallel group intervention study**

|                                        |                                                                |                                                                                                   |
|----------------------------------------|----------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| <b>Submission date</b><br>08/05/2007   | <b>Recruitment status</b><br>No longer recruiting              | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol |
| <b>Registration date</b><br>03/07/2007 | <b>Overall study status</b><br>Completed                       | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>17/04/2019       | <b>Condition category</b><br>Nutritional, Metabolic, Endocrine | <input type="checkbox"/> 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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## **Additional identifiers**

EudraCT/CTIS number

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

DCpred001

## **Study information**

### **Scientific Title**

PANTHEON-II: The peripheral effects of prednisolone on glucose metabolism, metabolic hormones, insulin sensitivity and insulin secretion in healthy young males and males with metabolic syndrome: a randomised, placebo controlled, double blind, dose-response, parallel group intervention study

### **Acronym**

PANTHEON-II

### **Study objectives**

Glucocorticoids (GCs), like prednisolone, are the most commonly prescribed anti-inflammatory and immunosuppressive drugs. Although GCs display excellent efficacy in a great number of (auto-immune) diseases, the side effect profile often limits their therapeutical benefit. Major side effects associated with GC treatment include changes in glucose, lipid and protein metabolism, leading to adult onset (a.o.) insulin resistance, glucose intolerance, muscle wasting and dyslipidemia. Currently a renewed interest exists in these poorly understood diabetogenic side effects, with the development of so called 'dissociated glucocorticoid receptor activators', which seem to be lacking these deleterious effects. With this trial, we expect to obtain results that will aid the development of such compounds by a pharmaceutical company that is involved in this study project. This novel class of drugs could become of great importance for the millions of people currently requiring glucocorticoid therapy.

### **Hypotheses:**

What are the effects of a two-week treatment with 7.5 mg prednisolone daily or 30 mg prednisolone daily, versus placebo, on:

1. Metabolic fluxes such as endogenous glucose production, rate of lipolysis and proteolysis?
2. Peripheral and hepatic insulin sensitivity?

This trial is linked to the PANTHEON I study, registered under ISRCTN78149983. Although these trials have the same interventions, the outcomes being looked at are different.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Ethics approval received from the Ethics Committee of the VU University Medical Centre on the 11th October 2007 (ref: 2007/179).

### **Study design**

PANTHEON-II study is a randomised, placebo controlled, double blind, dose-response, parallel group intervention study

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet****Health condition(s) or problem(s) studied**

Metabolic syndrome

**Interventions**

The effects of a two-week treatment with either prednisolone 7.5 mg daily or prednisolone 30 mg daily, versus placebo, will be evaluated.

**Intervention Type**

Drug

**Phase**

Not Applicable

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

Prednisolone

**Primary outcome measure**

To assess the effects of a two-week treatment with 7.5 or 30 mg prednisolone daily, compared to placebo, in healthy males and males with the metabolic syndrome on:

1. Metabolic fluxes of glucose-, fat- and protein metabolism (rates will be calculated using Steele's equation), measured at Day 14
2. Hepatic and peripheral insulin sensitivity (insulin sensitivity index measured during a two-step hyperinsulinaemic-euglycaemic clamp procedure), measured at Day 14

**Secondary outcome measures**

To assess the effects of a two-week treatment with 7.5 or 30 mg prednisolone daily, compared to placebo, in healthy males and males with the metabolic syndrome on:

1. Circulating biomarkers (plasma), measured at Day 14
2. Body composition, measured at Day 13
3. Blood pressure and haemodynamic parameters, measured at Day 13
4. Body fat distribution (Magnetic Resonance Imaging [MRI]), measured at Day 13
5. Molecular mechanisms underlying prednisolone effects, measured at Day 14

**Overall study start date**

01/09/2007

**Completion date**

01/09/2010

## Eligibility

**Key inclusion criteria**

For all participants:

1. Written informed consent
2. Male caucasian
3. Smoking less than five cigarettes per day and capable of stopping during the trial period

For healthy participants:

1. healthy as determined by history taking, physical examination, laboratory examinations and Electrocardiogram (ECG):
  - 1.1. Aged 20 to 55 years
  - 1.2. Body Mass Index (BMI) between 20 and 25 kg/m<sup>2</sup>
  - 1.3. Fasting glucose less than 5.6 mmol/L and glucose less than 7.8 mmol/L at two hours after intake of 75 g glucose (Oral Glucose Tolerance Test [OGTT])

For participants with metabolic syndrome:

1. Aged 20 to 55 years
2. Waist circumference more than 94 cm
3. Three of following criteria:
  - 3.1. Triglycerides more than 1.7 mmol/L
  - 3.2. High Density Lipoprotein (HDL) cholesterol less than 1.03 mmol/L
  - 3.3. Blood pressure more than 130/85 mmHg
  - 3.4. Fasting glucose level less than 6.1 mmol/L and glucose less than 11.0 mmol/L at two hours after intake of 75 g glucose (OGTT)

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Male

**Target number of participants**

60

**Key exclusion criteria**

For all participants:

1. Idiosyncrasy/sensitivity to Glucocorticoids (GC)
2. GC use during the last three months prior to first study dose
3. Participation in an investigational drug trial within 90 days prior to the first dose
4. Donation of blood (more than 100 mL) within 90 days prior to the first dose
5. History of or current abuse of drugs or alcohol
6. Serious mental impairment or language problems, i.e., preventing to understand the study protocol/aim

For healthy participants:

1. Presence of a medical disorder
2. Medication use, except for incidental analgesic agents
3. First degree relative with type two diabetes mellitus
4. Performing intensive physical activity more than twice a week

For participants with metabolic syndrome:

1. Serious pulmonary, cardiovascular, hepatic (Alanine Aminotransferase [ALT], Aspartate Aminotransferase [AST] more than 3 x Upper Limit of Normal [ULN]) or renal disease (serum creatinine more than 135 mmol/L)
2. History of cardiovascular disease, such as myocardial infarction, cerebrovascular accident
3. Major psychiatric disorder
4. Depression
5. All diseases that induce changes in the Hypothalamic-Pituitary-Adrenal (HPA) axis
6. Malignant disease
7. All other relevant medical disorders that potentially interfere with this trial\*
8. All medication interfering with study drug or interfering with study endpoints/hypotheses\*

\* the study physician and internist will make an individual assessment per subject whether he is eligible for inclusion

**Date of first enrolment**

01/09/2007

**Date of final enrolment**

01/09/2010

## **Locations**

**Countries of recruitment**

Netherlands

**Study participating centre**

**Department of Endocrinology/Diabetes Centre**

Amsterdam

Netherlands

1081 HV

## **Sponsor information**

**Organisation**

Vrije University Medical Centre (VUMC) (The Netherlands)

**Sponsor details**

c/o Dr M. Diamant and Dr R.J. Heine

De Boelelaan 1117

Amsterdam  
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**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.vumc.nl/english/>

**ROR**

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

## Funder(s)

**Funder type**

Industry

**Funder Name**

Top Institute Pharma (TIP) (The Netherlands) - a collaborative structure consisting of industrial and academic research teams ([www.tipharma.com](http://www.tipharma.com))

## 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? |
|---------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a> | results | 01/08/2011   |            | Yes            | No              |
| <a href="#">Results article</a> | results | 01/03/2013   |            | Yes            | No              |
| <a href="#">Results article</a> | results | 01/07/2018   | 17/04/2019 | Yes            | No              |