# A randomized, double-blind, placebo-controlled study to investigate the effects of an 8-week recombinant human erythropoietin (NeoRecormon) treatment on well-trained cyclists and their cycling performance.

Published: 25-11-2015
Last updated: 19-04-2024

Primary Objective- To explore the effects of NeoRecormon on well-trained cyclists and their cycling performance by exercise parameters. Secondary Objectives- To explore the effects of NeoRecormon on well-trained cyclists and their cycling...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON44014

**Source**
ToetsingOnline

**Brief title**
Erythropoetine effects on cycling performance.

### Condition

- Other condition

**Synonym**
Cycling performance, slow cycling

**Health condition**

Fietsprestatie

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Centre for Human Drug Research
**Source(s) of monetary or material Support:** Centre for Human Drug Research

## Intervention

**Keyword:** Cycling performance, Doping, Epoetin beta

## Outcome measures

**Primary outcome**

Exercise tests

All subjects will breathe during the exercise test through a facemask that will

be connected to an oxymeter to collect inspired and expired gasses for

analyzing:

- Oxygen consumption, VO2 (L/min)

- Carbon dioxide production, VCO2 (L/min)

- Respiratory minute ventilation, VE (L/min)

- Tidal volume, Vt (L)

- Respiratory frequency, Rf

- Maximal oxygen consumption, VO2,max (ml kg-1 min-1)

During the exercise tests blood will be collected at predetermined stages to

measure:

- Lactate levels

- Tissue plasminogen activator

- Creatinine phosphokinase

- C-reactive protein levels

VO2 and VCO2 will be used to calculate:

- Ventilatory equivalent for oxygen (VE/VO2), eqVO2

- Ventilatory equivalent for carbon dioxide (VE/VCO2), eqVCO2

these values will be used to determine:

- Ventilatory threshold 1, VT1

- Ventilatory threshold 2, VT2

Physiological parameters that will be determined at VT1 and VT2:

- Oxygen consumption, VO2 (L/min)

- Oxygen consumption per kg, VO2 (L/min/kg)

- Percentage of maximal oxygen consumption, %VO2max (L/min)

- Power output, P (J/s)

- Power output per kg, P (J/s/kg)

Physiological parameters that will be determined at maximal effort:

- Maximal oxygen consumption, VO2max (L/min)

- Maximal oxygen consumption per kg, VO2max (L/min/kg)

- Maximal power output, Pmax (J/s)

- Maximal power output per kg, Pmax (J/s/kg)

- Lactate values

Other determinations:

- Lactate threshold 1, LT1

- Lactate threshold 2, LT2

- Cycling economy, CE (W L-1 min-1)

- Gross efficiency, GE (%)

- Heart rate (bpm)

- Systolic blood pressure (mmHg)

- Diastolic blood pressure (mmHg)

Competition

Maximal and submaximal exercise parameters that will be measured and calculated

during the competition:

- Power (W)

- Heart rate (bpm)

- Systolic blood pressure (mmHg)

- Diastolic blood pressure (mmHg)

**Secondary outcome**

Safety markers:

Monitoring vital signs

o Pulse Rate (bpm)

o Systolic blood pressure (mmHg)

o Diastolic blood pressure (mmHg)

o Temperature measurements (ºC)

Electrocardiogram (ECG)

o Heart Rate (HR) (bpm), PR, QRS, QT, QTcB, QTcF

Clinical Laboratory Assessments

o Haematology

Ht must be <52%.

o Chemistry

o Urinalysis

o Coagulation (F1+2, D-Dimer, bTG, PF4, P-selectin, E-selectin,

thrombomodulin, TXB2)

Doping detection:

Detection (positive/negative test) of EPO in urine samples from subjects.

RNA expression:

RNA expression levels in venous blood before and after a submaximal exercise

test

# Study description

**Background summary**

A recent report of the Union Cycliste Internationale gives an in-depth analysis of doping throughout cycling*s history, from 1890 to the present day. The report*s final conclusion is that cycling has had, and continues to have, a serious doping problem.
Although it could be argued that administering substances that improve performance is forbidden and nothing more needs to be known about it, research to investigate the effects, safety and tolerability of doping substances in this population is necessary.

There are number of reasons for this. In the first place it is often unknown if a forbidden substance really aids performance. If this is not the case the need for administration is strongly diminished. Additionally the adverse effects of such substances are often insufficiently known and athletes may be exposed to risks without being adequately informed about them.

## Study objective

Primary Objective
- To explore the effects of NeoRecormon on well-trained cyclists and their cycling performance by exercise parameters.

Secondary Objectives
- To explore the effects of NeoRecormon on well-trained cyclists and their cycling performance by performance in a competition.
- Evaluate the safety of NeoRecormon in well-trained cyclists.
- Evaluate the performance of doping detection methods for NeoRecormon use in well-trained cyclists.

Exploratory objectives:
- To explore how a standardized submaximal exercise affects gene expression patterns in well-trained individuals.
- To explore the difference in RNA-profiles between individuals treated with rHuEPO and placebo
- To identify potential transcripts that can be used as biomarkers for rHuEPO use
- To explore correlations between changes in whole blood gene expression patterns observed before and after a submaximal exercise test in individuals and their performance

## Study design

Randomized, double-blind, placebo-controlled study to investigate the effects and safety of NeoRecormon in well-trained cyclists.

## Intervention

Weekly subcutaneous doses of Neorecormon (5000 IU, or adjusted to reach the desired Hemoglobin increase, maximum dose is 10.000 IU). Additionally, all subject will receive Vitamin C and iron supplementation.

## Study burden and risks

NeoRecormon is a registered drug. The safety profile of this compound is known. Because side effects might occur and anaphylactoid reactions were observed in isolated cases (*1/10.000) (see SmPC), the study drug administrations will be

done in the clinic under medical supervision. Subjects will be closely monitored and will only be discharged from the unit if their medical condition allows this.

Subjects will receive a dose of 2000, 5000 or *6000IU with a maximum of 10.000IU/week of NeoRecormon once a week for 8 weeks. The dosage depends on haemoglobin (Hb) concentration and haematocrit (Ht) measured prior to administration. If Ht is *52% dosage will be interrupted. If Ht is <52% the dosage depends on the Hb concentration (see Figure 1).
The effects of NeoRecormon used in patients in an autologous blood predonation programme most closely resembles the effects of NeoRecormon in healthy volunteers. For the use of NeoRecormon in an autologous blood predonation programme, the SmPC states that the maximum dose should not exceed 1200IU/kg (or 90.000 IU for a 75kg subject) per week for subcutaneous administration. Planned doses of 2000IU, 5000IU or *6000IU with a maximum of 10.000IU/week of NeoRecormon will be well below this maximum dose and are therefore considered safe. The risk is considered small and therefore acceptable compared to the scientific benefit.

No benefit for the subjects is expected, however, their cycling performance might be increased by EPO treatment.

# Contacts

**Public**
Centre for Human Drug Research

Zernikedreef 8
Leiden 2333CL
NL
**Scientific**
Centre for Human Drug Research

Zernikedreef 8
Leiden 2333CL
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Well-trained (as determined by cycling history and maximal power output >4 W/kg) male subjects, 18 to 50 years old (inclusive);
2. Subjects must be healthy / medically stable on the basis of clinical laboratory tests, medical history, vital signs, and 12-lead ECG performed at screening, including exercise ECG.
3. Each subject must sign an informed consent form prior to the study. This means the subject understands the purpose of and procedures required for the study.

## Exclusion criteria

1. Any clinically significant abnormality, as determined by medical history taking and physical examinations, obtained during the screening visit that in the opinion of the investigator would interfere with the study objectives or compromise subject safety.
2. Unacceptable known concomitant diagnoses or diseases at baseline, e.g., known cardiovascular, pulmonary, muscle, metabolic or haematological disease, renal or liver dysfunction, ECG or laboratory abnormalities, etc.
3. Unacceptable concomitant medications at baseline, e.g., drugs known or likely to interact with the study drugs or study assessments.
4. Unacceptable potential cycling performance enhancing medications at baseline, e.g. Erythropoiesis-stimulating agents, Anabolic Androgenic Steroids, Growth Hormone, Insulin, IGF-I and Beta-Adrenergic Agents or methods, e.g. altitude tents.
5. Blood transfusion in the past three months.
6. Loss or donation of blood over 500 mL within three months.
7. Participation in a clinical trial within 90 days of screening or more than 4 times in the previous year.
8. Known hypersensitivity to the treatment or drugs of the same class, or any of their excipients.
9. Any known factor, condition, or disease that might interfere with treatment compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.
10. Positive urine drug test at screening
11. Positive alcohol breath test at screening
12. Haemoglobin (Hb) concentration > 9.8 mmol/l at screening.
13. Hb concentration < 8 mmol/l at screening.
14. Haematocrit (Ht) * 48% at screening.
15. Being subject to WADA*s anti-doping rules, meaning being a member of an official cycling

union or other sports union for competition (such as the KNWU) or participating in official competition during the study.
16. Positive results from serology at screening (except for vaccinated subjects or subjects with past but resolved hepatitis)
17. Previous history of fainting, collapse, syncope, orthostatic hypotension, or vasovagal reactions.
18. Any circumstances or conditions, which, in the opinion of the investigator, may affect full participation in the study or compliance with the protocol.

# Study design

## Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 07-03-2016 |
| Enrollment: | 48 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | NeoRecormon |
| Generic name: | Epoetin beta |
| Registration: | Yes - NL outside intended use |

# Ethics review

| | |
|---|---|
| Approved WMO Date: | 25-11-2015 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 13-01-2016 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 18-02-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 01-03-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 22-03-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 23-03-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 22-04-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 04-05-2016 |
| Application type: | Amendment |

| | |
|---|---|
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 23-05-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 25-05-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2015-003269-27-NL |
| CCMO | NL54516.056.15 |

# Study results

| | |
|---|---|
| Date completed: | 15-08-2016 |
| Actual enrolment: | 48 |

**Summary results**
Trial is onging in other countries