# a pilot study to investigate the hepcidin levels in patients with rheumatoid arthtitis treated with IL-6R blockade

Published: 29-05-2009
Last updated: 04-05-2024

Primary objective:To determine the hepcidin levels before, 2, 4, 8 and 24 hours after the administration of anti-IL-6R in patients with RA.Secondary objective:To determine the levels of Iron, transferrin , (calculation of transferrin saturation),...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Anaemias nonhaemolytic and marrow depression |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON33066

**Source**
ToetsingOnline

**Brief title**
The Hepblock study

### Condition

- Anaemias nonhaemolytic and marrow depression
- Synovial and bursal disorders

**Synonym**
anemia of chronic disease

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** HagaZiekenhuis
**Source(s) of monetary or material Support:** eigen onderzoeks budget

## Intervention

**Keyword:** Hepcidin, IL-6 receptor blockade, Rheumatoid arthritis

## Outcome measures

### Primary outcome

To determine the hepcidin levels before, 2, 4, 8 and 24 hours after the administration of anti-IL-6R in patients with RA.

### Secondary outcome

To determine the levels of Iron, transferrin , (calculation of transferrin saturation), ferritin, Hb, CRP and IL-6 before, 2, 4,8 and 24 hours after anti-IL-6R administration in patients with RA.

# Study description

### Background summary

Anemia is a common condition in patients. Anemia is most frequently due to absolute iron deficiency (i.e. blood loss) or functional iron deficiency due to chronic inflammatory conditions (Anemia of Chronic Disease , ACD).
This latter form of iron deficiency can largely be attributed to the inhibition of the release of stored iron from the Reticulo-Endothelial System (RES) as a result of increased levels of circulating hepcidin (1,2).
The peptide hormone hepcidin is produced by the hepatocytes and the key regulator of systemic iron homeostasis (2,3). Hepcidin leads to internalization and subsequent degradation of iron exporter ferroportin, which is present on the cell surface of macrophages and enterocytes (4).
In chronic inflammatory diseases such as rheumatoid arthritis, Chron*s disease, chronic renal or heart failure and cancer, hepcidin production is elevated.
This results in a decrease of iron absorption from the intestine and the sequestration of iron in the RES (5), leading to hypoferremia, a reduction of iron available for erythropoiesis, and anemia.
This induction of hepatic hepcidin production upon inflammatory stimuli has been shown to be predominantly induced by interleukin (IL)-6 by Janus Kinase (JAK)-signal transducer and activator of transcription (STAT)-3 signalling (6,7,8,9). More specific, Nemeth, Rivera, and colleagues showed that IL-6 induced hepcidin expression in hepatic cells (10). They have replicated this

effect using conditioned medium from endotoxin-treated macrophages and shown that a neutralizing antibody against IL-6 blocked hepcidin induction. Other inflammatory cytokines did not stimulate hepcidin production; in fact, TNF-* inhibited it. Complementary experiments carried out in human volunteers by 2 different research groups in LA (USA) and Nijmegen (the Netherlands) showed that IL-6 and LPS infusion stimulated urinary hepcidin excretion within 2 hours and 6 hours, respectively, and induced hypoferremia (7,10). Accordingly, treatment with an IL-6 antibody significantly reduced serum hepcidin levels in two patients with multicentric Castleman*s disease. In both cases , the level of serum hepcidin dramatically dropped within 24 h after the first dose of anti-IL-6R(11).
Taken together, these data provide strong support for the conclusions that IL-6 is a primary inducer of hepcidin expression and that increased hepcidin expression results in hypoferremia. This is gratifyingly consistent with clinical observations that hypoferremia occurs very quickly after the onset of inflammation.
If inflammatory induction of hepcidin by IL-6 causes hypoferremia, it is logical to predict that inhibition of hepcidin expression, activity or blockage of the IL-6 receptor will ameliorate the anemia of inflammation. Anti-IL-6R is the most readily available antagonist of hepcidin. Clinical trials on effectivity and safety will be required to define appropriate indications for its use in anaemia of chronic disease. This pilot study investigates hepcidin kinetics in RA patients treated with anti-IL-6R.

## Study objective

Primary objective:

To determine the hepcidin levels before, 2, 4, 8 and 24 hours after the administration of anti-IL-6R in patients with RA.

Secondary objective:

To determine the levels of Iron, transferrin , (calculation of transferrin saturation), ferritin, Hb, CRP and IL-6 before, 2, 4,8 and 24 hours after anti-IL-6R administration in patients with RA.

## Study design

The study is an observational pilot study.
Blood samples will be taken before, 2, 4, 8 and 24 hours after the administration of anti-IL-6R in patients with RA

## Study burden and risks

No burden or risks with participation.

# Contacts

**Public**
HagaZiekenhuis

Postbus 40551
2504 LN
Nederland
**Scientific**
HagaZiekenhuis

Postbus 40551
2504 LN
Nederland

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Moderate to severe active RA
Age > 18
treatment with anti-IL-6R

## Exclusion criteria

Major surgery within 8 weeks prior to screening

Prior history of inflammatory (joint) disease other than RA

# Study design

## Design

**Study type:** Observational invasive

| | |
|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Other |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 26-04-2010 |
| Enrollment: | 20 |
| Type: | Actual |

# Ethics review

Approved WMO

| | |
|---|---|
| Date: | 29-05-2009 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

# 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 |
| --- | --- |
| CCMO | NL27910.098.09 |