# Dose REduction Strategy Study of TNF inhibitors in Psoriatic arthritis and axial Spondyloarthritis patients.

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The aim of the study is to compare the proportion of patients (for PsA and axSpA together) having LDA at 12 months between a T2T strategy with versus without tapering attempt against a pre-set non-inferiority margin of 20%.

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

## Summary

### ID

NL-OMON49692

**Source**
ToetsingOnline

**Brief title**
DRESS-PS

### Condition

- Autoimmune disorders
- Joint disorders

**Synonym**
chronic inflammation of the joints, Psoriatic arthritis and axial spondyloarthritis

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Sint Maartenskliniek
**Source(s) of monetary or material Support:** Reumafonds / ReumaNederland

## Intervention

**Keyword:** Axial spondyloarthritis, Dose reduction, Psoriatic arthritis, TNF inhibitors

## Outcome measures

### Primary outcome

The difference in proportion of patients between T2T strategy with or without tapering attempt who are in LDA state (PASDAS <= 3.2 and modified BSA <= 3% of the skin (PsA), ASDAS < 2.1 (axSpA) and an absence of active extra-axial symptoms) at 12 months follow-up, compared to the prespecified non-inferiority margin of 0.2 (20%).

### Secondary outcome

- To assess the proportion of patients in the intervention group able to reduce their TNFi dose, able to discontinue TNFi altogether, or not able to reduce TNFi dose without an increase in disease activity, respectively,

- To compare the differences in efficacy between the intervention versus control group with TNFi measured by change in PASDAS and BSA of the skin and/or ASDAS at 3, 6, 9 and 12 months follow-up,

- To assess the difference in the change from baseline in functioning measured by the Health Assessment Questionnaire Disability Index (HAQ-DI) and Bath Ankylosing Spondylitis Functional Index (BASFI - axSpA only) between both groups with TNFi at 3, 6, 9, and 12 months follow-up,

- To estimate cost-effectiveness ratio of the T2T strategy with tapering attempt of TNFi compared to the T2T strategy without tapering attempt,

- To compare (dosage and) proportion of patients using NSAID, corticosteroid*s or cs/b/tsDMARDs between intervention and control group at 12 months follow up,

- To predict in the intervention group which baseline factors (including

[change in] serum drug levels and antidrug antibody levels) are associated with

successful and maintained dose reduction,

- To compare the difference in cumulative incidence of flare between the

intervention and control group at 12 months follow up,

- To assess the safety of this strategy with respect to proportion of patients

developing adverse events with special attention to allergic (injection)

reactions and infections

# Study description

**Background summary**

Spondyloarthritis, notably psoriatic arthritis (PsA) and axial Spondyloarthritis (axSpA), can successfully be treated with Tumour Necrosis Factor inhibitors (TNFi) therapy. When patients are in low disease activity (LDA), the question arises whether patients may be able to maintain LDA with a lower dose or without TNFi, as overtreatment with TNFi is associated with risk for infections and higher costs. A few non-randomised studies have previously explored the possibility of disease activity guided dose reduction in PsA and axSpA, but data is scarce and evidence from randomised trials is lacking. Also, no cost-effectiveness analysis has been performed to provide insight into the potential cost savings of effective dose reduction of TNFi. In contrast, the safety and efficacy of disease activity guided dose reduction of TNFi have already been shown in Rheumatoid Arthritis (RA), and similar strategy trials in Crohns* disease and psoriasis are ongoing in the Netherlands. Both PsA/axSpA treatment strategy studies as well as specifically TNFi tapering studies have been identified in the most recent 2017 European research agenda on PsA/axSpA.

**Study objective**

The aim of the study is to compare the proportion of patients (for PsA and axSpA together) having LDA at 12 months between a T2T strategy with versus without tapering attempt against a pre-set non-inferiority margin of 20%.

**Study design**

This study is a pragmatic, open-label, randomised controlled, non-inferiority strategy trial. 95 (PsA and AxSpA together) patients already receiving TNFi and having LDA for at least 6 months will be randomised to a T2T strategy with versus without tapering attempt of TNFi therapy using a concealed randomisation procedure, stratified for PsA and axSpA and csDMARDs. Follow up duration will be 12 months for all patients. The control arm will receive a T2T strategy without tapering attempt and the intervention arm will receive aT2T strategy with tapering attempt following a dose reduction strategy for each TNFi in which the dose interval will be increased every 3 months when disease activity remains low. As the final step of dose reduction, TNFi therapy is discontinued. When a persistent loss of response/flare occurs, the treatment is intensified to the last effective interval/dose.

**Intervention**

The following T2T strategy will be adviced to rheumatologists: For patients allocated to the T2T strategy with tapering attempt group the TNFi dose will be reduced about one third by extending the interval every 3 months from 14 to 21 to 28 days for adalimumab and certolizumab, from 7 to 10 to 14 days for etanercept, from 4 to 6 to 8 weeks for golimumab, after which the TNFi will be stopped. For infliximab, the interval will remain 8 weeks but the dose will be reduced every 3 months from 3 to 2.25 to 1.5 mg/kg bodyweight after which infliximab will be stopped. When a persistent loss of response/flare occurs, the treatment is intensified to the last effective interval/dose. Patients allocated to the T2T strategy without tapering attempt group will continue treatment following a standardized protocol that is aimed to maintain LDA, at the discretion of the rheumatologist and patient.

**Study burden and risks**

In daily practice, rheumatologists monitor their patients on a ongoing basis once every three or six months. Normally, disease activity is measured and blood samples are collected during regular visits. In this study patients will be scheduled to a visit once every three months. At the baseline visit, patients are asked for baseline characteristics. Radiographs will be made of the hands, feet and cervical, lumbar spine and SI-joints at baseline and the last visit. If necessary, radiographs will be taken of other joints. During all visits two blood samples will be collected. Several short questionnaires will be completed HAQ-DI, BASFI, EUROQOL-5D-3L, SF-12, ASAS-HI, transition scale and PASS question during all visits. The extra time required for this study is estimated to be approximately 1 hour for the first visit and 15 minutes for the other visits. This results in a total of 2,15 hours of extra time required for a patient to take part in the study (excluding travel time). Risks of participation in this study includes the chance of a temporary increase in disease activity in the patients receiving a lower dose than they used to. However, if this happens, the increase in disease activity will be short-lived

as the rheumatologist will immediately act. On the other hand, patients receiving a lower dose of TNFi will have a reduced chance on TNFi related side effects

## 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

- Eligible patients are >= 16 years of age at the time of signing the informed consent form AND
1) have peripheral SpA of the psoriatic arthritis subtype diagnosed clinically by the rheumatologist , supported by the Classification Criteria for Psoriatic Arthritis (CASPAR) and/or
2) have axial SpA of the axial spondyloarthritis subtype, supported by the Assessment of SpondyloArthritis international Society (ASAS) classification

criteria for axSpA, AND
- Are using full dose, or at least > 50% of the authorized defined daily dose (DDD), of an originator or biosimilar TNFi (adalimumab, certolizumab, etanercept, golimumab, infliximab);
- Patients have to have stable LDA, Psoriatic Arthritis Disease Activity Score (PASDAS) <= 3.2 and a skin measure of body surface area involvement (modified BSA) using a target of 3% as used by rheumatologists in clinical practice for PsA and/or Ankylosing Spondylitis Disease Activity Score (ASDAS) < 2.1 and an absence of active extra-axial symptoms such as Crohn*s disease, uveitis, colitis or psoriasis for axSpA, for at least 6 months, or when formal measurements are not available, judgement of physician and patient.

### Exclusion criteria

- Previous recorded unsuccessful dose reduction of TNFi in the previous 24 months,
- Comorbidities expected to hamper successful dose reduction (e g Crohns disease, Ulcerative colitis, Psoriasis, Uveitis),
- Not able to have 12 months follow-up (life expectancy, planned relocation),
- Not able to measure outcome (language, other limitations)

## Study design

### Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

### Recruitment

NL

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|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 09-01-2019 |
| Enrollment: | 95 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Humira®, Cimzia®, Simponi®, Benepali®, Enbrel®, Erelzi®, Flixabi®, Inflectra®, Remicade®, Remsima® |
| Generic name: | Adalimumab, Certolizumab, Golimumab, Etanercept, Infliximab |
| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 13-09-2018 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 19-10-2018 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 23-10-2018 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 17-03-2020 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

## Study registrations

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

No registrations found.

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

ID: 29006
Source: Nationaal Trial Register
Title:

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2018-003432-72-NL |
| CCMO | NL66181.091.18 |
| OMON | NL-OMON29006 |

# Study results

Date completed: 17-06-2021

Results posted: 08-07-2022

**First publication**
30-05-2022