# Therapeutic drug monitoring in tocilizumab-treated rheumatoid arthritis patients: Pilot study of a double-blind randomised controlled trial

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To evaluate the feasibility of the study after 20 weeks of follow-up, which includes the evaluation of the dose-reduction algorithm in tocilizumab-treated patients with RA.

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Autoimmune disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON44574

**Source**
ToetsingOnline

**Brief title**
TDM tocilizumab

### Condition

- Autoimmune disorders

**Synonym**
rheuma, rheumatoid arthritis

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Amsterdam Rheumatology and immunology Center | Reade
**Source(s) of monetary or material Support:** Reade reumatologie fonds

## Intervention

**Keyword:** rheumatoid arthritis, therapeutic drug monitoring, tocilizumab

## Outcome measures

### Primary outcome

The primary study outcome is the feasibility of the study logistics

This will be evaluated according to the following endpoints:

- Percentage of patients completing 20-weeks follow-up. We accept a drop out of 10%.

- We only accept a few protocol deviations, when there are more than 3 protocol deviations, the protocol should be adjusted according to this deviations.

- The opinion of approached and participating patients about the study protocol.

### Secondary outcome

The secondary study outcome is the feasibility of the dose reduction algorithme. The algorithm is feasible if 80% of the patients achieve serum concentration in the range of 4-6 mg/L and none of the patients has a drug concentration below 1 mg/L. If between 50% and 80% of the patients achieve the targeted range, the algorithm must be adjusted before implementation in further studies. When less than 50% of the patients achieve the targeted drug concentration range, a new algorithm must be designed.

# Study description

## Background summary

A wide range of serum trough concentrations is observed in tocilizumab-treated rheumatoid arthritis (RA) patients, while 1 mg/L tocilizumab is sufficient to block systemic interleukin 6 receptor. Substantial proportion of patients have higher serum tocilizumab concentrations and are likely to be overexposed. We expect that patients can at least reduce the dose aiming for a concentration of 5 mg/L without reducing efficacy.

## Study objective

To evaluate the feasibility of the study after 20 weeks of follow-up, which includes the evaluation of the dose-reduction algorithm in tocilizumab-treated patients with RA.

## Study design

Double-blind randomised controlled pilot study with a follow up of 20 weeks.

## Intervention

Patients with a concentration below 5 mg/L will continue the dose. Those patients with a tocilizumab concentration above 5 mg/L are randomly assigned (2:1) to dose reduction or to continuation of the standard care tocilizumab dose. In the intervention group, the precise dose-reduction is calculated per patient in order to achieve a tocilizumab concentration of 5 mg/L (range 4-6 mg/L).

## Study burden and risks

Dose-reduction will lead to lower drug costs and possibly to reduce the risk of adverse events. Since we lower the tocilizumab concentration in a proportion of the patients, risk of a exacerbation of the disease exists. In this case, patients will receive their original dose. Previous studies showed that disease activity is controlled adequately after returning to the standard dose. However, our algorithm is designed to reach concentrations of 5 mg/L (range 4-6 mg/L) and studies showed that 1 mg/L of tocilizumab is sufficient to maintain clinical effect. The expected burden of this study is low, since study visits are planned at the time of infusion and therefore do not take extra time. The additional burden consists of an extra blood sample taken every visit and the fingerprick that is performed once at home.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

RA according to the ACR 1987 or 2010 criteria;
Current use of tocilizumab iv, with a consistent interval of 4 weeks for at least 24 weeks.

## Exclusion criteria

Scheduled surgery in the next 20 weeks or other preplanned reasons for treatment discontinuation.

# Study design

## Design

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| Study phase: | 4 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |

**Primary purpose:** Treatment

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 28-06-2018 |
| Enrollment: | 30 |
| Type: | Actual |

# Ethics review

Approved WMO

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| Date: | 28-11-2017 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

# 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 | NL63658.048.17 |