Prediction aided tapering in reumatoid arthritis patients treated with biologicals

Published: 11-10-2021
Last updated: 07-06-2025

To assess the effect of adding a tapering decision aid on a dynamic flare prediction model to disease-activity-guided dose optimisation (DGDO) on the incidence of flares and medication use.

Ethical review	Approved WMO
Status	Recruitment started
Health condition type	Autoimmune disorders
Study type	Interventional research applied for the first time in human subjects

Summary

ID

NL-OMON56102

Source
ToetsingOnline

Brief title
PATIO

Condition

- Autoimmune disorders
- Joint disorders

Synonym
rheumatism, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW

Intervention

- Medical device

Keyword: algorithm, biological, rheumatoid arthritis, tapering

Explanation

N.a.

Outcome measures

Primary outcome

Primary endpoint: the number of flares per patient over 18 months.

Secondary outcome

Main secondary endpoint: dose reduction (expressed as percentage of full-dose)
 over 18 months.

Study description

Background summary

Biological Disease Modifying Anti Rheumatic Drugs (bDMARDs) are effective in the treatment of rheumatoid arthritis, but they have several sometimes dose-dependent drawbacks. These include the patient*s need for self-injection, increased risk of infection and malignancy, and high costs. Thus, the question arises whether this adequate level of disease control can be maintained with less medication. Recent studies have shown that disease activity guided dose optimisation (DGDO) of bDMARDS, with trial and error dose reduction or even discontinuation in RA, is non-inferior to usual care. Results showed no difference in functional status, quality of life, relevant radiographic progression or adverse events between DGDO and usual care, although long-term effects are not fully clear. DGDO does however inherently increase the risk of short-lived flares, estimates in the DRESS study being 73% vs 27%. This can make doctors and patients hesitant to start the DGDO process. Therefore, the need arises to better predict and prevent flares during tapering.
We previously developed and externally validated a dynamic prediction model to predict the probability of a flare occurring within 3 months. By predicting a flare, tapering may be halted in time to prevent a flare. Our dynamic prediction model performed moderately well with an area under the ROC curve after cross-validation of 0.76 (95% CI 0.69-0.83). Using dynamic predictions

added to DGDO to guide tapering reduced the number of flares and retained most of the reduction in bDMARD dose compared to DGDO alone. These promising simulation results should however be confirmed in a controlled study.

Study objective

To assess the effect of adding a tapering decision aid on a dynamic flare prediction model to disease-activity-guided dose optimisation (DGDO) on the incidence of flares and medication use.

Study design

Pragmatic, open, randomized, superiority, multi-centre strategy trial with 18 months follow-up.

Intervention

A tapering decision aid based on a dynamic flare prediction model in addition to disease-activity-guided dose optimisation (DGDO) in regular patient care.

Study burden and risks

In the control group RA patients with stable low disease activity will taper their bDMARD according to disease-activity guided dose optimisation. This has been shown to be non-inferior to full-dose treatment and is in line with the advice of a review of 45 tapering studies and a recent Cochrane review. However, because this strategy may increase the risk of short-lived flares, the tapering in the intervention group will be assisted by a tapering decision aid aiming to halt tapering before a flare occurs. Thus, by definition there will be less flares in the intervention group. When a flare occurs (or when a flare is predicted in the intervention group), tapering will be halted in both groups, and no further tapering attempts will be taken. The treating rheumatologist is free to deviate from the protocol if he/she deems this medically necessary. Participation in the trial requires only very limited extra work for patients, as the 3-monthly visits with assessment of disease activity are standard in regular care. In addition, patients will be asked to fill out a limited set of questionnaires at regular intervals.

Contacts

Scientific
Universitair Medisch Centrum Utrecht
P.M.J. Welsing
Heidelberglaan 100

Utrecht 3584 CX
Netherlands
088-7550459
Public
Universitair Medisch Centrum Utrecht
P.M.J. Welsing
Heidelberglaan 100
Utrecht 3584 CX
Netherlands
088-7550459

Trial sites

Trial sites in the Netherlands

Sint Maartenskliniek
Target size: 40

Medisch Spectrum Twente (MST)
Target size: 18

St. Antonius Ziekenhuis
Target size: 17

Universitair Medisch Centrum Utrecht
Target size: 30

Meander Medisch Centrum
Target size: 20

St. Jansdal
Target size: 25

Reuma Zorg Zuid West Nederland
Target size: 10

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• A clinical diagnosis of rheumatoid arthritis as assessed by the treating rheumatologist.
It will be registered if patients meet ACR 1987 or EULAR/ACR 2010 criteria. If these criteria are not met, the separate components of the criteria will be registered.
• Treatment of their RA with one of the following bDMARDs that are registered for RA in >=66% of the standard dose (i.e. maximally one dose reduction step previously taken): adalimumab, certolizumab, golimumab, infliximab, etanercept, sarilumab, tocilizumab or abatacept).
• Patient is eligible to taper bDMARD according to treating physician (i.e. no other indication for bDMARD such as psoriasis or IBD, i.e. no recent relevant radiographic progression).
• Stable low disease activity with current bDMARD for >= 6 months according to treating physician
• Current DAS28-CRP <= 2.9 (low disease activity)
or
Current stable low disease activity according to treating physician and patient with a maximum DAS28-CRP <=3.5 (i.e. 2.9 + measurement error in DAS28 (~0.6)(33)).
• Patient is willing to taper (and if possible, stop) his/her bDMARD as well as to continue his/her current bDMARD dose.
• At least 18 years of age

Exclusion criteria

• Recent earlier (<6 months) tapering attempt(s) with the same bDMARD that failed according to treating physician
• Inability to comply with protocol, e.g. no possibility to measure outcome over 18 months, e.g. insufficient knowledge of the Dutch language

Study design

Design

Study phase:	N/A
Study type:	Interventional research applied for the first time in human subjects
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	No intervention
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	10-11-2021
Enrollment:	160
Duration:	18 months (per patient)
Type:	Actual

Medical products/devices used

Product type:	Medical device
Generic name:	Tapering decision aid (TAPER)
Registration:	No

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO Date:	11-10-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	21-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-12-2021

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-11-2022
Application type:	Amendment
Review commission:	METC NedMec
Notification accepted Date:	26-03-2025
Application type:	Amendment
Review commission:	METC NedMec

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: 19954
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL74537.041.21
Research portal	NL-008028